

New approach for calculating ideal chromatograms from arbitrary composite distribution isotherms

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ABSTRACT

A new method for the calculation of ideal chromatograms is presented. It is based on the solution of the eigenvector problem as occurs in the consideration of system peaks. As the resulting eigenvectors are tangential to the paths governing the shape of ideal chromatograms, these paths can be found by following the direction of the eigenvectors in composition space, this process being equivalent to the numerical integration of simultaneous differential equations, with the eigenvectors as the derivatives. The method has the advantage that new shapes of composite isotherms do not require more mathematical effort than inserting the corresponding expressions in the program source. So far the method has been developed for describing the phenomena at the front and the rear of a rectangular band that still has a region where the injected concentration is preserved. However, the application to fully deformed bands peaks and to systems with more than two components seems entirely feasible.

INTRODUCTION

As argued by Guiochon and Katti [1], the prediction of overloaded chromatograms can be approached from two extremes: on the one hand one can start from the solution of the chromatographic transport equations for the infinite dilution, linear situation, and treat the non-linearity as a perturbation to that solution. The treatment by Haarhof and van der Linde [2] has been shown to be extremely useful in that respect [1,3–5]. On the other hand, one can start with the solution for dispersionless or ideal chromatography. Often, *i.e.*, in heavily overloaded situations, this gives already [1,6,7] a fairly accurate impression of the chromatogram that is obtained when dispersion is also active both in experiment and in simulations of the process. A next step could be to try to correct these ideal chromatograms for dispersion, without resorting actually to carrying out experiments or simulations, which are both time consuming and expensive.

As the first approach is limited to relatively small overload (the perturbation should be small), the second approach is probably of great future importance for the development of preparative liquid chromatography (LC). It is therefore very unfortunate that ideal solutions in themselves can be calculated only for a few specific cases.

The best known solution of the ideal chromatography problem is probably that given decades ago by Helfferich and Klein in their classic book [8] on multi-component chromatography. However, their solution with the h -transform applies only to the case of so-called stoichiometric exchange, with constant selectivity coefficients. This is an appropriate model for ion exchange, but a great variety of phase systems in use in high-performance liquid chromatography (HPLC) cannot be forced into this model.

Recently, Golshan-Shirazi and Guiochon [6,7,9] performed the tremendous task of solving the ideal chromatography problem for a two-component competitive Langmuir equilibrium. First [6], they derived the solution in a new way, solving the equation for the "paths" (see Theory section) with the Clairaut and Offord equations, and then derived the complete elution pattern for the two components, for different degrees of separation. Second, they compared these results with an adapted version of the h -transform (already indicated as being useful by Helfferich and Klein [8]) and showed mathematical equivalence [9].

As indicated by them, the prospects for using this analytical approach for more complicated cases, *e.g.*, for more complicated isotherm expressions and for three- or more-component cases, look poor. The analytical equations become very complicated, and it is probably too much to expect that the path analysis can be performed in such cases.

The approach taken during this work was to use a numerical version of the path analysis.

THEORY

Paths and hodogram

As explained at length in Helfferich and Klein's book [8], the concept of coherence is central to the understanding of ideal multi-component chromatography with interference. Briefly, it appears that coherence is the ultimate situation towards which these systems tend to develop. Coherence means that a given concentration of a component is accompanied by the same set of concentrations of the $n-1$ other components, although the time and position of the observation point may vary. A propagation velocity is associated with each of such sets of concentrations.

These coherent changes in concentrations may occur in two versions: those with finite slope of concentration against time (or position) curves, *i.e.*, continuous changes, and abrupt, *i.e.*, discontinuous changes. Which one occurs depends on the mathematical properties of the system, which are complicated and abstract to formulate, but can be derived easily from physical principles, as will be discussed below. However, the continuous changes, indicated by Helfferich and Klein [8] as diffuse boundaries, will be discussed first.

When a given concentration of one component is associated with a given set of $n-1$ other concentrations, this represents a point in an n -dimensional space, the composition space. A two-dimensional example is shown in Fig. 1. A diffuse boundary is represented in this composition space by a line, each point of which connects a concentration with $n-1$ others. A collection of such lines may be called a hodogram. Each point on such a line, called a path (or Γ [10]), is associated with a retention parameter such as the equivalent of the capacity factor k' or of the R_F value. This

retention parameter tells how fast the particular point will move through the column in relation to the mobile phase velocity. When the coherent boundary is present immediately after the injection (this often occurs at the rear of the peak), the position in the column after a given time, or the retention time, *i.e.*, the time of occurrence of that concentration at the column exit, can be predicted by familiar equations such as

$$z(c_1, c_2, c_3 \dots c_n) = vtR_F = vt \cdot \frac{1}{(1 \pm k')} \quad (1)$$

$$t(c_1, c_2, c_3 \dots c_n) = (L/v) (1 + k') = (L/v) \cdot \frac{1 - R_F}{R_F} \quad (2)$$

where

$(c_1, c_2, c_3 \dots c_n)$	represents the particular combination of concentrations;
v	is the mobile phase velocity;
t	is time, from injection to the moment that the combination $(c_1, c_2, c_3 \dots c_n)$ elutes;
L	is the column length
z	is the position in the column of the combination $(c_1, c_2, c_3 \dots c_n)$
k'	is the "capacity factor"; and
R_F	is the retardation factor.

It is important to distinguish the "capacity factor" k' as used here from the meaning usually associated with it, namely the ratio of amounts of a solute in the stationary and mobile phases. Here the value of k' just describes the migration velocity of the particular point in concentration space.

