

Comparison between the hodograph transform method and frontal chromatography for the measurement of binary competitive adsorption isotherms

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ABSTRACT

Frontal analysis is an accurate method of isotherm determination. However, for the study of binary competitive isotherms, it requires a large number of measurements, it is time consuming and it needs excessive amounts of pure chemicals. The hodograph transform method is of considerable interest because it uses much smaller amounts of chemicals. It requires validation. In this work, the potential precision and accuracy of the two methods were compared and the optimum experimental conditions for each were determined on the basis of simulation study.

INTRODUCTION

The determination of multi-component adsorption isotherms and the investigation of their properties are important in several different areas. In physical chemistry, these isotherms offer another angle for the study of adsorbate–adsorbate and adsorbate–surface interactions. In chemical engineering, a knowledge of competitive adsorption isotherms is essential for process design. With the development of high-performance liquid chromatography (HPLC) and of its preparative applications, the study of competitive isotherms is gaining increasing attention as liquid–solid adsorption is one of the most important retention mechanisms. The competitive adsorption isotherms permit a better understanding of the phenomena responsible for retention and separation. Further, a method for the rapid, precise and accurate determination of com-

petitive adsorption isotherms would permit the rapid optimization of the design and operating conditions of a preparative chromatograph for performing a given purification. This is currently a crucial need in the pharmaceutical and biotechnical industries.

There are currently three types of methods for the determination of competitive isotherms, frontal analysis [1], pulse methods [2–4] and the application of the non-linear wave theory known as the hodograph plot [5–7]. Frontal analysis uses to advantage the formation and propagation of self-sharpening fronts in a chromatographic column as a response to the injection of a concentration step. If the isotherm is convex upward, these sharp fronts are observed for positive steps whereas they are recorded with negative steps with concave upward isotherms. For a binary mixture, Jacobson *et al.* [1] have shown how the measurement of the retention volumes of these self-sharpening fronts permits the determination of the amount of each component adsorbed at equilibrium with a solution of given composition, using an integral mass balance equation. This method is

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accurate but tedious and requires large amount of materials. It remains the most frequently used.

Helfferich and Peterson [2] have shown that the equilibrium isotherm can be related to the retention times of pulses of the mixture components injected on a concentration plateau. Two types of procedures have been developed, depending whether the pulses can be identified by using isotopically labeled components or not. In the former procedure, the elution pulse is identified using a radioactivity detector (radiolabeled components), an LC–mass spectrometric or LC–NMR instrument (stable isotopes) and the retention time of the pulse of the material actually injected in the column is measured. It gives directly, in a single experiment, the stationary-to-mobile phase partition coefficients of all tagged solutes at the mobile phase composition of the experiment, hence $q_i(C_1, C_2)$, the isotherm. Because of current safety regulations, however, the use of radioactive isotopes has become extremely cumbersome; the use of stable isotopes requires complex and expensive equipment which is difficult to tune and rarely available. Finally, in all instances, the synthesis of the appropriately labeled compounds needed is required. All these requirements combined make the tracer pulse method too expensive to be practical in an academic laboratory.

In the latter procedure, the injection of a small amount of one component on a concentration plateau of both components generates a series of peaks as the response of the column, the system peaks [8]. There are as many system peaks as there are degrees of freedom in the composition of the system. This number is equal to the total number of components of the eluent minus one, as we inject one of the mobile phase components. The retention time of the system peak gives the slope of the tangent to the corresponding isotherm, $\partial q_i / \partial C_i$. Thus, the method does not provide enough information to calculate the competitive isotherms as the four derivatives, $\partial q_i / \partial C_j$, are required.

Recently, a new method for the determination of the competitive equilibrium isotherms of binary mixtures has been introduced [5–7]. This method employs the non-linear wave effect which takes place when the column is overloaded both in concentration and in volume, to the degree that a concentration plateau at the feed composition is eluted between the band front and its rear. Under such

conditions, we have a non-linear wave solution of the system of partial differential equations made of the mass balances of the sample components [5,9–11]. It can be shown that, under such conditions, the hodograph transform of the band profiles, *i.e.*, a plot of the concentration of the first component *versus* the concentration of the second at the same time (see below), is made of two lines (one for the band front and the other for its rear) which intersect at the point corresponding to the feed composition (constant state). This plot is called the hodograph plot or hodogram [5–7,11–13]. The theory of partial differential equations shows that the hodogram contains all the information regarding the interaction of the mixture components, but no information on the extent of adsorption [11].

When the competitive isotherms of the components of a binary mixture follow the competitive Langmuir model, the hodogram consists of two straight lines. The slopes and intercepts of these two lines are simply related to the four parameters of the competitive Langmuir isotherms [5]. As a conventional chromatographic system with an automatic fraction collector and an autoinjector system [6] permits a rapid determination of the individual elution profiles, this provides a convenient method for the determination of these coefficients [5,7]. When the competitive Langmuir isotherm model fails, however, the lines are no longer straight and more experimental data are required in order to determine the isotherms. Repeating the experiment while varying the composition of the wide pulse can provide these data.

Among the obvious advantages of the new method compared with frontal analysis are the much smaller amount of material needed and the lesser dependence of the accuracy on some important experimental conditions, such as the column efficiency and the column dead volume. Conversely, a serious disadvantage is the need for an isotherm equation to which the data have to be fitted. The derivation of a direct isotherm plot from the hodogram is not possible. We present here a theoretical comparison between data obtained by frontal analysis and by the hodograph method.

