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RAPID METHOD FOR DETERMINING MULTICOMPONENT LANGMUIR PARAMETERS FOR DISPLACEMENT CHROMATOGRAPHY

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SUMMARY

A new method, based on the coherence theory of chromatography, has been presented for determining Langmuir equilibrium coefficients in multicomponent systems. The method provides a quick and simple technique for obtaining equilibrium data for the simulation of displacement chromatography, and is applicable to mixtures involving any number of components. In essence, the method uses a combination of elution and frontal chromatography experiments to characterize the equilibrium behavior. Pure component samples are not necessary, and sample preparation involves simple dilution or concentration steps with the process mixture and displacer. Furthermore, if the equilibrium behavior of the displacer in the Henry's law region is known, the characterization can be achieved, in most cases, with a single elution and single frontal chromatogram. Explicit equations relating the Langmuir coefficients to characteristics of the elution and frontal chromatograms have been derived. These equations have been successfully applied to a four-component adsorption system.

INTRODUCTION

It has been recognized for sometime that liquid chromatography (LC) has considerable potential as a large-scale purification and separation process in the production of biological and specialty chemical products. The strengths of this technique are its ability to achieve very high degrees of product purity, and its potential for achieving two operations, concentration and purification, in a single step. This reduction in the number of steps in the purification scheme can result in a significant economic advantage, as has been demonstrated in the production of streptomycin and cephalosporin[1].

Currently, the quickest and most commonly used approach for developing large-scale chromatographic processes is the direct scale-up of analytical systems[2]. Consequently, an overwhelming number of preparative processes are based on elution development, both linear and non-linear. Though elution chromatography is commonly used for large-scale purifications, this development technique can result in

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a chromatographic process that is economically less favorable than one using displacement development[3]. This fact has been recognized for sometime, but elution chromatography continues to be the technique of choice, because it is based on the wealth of knowledge accumulated from analytical chromatography. Correspondingly, the lack of bench-scale experience with displacement chromatography has hindered its acceptance in large-scale chromatographic processes.

The paucity of experimental data with regard to displacement chromatography can be compensated for, to a degree, by appropriate computer simulations of the process. These simulations allow the determination of optimal operating conditions for the desired separation. Essential to this approach is the availability of a suitable model for non-linear, multicomponent chromatography. Such a model is available[4], but the use of this model requires that multicomponent equilibrium behavior be known *a priori*; since equilibrium behavior establishes the primary response characteristics of the chromatographic process.

Multicomponent equilibrium data for liquid–solid systems have been traditionally obtained by batch methods. Briefly, the method involves generating the isotherm by equilibrating solution of known composition with a known weight of the adsorbent. Once equilibrated, the liquid solution is analyzed usually by chromatography, and its change in composition is used to locate a point on the isotherm. The disadvantage of this approach is that it is time consuming and tedious. Consequently, it is generally not suitable for the industrial environment, especially when only a preliminary analysis of competing separation techniques is being conducted.

An alternative method for obtaining equilibrium data is based on chromatography. Advantages of this method are speed and accuracy. The chromatographic approach was first used by Glueckauf[5] to study solid–liquid equilibria. Since then, various other chromatographic procedures have been proposed[6]. For multicomponent systems specifically, two chromatographic methods are commonly used. In the tracer pulse (TP) method proposed by Helfferich and Peterson[7], the column is initially equilibrated with a carrier fluid of constant, known composition. After equilibration, a small sample with the same composition as the carrier but containing a detectable isotope of the species of interest is injected into the fluid stream. The retention time of the isotope is measured, and this is used to calculate one point on the isotherm. The experiment is repeated at a number of carrier compositions to generate the required portion of the multicomponent isotherm. Though the TP method is applicable to any number of components and any equilibrium behavior, its major disadvantages are the need for a separate measurement for each point on the isotherm, and the need to have a detectable isotope of each species being studied.

The second chromatographic method is the elution on a plateau (EP) method (also called perturbation chromatography) introduced by Reilley *et al.*[8]. In this method, the column is first equilibrated with a fluid of known composition. It is then perturbed slightly from this state, and the response is observed. This experiment is repeated over a suitable composition grid, and the data are used with a non-linear parameter estimation method developed by Glover and co-workers[9,10] to determine the adsorption isotherm. While the EP method does not use isotopes, like the TP method it requires substantial chromatographic data. Furthermore, the method involves a complex parameter estimation method.

Despite the potential of the chromatographic approach for measuring equilib-

rium data, the use of this approach has been almost exclusively limited to gas chromatography (GC). This is due to the fact that, until recently, LC was used primarily for analytical purposes. In this case, the process is restricted to the linear portion of the isotherm, and a detailed knowledge of the adsorption behavior at high concentrations is not necessary. However, with the increasing use of LC in large-scale separations and purifications there is a need for a simple and quick procedure for measuring multicomponent isotherms. Both the TP and EP methods used in GC are directly applicable to LC. However, for reasons outlined earlier, neither one of these serves as a simple and quick method for determining multicomponent isotherms. Consequently, other, more suitable methods have to be developed.

