

CHROM. 21 519

INFLUENCE OF CALCULATION ERRORS IN THE NUMERICAL SIMULATION OF CHROMATOGRAPHIC ELUTION BAND PROFILES USING AN IDEAL OR SEMI-IDEAL MODEL

BINGCHANG LIN, ZIDU MA and GEORGES GUIOCHON*

**Department of Chemistry, University of Tennessee, Knoxville, TN 37996-1600, and Division of Analytical Chemistry, Oak Ridge National Laboratory, Oak Ridge, TN 37831-6120 (U.S.A.)*

SUMMARY

The theoretical models of chromatography, whether they assume or not quasi-equilibrium between the phases of the chromatographic system, lead to a set of partial differential equations that cannot be integrated but must be solved by numerical calculations. This procedure leads to computational errors. An analysis of the origin and importance of these errors is presented. A comparison is made between the errors introduced by different calculation procedures (mainly the characteristic and the Lax–Wendroff methods). The concentration dependence of the artificial diffusion introduced by the characteristic algorithm is discussed.

INTRODUCTION

Much attention has been given recently to the numerical solution of the set of mass balance equations of chromatography. Preparative chromatography has become a separation and purification method of considerable importance in the pharmaceutical industries. The operation of preparative chromatographs must be carried out at high feed concentrations in order to achieve economical production. The prediction of the column performance and the optimization of the experimental conditions require a knowledge of the breakthrough curves for different injection conditions, corresponding to elution, frontal analysis or displacement, for samples of various composition.

The only possibility for calculating these band profiles is by solving one of the relevant models of chromatography. The main feature of these models is the set of mass balance equations for the various compounds involved in the problem, the components of either the feed or the mobile phase. We can eliminate only the weakest solvent mass balance, by assuming that this solvent does not interact with the stationary phase, which sets a reference convention. The set of these mass balance equations must be completed by equations relating the concentrations of each component in the two phases of the chromatographic system at each time.

In most instances, we can assume that we are near equilibrium, *i.e.*, that the column efficiency is high, and we can replace the diffusive term of the mass balance

equations by a term that accounts for the rapid kinetics of radial mass transfer in modern columns¹⁻³. In some rare instances, kinetic equations must be used⁴⁻⁶. These equations relate the time differential of the concentration of each compound involved in the stationary phase to the concentration of this component in the stationary phase and to the concentrations of all the compounds involved in the mobile phase, in a given slice of column. The former models are called equilibrium or ideal models (if the column efficiency is infinite and equilibrium between both phases of the chromatographic system always takes place) or semi-ideal models (if equilibrium is not achieved but the deviation from equilibrium remains small, *e.g.*, the column efficiency exceeds a few hundred theoretical plates). The latter models are called kinetic models. This paper is mainly concerned with semi-ideal models.

The mass balance equation obtained for a pure compound is a partial differential equation that cannot be solved analytically and for which numerical solutions must be calculated. The numerical integration of a partial differential equation always introduces truncation errors because finite increments of the variable must be considered. As a huge number of loops must be circled during the integration, the errors made during the numerical calculation propagate and accumulate from one stage to the next. In some instances these errors have most undesirable consequences, as they lead to numerical instability of the solution, and must be avoided. In other instances they may be used to advantage. In this paper, we present an analysis of the nature and extent of these errors, with emphasis on those resulting from the characteristic and the Lax-Wendroff algorithms.

In a previous paper⁷ we showed that, for a linear equilibrium isotherm between the two phases of a chromatographic system, the truncation error introduced by using the first-order characteristic type calculation scheme for the numerical integration of the partial differential equation has the same effect as a dispersion term on the band profile. If proper values are chosen for the space and time increments, this artificial dispersion term permits a successful account of the effect on the band profile of a finite column efficiency. With a non-linear isotherm, however, the artificial dispersion effect is different from that with a linear isotherm and the consequences are analyzed below.