THEORY

The mass balance equation of the two compo-

nents of a binary mixture in a chromatographic system is

$$\frac{\partial C_i}{\partial t} + F \cdot \frac{\partial q_i}{\partial t} + u_0 \cdot \frac{\partial C_i}{\partial x} = D_a \cdot \frac{\partial^2 C_i}{\partial x^2} \quad (1)$$

As usual in the non-ideal or equilibrium-dispersive model of chromatography, the stationary phase concentration, q_i , and the mobile phase concentration, C_i , are related by the equilibrium isotherm; F is the phase ratio and u_0 the mobile phase velocity. The apparent dispersion coefficient, D_a , accounts for axial diffusion and for the mass transfer kinetics [14]. This assumption is valid as long as the column efficiency exceeds a few hundred theoretical plates [11,14]. The initial and boundary conditions of the problem are

$$C_i(t, x = 0) = \phi_i(t) \quad (2a)$$

$$C_i(t = 0, x) = 0 \quad (2b)$$

with $i = 1, 2$. In practice, we assume a rectangular injection of a mixture of constant composition, $C_{1,0}$, $C_{2,0}$, during a time t_p .

In the case of a competitive Langmuir isotherm:

$$q_i = \frac{a_i C_i}{1 + \sum_{j=1}^2 b_j C_j} \quad (3a)$$

When C_i becomes large, q_i tends towards a limit, the column saturation capacity, $q_{si} = a_i/b_i$. We can simplify the equations in the following derivation by letting $\bar{Q}_i = q_i/q_{si}$, $\bar{C}_i = b_i C_i$. Eqn. 3a becomes

$$\bar{Q}_i = \frac{\bar{C}_i}{1 + \sum_{j=1}^2 \bar{C}_j} \quad (3b)$$

Frontal chromatography method

In this method, a solution of the two components is pumped into a column previously equilibrated with the pure mobile phase. A front of the first component is eluted, followed by a front of the second component. When the eluent composition is constant and equal to the feed composition, the experience is repeated, the feed solution being replaced with a more concentrated solution of the two components, usually keeping constant the ratio of these two components. Because of the competi-

tion between the two components, an intermediate plateau appears after the elution of the front of the first component. During the elution of this intermediate plateau, the eluent concentration of the first component is higher than its concentration in the new feed while the eluent concentration of the second component is intermediate between its concentrations in the old and the new feed (see Fig. 1).

In the assumption of ideal chromatography (*i.e.*, if $D_a = 0$), the integral mass balance equations of

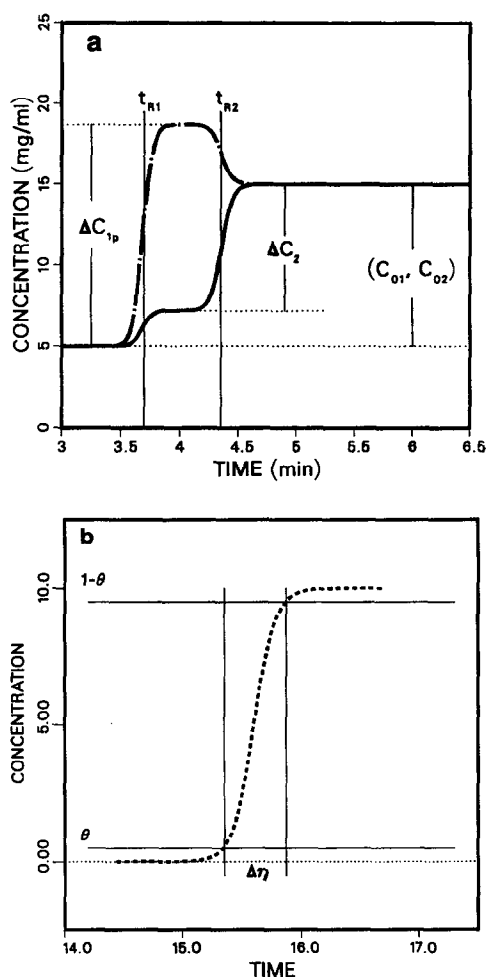


Fig. 1. Breakthrough profiles of the two components in frontal analysis and definition of symbols. (a) Schematic diagram of the individual breakthrough profiles in binary frontal analysis (assuming $C_{01} = C_{02}$), and definitions. (b) Schematic diagram of a shock layer and definition of its thickness. All figures: concentration is in mg/ml; time is in min.

the two components are written (see Symbols and Fig. 1a)

$$\frac{t_{R1} - t_0}{Ft_0} = \frac{\Delta q_1}{\Delta C_{1p}} \quad (4a)$$

$$\frac{t_{R2} - t_0}{Ft_0} = \frac{\Delta q_2}{\Delta C_2} \quad (4b)$$

where Δq_i and ΔC_i are the amplitudes of the concentration shock in the stationary and the mobile phases, respectively. The relationship which was derived by Jacobson *et al.* [1] as an integral mass balance equation can also be derived from the above equations which relate the retention times of the two breakthrough curves, the mobile phase concentration jumps of each solute corresponding to the injection step and the corresponding changes of each solute concentration in the stationary phase. However, when accounting for experimental data, different results are obtained when fitting these data to eqns. 4 or to the equations reported in ref. 1. The differences can be significant if the data are not very precise.

In practice, D_a is different from zero. The axial dispersion and the finite rate of mass transfer combine to erode the concentration discontinuities predicted by the ideal model. As these shocks are caused by non-linear thermodynamic effects which are constantly at work, the fronts remain very steep. Shock layers appear, which propagate at the same velocity as the shocks of the ideal model but have a finite width [9,11,15]. As a result, the formation of the intermediate concentration plateau is not instantaneous and this plateau is narrower than predicted by the ideal model [13], as allowance must be made for the thickness of the two shock layers.