Jacobson *et al.*[11,12] have used LC to successfully study adsorption behavior. In one study[11], they measured the adsorption of single solutes on silica-bound hydrocarbonaceous sorbents by frontal chromatography. More recently[12], they have presented two methods, both based on frontal chromatography, for the measurement of competitive adsorption isotherms. In one method, the method of mass balance (MMB), the effluent composition history is used in conjunction with the column mass balance to generate a point on the adsorption isotherm. The advantage of this method is that it is applicable to any type of adsorption behavior. However, MMB requires detailed effluent composition histories, and a substantial amount of frontal chromatography data; since a single frontal chromatogram generates only one point on the isotherm. The second method, the method of composition velocities (MCV), is based on the coherence theory of chromatography[4]. In this method, migration velocities of concentration waves generated by frontal chromatography are regressed to yield parameters of the complex Langmuir isotherm. The advantage of MCV over MMB is that it requires only retention volumes and not composition histories. It is, however, restricted to systems obeying the complex Langmuir isotherm. A further disadvantage of MCV is that, though the method is in principle applicable to any number of components, the regression procedure becomes increasingly complex, and the regression parameters more uncertain, as the number of components increases.

In this paper, a new method, called the *h*-root method (HRM), will be presented. This new method is geared toward obtaining equilibrium data for displacement chromatography. Like MCV, it is restricted to systems obeying the compound Langmuir isotherm. The new method uses a combination of elution and frontal chromatography. It is based on propagation velocities of the composition fronts and compositions of the effluent plateaus, but requires no parameter estimation. Furthermore, if equilibrium data for the displacer are known in the linear region, the multicomponent isotherm can be established with a single elution and single frontal experiment, regardless of the number of components present. Also, samples required for both experiments can be obtained directly from process solutions, without extensive sample preparation.

THEORY

Equilibrium isotherm

The equilibrium distribution of species between the stationary and mobile phases in chromatography establishes the primary characteristics of the effluent composition history. For LC with a single solute, a commonly used isotherm is the Langmuir isotherm[13]:

$$q_i = \frac{a_i c_i}{1 + b_i c_i} \tag{1}$$

For multicomponent systems eqn. 1 is readily extended to give:

$$q_i = \frac{a_i c_i}{1 + \sum_{j=1}^{n} b_j c_j} \tag{2}$$

With $b_j > 0$, eqn. 2 allows for competitive behavior between species. Eqn. 2 is the only multicomponent isotherm for which a comprehensive theory of chromatography exists[4]. Consequently, this isotherm is frequently used for modeling large-scale chromatographic separation processes[3].

Summary of coherence theory

The coherence theory of chromatography[4] is a useful equilibrium theory that has been applied successfully to a variety of chromatographic processes[14–20]. No attempt will be made in this article to outline the theory in detail; only features essential to the current development will be given.

Fundamental to the coherence theory is the recognition of the phenomenon of coherence. A chromatographic column subject to a disturbance will, after a period, settle into a "resolved" state, which consists of a series of composition waves each subject to the coherence condition:

$$v_{c_i} = v_{c_j} \tag{3}$$

for all i and j. Using DeVault's[21] equation for concentration velocity,

$$v_{c_i} = \frac{v_0}{1 + \frac{\rho}{\varepsilon}\left(\frac{\partial q_i}{\partial c_i}\right)_z} \tag{4}$$

and the compound Langmuir isotherm, eqn. 2, it can be shown that the coherence condition defines a grid of coherent composition paths to which the system is restricted once the coherence condition, eqn. 3, is satisfied. Thus, given the feed history, this grid can be used to find the composition route for the column, and, therefore, the column effluent history can be predicted.

In order to allow the use of this approach to any number of components, Helfferich and Klein[4] have orthogonalized the composition path grid by defining the h-composition space with the non-linear transformation:

$$\sum_{i=1}^{n} \left(\frac{b_i c_i}{h a_i / a_1 - 1}\right) - 1 = 0 \tag{5a}$$

and

$$h_{j-1} = a_1/a_j \text{ or } h_j = a_1/a_j \text{ if } c_j = 0 \quad (1<j\leq n) \tag{5b}$$

$$h_1 = 1 \qquad \text{if } c_1 = 0 \tag{5c}$$

In the h-space, the velocity of the composition front with kth h-root as the variable root is given by:

$$u_k = h_k \prod_{i=1}^{n} h_i \prod_{i=1}^{n+1} \alpha_{i1} \tag{6}$$

for a diffuse wave, and

$$u_k = h_k' h_k'' \prod_{\substack{i=1 \\ i\neq k}}^{n} h_i \prod_{i=1}^{n+1} \alpha_{i1} \tag{7}$$

for a sharp wave. Eqns. 6 and 7 are written for an n-component non-stoichiometric system obeying eqn. 2, that has been converted to an equivalent $n+1$ component stoichiometric system[4]. The velocities in eqns. 6 and 7 are adjusted velocities and are related to real velocities by the equation:

$$v_k = \frac{v_0}{1 + \dfrac{R\rho}{u_k \varepsilon}} \tag{8}$$

where R is an adjustable parameter used in the conversion of the n-component non-stoichiometric system to an $n+1$ component stoichiometric system[4]. The separation factors α_{i1} in eqns. 6 and 7 are related to the Langmuir equilibrium constants as follows:

$$\begin{aligned} \alpha_{i1} &= a_i/a_1 \quad i\neq p \\ \alpha_{p1} &= R/a_1 \end{aligned} \tag{9}$$

where p is the dummy species in the $n+1$ component stoichiometric system. In this development, the R value will be selected in the range $0<R<a_n$, to ensure that the dummy species is the least retained species ($p = n+1$).