The investigation of the elution band profile of a pure compound is interesting as a necessary step in the study of the chromatographic separation of complex mixtures. In itself, however, it does not provide much useful information. As chromatography is a separation method, the elution of a binary mixture should be investigated. For the more practical and relevant discussion of the calculation of elution profiles of multicomponent samples, the use of the artificial dispersion introduced by the finite difference method and the characteristic algorithm is not suitable, in principle. In practice, it is acceptable only when the relative retention of the compounds considered is close to unity. The basic reason for the method being unsuitable is that the artificial dispersion it introduces depends on the slope of the isotherm. The simulation of the elution profiles of different compounds for which the column has the same efficiency requires different values of the space and time increments for the different compounds, a procedure which is at best complicated and impractical.

For this reason, considerable difficulties are encountered when trying to extend our previous results to the simulation of non-linear chromatography in the gradient elution mode. In this particular case, a numerical procedure that is easy to implement and is accurate would be very attractive for simulating the separation of multi-

component systems. A satisfactory approach is in the use of a higher order method, *i.e.*, a method with which the truncation errors introduced by replacing the exact partial differential equation by an approximate difference algebraic equation are of second order with respect to the time and length increments.

ERROR ANALYSIS IN THE CASE OF THE CHARACTERISTIC TYPE DIFFERENCE METHOD

The ideal model of chromatography assumes constant equilibrium between the two phases and a column of infinite efficiency. Hence the diffusion term of the mass balance equation written for a pure compound in a slice of column is zero and the concentration in the stationary phase (C_s) which appears in this mass balance is replaced by the value given by the equilibrium isotherm. The mathematical model of ideal chromatography for a pure compound is

$$\left(1 + F \cdot \frac{\partial q}{\partial C}\right) \frac{\partial C}{\partial t} + u \cdot \frac{\partial C}{\partial z} = 0 \quad (1)$$

The isotherm is an equation [$C_s = q = f(C_m)$] which relates the concentrations at equilibrium in the mobile (C_m) and the stationary phases. In eqn. 1, F is the phase ratio of the chromatographic column, u the cross-section average velocity of the mobile phase, t the time and z the abscissa along the column.

The boundary and initial conditions for the integration in the case of a rectangular pulse injection, with a concentration C_0 and a time τ , are

$$C(z = 0, t) = C_0, \quad 0 \leq t \leq \tau \quad (2)$$

and

$$C(z = 0, t) = 0, \quad t > \tau$$

with

$$C(z, t = 0) = 0 \quad (3)$$

Eqn. 1 is not the canonical form of this type of partial differential eqn. 2 (ref. 8). It is frequently encountered in aerodynamics and hydraulics, where it is discussed by mechanical engineers in the form

$$\frac{\partial C}{\partial z} + B \cdot \frac{\partial H}{\partial t} = 0 \quad (4)$$

where

$$B = \frac{1}{u} \quad (5)$$

and

$$H = C + Fq \quad (6)$$

In the general case, there is no analytical solution known for eqn. 1. When solutions are needed, they must be calculated.

The principle of the calculation of numerical solutions of eqn. 1 is to replace the continuous (z, t) plane by a grid and to calculate the numerical values of the concentration C of the compound studied in the mobile phase at each point (n, j) of this grid. The space and time increments of the grid are h and τ , respectively. The injection profile is discretized. Then, for each time $t = j\tau$, the concentration at each point in the column, $z = nh$, $0 < n < L/h$, is calculated from the similar profile, $C(n, j)$, obtained at the previous instant, $t = (j - 1)\tau$ and from the initial and boundary conditions. The set of values of the concentration for $z = L$ ($L =$ length of the column) for each time frame constitutes the elution chromatogram. In this paper, we discuss two numerical schemes for the numerical calculation of profiles which are solutions of eqn. 1. The first type has been used for writing the computer program we have developed and used for the calculation of the elution band profiles of pure compounds^{3,7,8}, binary mixtures⁹ or system peaks¹⁰ and of the profiles of displacement bands¹¹.