The thickness of the shock layer was calculated by Rhee and Amundson [16]. They showed that a steep but steady concentration change, the shock layer, propagates along a real column (*i.e.*, a column where D_a is different from zero), that it propagates at the same velocity as the concentration shock would propagate along an ideal column with the same isotherms and they calculated the thickness of this shock layer. The velocity of a shock depends only on its height and is given by the equation

$$U_s = \frac{u_0}{1 + Fa_i \cdot \frac{\Delta \bar{Q}_i}{\Delta \bar{C}_i}} \quad (5)$$

From the study performed by Rhee and Amundson, we can derive the width, $\Delta \eta$, of the shock layer on the front of the first component band in frontal analysis and the time, Δt , needed for the formation of the intermediate plateau [13]. The width of the shock layer depends on the fractional height, θ , at which it is measured. It is given by

$$\Delta \eta(\theta) = D_a \cdot \frac{(1 + K)^2}{K} \cdot \frac{2 + \bar{C}_0}{C_0} \cdot \ln\left(\frac{1 - \theta}{\theta}\right) \approx \frac{H(1 + K)^2}{2u_0K} \cdot \frac{2 + C_0}{C_0} |\ln \theta| \quad (6)$$

with

$$K = k'_0 / (1 + \bar{C}_0) \quad (7a)$$

$$\theta = \frac{C_1^* - C_l}{C_1^* - C_r^*} = \frac{C_r - C_r^*}{C_1^* - C_r^*} \quad (7b)$$

$k'_{1,0} = a_1 F$ is the retention factor of the first component at infinite dilution; C_1^* and C_r^* are the concentrations at the left and right of the shock which are used to define θ and indicate at which fractional height of the shock layer we measure its width (see Fig. 1b). In eqn. 7b, either the true concentrations or the dimensionless concentrations (eqn. 3b) can be used. As the front of the first component elutes pure, we calculate the thickness of the first shock by combining eqns. 6 and 7a with

$$\begin{aligned} \bar{C}_0 &= \bar{C}_{1,0} \\ k'_0 &= Fa_1 \\ D_a &= H/2u_0 \end{aligned} \quad (8a)$$

where H is the column height equivalent to a theoretical plate. It would probably be more exact to use $D_a = H/2u_0 + U_s(u_0 - U_s)/k_f$, where k_f is the lumped mass transfer coefficient [17].

This question deserves a more thorough investigation, currently undergone in connection with an experimental study. For the thickness of the second component, we use

$$\bar{C}_0 = \bar{C}_{2,0}$$

$$k'_0 = \frac{Fa_2}{1 + b_1 \cdot \frac{1 - \alpha}{\alpha b_1 + b_2/\xi}} \quad (8b)$$

where ξ is the solution of the second degree algebraic eqn. 12a in ref. 13. This equation is also eqn. 10 in the next section of this paper.

From the combination of eqns. 6 and 8a, it results that the shock layer thickness increases in proportion to the column HETP [11,13]. This conclusion is supported by experimental results [13].

The time required before stabilization of the elution front of the first component and formation of the enriched plateau is

$$\Delta t = \frac{1}{2} \cdot \frac{\Delta C_{1p}(\Delta\eta_1 + \Delta\eta_2)}{C_{1,0}U_{s1} - C_{2,0}U_{s2}} \quad (9)$$

where ΔC_{1p} is the concentration height of the enriched plateau of the first component, $\Delta\eta_{s,1}$ and $\Delta\eta_{s,2}$ are the width of the shock layers before and after the enriched plateau and $U_{s,1}$ and $U_{s,2}$ are the shock velocities of the two injection concentrations, $C_{1,0}$ and $C_{2,0}$, respectively.

From eqn. 9, we can derive the conditions required for an accurate determination of the amounts of the two components adsorbed at equilibrium with the concentrations $C_{1,0}$ and $C_{2,0}$ in the mobile phase. The column length and efficiency must be such that the elution of the band front takes a time longer than Δt under all the experimental conditions investigated, so the intermediate plateau is always formed and its composition can be measured.

Hodograph method

As demonstrated previously [9,11,18–20], the following relationship can be derived between the derivatives and differentials of the concentrations, when the apparent diffusion coefficient is zero:

$$\xi^2 f_{21} + \xi(f_{22} - f_{11}) - f_{12} = 0 \quad (10)$$

where

$$\xi = dC_1/dC_2 \quad (11a)$$

and

$$f_{i,j} = \partial q_i / \partial C_j \quad i, j = 1, 2 \quad (11b)$$

ξ is the derivative associated with the characteristic direction in the C_1, C_2 space [9,18,19]; it defines the

slope of the lines in the hodograph plot. Eqn. 10 is a Clairaut differential equation with respect to dC_1/dC_2 . Its solutions are well known [9]: they consist of two families of straight lines whose slopes and ordinates are related to the partial differentials of the isotherm, which are the characteristics in the concentration domain. Each of the two roots defines a family of characteristic lines in each point of the (C_1, C_2) plane having the slopes ξ_+ , ξ_- , where ξ_+ and ξ_- are the positive and negative roots of eqn. 10, respectively. In the case of the competitive Langmuir isotherm, combining eqns. 3 and 10 gives

$$C_1 = \xi_+ C_2 + \frac{a_1 - a_2}{a_2 b_1 + a_1 b_2 / \xi_+} \quad (12a)$$

$$C_1 = \xi_- C_2 - \frac{a_1 - a_2}{a_2 b_1 + a_1 b_2 / \xi_-} \quad (12b)$$

The hodogram, *i.e.*, the plot of C_1 versus C_2 during the elution of the band, is made of two straight lines intersecting at the point of coordinates $C_{1,0}$, $C_{2,0}$, corresponding to the feed composition [5,11–16]. These lines are the characteristics of the point $C_{1,0}$, $C_{2,0}$. As a consequence, the product of their slopes is

$$\xi_- \xi_+ = -\frac{a_1 b_2}{a_2 b_1} \cdot \frac{C_{1,0}}{C_{2,0}} = \frac{1}{R_q R_c} \quad (13)$$

where R_q and R_c are the ratios $q_{s,2}/q_{s,1}$ and $C_{2,0}/C_{1,0}$, respectively [21]. This equation is derived directly from eqn. 10. Thus, if experiments are made with the same two components (R_q constant) and the same composition (R_c constant), the product of the two slopes should remain constant if the competitive isotherm is accounted for by the Langmuir isotherm.