Tracer pulse elution

Tracer pulse elution is a special case of elution chromatography in which the injected pulse contains trace concentrations of all components except the eluent. In this case, the response pulses will travel at the trace-species velocities, and it can be shown that the pulse containing the species j on a background of the eluent, k, will have an adjusted velocity[4]:

$$u_j = \alpha_{kj} \tag{10}$$

Using eqn. 8, the adjusted velocity in eqn. 10 can be replaced with the real velocity:

$$\alpha_{kj} = \frac{R\rho}{\varepsilon}\left(\frac{1}{\frac{v_o}{v_j} - 1}\right) \tag{11}$$

Applying eqn. 11 to species 1, the most strongly retained species, and dividing the resultant equation by eqn. 11, we obtain:

$$\alpha_{j1} = \frac{\frac{v_0}{v_j} - 1}{\frac{v_0}{v_1} - 1} \tag{12}$$

Frontal chromatography

In frontal chromatography, a column initially equilibrated with a solution containing no solutes is subject to a step change in the influent fluid composition. If the step change involves n solutes, n sharp composition waves will be generated in the column. Fig. 1 is a convenient, schematic representation of the column profile during frontal development. The horizontal lines represent sharp waves generated by the development, and the fastest wave, wave n, is furthest downstream. Also shown in Fig. 1 are the plateau compositions, defined in the h-composition space. These h-root values establish the velocities of the concentration fronts, as can be seen from eqn. 7.

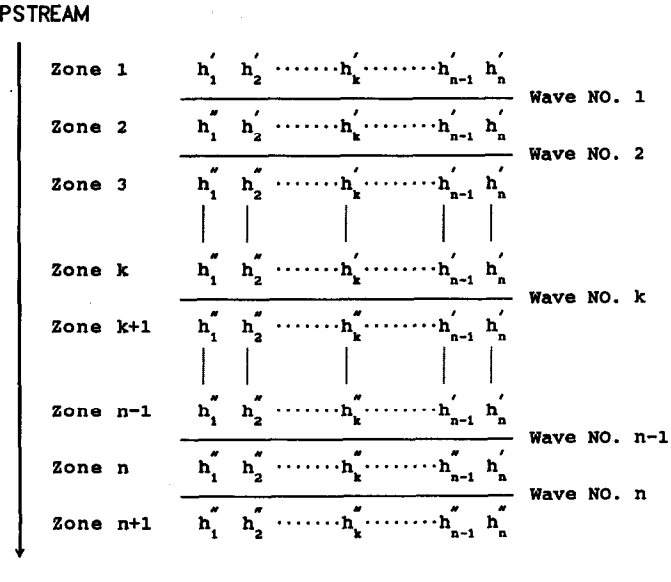

Fig. 1. Schematic representation of frontal development.

For the nth wave, the fastest wave,

$$u_n = h_n' h_n'' \prod_{i=1}^{n-1} h_i'' \prod_{i=1}^{n+1} \alpha_{i1} \tag{13}$$

Since the column does not contain any solutes initially, we have from eqn. 5b and c,

$$h_j'' = a_1/a_j \quad j = 1, \ldots, n \tag{14}$$

With the dummy species as the $(n+1)$th species, eqns. 9 and 14 give:

$$h_j'' = \alpha_{1j} \quad j = 1, \ldots, n \tag{15}$$

Substituting eqn. 15 in eqn. 13, and solving for h_n':

$$h_n' = u_n \alpha_{1n+1} \tag{16}$$

Finally, eqn. 9, applied to the dummy species, can be substituted in eqn. 16 to give:

$$h_n' = \frac{u_n a_1}{R} \tag{17}$$

From eqn. 7, the wave velocity of the $(n-1)$th wave is:

$$u_{n-1} = h_n' h_{n-1}' \prod_{i=1}^{n-1} h_i'' \prod_{i=1}^{n+1} \alpha_{i1} \tag{18}$$

Substituting eqns. 15 and 17 in eqn. 18 and solving for h_{n-1}', we obtain:

$$h_{n-1}' = \frac{a_1 u_{n-1}}{a_n u_n} \tag{19}$$

This procedure can be repeated for all slower waves, and it can be shown that

$$h_k' = \frac{a_1 u_k}{a_{k+1} u_{k+1}} \qquad k = 1, \ldots, (n-1) \tag{20}$$

DETERMINATION OF LANGMUIR CONSTANTS

HRM determines the Langmuir constants, a and b in eqn. 2, through a combination of tracer elution and frontal chromatography experiments. Tracer pulse elution is used to estimate dilute solution equilibrium behavior, and frontal chromatography establishes equilibrium behavior in the high-concentration region. The method will be described for the situation where the equilibrium behavior of the displacer in the dilute concentration region (Henry's law region) is known. If the dilute

solution behavior of the displacer is not known, it can be obtained from simple frontal chromatography experiments, and these will be described in more detail later.