Consider a simple case of a transition from one composition, A, to another, B, *i.e.*, when both points A and B are on the same path, and B is the injected solution (with a long injection block and chosen carefully to be on the path of A) and A is the composition of the mobile phase. The retention along the path will vary (see the Langmuir hodogram in Fig. 1). Assume that it continuously decreases (it does for the Langmuir case when both concentrations in B are larger) when moving from A to B. Drawing the rear of such a peak presents no problems; the concentrations close to B have moved fast, those close to A have moved less and a "reasonable", *i.e.*, physically acceptable shape is obtained. However, at the front the procedure would yield double-valued concentrations, a curve that retreats in space or time, which is physically unacceptable.

The mathematics of such phenomena is that of shock waves, as discussed by Golshan-Shirazi and Guiochon [6]. It is abstract and difficult. In this paper the mathematical approach to deal with this will not be taken, rather physical arguments will be used to handle situations such as these. However, it should be recognized that eventually, if the approach given here is to be of much use, formal rules for substituting the physical reasoning often applied here have to be found in the literature or be derived.

Anyway, rather than an impossible retreating diffuse boundary, a steep concentration change, discontinuity, from B to A, occurs at the front of the band. The analysis of it is easiest when B represents the composition of the injected solution, and

is not yet deformed after or before the shock. Its velocity can then be derived from consideration of mass preservation. This is most easily done when graphs (such as used here) plot total concentration against position in column, or when elution functions of mobile phase concentrations against time are used. In both instances the position of the shock can be found as the mean value of the found positions or times, respectively (retreating), as this is the position of the shock that gives the proper amount of material. "Mean value" is to be understood here as the integral of position integrated with respect to concentration, divided by concentration difference. That this gives a mass-preserving solution can be derived as follows.

The retreating solution of the differential equation is one that "conserves mass"; the total amount present does not change with time. This amount equals the integral with respect to position of the total concentration, or of the mobile phase concentration with respect to time. Taking the average position or time in both graphs therefore does give the proper location of the shock.

However, this reasoning can be applied only in this simple form when the two extreme composition points of the shock remain the same during column transport; if there is no flat profile on both sides, the intensity of the shock is changing all the time and a more intricate form of the mass balance has to be applied.

The Followpath procedure

In a previous paper [11] and a paper by Golshan-Shirazi and Guiochon [12] it was discussed how the eigenvectors and eigenvalues describe the properties of system peaks and the possibilities for indirect detection, in both chromatography and electrophoresis. In the following we shall limit the discussion to chromatography. Briefly, it was shown [11,12] that, for small deviations from the mobile phase composition, the distribution equilibrium in general can be described by a matrix equation, given the vector, c_s , consisting of the changes in each of the n stationary phase concentrations $c_{s,j}$, as a function of the vector c_m of changes in the mobile phase concentrations, $c_{m,j}$:

$$c_s = S_from_M \cdot c_m \quad (3)$$

The matrix S_from_M usually has n eigenvalues, λ_0 through λ_{n-1} with associated eigenvectors e_0 through e_{n-1} . The n values of λ represent capacity factors, k' , at which the particular coherent disturbances are eluted. The set of n resulting eigenvectors describe the proportions in which the n constituents vary in concentration in each of the n disturbances. That is, if one injected a composition that differs from the mobile phase by exactly the $e_{j,i}$ values multiplied by a small number (j giving the number of the eigenvalue, i giving the number of the component to which the component of eigenvector e_j applies), it is transported as one peak with capacity factor λ_j . Injected compositions that cannot be described as one eigenvector will be split up, in general into n peaks of which the capacity factors are the λ 's.

This approach has been shown [12-15] to give an adequate description of system peaks and indirect detection phenomena, which had previously puzzled many workers. However, it was also noted in the earlier paper [11] that the eigenvectors thus obtained are the tangents to the paths in the n -dimensional composition space and that they describe the coherent boundaries that would develop in ideal chromatography.

It follows that one can move approximately from one point on a path to another in its vicinity, after the eigenvector has been calculated. Thus there is a way, at least an approximate one, to find a full path starting from a given point in composition space. It consists of repeatedly computing the eigenvector and moving to a new point on the path. By starting at several points one can derive the picture of the hodogram with any degree of detail.

The program that forms the basis of this report relies on a procedure called "Followpath", taking a starting solution, "sol", as the argument. Sol is a vector of n numbers (2 in the implementations described in this paper), giving the concentrations in the mobile phase. With any given expression for the distribution of the n components to the stationary phase (e.g., Langmuir, ion-pair distribution equations) the concentrations of the stationary phase can be calculated. (A short comment on the forms used, especially the omission of certain factors such as the phase ratio and the surface necessities for a composite Langmuir adsorption is to be found at the end of this section.)

As the eigenvector treatment works with the changes in the concentrations, the derivatives of these expressions are needed. These have been obtained during this work by numerical differentiation: the concentrations of compounds $j = 0$ to $n-1$, $c_{m,j}$, are changed by a small amount, "eps", successively and the resulting changes in the stationary phase concentrations $c_{s,i}$ are noted. Divided by eps these form the elements $[i,j]$ of the matrix that is needed. This matrix was above indicated by "S from M".

Numerical differentiation has the important advantage that the study of a new type of distribution behaviour merely involves introducing other distribution equations in integral form; the often painstaking analytical differentiation to obtain all the matrix elements is not needed. The full procedure could be carried out by just using S from M with, as indicated, eigenvalues corresponding to capacity factors, k' . However, it is useful to consider also other matrices carrying the same information; these are as follows:

(i) M from S, calculation of mobile phase concentration changes from stationary phase concentration changes. This is unusual; however, at least one [16] model exists where explicit expressions are obtainable only for this case. M from S is the inverse of S from M, and numerical values were obtained by the Gauss-Jordan algorithm. Its eigenvalues correspond to $1/k'$.