An interesting question on which calculations may shed useful light is whether or not the accurate determination of isotherm data by the hodograph method requires experimental conditions under which the intermediate plateau of the first component is formed, which is an absolute requirement with the frontal analysis procedure. We have calculated the elution profile of a wide rectangular band at the end of columns of increasing lengths (Fig. 2a) and otherwise identical (*e.g.*, same height equivalent to a theoretical plate). For the sake of clarity, only the front part of these bands is shown. We see that the intermediate plateau is formed progressively, the height of the first component front increasing until it

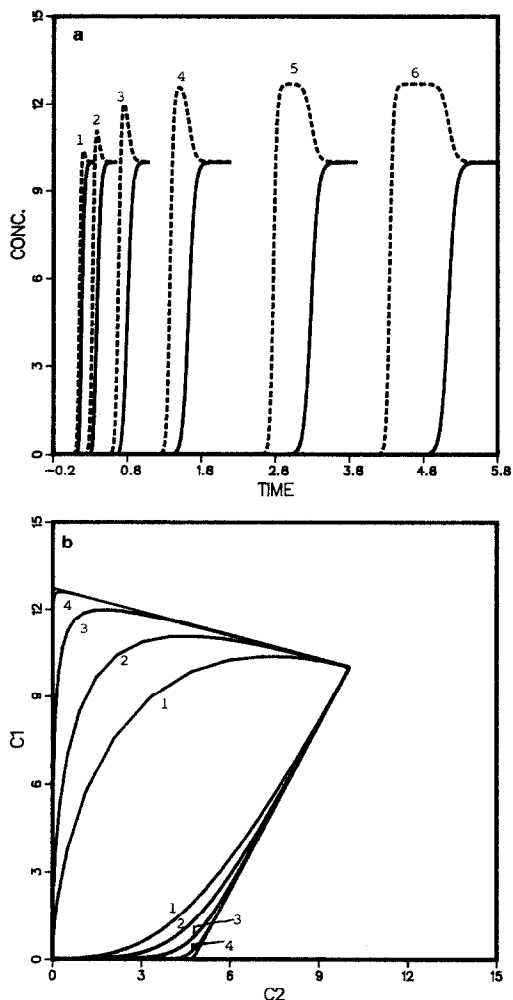


Fig. 2. Influence of the width of the intermediate plateau on the accuracy of the hodograph plot method. (a) Band profiles for a wide rectangular injection of a binary mixture at the exit of columns of increasing lengths. Column length: (1) 1 cm; (2) 2 cm; (3) 4 cm; (4) 8 cm; (5) 16 cm; (6) 25 cm. The rear boundaries of the elution profiles are not shown. (b) Hodograph plots corresponding to the elution profiles detected at 16 and 25 cm are superimposed on each other and cannot be distinguished.

reaches the plateau concentration, which it does for the fourth profile. The minimum column length required in frontal analysis is that corresponding to the fourth profile. In practice, a longer column would be needed as the plateau has to be wide enough to permit grabbing an eluent sample for its analysis. In Fig. 2b, the hodograph transform of

these bands is shown. The plot corresponding to the fourth profile permits essentially the same accuracy as any further experiment for which the intermediate plateau is fully developed. Satisfactory results could be obtained from the hodogram corresponding to the third profile, provided that about a third of the experimental data points, near the two concentration axes, be eliminated when the data processing is done to estimate the isotherm parameters.

Comparison between the frontal analysis and the hodogram methods for isotherm determination

Both methods are based on the solution of the mass balance eqns. 1 in the assumption of the ideal model. The errors made will derive from the consequences of having to use real, non-ideal columns and they will strike differently.

In frontal analysis, we assume that the two shock layers, at the front of the first component band and between the bands of the first and second components, have had time to form before the breakthrough of the concentration step. The formation of two stable shock layers and of a plateau wide enough to be recorded and collected is necessary to permit the determination of the concentrations of the two components on this intermediate plateau. This measure, in turn, is necessary for the calculation of the integral mass balance of the two components of the binary mixture. Under non-ideal conditions, this phenomenon takes a finite time, as mass transfers are no longer infinitely fast. This is especially true with a mixture, as the concentration of the first component at the breakthrough time is higher than in the injected feed [1]. The time, Δt (eqn. 9), required for the formation of this plateau depends on the column efficiency, on the relative retention of the components and on the injection profile. As a consequence, the minimum time required for the determination of a series of competitive isotherms at different relative concentrations R_{C_0} depends strongly on the efficiency of the column used and on the relative retention of the components studied.

The accuracy of the mass balances measured by frontal analysis relies on the assumption that the shock layers are symmetrical, so the retention time of the inflection point of the breakthrough profile is also the retention time of the mass center of the front. If the kinetics of mass transfer or of the retention mechanism are slow, this assumption may

lead to a significant error. This kind of error seems insignificant in most determinations carried out with most HPLC systems, where the kinetics are fast. It might be significant in affinity chromatography or in other applications involving biopolymers.

These limitations similarly affect the hodograph method. This method is valid only if the intermediate plateau at the front of the first component band has fully developed. Otherwise, there would not be any meaning to the slope and intercept of the first straight line of the hodogram. Although the method is fairly immune to slow mass transfer or reaction kinetics, if one of these types of kinetics is slow enough to generate a strongly unsymmetrical shock layer, it will render meaningless the parts of the plot close to the concentration axis and make it nearly impossible to select the experimental points which must be kept in the calculation of the slopes and intercepts of the two straight lines.