Dilute solution behavior

The elution experiments involve the following sequence of steps: (1) equilibration of the column with a suitable eluent; (2) injection of a short pulse of a mixture of the multicomponent process solution, the displacer, and the eluent; and (3) development of the chromatogram with the eluent.

The preparation of injection samples for the elution experiments is straightforward. The selected displacer is mixed with a sample of the process solution to give a product that has a displacer concentration that is no greater than that of the most concentrated components in the process solution; this will ensure that the displacer does not dominate over process components. This mixture is then diluted appropriately with the eluent. The degree of dilution depends on the total concentration of the solutes, the maximum concentration of any one solute, and the competitive adsorption behavior between solutes. The degree of dilution necessary cannot be established *a priori*, but can be determined quickly through a simple procedure.

The objective of the dilution process is to ensure that the elution occurs in the linear portion of the isotherm. From eqn. 2, this requires that

$$\sum_{j=1}^{n} b_j c_j \ll 1 \tag{21}$$

In order to identify dilution conditions that satisfy eqn. 21, the elution experiment is first performed with a sample diluted to a known but arbitrary degree. For an n-component process solution, this experiment will give $n+1$ concentration pulses. The first pulse eluting, pulse $n+1$, will correspond to the least retained component in the process solution. The most highly retained component will be the displacer, which will elute last (pulse 1). Between pulse $n+1$ and pulse 1, the other components in the process solution will elute, with retention times increasing with increasing affinity. As

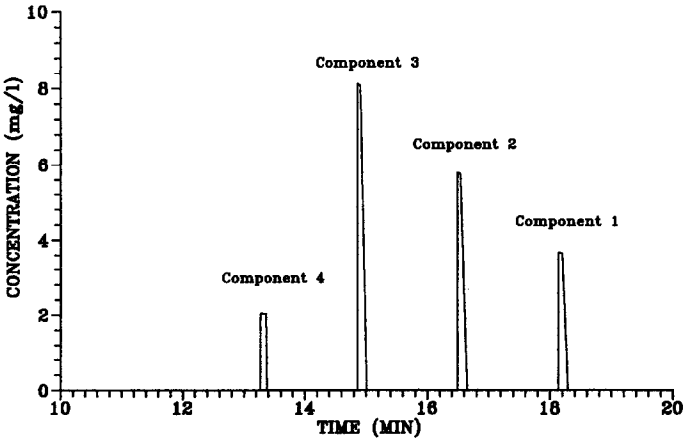

Fig. 2. Elution chromatogram for sample No. 3.

TABLE I
LANGMUIR CONSTANTS FOR CHROMATOGRAPHIC SIMULATIONS

Component No.	*a (l/g)*	*b (l/mg)*
1	5	0.25
2	4	0.25
3	3	0.25
4	2	0.25
5	1	0.25

an example, an ideal elution chromatogram for a three-component process solution is shown in Fig. 2. The peak retention times for each of the pulses is recorded. The elution experiment is now repeated with a sample that is ten times more dilute than the sample used in the first experiment. The new peak retention times are noted, and compared to the set obtained earlier. If the degree of dilution first selected is adequate, the retention times obtained from the two experiments will be essentially the same. If they are not, the process has to be repeated until a degree of dilution consistent with the requirements of tracer elution chromatography is established.

The procedure for identifying adequate dilution is illustrated for the five-component system shown in Table I. Component 1 is the displacer, and component 5 is the eluent. Components 2–4 are solutes in the process solution for which the displacement scheme is being developed. For this system, the coherence theory of chromatography[4] was used in conjunction with the operating conditions given in Table II, to simulate the column response during the isocratic elution of various samples, each diluted to a different degree. The results of these simulations are summarized in Table III. Sample 1 corresponds to the initial sample prepared with an arbitrarily selected degree of dilution. Sample 2 corresponds to a ten-fold increase in the dilution, relative to sample 1. It is clear from a comparison of the retention times obtained with these two samples, that the initial degree of dilution is insufficient for linear elution chromatography. Sample 3 corresponds to a further ten-fold increase in the degree of dilution. Once again, the change in retention times exhibited between samples 2 and 3 indicate that the degree of dilution represented by sample 2 is insufficient. In contrast, a comparison of retention times obtained with samples 3 and 4 indicates that the dilution represented by sample 3 is sufficient to satisfy eqn. 21.