(ii) T from M, calculation of the total concentration changes (see the remark at the end of the section on expressions and units) from the mobile phase concentration changes. It is obtained by adding 1 to the diagonal elements of S from M. The eigenvalues equal $k' + 1$.

(iii) M from T, calculation of the mobile phase concentration changes from the changes in the total concentrations. This matrix is obtained by inversion of T from M. Its eigenvalues are the R_F values of the corresponding disturbances. The use of this form might be useful in cases where mass preservation is to be considered in studies involving spatial distribution, rather than elution function (see below).

It should be noted that when finding eigenvalues and eigenvectors for all these four matrices one obtains different eigenvalues [although the one set can be easily found from the other, e.g., by $R_F = 1/(1+k')$], but the same eigenvectors. This is easily seen when one considers that for an eigenvector e_j with eigenvalue λ_j it holds that

$$\underline{S}_{\text{from } M} \cdot \mathbf{e}_j = \lambda_j \cdot \mathbf{e}_j \quad (4)$$

Stationary phase and mobile phase changes are in the same proportion λ_j for all components. Thus the changes of, e.g., the sum of both concentrations are also in proportion.

After the n eigenvectors have been found for the first time it is to be decided which one of these gives the direction to be followed (e.g., one can choose the one with the largest capacity factor). Denoting this one by $j = f$ (f for "follow this one"), a next point on the path is found by adding the components of the vector \mathbf{e}_f to the components of "sol". The size of the step is controlled by a parameter β , by which the eigenvector components are multiplied before carrying out the addition. Thus, for the two-component system considered in this paper:

$$\begin{aligned} \text{sol}_0 &= \text{sol}_0 + \beta \cdot \mathbf{e}_{f,0} \\ \text{sol}_1 &= \text{sol}_1 + \beta \cdot \mathbf{e}_{f,1} \end{aligned} \quad (5)$$

In fact, as the \mathbf{e}_j emerge normalized from the eigenvector procedure (i.e., the sum of the squares of the components is 1, the euclidian length is 1), the value of β is the distance travelled in composition space during such a step.

For the new point described by the new value of "sol", the eigenvector is again calculated, and a new step is taken in the new direction. It might occur during the Followpath procedure that the step size, β , is too large: following the tangent rather than the path curve itself is only sufficiently accurate if either the curvature is small or the step size is small. Therefore, after each tentative step it is checked if the direction indeed has changed only insignificantly.

The change in direction is measured by the correlation coefficient, r , sum of the cross-products of the elements of previous and newly considered vector (division by the square root of the euclidian lengths of both is not needed as both are 1). A value $r = 1$ corresponds to exactly the same direction. In that case the path is linear in composition space, a situation occurring with competitive Langmuir adsorption, as discussed at length by Guiochon and co-workers.

Values of r larger than 0.9999 were treated as acceptable. When smaller values occurred, the value of β was decreased repeatedly by a factor of two until a sufficiently large value of r was obtained. When r exceeded 0.99999, the step size β was doubled, in order to speed up calculations.

A rough guess of the errors made this way can be made as follows. A correlation coefficient of 0.9999 means that the angle between the vectors equals $\sqrt{(1-r)} = 0.01$ rad. Thus on each step of size β one deviates 0.01β from the correct path. Suppose a path is a full circle (an extreme case; for useful phase systems curvature in general will not be very strong) with radius 1. One return to the point of origin there would be a deviation of 0.0628. Thus the procedure is probably accurate to better than a few percent in composition space.

The calculation of r was needed for another reason: as indicated, from each point in composition space n paths emerge (2 in this work). The eigenvalue-eigenvector procedure gives the n results in an unpredictable order, and precautions have to be taken to avoid hopping from one direction to another that is more or less orthogonal

to it. Thus, each time the relevant eigenvalue λ_f and corresponding vector e_f were identified as the one having the highest correlation, r , with the previous vector.

As indicated, the eigenvalues obtained during the iteration, either in terms of k' (when **S from M** is used) or in terms of R_F (when **M from T** is used) contain essential information; they can be used to predict either the retention time or the spatial position in the column of the specific composition point. Thus, the full information on the behaviour of the components in the phase system used is contained in an $(n+1)$ -dimensional plot, composition space with an additional dimension in which the λ (k' or R_F) value is plotted. In Figs. 1, 3 and 5 this is approached by inserting the numbers for the k' values on the path lines.

The program needs additional tricks for the following reasons:

(1) To make sure that a path is followed in both directions. Thus, after a path is followed until the edge of considered composition space is reached, one has to return to the original composition and "go the other way".

(2) To make sure that the n (2 here) paths emerging from one point are plotted. Thus, e.g., first the higher capacity factor (at the point of origin) is handled, and next the smaller capacity factor. Altogether, $2n$ (here 4) "rays" emanate from a point.

(3) To obtain a reasonable distribution of plotted paths over the composition space considered to be of interest. This was done here by choosing a rather arbitrary starting composition. In each of the resulting four main "rays", a stop was made when a given distance had been travelled. From there the other path was followed leading to two new rays. In this way usually a reasonably filled but not overcrowded hodogram was obtained.

Description of the distribution equilibrium

In the following the two-component composite Langmuir isotherm will be used to demonstrate the principles used here.

The concentration in the stationary phase, either per unit of surface area or per gram of adsorbent, is generally modelled as

$$c_{s,j} = \frac{K_i c_{m,j}}{1 + K_1 c_{m,1} b_1 + K_2 c_{m,2} b_2} \quad (6)$$

where the b s represent the areas covered by a mole of material. They have been the subject of interesting discussions [17], when it was noted that widely different b 's for the two components can lead to intersecting isotherms, i.e., at low concentration the one component is better adsorbed, whereas at higher concentrations the reverse case occurs.