If we consider eqns. 4 and 12, we observe that frontal analysis requires the determination of the retention times of the two fronts, the phase ratio and the concentrations of the intermediate plateau. Both methods require the determination of the dead time (the hodograph method, in order to derive the value of the a_i coefficients). The hodograph method requires the collection of a large number of fractions and the accurate determination of their composition. Further, frontal analysis gives a single point of the isotherm for each breakthrough curve, while the hodogram samples the isotherm over an entire arc, *i.e.*, over a wide composition range, using a much smaller amount of sample and mobile phase in the process.

Experimentally, the hodograph method requires the acquisition of a large number of fractions and their analysis. A number of experimental problems have to be solved. A fast fraction collector is needed to collect enough fractions during the elution of the second shock layer (the elution of the first one does not give useful hodograph data). The collected fractions must be analyzed rapidly and accurately. Practical solutions have been discussed previously [6,7]. The errors made on the fraction concentrations result in a significant scatter of the data points [5–7,22], which limits the accuracy of the coefficients obtained by fitting the hodogram to an isotherm model that is more sophisticated than the competitive Langmuir equation. This is probably the most important drawback of the method.

Finally, the experimental data acquired in frontal analysis are transformed directly into isotherm points. The experimental data supplied by the hodogram cannot be transformed directly into isotherm points. They may be fitted to the equation of an isotherm model and used to calculate the best estimates of the parameters of this model. A model is necessary; the fitting of the isotherm data points to a spline is impossible as there are no isotherm data points.

In summary, the two methods have similar requirements regarding the column characteristics. The equipment needed for the hodograph method is standard whereas two chromatographs must be used in binary frontal analysis, the second for the analysis of a sample of the intermediate plateau. The hodograph transform is more precise, faster and uses much smaller amounts of chemicals but the data it collects are more difficult to process and require an isotherm model. Binary frontal analysis is very accurate but requires tight control of experimental conditions. A comparison between the accuracies of the two methods is difficult. The hodograph method does not require the determination of t_0 , whereas frontal analysis does. Flow-rate fluctuations during the experiment affect the frontal analysis measurement if made after the recording of detector signal *versus* time. They will not affect the hodogram, which merely uses the two concentrations.

The two methods appear to have complementary natures. An attractive synthesis would be to conduct a series of experiments designed for the hodograph method, injecting different concentration steps, with different concentration ratios. The retention times of the fronts of the breakthrough curves can be used to calculate the concentrations of each solute in the stationary phase, using eqns. 4, while the concentration profiles of the whole bands can be used with the hodograph method. This would provide some check on consistency and accuracy.

Simulation experiments

Using the computer programs previously developed for the calculation of solutions of the equilibrium-dispersive model [21–24], we have calculated the elution profiles for a series of four wide band injections of a binary mixture (concentration $C_1^0 = 15.0, 10.0, 5.0$ and 2.5 mM, respectively, with

$C_1^0/C_2^0 = 1$) and the breakthrough profiles for various steps of the same mixture [5]. A fraction of the points (one every 80) is kept as a data point. To each of these data points, a number taken from a simulated noise sequence is added. The uniform distribution random number generator DRNUN of

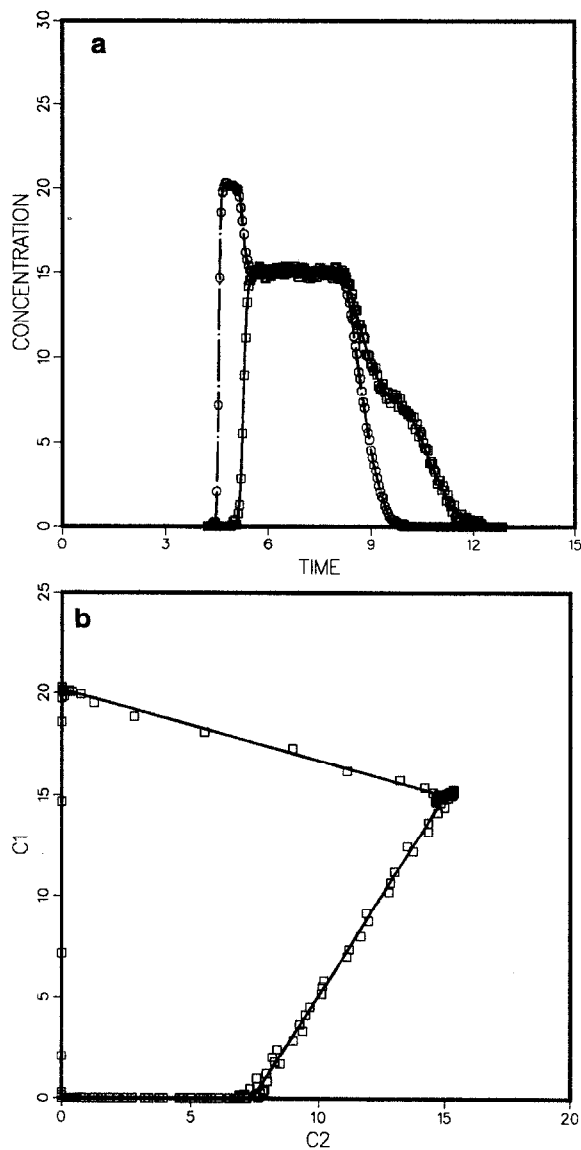


Fig. 3. Elution profiles and hodograph plot of experiment No. 1 shown in Table I. (a) Elution profiles. The points are simulated experiment points and the lines are the theoretical lines. (b) Hodograph plot corresponding to the elution profiles shown in (a).

the IMSL library gives random numbers between 0 and 1. A random number series of appropriate length is scaled to a mean of 0 and a standard deviation of 5% of the height of the rectangular pulse or of the concentration step injected.