Once an adequate degree of sample dilution has been identified, the corres-

TABLE II
OPERATING CONDITIONS FOR ELUTION SIMULATIONS

Column length	100 cm
Packing density	20 g/l of column
Column porosity	0.97
Interstitial fluid velocity	10 cm/min
Injection time	0.1 min
Eluent	500 mg/l component 5 in inert carrier

TABLE III
EFFECT OF DEGREE OF DILUTION ON RETENTION TIME

Sample No.[a]	*Relative degree of dilution*	*Retention time (min) for peak No.*			
		1	*2*	*3*	*4*
1[b]	1	16.7	15.0	13.5	12.6
2	10	17.8	16.2	14.5	13.2
3	100	18.1	16.5	14.9	13.3
4	1000	18.2	16.5	14.9	13.3

[a] All samples prepared in a solution containing 500 mg/l of eluent in an inert carrier.
[b] 400 mg/l component 1; 600 mg/l component 2; 800 mg/l component 3; 200 mg/l component 4; 500 mg/l component 5.

ponding elution chromatogram can be used to calculate the separation factors, α_{j1}, of all components except the eluent. For example, for sample 3 in Table III, the elution chromatogram is shown in Fig. 2. From the retention times of each of the peaks in this chromatogram, the propagation velocities of the peaks are calculated. These velocities are reported in Table IV. Once peak velocities are known, eqn. 12 is used to calculate the separation factors. For the case being considered, the separation factors calculated in this manner are given in Table IV. The dilute solution constants, a_j, for the process solution components ($1 < j \leq n$), can now be calculated from eqn. 14 and the value of a_1, which is assumed to be known. As shown in Table IV, the values of a_j used in the simulation are recovered.

From this development, it is clear that tracer elution allows the explicit determination of the dilute solution Langmuir constants from a single chromatogram, once an appropriate degree of dilution has been identified. Notice that the method works regardless of the number of components present in the process solution. Furthermore, injection samples are obtained directly from the process solution, and the sample preparation process involves only dilution.

Characterization of competitive behavior

The characterization of competitive behavior between adsorbing species can be

TABLE IV
DILUTE SOLUTION LANGMUIR CONSTANTS FROM ELUTION CHROMATOGRAM OF SAMPLE No. 3

Species No., j	*Peak velocity, v_j (cm/min)*	*Separation factor, α_{j1}*	*Calculated constant a_j (l/g)*
1	5.52	1.0	–
2	6.06	0.8	4.0
3	6.71	0.6	3.0
4	7.52	0.4	2.0

achieved with frontal chromatography. The frontal chromatogram should be obtained for an appropriate mixture of the process solution and the displacer; the concentration of displacer in the injected mixture should, for the reason outlined earlier, be no greater than that of the most concentrated components in the process solution. Before performing the frontal experiment, it is necessary to ensure that the chromatographic process will occur in the non-linear regime. This can be established with the elution experiments described earlier. If it is found that the adsorbate content in the process solution is low, concentration of this solution will be necessary.

As was stated earlier, frontal chromatography with n components will produce n sharp concentration boundaries in the column, each travelling with a different, but constant, velocity (Fig. 1). Since for frontal chromatography the resolution from non-coherence to coherence is instantaneous, the waves maintain their positions in the sequence from the start of the operation to the time they exit the column; *i.e.*, there will be no interference between the migrating waves. Thus, the plateau regions between the waves will be conserved.

From the frontal chromatography experiment, the retention time for each of the boundaries can be obtained. These retention times can then be used to calculate the velocities of the corresponding boundaries. From the real velocities, adjusted velocities are calculated with eqn. 8. At this point, it is necessary to obtain the value of the nth h-root in the injected solution (the h_n' value in Fig. 1). This is achieved with eqn. 17, using an R value that is arbitrarily selected in the range $0 < R < a_n$. Helfferich and Klein[4] have shown that the value of R selected does not affect the computation. However, selecting a value in the range specified will ensure that the concentrations of all physically existing species will be positive.

The frontal chromatography experiment will also provide the compositions of each of the plateau regions between the migrating boundaries. These compositins can be used in eqn. 5a with the calculated value of h_n' to systematically determine the values of the competitive binding coefficients b_i. Eqn. 5a is first applied to plateau zone n in Fig. 1. For this zone, the concentrations of all components except component n, the least retained component in the process solution, are zero. Thus, eqn. 5a simplifies to:

$$\frac{b_n c_n}{h a_n/a_1 - 1} - 1 = 0 \tag{22}$$

Since h_n' is a non-trivial root in zone n, it will satisfy eqn. 22. Therefore, the only unknown in eqn. 22 is b_n;

$$b_n = \frac{h_n' a_n/a_1 - 1}{c_n} \tag{23}$$

Eqn. 5a is now applied to zone $n-1$. In this case, all concentrations except those of components n and $n-1$ are zero. Therefore, eqn. 5a simplifies to:

$$\sum_{i=n-1}^{n} \left(\frac{b_i c_i}{h a_i/a_1 - 1} \right) - 1 = 0 \tag{24}$$