First difference type

In the calculation procedure described above, eqn. 1 is replaced by the following algebraic equation, which is its finite difference equivalent:

$$\frac{C_j^{n+1} - C_j^n}{h} + \frac{1}{u} \cdot \frac{C_j^n - C_{j-1}^n}{\tau} + \frac{F}{u} \cdot \frac{q_j^n - q_{j-1}^n}{\tau} = 0 \quad (7)$$

Eqns. 1 and 7 would be entirely equivalent only if the increments, h and τ , could be made zero, which, in turn, would require an infinite computation time, not a realistic proposition. As the increments must be finite, a numerical error results from the replacement of eqn. 1 by eqn. 7. During the calculation process, these errors propagate and build up. If the values of the space and time increments are not properly chosen, divergence and oscillations may occur and the numerical solution does not bear any resemblance to the exact solution of the partial differential equation studied. The stability condition for this method, in the ideal approximation, is

$$\frac{h}{u_z \tau} < 1 \quad (8)$$

where u_z is given by eqn. 16b (see below)^{2,7}. This condition is called the Courant condition of the problem and $u_z \tau / h$ is its Courant number. It has been demonstrated that, when h and τ satisfy it, the numerical solution obtained converges towards the exact solution of the partial differential equation with decreasing increment values².

In order to calculate the error made by replacing eqn. 1 by eqn. 7 in the calculation of the elution band profile, we may replace the different concentration terms by their three-term expansion:

$$C_j^{n+1} = C_j^n + h \left(\frac{\partial C}{\partial z} \right)_j^n + \frac{h^2}{2} \left(\frac{\partial^2 C}{\partial z^2} \right)_j^n \quad (9)$$

and

$$C_{j-1}^n = C_j^n - \tau \left(\frac{\partial C}{\partial t} \right)_j^n + \frac{\tau^2}{2} \left(\frac{\partial^2 C}{\partial t^2} \right)_j^n \quad (10)$$

We shall assume here that the equilibrium isotherm is given by the classical Langmuir equation, although most of the conclusions are valid with other equilibrium equations. With a Langmuir isotherm we have

$$q_j^n = f(C_j^n) = \frac{GC_j^n}{1 + bC_j^n} \quad (11)$$

where G and b are constants. Therefore,

$$q_{j-1}^n = \frac{GC_{j-1}^n}{1 + bC_{j-1}^n} \quad (12)$$

The three difference terms in eqn. 7 become

$$\frac{C_j^{n+1} - C_j^n}{h} = \left(\frac{\partial C}{\partial z} \right)_j^n + \frac{h}{2} \left(\frac{\partial^2 C}{\partial z^2} \right)_j^n \quad (13)$$

$$\frac{C_j^n - C_{j-1}^n}{\tau} = \left(\frac{\partial C}{\partial t} \right)_j^n - \frac{\tau}{2} \left(\frac{\partial^2 C}{\partial t^2} \right)_j^n \quad (14)$$

and

$$F \cdot \frac{q_j^n - q_{j-1}^n}{\tau} = \frac{FG(C_j^n - C_{j-1}^n)}{(1 + bC_{j-1}^n)(1 + bC_j^n)\tau} \quad (15a)$$

which is equivalent to

$$F \cdot \frac{q_j^n - q_{j-1}^n}{\tau} \approx \frac{FG(C_j^n - C_{j-1}^n)}{(1 + bC_j^n)^2\tau} = F \left(\frac{\partial f}{\partial C} \right)_j^n \left[\left(\frac{\partial C}{\partial t} \right)_j^n - \frac{\tau}{2} \left(\frac{\partial^2 C}{\partial t^2} \right)_j^n \right] \quad (15b)$$

Combining eqn. 7 with eqns. 9–15 gives

$$\left(1 + F \cdot \frac{\partial f}{\partial C} \right) \frac{\partial C}{\partial t} + u \cdot \frac{\partial C}{\partial z} = \frac{\tau}{2} \left(1 + F \cdot \frac{\partial f}{\partial C} \right) \frac{\partial^2 C}{\partial t^2} - \frac{hu}{2} \left(\frac{\partial^2 C}{\partial z^2} \right) \quad (16)$$