The elution profiles of the four wide rectangular pulses considered are shown in Figs. 3a-6a. In these figures, the points are the "experimental" results of the simulated experimental data obtained as just

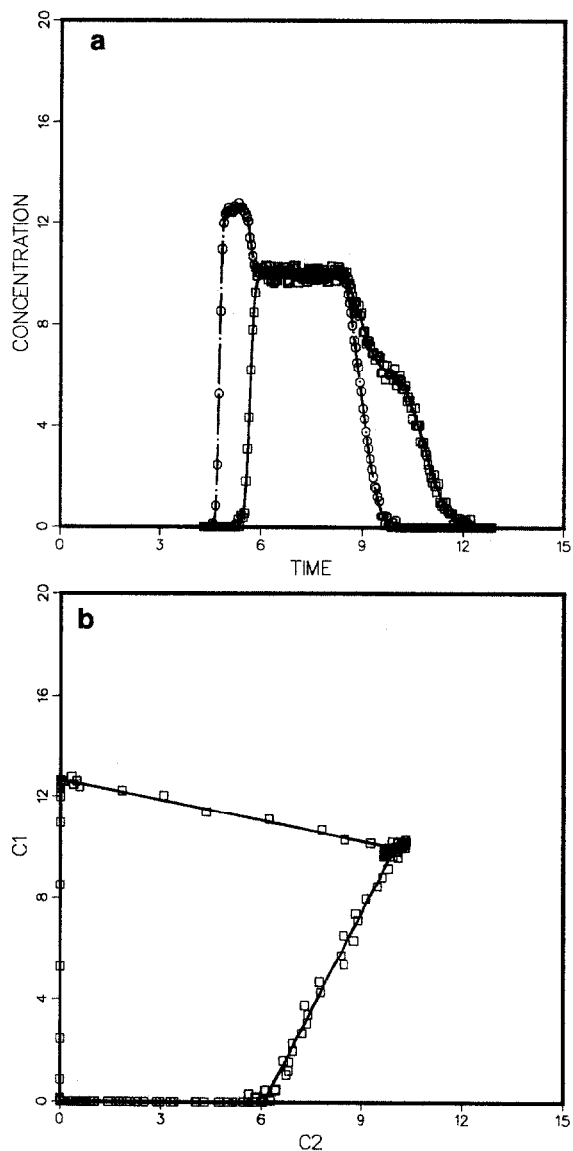


Fig. 4. As Fig. 3 for experiment No. 2 shown in Table I.

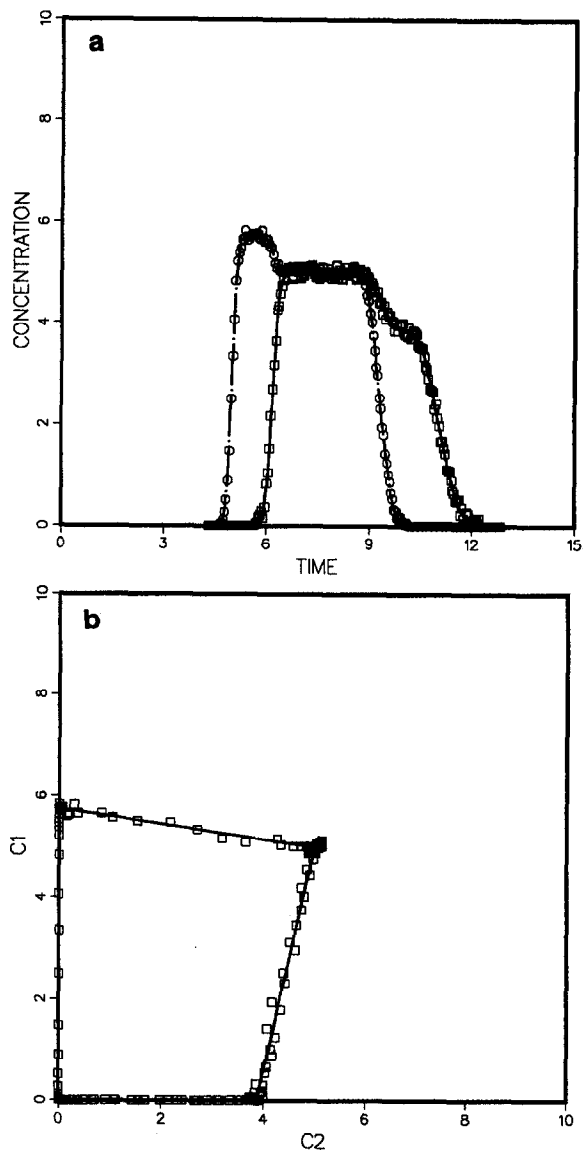


Fig. 5. As Fig. 3 for experiment No. 3 shown in Table I.