In order to correlate the k' values in the column with eqn. 4, one needs in addition the phase ratio, q , e.g., in square metres per millilitre of mobile phase. Altogether, one ends up with unwieldy expressions that are especially impractical in general considerations, because of the lengthy equations, and in simulations, because of increased program run times. It is our opinion that in such general discussions, as well as in simulations, it is very profitable to "normalize out" the b 's in addition to q . This can be done as follows.

In the first place the concentrations in the stationary phase are defined as the

amount adsorbed in a given infinitesimal part of the column, divided by the volume of mobile phase in that part. As there is a constant ratio between square metres and the mobile phase volume, there is no loss of generality when doing this. The result is that k' and the distribution constant K are the same. The sum of c_m and c_s is now equal to the "total concentration" used above, c_t , total amount in an infinitesimal section of the column over the associated volume of mobile phase.

In the second place, it can be noted that the way amounts and concentrations are expressed is arbitrary. Also, different units can be used for different components. It lies at hand to multiply the concentration $c_{m,j}$ by b_j to form normalized concentrations (in both phases). Again, there is no loss in generality, and all situations can still be expressed. The Langmuir expression can then be written as

$$c_{s,j} = \frac{K_j c_{m,j}}{1 + K_1 c_{m,1} + K_2 c_{m,2}} \quad (7)$$

the K 's being the same as those in eqn. 6. From this approach, which is used throughout this work, it follows, *e.g.*, that special phenomena brought about by strongly differing b values can be studied (simulation, analytical) by means of the regular model given in eqn. 7, by simply increasing the amount injected of compounds having a large b .

The advantage of this is that the great multitude of different cases met with in discussions or preparative chromatography are at least partly reduced. All situations that can be modelled, *e.g.*, by the simple composite Langmuir expressions can be represented by choosing proper values for K 's and the injected concentrations.

EXPERIMENTAL

All programs were written in Turbo Pascal (Borland International, Scotts Valley, CA, USA) version 4.0. For the present two-component case the eigenvector problem was solved by solving the quadratic equation, with the procedure as described in ref. 18. For three and higher component systems the procedures ELMHES, HQR and SVDCMP from the same source were applied. A custom-written package for translating graphic calls in Turbo 4.0 into graphics commands for a laser printer was used to obtain the figures shown.

Column transport simulations were implemented according to the approach described by Golshan-Shirazi and Guiochon [19]. However, the code as described by them was first translated into Pascal, and next modified to allow the presentation of spatial distributions in the column rather than elution functions. Also, in many cases another choice of the time and position increments, Δt and Δz , was made. In those cases the numerical dispersion was made practically zero (at least for the most retained disturbance), rather than equal to a predetermined amount of dispersion, as the purpose here was to compare results from two approaches for ideal chromatography. The simulation program was thoroughly checked for conceptual or programming errors by running experiments with predictable results, such as those with only one component, or with minor disturbance injections leading to "system peaks" and indirect detection phenomena. Retentions and peak intensities as well as mass conservation agreed entirely satisfactorily (*i.e.*, deviations could be explained as the result of numerical truncations).

RESULTS AND DISCUSSION

Langmuir case

Fig. 1 gives the paths as calculated for a two-component Langmuir isotherm, according to eqn. 5, with $K_0 = 2$ and $K_1 = 3$. This result is trivial, in the sense that the lines can be much more easily calculated according to the procedure given by Golshan-Shirazi and Guiochon [6] using the Offord and Clairaut equations. Indeed, doing this produces (not shown) an identical figure.

In Fig. 1 the numbers written along the lines represent the capacity factor, k' , corresponding to the retention of the path at that position. Thus, if the path exists from the very start of the elution, the position of the composition point in the chromatogram, or in the column at a given time, can be predicted. This concept, in combination with the general method for finding the paths, would allow the prediction of the column history for any kind of composite distribution isotherm.

The implementation of this concept is, however, not without difficulties, and at present requires the application of intuitive notions or physical insight. This will be illustrated while discussing the results obtained with this form of isotherm, although in themselves these results are no more than a partial reproduction of the results of Golshan-Shirazi and Guiochon [6] who derived the complete set of expressions for the elution curves of a still partially mixed band.

In Fig. 1 point I represents a hypothetical composition of an injected plug. This