Since h'_n is also a non-trivial root in zone $n-1$, it will satisfy eqn. 24. Thus, b_{n-1} can be calculated from the equation:

$$b_{n-1} = \frac{h'_n a_{n-1}/a_1 - 1}{c_{n-1}} \left(1 - \frac{b_n c_n}{h'_n a_n/a_1 - 1}\right) \tag{25}$$

In this manner, successive zones from the downstream end to the upstream end can be used to calculate the remaining b constants. For the kth component ($k \neq n$), b_k will be given by:

$$b_k = \frac{h'_n a_k/a_1 - 1}{c_k} \left(1 - \sum_{i=k+1}^{n} \frac{b_i c_i}{h'_n a_i/a_1 - 1}\right) \tag{26}$$

This approach has been applied to the four-component system of Table I. For this system, with the operating conditions of Table V, the coherence theory predicts the chromatogram shown in Fig. 3. As expected, four sharp boundaries are obtained. The retention time for each of these boundaries, and the compositions of the plateaus between the boundaries are given in Table VI. Using the retention time for the fastest wave with eqn. 17, h'_4 in Table VII was calculated. This h-root and the composition of the zone upstream of wave 4 were used in eqn. 23 to calculate b_4. The computation was repeated with the other plateau compositions, using eqn. 26 instead of eqn. 23. The values of b thus obtained are reported in Table VII. Comparing these values with the values used for the simulation (Table I), it can be seen that the Langmuir b parameters are recovered.

In the calculation method described, only h'_n was used. It is also possible to calculate the b values by using the other h-roots in the injected solution (h' roots in Fig. 1). In this case, the retention time data are used in conjunction with eqn. 20 to obtain the desired h-roots. These non-trivial h-roots are then used in eqn. 26, with appropriate plateau compositions, to calculate the b parameters.

Two characteristics of the Langmuir coefficients used in the sample simulation need to be highlighted. First, the a_i/b_i ratio for each of the components in the mixture is different. This usually represents the situation when Langmuir coefficients for multicomponent systems cannot be obtained from single-component adsorption

TABLE V
OPERATING CONDITIONS FOR FRONTAL SIMULATIONS

Column length	30 cm
Packing density	400 g/l of column
Column porosity	0.4
Interstitial fluid velocity	10 cm/min
Injected fluid composition	
Component 1	400 mg/l
Component 2	600 mg/l
Component 3	800 mg/l
Component 4 (inert carrier)	200 mg/l

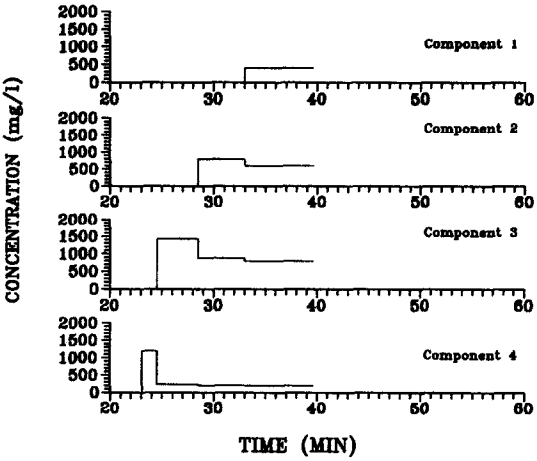

Fig. 3. Frontal chromatogram of four-component mixture with diverging isotherms.

data[12]. Secondly, the values of the constants selected give divergent isotherms. However, HRM is not restricted to divergent isotherms. Shown in Fig. 4 is the frontal chromatogram predicted with the coherence theory for the equilibrium conditions in Table VIII and the operating conditions in Table V; the parameters of Table VIII allow for crossing of the isotherms of components 2 and 3. Using the retention times and plateau compositions of this chromatogram with the procedure described earlier, the *b* parameters in Table IX were obtained. Once again, the calculated values coincide with the values used in the simulation.

TABLE VI
DATA FROM FRONTAL CHROMATOGRAM

Wave No.	*Retention time (min)*	*Component*	*Concentration (mg/l)*	
			Downstream	*Upstream*
4	23.1	1	0.0	0.0
		2	0.0	0.0
		3	0.0	0.0
		4	0.0	1190
3	24.5	1	0.0	0.0
		2	0.0	0.0
		3	0.0	1429
		4	1190	239
2	28.5	1	0.0	0.0
		2	0.0	794
		3	1429	880
		4	239	208
1	33.0	1	0.0	400
		2	794	600
		3	880	800
		4	208	200

TABLE VII
COMPETITIVE BINDING PARAMETERS FROM FRONTAL DATA
$h'_4 = 747.126$.

Component No.	*Calculated h_i (l/mg)*
2	0.25
3	0.25
4	0.25

It can be seen that HRM provides an explicit method for characterizing competitive binding coefficients in systems obeying the Langmuir isotherm. Regardless of the number of components present in the process solution, only one complete frontal chromatogram is necessary for the computation. Also, the injected sample is obtained directly from the process solution.