From eqn. 1 we can derive a relationship giving the velocity, u_z , associated with a concentration⁸:

$$\frac{\partial C}{\partial t} = -u_z \cdot \frac{\partial C}{\partial z} \quad (17a)$$

with

$$u_z = \frac{u}{1 + F \cdot \frac{\partial f}{\partial C}} \quad (17b)$$

From eqns. 17a and 17b we obtain

$$\frac{\partial^2 C}{\partial t^2} = \frac{\partial}{\partial t} \left(-u_z \frac{\partial C}{\partial z} \right) = -\frac{Fu_z^2}{1 + F \cdot \frac{\partial f}{\partial C}} \cdot \frac{\partial^2 f}{\partial C^2} \left(\frac{\partial C}{\partial z} \right)^2 + u_z^2 \cdot \frac{\partial^2 C}{\partial z^2} \quad (18)$$

Substituting eqn. 18 into eqn. 16 permits the determination of the error made in the calculation of the profile when using eqn. 7. We have

$$\left(1 + F \cdot \frac{\partial f}{\partial C} \right) \frac{\partial C}{\partial t} + u \cdot \frac{\partial C}{\partial z} = \frac{hu}{2} (a - 1) \frac{\partial^2 C}{\partial z^2} - \frac{\tau}{2} \cdot u^2 F \cdot \frac{\partial^2 f}{\partial C^2} \left(\frac{\partial C}{\partial z} \right)^2 \left/ \left(1 + F \cdot \frac{\partial f}{\partial C} \right)^2 \right. \quad (19)$$

where a is the Courant number [$u_z \tau / h = u \tau / (1 + k'_0) h$], which we have taken as equal to 2, by selecting properly the time increment, τ , as a function of the space increment^{3,7,9}. The choice of a Courant number of 2 ensures numerical stability of the calculated solution (eqn. 16), *i.e.*, avoids widely oscillating profiles with negative values of the concentration, results which have no physical sense.

The right-hand side of eqn. 19 represents the error made. This error is of first order with respect to h and τ [*i.e.*, $O(h + \tau)$]. It is the sum of two terms, the first being a dispersion term, proportional to the space increment, h , and the second, proportional to the time increment, τ , being non-linear. It vanishes when $\tau \rightarrow 0$ or when $\partial^2 f / \partial C^2 \rightarrow 0$. In the case of a Langmuir isotherm, $\partial^2 f / \partial C^2 = -2Gb / (1 + bC)^3$, and is never zero. $\partial^2 f / \partial C^2$ can be zero only for a linear isotherm. The sign of this second term is determined by the curvature of the isotherm.

In the case of a Langmuir isotherm, or of an isotherm convex towards the axis of stationary phase concentrations, the profile predicted by the ideal model exhibits a front shock^{2,3,8}. The second differential of the isotherm is negative and the two terms add to each other. The effect of the error is in the appearance of a dispersion term, the replacement of the concentration discontinuity by a shock layer, with a finite thickness and a decrease in the shock amplitude. If the isotherm is concave, in contrast, the shock appears on the rear of the profile, but the qualitative influence of the numerical errors remains the same.

Second difference type

An alternative form of the general equation of the ideal (equilibrium) model of chromatography, equivalent to eqn. 1, is the following:

$$\frac{\partial C}{\partial t} + F \cdot \frac{\partial q}{\partial t} + u \cdot \frac{\partial C}{\partial z} = 0 \quad (20)$$

In this case, the equivalent finite difference equation is written as

$$\frac{C_j^{n+1} - C_j^n}{\tau} + F \cdot \frac{q_j^{n+1} - q_j^n}{\tau} + u \cdot \frac{C_j^{n+1} - C_{j-1}^{n+1}}{h} = 0 \quad (21)$$