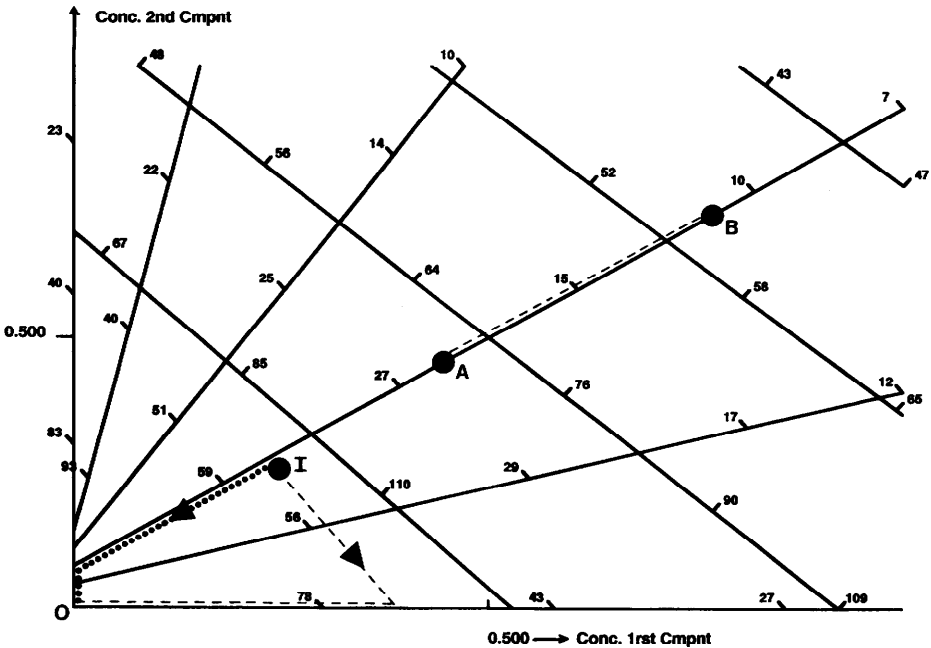


Fig. 1. Hodogram for Langmuir isotherm, according to eqn. 7, with $K_0 = 2$, $K_1 = 3$. Numbers on the path lines are capacity factors, multiplied by 100. Concentrations on axes are mobile phase concentrations. Cmpnt = Component.

is supposed to be already in equilibrium with the stationary phase, so that in fact much more is injected. (This rather artificial modelling of injection is chosen in these first exercises just to facilitate insight; in later, more practical, applications one should of course consider the influx of a solution into an empty column.)

The rear of this plug represents a transition in the composition space from the origin, O, the empty solvent, to I; at the front the opposite transition occurs. For such transitions, following the paths in the hodogram, there are in general two routes (in fact, the Langmuir case gives three routes, as can be seen, but one is ruled out for physical reasons). Which way is taken depends on whether the front or the rear of the peak is considered. At the very rear of the band, still close to the origin, one should find a path with the highest capacity factor. That is the path coinciding with the vertical axis ($c_{m,0} = 0$), corresponding to pure component 1 (the most retained one). This path is followed until arrival on the intersection with the path through I. Next this mixed band path is followed; see the dotted lines in Fig. 1 starting at point I.

Note that on both paths the capacity factor decreases, and position increases, while following the path, and thus approaching the original injected concentration at the (still) flat top of the band. This indicates that no physical impossibilities are implied by this solution and indeed a diffuse boundary is described.

As noted by Golshan-Shirazi and Guiochon [9], the difference in k' value for the two paths at the same composition (the intersection point) explains the occurrence of a plateau of constant concentration of component 1, where it seems that this component leaks out of the mixed band.

It should be noted that in the algorithm (Followpath) that produced the circles in, e.g., Fig. 2, the opposite route was followed, starting from the injected concentrations. For the description of the rear of the band the path with the smallest capacity factor was first followed, making sure that both concentrations decreased. When the concentration of the least retained component was found to be zero (the procedure was targeted to reach that point), the procedure switched to the alternative path, that following the vertical axis in Fig. 1, leading to a classical one-component Langmuir boundary.

In the algorithm for the calculation of the front of the band the path with the highest capacity factor was first followed, making sure that the concentration of component 1 decreased, that of 0 increased, because (one of the physical reasonings resorted in this work to make the system work) it is known that by displacement a concentration effect on the less retained component occurs. When the concentration of the most retained component was found to be zero, the procedure switched to the alternative path, that again giving a classical one-component Langmuir boundary, albeit retreating. This route corresponds to that indicated by the dashed lines starting at point I in Fig. 1.

All R_F values found were multiplied with the time (velocity assumed to be 1), added to the starting position of the rear or front, respectively, and plotted in Fig. 2 as circles. Fig. 2 shows the graphical implementation in terms of column "maps" for the two components. The full line gives the results of a simulation with this distribution equilibrium. Best efforts were made to make dispersion as small as possible in this simulation experiment; for one thing it takes several hours to reach this point of $t = 4000$. Superimposed on this are circles that were calculated from the Followpath approach. As the starting point the injection was taken.