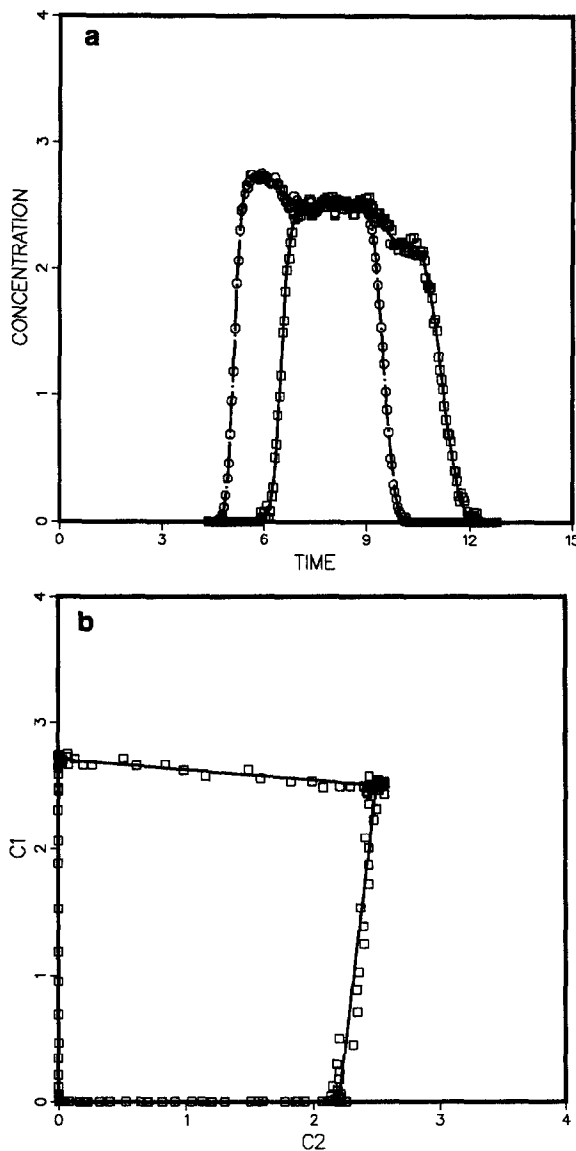


Fig. 6. As Fig. 3 for experiment No. 4 shown in Table I.

described. The data points obtained for the elution of a wide rectangular pulse are stored into two groups. The former includes the points for which the second component concentration is positive and the first component concentration is larger than the injection concentration augmented with the largest noise number. This set of data is used to calculate the negative slope, ξ_- , and the corresponding intercept

(Table I) by fitting the points to a straight line. The latter data group includes the points for which the first component concentration is positive and the second component concentration is lower than the injection concentration less the smallest random number. This second set of data is used to calculate the positive slope, ξ_+ , and the corresponding intercept (Table I). The hodograph plots and the best

TABLE I
SLOPES AND INTERCEPTS

Concentrations of the rectangular injection plug, $C_1^0 = C_2^0$: (1) 15 mM; (2) 10.0 mM; (3) 5.0 mM; (4) 2.5 mM. A_+ and A_- are the intercept of the straight lines shown in Fig. 3a, corresponding to the positive and the negative slope, respectively. Column length, $L = 25$ cm; flow-rate, 1 ml/min; hold-up time, 3.00 min; phase ratio, $F = 0.35$; column efficiency, 2500 theoretical plates. True values: $a_1 = 2.1556$, $a_2 = 3.7566$, $b_1 = 0.0216$, $b_2 = 0.0256$.

No.	ξ_-	ξ_+	A_+	A_-	b_1	b_2
1	0.3381	1.9594	14.3714	20.0927	0.02217	0.02556
2	0.2585	2.4854	14.9240	12.6399	0.02268	0.02541
3	0.1461	4.2905	16.4198	5.7550	0.02266	0.02463
4	0.07730	7.3592	15.9042	2.6922	0.02487	0.02468

straight lines obtained for the four simulated experiments are shown in Figs. 3b–6b.

The data points from the breakthrough curve are used to calculate the retention times of the two fronts and the intermediate concentration (Table II). Then, the equations in ref. 1 were used to calculate the corresponding stationary phase concentrations for the two components. To fit the frontal analysis data to the equations of the model, we used the SYNLIN procedure from the SAS package. This program permits the fitting of a set of experimental data to more than one equation.

RESULTS AND DISCUSSION

As indicated in the previous section, a comparison

of the accuracies of the two methods based on the use of experimental data is difficult, as the exact isotherm can never be known. A comparison based on the use of simulated data is useful to search for possible bias or errors. Experimental data comparing the precisions of the two methods will be reported later [25].

The parameters of the Langmuir isotherms are derived from the slopes and intercepts of the two straight lines of the hodograph plots (Table I) [5]. The deviations between the values of the parameters obtained with the hodograph method and the theoretical values increase from 2.6% to 15% for b_1 and from 0.2 to 3.6% for b_2 when the pulse concentration decreases from 15 to 2.5 mM. The results derived from the three highest concentration injec-

TABLE II
FRONTAL ANALYSIS RESULTS

Nos. 1–10 are the ten steps of a frontal analysis experiment. The concentrations C_{int} are the intermediate mobile phase concentrations of the first component corresponding to its mobile phase concentration on the intermediate plateau. From eqn. 4a, Q_1 and Q_2 are the stationary phase concentrations of the first and the second component corresponding to the mobile phase concentration of the injected step. All concentrations are in mM and all times in min. A hold-up time of 2.97 min was used to calculate the stationary concentrations.

No.	t_{R1}	t_{R2}	C_{int}	Q_1	Q_2
1	4.581	5.192	19.920	20.552	32.385
2	4.757	5.706	12.832	14.751	26.588
3	4.915	6.063	5.849	8.503	15.028
4	5.042	6.625	2.762	4.631	8.879
5	4.635	5.632	16.184	23.120	12.933
6	5.026	6.316	7.948	14.420	8.128
7	5.180	6.589	3.959	7.766	4.396
8	4.991	5.693	8.014	7.761	39.691
9	5.103	6.274	3.266	4.310	24.076
10	5.315	6.358	1.446	2.699	12.346

TABLE III
PARAMETERS OBTAINED BY FITTING THE EXPERIMENTAL RESULTS TO VARIOUS ISOTHERMS

Isotherm	Parameters					
	a_1	a_2	b_1	b_2	R^2	
(a) Competitive Langmuir isotherm equation, using eqn. 4						Q_1
						Q_2
	2.3568	3.9007	0.0269	0.0234	0.9976	0.9978
(b) Langmuir isotherm equation, using eqn. 4			b_1	b_2	R^2	
						Q_1
			0.0198	0.02236	0.9967	0.9951
(c) Competitive Langmuir isotherm equation	a_1	a_2	b_1	b_2	R^2	
						Q_1
	2.3389	3.9075	0.0233	0.0276	0.9944	0.9979
(d) Langmuir isotherm equation			b_1	b_2	R^2	
						Q_1
			0.0221	0.0214	0.9925	0.9961

tions are all within 5% of the true value. Thus, when the adsorption behavior of the binary mixture is well described by the Langmuir model, the determination of the model parameters is reasonably accurate.