In eqn. 20, n is the time index and j is the space index. For this type of finite difference equation, the Courant condition (see above), in the ideal approximation, is $u_z \tau / h > 0$. It is, of course, always satisfied. Expansion of the different terms gives

$$C_j^{n+1} = C_j^n + \tau \left(\frac{\partial C}{\partial t} \right)_j^n + \frac{\tau^2}{2} \left(\frac{\partial^2 C}{\partial t^2} \right)_j^n \quad (22)$$

and

$$C_{j-1}^{n+1} = C_j^n + \tau \left(\frac{\partial C}{\partial t} \right)_j^n - h \left(\frac{\partial C}{\partial z} \right)_j^n + \frac{\tau^2}{2} \left(\frac{\partial^2 C}{\partial t^2} \right)_j^n + \frac{h^2}{2} \left(\frac{\partial^2 C}{\partial z^2} \right)_j^n - \tau h \left(\frac{\partial^2 C}{\partial z \partial t} \right)_j^n \quad (23)$$

The equilibrium isotherm is again given by eqn. 12 (Langmuir isotherm). In a practical calculation, we could use the following approximation:

$$q_j^{n+1} \approx \frac{GC_j^{n+1}}{1 + bC_j^n} \quad (24)$$

Combining eqns. 22-24 gives the second term of eqn. 21:

$$\begin{aligned} \frac{q_j^{n+1} - q_j^n}{\tau} &= \frac{1}{\tau} \cdot \frac{G(C_j^{n+1} - C_j^n)}{1 + bC_j^n} = \frac{1}{\tau} \cdot \frac{G(C_j^{n+1} - C_j^n)}{(1 + bC_j^n)^2} (1 + bC_j^n) \\ &= \left[\left(\frac{\partial f}{\partial C} \right) \left(\frac{\partial C}{\partial t} + \frac{\tau}{2} \cdot \frac{\partial^2 C}{\partial t^2} \right) (1 + bC) \right]_j^n \end{aligned} \quad (25)$$

By combining eqns. 21 with eqns. 22-25, we obtain

$$\begin{aligned} \left(1 + F \cdot \frac{\partial f}{\partial C} \right) \frac{\partial C}{\partial t} + u \cdot \frac{\partial C}{\partial z} = \\ -\frac{\tau}{2} \left(1 + F \cdot \frac{\partial f}{\partial C} \right) \frac{\partial^2 C}{\partial t^2} + \frac{hu}{2} \cdot \frac{\partial^2 C}{\partial z^2} - \tau u \cdot \frac{\partial^2 C}{\partial z \partial t} - FbC \cdot \frac{\partial f}{\partial C} \left(\frac{\partial C}{\partial t} + \frac{\tau}{2} \cdot \frac{\partial^2 C}{\partial t^2} \right) \end{aligned} \quad (26)$$

From eqn. 17, we can derive that

$$\frac{\partial^2 C}{\partial z \partial t} = \frac{u_z}{1 + F \cdot \frac{\partial f}{\partial C}} \cdot F \cdot \frac{\partial^2 f}{\partial C^2} \left(\frac{\partial C}{\partial z} \right)^2 - u_z \cdot \frac{\partial^2 C}{\partial z^2} \quad (27)$$

Combination of eqns. 18, 26 and 27 gives

$$\left(1 + F \cdot \frac{\partial f}{\partial C}\right) \frac{\partial C}{\partial t} + u \cdot \frac{\partial C}{\partial z} = -FbC \cdot \frac{\partial f}{\partial C} \cdot \frac{\partial C}{\partial t} + \frac{hu}{2}(a+1) \frac{\partial^2 C}{\partial z^2} - \tau \left\{ Fu_z^2 \cdot \frac{\partial^2 f}{\partial C^2} \left(\frac{\partial C}{\partial z}\right)^2 - FbC \cdot \frac{\partial f}{\partial C} \left[u_z \cdot \frac{\partial^2 C}{\partial z^2} - \frac{Fu_z^2}{1 + F \cdot \frac{\partial f}{\partial C}} \left(\frac{\partial^2 f}{\partial C^2}\right) \left(\frac{\partial C}{\partial z}\right)^2 \right] \right\} \quad (28)$$