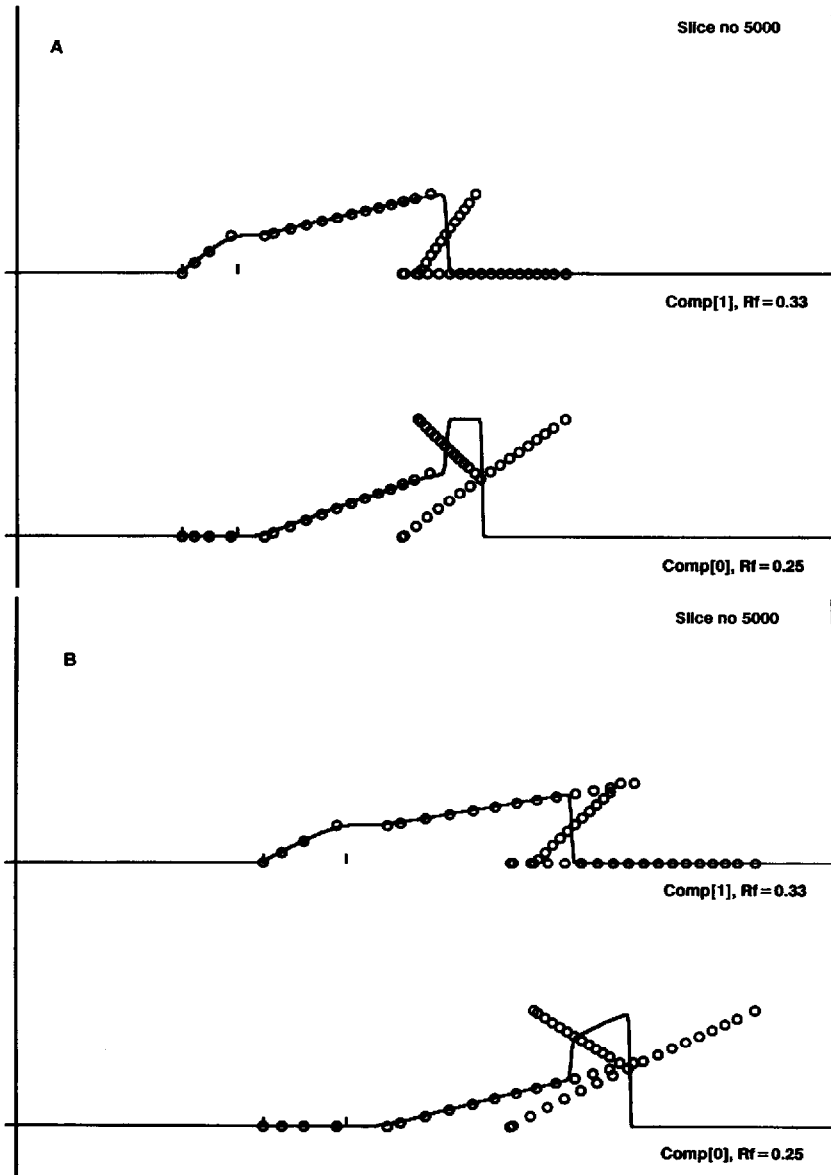


Fig. 2. Distribution of the two components along the length of the column after a time lapse of (A) 4010 units or (B) 6007 units, for Langmuir isotherm as in Fig. 1. Injection was done by saturating slice No. 50 (vertical line at left) to 1050 with a mobile phase with $c_0 = 0.2$ and $c_1 = 0.2$, and forcing the stationary phase concentration to be in equilibrium with that mobile phase. Mobile phase velocity assumed to be 1 slice per time unit. Component concentrations plotted are total concentrations. $c_1 = c_s + c_m$. Full line, results of Guiochon-type simulation; circles, results from path calculation.

As can be seen in Fig. 2, the Followpath approach yields a fairly accurate estimate of the distribution functions for the components. Where diffuse boundaries occur, the (full) lines obtained by simulation are a very good match with the circles

obtained with the Followpath procedure. At the front of the peak the two lines formed by the circles represent physically impossible retreating lines. However, the shocks given by the numerical simulation are indeed at the average position of the circles. Note that two paths follow the axis of component 0 or component 1 in the hodogram, *i.e.*, the circles in the column map in Fig. 2 are on the axis for one of the components.

However, as soon as the flat top of the band at the injected concentration is "eroded away" [9], the applied procedure fails (Fig. 2B). As indicated above, the shocks then no longer have a constant intensity, and their positions have to be calculated with a more complicated mass balance consideration. Also, another diffuse boundary develops. The latter can be handled in the indicated way, with the exception that its time and place of birth differ from the injection time and either front or rear of the injection plug. Rather the place and time of birth should be calculated separately.

Such problems cannot be handled yet, although we have confidence that they can be solved and that the solutions can be put into fairly general code. However, at this stage meaningful results can only be obtained for situations where the injected concentrations are still present in the band.

Quadratic Langmuir-type equilibrium expression

Guiochon's group [20] have argued that the composite Langmuir expression can be generalized by substituting polynomes in the various mobile phase concentrations for the expressions $K_i c_i$. In order to demonstrate the flexibility of our approach, we carried out calculations with such an isotherm. Its exact shape was as follows:

$$c_{s,0} = \frac{K_{00}c_{m,0} + Q_{00}c_{m,0}^2 + Q_{01}c_{m,0}c_{m,1}}{1 + K_{00}c_{m,0} + K_{11}c_{m,1} + Q_{00}c_{m,0}^2 + Q_{11}c_{m,1}^2 + Q_{01}c_{m,0}c_{m,1}}$$

$$c_{s,1} = \frac{K_{11}c_{m,1} + Q_{11}c_{m,1}^2 + Q_{01}c_{m,0}c_{m,1}}{1 + K_{00}c_{m,0} + K_{11}c_{m,1} + Q_{00}c_{m,0}^2 + Q_{11}c_{m,1}^2 + Q_{01}c_{m,0}c_{m,1}} \quad (8)$$

Followpath calculations were carried out and compared with transport simulations for such an isotherm with $K_{00} = 1$, $K_{11} = 1.5$, $Q_{00} = 2$, $Q_{11} = 3$, $Q_{01} = 1$. The results are shown in Fig. 3 as a hodogram and in Fig. 4 as a prediction of column maps (circles), together with the result of the numerical simulation (full lines).

Inspection of the hodogram shows that the paths are curves, as is to be expected. Still, the structure of the Langmuir hodogram can be distinguished. More important, on a number of paths (those with a negative slope) the retention does not change monotonously, but first goes up and then goes down. This means that, no matter if one considers the front or the rear of the band, a transition is possible consisting partly of a shock and partly of a diffuse boundary. This is similar to what occurs in the one-component case when the isotherm has a sigmoid shape, *i.e.*, the second derivative changes sign over the range of interest.