Dilute solution behavior of displacer

HRM, as described, is dependent on a knowledge of the dilute solution parameter, a_1, for the displacer. When a_1 is not known, it can be obtained with the existing method of single component frontal analysis (FA)[11], applied to the displacer in the dilute solution region; the dilute solution region can be established with elution experiments of the type described earlier. FA is appropriate because the displacer will in general be available as a pure component, separate from the components in the process solution. Furthermore, only a_1 is being determined with the single-component experiments, while competitive behavior is characterized with high concentration, multicomponent experiments. In principle, the retention time of the single, sharp concentration front obtained from a single FA experiment in the dilute solution region will give the value of a_1.

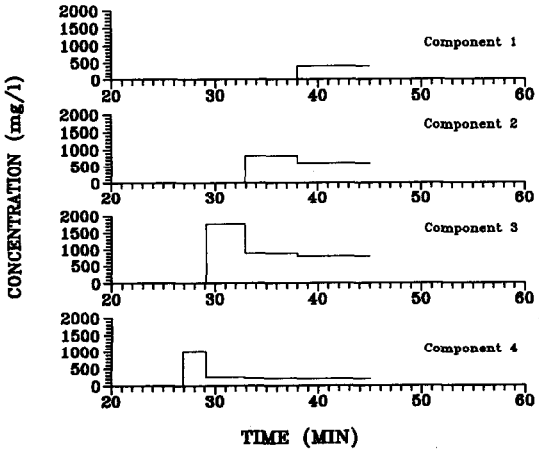

Fig. 4. Frontal chromatogram of four-component mixture with crossing isotherms.

TABLE VIII
LANGMUIR CONSTANTS FOR SYSTEM WITH CROSSING ISOTHERMS

Component No.	*a (l/g)*	*b (l/mg)*
1	5	0.25
2	4	0.25
3	3	0.16
4	2	0.25

TABLE IX
COMPETITIVE BINDING PARAMETERS FROM FRONTAL CHROMATOGRAM FOR CROSSING ISOTHERMS CASE
$h_4' = 624.297$.

Component No.	*Calculated b_i (l/mg)*
2	0.25
3	0.16
4	0.25

Trace components

In some applications of displacement chromatography, the concentrations of some components in the process solution may be at trace levels. In such cases, it may be difficult to establish the effluent concentration history of the more dilute components during frontal chromatography. For example, for the operating conditions of Table V, if the concentration of component 3 is dropped from 800 to 20 mg/l, the coherence

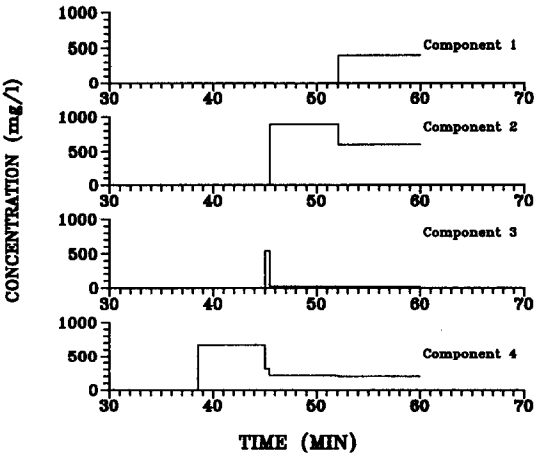

Fig. 5. Frontal chromatogram of four-component system with one trace component.

TABLE X

OPERATING CONDITIONS FOR DISPLACEMENT CHROMATOGRAPHY

Column length, 122 cm; packing density, 400 g/l of column; column porosity, 0.4; interstitial fluid velocity, 10 cm/min.

	Time (min)	*Component No.*	*Concentration (mg/l)*
Presaturant	–	1	0.0
		2	0.0
		3	0.0
		4	0.0
Sample	0.0	1	0.0
		2	600
		3	20
		4	200
Displacer	2.0	1	2000
		2	0.0
		3	0.0
		4	0.0

theory predicts the frontal chromatogram shown in Fig. 5. Depending on the sensitivity of the detection technique, the very short plateau region corresponding to the first appearance of component 3 may not be detected at all. Thus, it may not be possible to determine the coefficients b_i for trace components.

Fortunately, the determination of b values of trace components is not essential for simulation major features of the displacement chromatogram. As an example, consider the displacement experiment described in Table X. In this case, component 3 is the trace component. For the equilibrium constants of Table I, the coherence theory predicts the displacement chromatogram shown in Fig. 6. Repeating the

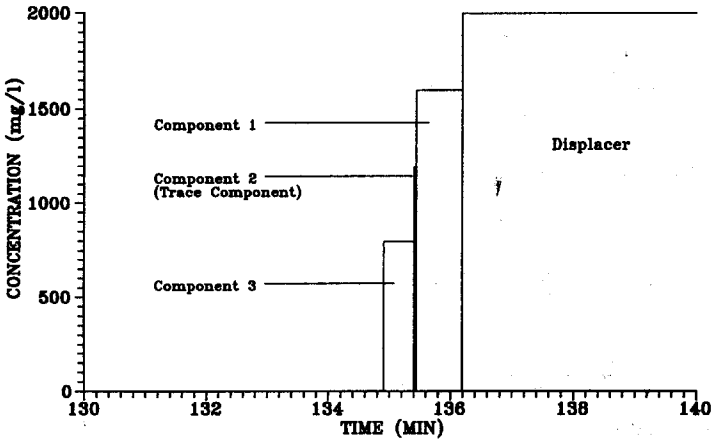

Fig. 6. Displacement chromatogram of three-component system with one trace component.