The essential difference between the equation derived in the case of a linear isotherm and eqn. 28 is in the first term of the right-hand side, equal to $-FbC \partial f / \partial C \cdot \partial C / \partial t$, i.e., to $k'bC \partial C / \partial t$. This term is independent of the value of the integration increments. The error cannot be made infinitely small by increasing the computer time: the solution converges towards a solution of the top part of eqn. 28, i.e., without the lower term, proportional to τ , which is not eqn. 20. Actually, the term which contains FbC comes from the approximation made above (see eqn. 24). The error is complex and the numerical solution obtained by this method cannot be trusted entirely. Of course, in the linear case the coefficient b is zero.

If an approximation other than eqn. 24 is taken for q_j^{i+1} , e.g., $q_j^{i+1} \approx GC_j^{i+1} / (1 + bC_j^{i+1})$, the term which contains FbC can also be eliminated, and the results may be better.

This analysis illustrates the difficulties and pitfalls which may be encountered in non-linear chromatography when a numerical algorithm is not very carefully studied before it is implemented.

Comparison between the two difference types

If the non-linear contribution can be ignored (small deviation from the linear isotherm), the apparent dispersion coefficient in the case of the first difference type studied becomes

$$D_a = \frac{hu}{2} \left[\frac{\tau u}{(1+k')h} + 1 \right] \quad (29)$$

and in the case of the second difference type

$$D_a = \frac{hu}{2} \left[\frac{\tau u}{(1+k')h} - 1 \right] \quad (30)$$

In practice, we want to use the apparent diffusion coefficient, D_a , to account for the diffusion term, D , which we neglected when we replaced the exact mass balance equation by the equation of the ideal model (eqns. 1 and 20). In fact, D_a could be used to simulate the finite column efficiency. Then it is necessary to keep the apparent dispersion coefficient constant during the entire calculation. The Courant number will be kept constant, hence we must have

$$\frac{\tau u}{\left(1 + F \cdot \frac{\partial f}{\partial C}\right) h} = \text{constant} \quad (31)$$

If one takes, for the sake of simplicity and clarity, the space increment to be equal to the column height equivalent to a theoretical plate ($h = H$), the time increment is given by

$$\tau = \text{constant} \cdot (1 + k') \frac{H}{u} \quad (32)$$

In all our calculations^{3,7-10}, we have taken the Courant number as equal to 2, hence

$$\tau = \frac{2 \left(1 + F \cdot \frac{\partial f}{\partial C} \right) H}{u} \quad (33)$$

Our first requirement is the numerical stability of the solution. This does not require that we keep the Courant number constant, but merely that we make sure that it exceeds unity⁷. One simple way to satisfy this condition, in the case of a Langmuir-type isotherm, would be to take τ equal to $2(1 + k'_0)h/u$, where k'_0 is the limit value of $\partial f/\partial C$ for an infinitely small sample. However, then the apparent diffusion coefficient increases during the elution of the band (see eqn. 29). If we adopt a variable time increment, $\tau = \tau(C)$, the error term introduced will have certain effects on the results of the simulation of the migration of the chromatographic band. Comparison between the exact analytical solution of eqn. 1 in the case of a Langmuir isotherm and the numerical solution obtained with the first difference type shows, however, that the difference between the two profiles, *i.e.*, the error introduced by the numerical calculation and accounted for by eqn. 19, is small and cannot be very different from that predicted by eqn. 29 with a constant value of the Courant number¹².

In the case of the first difference type, the error contains two terms (eqn. 19). The first one is the artificial dispersion term just discussed. The second one is smaller but, in the case of a Langmuir type isotherm, it tends to enhance the self-sharpening effect of the band due to the non-linear behavior of the equilibrium isotherm and to the strong concentration dependence of the velocity associated with a concentration u_z .

The second difference method should be avoided because of the presence of a constant term in its error function, a term which is independent of the integration increments.