Table II gives the results of a frontal analysis experiment involving the simulation of ten consecutive steps. For each step, the values of the intermediate concentration of the first component and of the retention times of the two fronts contain a random error resulting from the noise added to the detector signal, as explained in the previous section. The largest error made on the intermediate concentration is 2.2% and that made on the retention time of the two fronts is 2.3%. We have used two methods to fit these results to a Langmuir model. The data in Table III(a) and (c) were obtained using eqn. 4. First, the data for the first component are fitted to the single-component Langmuir equation, using C_{int} as the concentration in the mobile phase, and calculating the stationary phase concentration from eqn. 4a. The data for the second component are then

fitted to the competitive Langmuir equation, using the injection concentrations as mobile phase concentrations and deriving the stationary phase concentrations from eqn. 4b. The data in Table III(b) and (d) were obtained by determining the coefficients a_1 and a_2 from the infinite retention times and deriving the coefficients b_1 and b_2 by fitting the data in Table II using the equations derived by Jacobson *et al.* [1].

The largest deviation is about 24% [Table III(a)]. The best results are in Table III(c) (ca. 8% error for a_1 , b_1 and b_2 and 4% for a_2). We conclude that in the case of a true Langmuir isotherm, the frontal analysis data are slightly less accurate than the hodograph data. From this numerical comparison, we may conclude that the two methods give comparable performances. Both require fast mass transfer in the column for an accurate determination of the isotherm data. From a theoretical viewpoint, frontal analysis has the advantage of supplying as an intermediate result the absolute concentrations of the two solutes in the stationary phase at equilib-

rium. The hodograph method cannot give this result. With this second method, an isotherm model is always required, so the experimental data can be fitted to this equation. On the other hand, the hodograph method does not need the prior determination of the dead time whereas frontal analysis does. However, this advantage is due to the fact that the hodograph method supplies only the ratio $\alpha = a_2/a_1$, not the value of each of these two coefficients, so the measurement of t_0 is eventually necessary. Finally, only random errors on the composition of the collected fractions affect the results of the hodograph method. Random errors on the flow-rate and the influence of the signal noise on the error made in the determination of the retention time of the breakthrough curve affect the results of frontal analysis. This could sometimes be an advantage.

From a practical point of view, the hodograph method has several important advantages over the frontal analysis method. (1) The experimental procedure is simpler than that described in ref. 1 and it is much easier to automate. The equipment required includes an ordinary liquid chromatograph, an automatic fraction collector and an automated analyzer. (2) The requirements for the control of the experimental conditions are less demanding than for frontal analysis. For example, flow-rate fluctuations do not affect the results of the hodograph method whereas they directly affect the results of frontal analysis. (3) Finally, but most important, the amount of sample needed for the determination of an isotherm is much less than in frontal analysis, often several orders of magnitude less. (4) On the other hand, the data processing required for the application of the hodograph method is much more complicated than the simple fit of the stationary phase concentrations to an adsorption equation needed in frontal analysis. This is especially true in the case of non-Langmuir isotherms. If the isotherm function has one or several inflection points, however, unexpected difficulties arise in the use of the frontal analysis method, *i.e.*, in the identification of the self-sharpening boundary and in the measurement of the correct retention time [26]. The hodograph method is easier to apply if the isotherms of the two components are similar.

SYMBOLS

a_i	first coefficient of the Langmuir isotherm (eqn. 3)
b_i	second coefficient of the Langmuir isotherm (eqn. 3)
$C_{i,0}$	concentration of the component i in a rectangular injection pulse (eqn. 2)
C_i	mobile phase concentration of the component i ($i = 1$ or 2) (eqn. 1)
\bar{C}_i	normalized mobile phase concentration of the component i (eqn. 3)
C_1^*	concentration of the plateau before the shock layer (eqn. 7b)
C_2^*	concentration of the plateau after the shock layer (eqn. 7b)
D_a	coefficient of axial dispersion (eqn. 1)
F	phase ratio [$F = (1 - \epsilon)/\epsilon$] (eqn. 1)
H	column HETP (eqn. 6)
K	retention parameter, eqn. 7a
i	rank of the component (here, $i = 1$ or 2) (eqn. 1)
\bar{Q}_i	normalized stationary phase concentration of the component i (eqn. 3)
q_i	stationary phase concentration of the component i ($i = 1$ or 2) (eqn. 1)
q_{si}	column saturation capacity for the component i (eqn. 3)
t	time (eqn. 1)
t_0	hold-up time (eqn. 4)
t_p	width of a rectangular injection profile (eqn. 2)
t_{Ri}	retention time of the component i (elution time of the center of the breakthrough curve)
U_s	velocity of a shock (eqn. 5)
u_0	mobile phase velocity (eqn. 1)
x	distance along the column (eqn. 1)

Greek symbols

α	relative retention of the two components, $\alpha = a_2/a_1$ (eqn. 8b)
ϵ	total column porosity
ΔC_i	amplitude of the concentration shock or step in the mobile phase (eqn. 4)
ΔC_{1p}	concentration height of the intermediate plateau (eqn. 9)
Δq_i	amplitude of the concentration shock or step in the stationary phase (eqn. 4)
Δt	time necessary to form the intermediate pla-

- teau in the case of frontal analysis of a binary mixture (eqn. 9)
- $\Delta\eta$ shock layer thickness (eqn. 6)
- $\phi_i(t)$ injection profile (eqn. 2)
- θ reduced concentration during the passage of the shock layer (eqn. 7b)
- ξ solution of eqn. 10. There are two roots, ξ_+ and ξ_-

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