Fig. 4, given the results of the Followpath procedure in comparison with those of the simulation, clearly shows this behaviour. Considering first the rear part of the curves, coming down from the injected concentration one first has a "normal" boundary, and in this part the agreement with the simulation is very good. However,

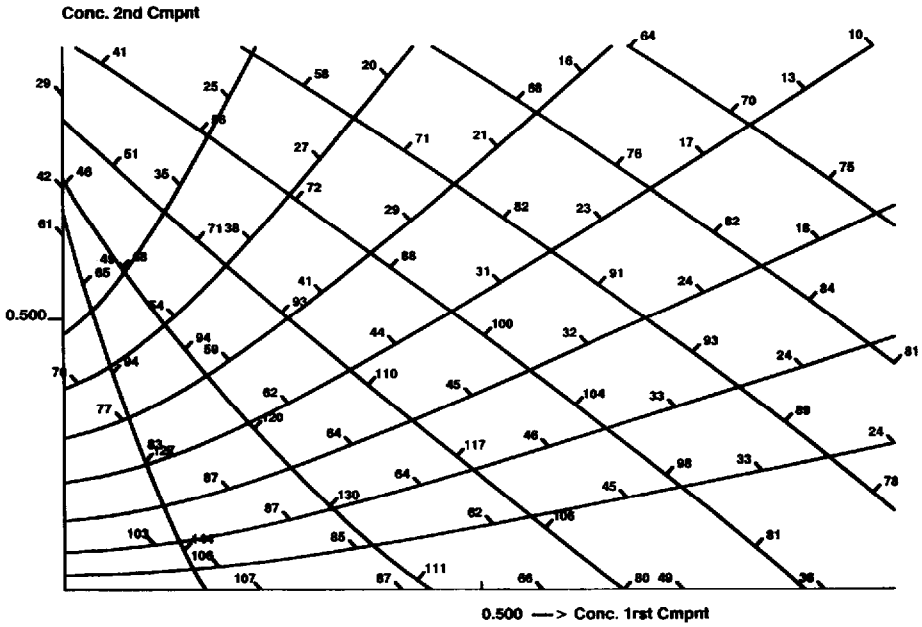


Fig. 3. Hodogram for quadratic Langmuir isotherm, according to eqn. 8, with $K_{00} = 1$, $K_{11} = 1.5$, $Q_{00} = 2$, $Q_{11} = 3$, $Q_{01} = 1$. Numbers on the path lines are capacity factors, multiplied by 100. Concentrations on axes are mobile phase concentrations.

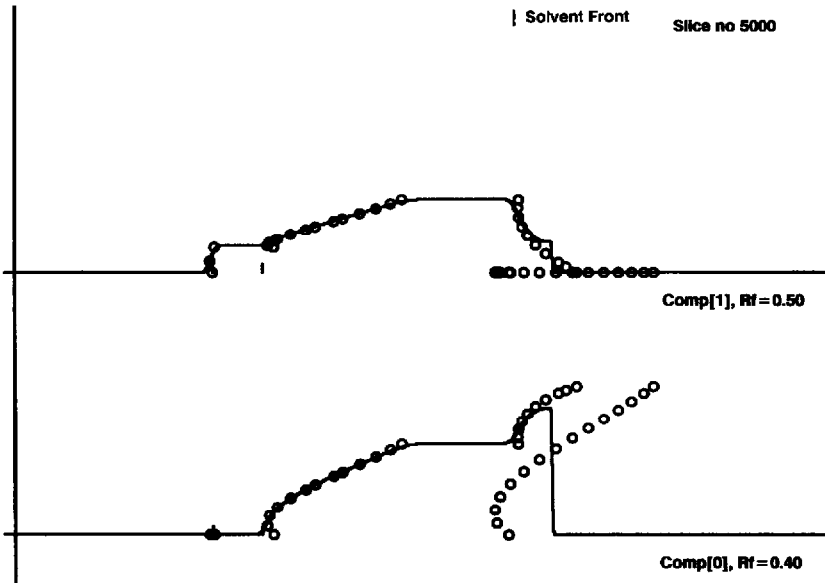


Fig. 4. Distribution of the two components along the length of the column after a time lapse of 3005 units, for quadratic Langmuir isotherm as in Fig. 3. Injection was done by saturating slice No. 50 (vertical line at left) to 1550 with a mobile phase with $c_0 = 0.7$ and $c_1 = 0.5$, and forcing the stationary phase concentration to be in equilibrium with that mobile phase. Mobile phase velocity assumed to be 1 slice per time unit. Component concentrations plotted are total concentrations, $c_s + c_m$. Full line, results of Guiochon-type simulation; circles, results from path calculation.

when the concentration of component 1 approaches zero, the curve formed by the circles changes to a retreating line, predicting a shock. This is not apparent from the simulation (full line); this is probably due to the influence of (numerical) dispersion. The line describing the transition to where both concentrations are zero (far left side of the band in Fig. 4) shows a similar behaviour. Also here the shock nature is not visible in the simulation.

The front part of the band in Fig. 4 shows reasonable agreement for the onset of the concentrated band of component 0, pushed forward by the other component. However, it can be seen that the Followpath procedure does predict a much higher concentration for component 0 than is actually observed. This can be explained as follows. The program as it moves along the path until the concentration of component 1 is zero. However, at that point its velocity is higher than that of the shock described by the alternative path starting from the point of injection composition; the upper part of the diffuse boundary moves faster than that shock. Thus the path should have been followed up to a point P where its velocity equals that of the shock connected with the transition from P to zero.

Synergistic sorption

Another example considered is that of synergistic sorption, an adequate model, *e.g.*, for ion-pair chromatography. Here the isotherm is

$$\begin{aligned}c_0 &= K_{00}c_0 + Q_{01}c_0c_1 \\c_1 &= K_{11}c_1 + Q_{01}c_0c_1\end{aligned}\tag{9}$$

where the term with Q_{01} stands for, *e.g.*, ion-pair formation and the K 's for simple sorption of the constituent ions. The hodogram obtained with $K_{00} = 2$, $K_{11} = 3$ and $Q_{01} = 2$ is shown in Fig. 5.

Note that the capacity factors along the axis are constant, 2 and 3, respectively, for the two components, in agreement with the fact that when the other component is absent eqn. 9 gives simple linear partition. The curvature of the paths is striking, as is the fact that above a given concentration of 1 there appear to be no intersections with the corresponding axis.