ERROR ANALYSIS IN THE CASE OF THE LAX-WENDROFF TYPE DIFFERENCE METHOD

The kinetic model for non-linear chromatography is more general than either the ideal or the semi-ideal models, which postulate near equilibrium between the two phases at any time and any location in the column. The only assumption made in this model is in the choice of the kinetic equation which relates the rate of change of the concentration in the stationary phase to the concentrations of the compound under study in both phases. In one of its simplest forms, the kinetic model can be written as

$$\frac{\partial C}{\partial t} + F \cdot \frac{\partial q}{\partial t} + u \cdot \frac{\partial C}{\partial z} = D \cdot \frac{\partial^2 C}{\partial z^2} \quad (34)$$

$$\frac{\partial q}{\partial t} = K[f(C) - q] \quad (35)$$

Eqn. 34 is the general mass balance of chromatography. Eqn. 35 is the kinetic model. In this equation, K is the rate constant or mass transfer coefficient and q is the concentration of the compound of interest in the stationary phase. First-order kinetics have been selected here. The classical initial and boundary conditions are written as

$$\begin{aligned} C(z = 0, t) &= C_0, & 0 \leq t \leq \tau \\ C(z = 0, t) &= 0, & t > \tau \\ C(z, t = 0) &= 0 & q(z, t = 0) = 0 \end{aligned} \quad (36)$$

There is no analytical solution for this system of equations, although Goldstein¹³ and Wade *et al.*¹⁴ derived an analytical solution in the closely related case when the kinetic equation is that of the classical Langmuir adsorption-desorption kinetics. Numerical solutions must be calculated, and the best approach seems to be the Lax-Wendroff method^{15,16}. Two cases can be distinguished, depending whether the problem discussed involves a near-equilibrium model (*i.e.*, fast kinetics of mass transfer between phases, so the number of transfer stages in the column is large⁶) or a true kinetic problem, in which case the mass transfers between phases are slow.

NEAR EQUILIBRIUM PROBLEM

Under the equilibrium approximation, the system of eqns. 33 and 34 can be replaced by a single partial differential equation¹⁷, which is written as

$$\frac{\partial C}{\partial t} + u_z \cdot \frac{\partial C}{\partial z} = D_z \cdot \frac{\partial^2 C}{\partial x^2} \quad (37)$$

where D_z stands for $D/(1 + F \cdot \partial f/\partial C)$. The corresponding finite difference equation is

$$\frac{C_j^{n+1} - C_j^n}{\tau} + u_z \cdot \frac{C_{j+1}^n - C_{j-1}^n}{2h} - \left(\frac{u_z^2 \tau}{2h^2} + \frac{D_z}{h^2} \right) (C_{j+1}^n - 2C_j^n + C_{j-1}^n) = 0 \quad (38)$$

where n is the time index and j the space index. For this method, the stability condition is $(u_z \tau/h)^2 + 2D_z \tau/h^2 < 1$ (ref. 16).

In order to calculate the truncation error introduced by the Lax-Wendroff procedure in the near equilibrium case, we write as follows the four-term expansion of the higher order terms in eqns. 34 and 35, at the index values n and j :

$$C_j^{n+1} = C_j^n + \tau \left(\frac{\partial C}{\partial t} \right)_j^n + \frac{\tau^2}{2} \left(\frac{\partial^2 C}{\partial t^2} \right)_j^n + \frac{\tau^3}{6} \left(\frac{\partial^3 C}{\partial t^3} \right)_j^n \quad (39)$$

$$C_{j+1}^n = C_j^n + h \left(\frac{\partial C}{\partial z} \right)_j^n + \frac{h^2}{2} \left(\frac{\partial^2 C}{\partial z^2} \right)_j^n + \frac{h^3}{6} \left(\frac{\partial^3 C}{\partial z^3} \right)_j^n \quad (40)$$

and

$$C_{j-1}^n = C_j^n - h \left(\frac{\partial C}{\partial z} \right)_j^n + \frac{h^2}{2} \left(\frac{\partial^2 C}{\partial z^2} \right)_j^n - \frac{h^3}{6} \left(\frac{\partial^3 C}{\partial z^3} \right)_j^n \quad (41)$$