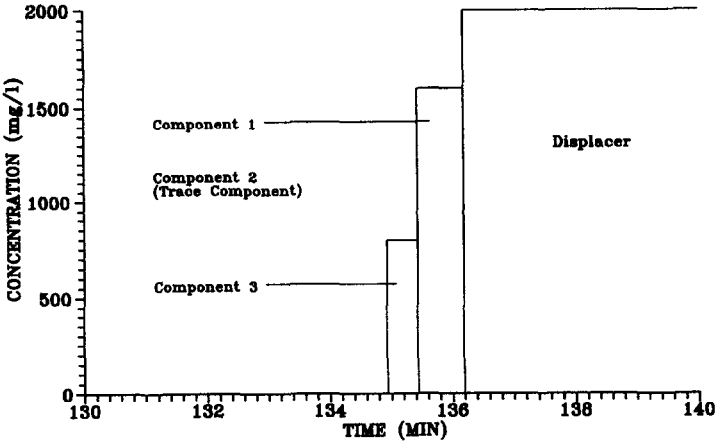

Fig. 7. Displacement chromatogram of three-component system neglecting trace component.

simulation with the same equilibrium and operating conditions, but assuming the absence of component 3, the chromatogram in Fig. 7 is obtained. Comparing Fig. 6 and 7 it is clear that the trace component has essentially no effect on the major features of the effluent composition history. If the location of the trace component zones in the chromatogram is desired, it is simply necessary to simulate the system with $b_i c_i \cong 0$, where i represents all trace components in the system; the values of a_i for the trace components will be available, since these can be determined from elution experiments using appropriate degrees of dilution.

CONCLUSION

In this paper, only theoretical aspects of HRM have been addressed. However, it must be noted that, in the practical application of this method, some difficulties may be encountered in obtaining the required experimental data. For the elution experiments, the theory has been presented for the isocratic case. The experimental difficulty with isocratic elution is that suitable eluents may not always be available to ensure efficient chromatographic development. Though the method can be extended to gradient elution, the computations are considerably more involved. For the frontal chromatography experiments, the determination of the concentrations of the fronts may require tedious analyses. Automated chromatographic analysis is likely to be useful in this case. These and other experimental aspects of HRM are currently being investigated in our laboratory.

A limitation of the coherence theory is that it is an equilibrium theory. In practice, secondary effects such as axial dispersion, mass transfer, and mixing will result in some degree of band spreading. This will affect the determination of the retention times of the concentration waves in the frontal chromatogram. Thus, care must be taken in establishing operating conditions, such as column packing, flow distribution, and support size, that minimize secondary effects during the frontal experiments. Under any circumstances some degree of spreading of the sharp concentration fronts will occur. In this case, the inflection points on the fronts can be used to approximate the retention times[12].

The coherence theory provides a potent framework for the rapid determination of equilibrium adsorption data. With a minimal number of experiments, the equilibrium behavior of multicomponent Langmuirian systems can be established. The theory gives a direct relationship between retention times and compositions and the coefficients of the multicomponent isotherm. Thus, the accuracy with which the equilibrium behavior can be characterized is dependent only on the accuracy of the experimental data. This is in contrast to other approaches, where parameter estimation techniques form an integral part of the method[10,12]. Another advantage of HRM relates to the determination of equilibrium characteristics of high-value products. Tracer elution experiments required by the method inherently use small quantities of solute, while frontal chromatograms can potentially be obtained by using automated, miniaturized chromatographic systems, similar to the one developed by Jacobson *et al.*[11]. Furthermore, pure samples of the solutes are not required, and equilibrium data are obtained from a minimal number of chromatographic experiments.

SYMBOLS

a_i Langmuir coefficient of species i (l/g)
b_i Langmuir coefficient of species i (l/mg)
c_i concentration of species i in external fluid (mg/l)
h_i the ith h-root
q_i concentration of species i in adsorbent (mg/g)
R conversion parameter (l/g)
u_i adjusted wave velocity of ith wave
v_{ci} concentration velocity (cm/min)
v_i real velocity of ith wave (cm/min)
v_0 interstitial fluid velocity (cm/min)
z distance coordinate (cm)

Greek symbols
α_{ij} separation factor
ε column porosity
ρ packing density (g/l of column)

Superscripts
$'$ upstream
$''$ downstream

Subscripts
i species i
n species n or number of component
p dummy spcies

ACKNOWLEDGEMENTS

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