The prediction of column maps is given in Fig. 6, again compared with the simulation experiment. As can be seen, the concentration of component 1 at the end of the band is predicted, with good quantitative agreement. Note that all paths are "natural"; there are no shocks. The paths with one component (far left and far right of the band) are vertical in the column map, as there is a constant capacity factor.

CONCLUSIONS

It has been shown that numerical procedures can be applied to derive the shape of paths in composition space, together with the corresponding retention data. The prediction of elution functions and column maps for ideal chromatography seems to be possible with this approach. The main drawback of the present implementation of the idea is that physical, more or less intuitive, arguments have to be used to decide

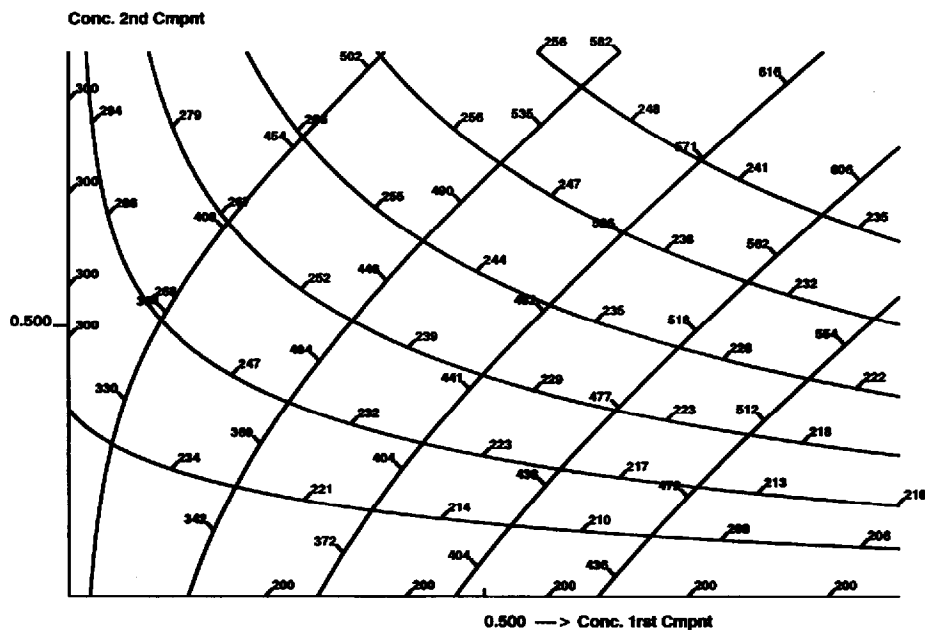


Fig. 5. Hodogram for synergistic isotherm, according to eqn. 9, with $K_{00} = 2$, $K_{11} = 3$, $Q_{01} = 2$. Numbers on the path lines are capacity factors, multiplied by 100. Concentrations on axes are mobile phase concentrations.

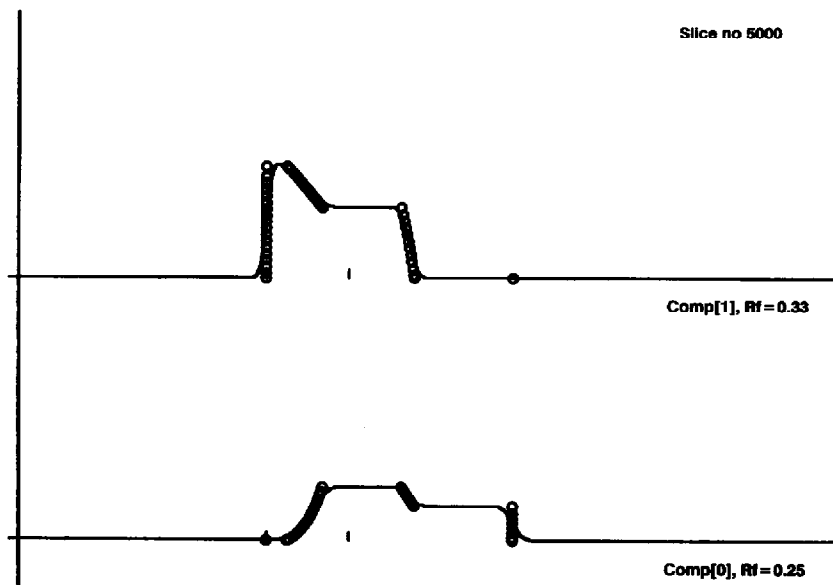


Fig. 6. Distribution of the two components along the length of the column after a time lapse of 6111 units, for synergistic isotherm as in Fig. 5. Injection was done by saturating slice No. 50 (vertical line at left) to 1050 with a mobile phase with $c_0 = 0.2$ and $c_1 = 0.2$, and forcing the stationary phase concentration to be in equilibrium with that mobile phase. Mobile phase velocity assumed to be 1 slice per time unit. Component concentrations plotted are total concentrations, $c_s + c_m$. Full line, results of Guiochon-type simulation; circles, results from path calculation.

which path is to be followed, and to what limit, and when to change path. Also, only a simple situation, just a broad band that broadens on one side and leading to displacement on the other, can be properly handled at this stage. However, it is believed that the rules for choosing paths can be formalized and put into automatic code. In addition, it is believed that the application of the calculation scheme can be extended, by proper calculation and decision schemes, to cases where, e.g., a diffuse band or shock originates during the chromatographic transport.

The potential advances that could be obtained when these aims can be reached are significant. It would be possible to predict ideal chromatograms in an easy manner, by just inserting the code for the distribution equilibrium into the program, for arbitrary isotherm shapes. There also appear to be no unsurmountable problems in applying this approach to systems with more than two components.

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