In the ideal approximation, we have (see above)

$$\frac{\partial}{\partial t} = -u_z \cdot \frac{\partial}{\partial z} \quad (42)$$

and

$$\frac{\partial^2}{\partial t^2} = u_z^2 \cdot \frac{\partial^2}{\partial z^2} \quad (43)$$

Combining eqns. 38–43 gives

$$\left(\frac{\partial C}{\partial t} \right)_j^n + u_z \left(\frac{\partial C}{\partial z} \right)_j^n - D \left(\frac{\partial^2 C}{\partial z^2} \right)_j^n = \frac{u_z}{6} \left[(u_z \tau)^2 - h^2 \right] \left(\frac{\partial^3 C}{\partial z^3} \right)_j^n \quad (44)$$

an equation which is equivalent to

$$\left(1 + F \cdot \frac{\partial f}{\partial C} \right) \left(\frac{\partial C}{\partial t} \right)_j^n + u \left(\frac{\partial C}{\partial z} \right)_j^n - D \left(\frac{\partial^2 C}{\partial z^2} \right)_j^n = \frac{u}{6} \left[(u_z \tau)^2 - h^2 \right] \left(\frac{\partial^3 C}{\partial z^3} \right)_j^n \quad (44a)$$

This relationship shows that the truncation error caused by the use of the Lax–Wendroff calculation procedure under equilibrium conditions, in the linear approximation, and by the replacement of eqn. 34 by eqn. 36 for the numerical calculation is equal to

$$\frac{u}{6} \left[(u_z \tau)^2 - h^2 \right] \frac{\partial^3 C}{\partial z^3} \quad (45)$$

The truncation error introduced by the Lax–Wendroff method is of second order, *i.e.*, $O(h^2 + \tau^2)$. Furthermore, no artificial dispersion term is introduced in the calculation.

If we assume the elution band to be a near Gaussian profile, we can fit the upper part of the peak (most of the portion above the inflection points) on a polynomial, *i.e.*, $C(z, t) = \sum_i a_i C^i$. If the profile is Gaussian, a parabola would suffice¹⁸ and the term in eqn. 44 is zero. If the profile is unsymmetrical, a third-degree polynomial, or a polynomial with a very small fourth-degree term, gives satisfactory results, hence, $\partial^3 C / \partial z^3 \approx a_3 + a_4 z \approx a_3$. The last term in eqn. 44 contains a constant, whose effect is to change the position of the solution, that is, to change the solution from $C(z, t)$ to $C(z, z - \alpha t)$, where α is the product of the coefficient of eqn. 44 and a_3 .

If we compare eqns. 28 and 44, we see that, whereas the truncation error introduced by the characteristic scheme is of second order with respect to h and τ , with

the Lax–Wendroff scheme the truncation error is only of the third order. The main effect of the former is to disperse the band, and in most instances to act mainly as an apparent diffusion term. In the latter instance, the effect is essentially a shift in the peak position.

Non-equilibrium problem

In this instance, the system of partial differential eqns. 34 and 35 is replaced by the following system of algebraic, finite difference equations:

$$\frac{C_j^{n+1} - C_j^n}{\tau} + F \cdot \frac{q_j^{n+1} - q_j^n}{\tau} + u \cdot \frac{C_{j+1}^n - C_{j-1}^n}{2h} - \left(\frac{u_z^2 \tau}{2h^2} + \frac{D_z}{h^2} \right) (C_{j+1}^n - 2C_j^n + C_{j-1}^n) = 0 \quad (46)$$

and

$$\frac{q_j^{n+1} - q_j^n}{\tau} = -K(q_j^n - f_j) \quad (47)$$

We combine now these equations with eqns. 39–41 and the equation similar to eqn. 39 which can be written for q_j^{n+1} :

$$\begin{aligned} \left(\frac{\partial C}{\partial t} \right)_j^n + F \left(\frac{\partial q}{\partial t} \right)_j^n + u \left(\frac{\partial C}{\partial z} \right)_j^n - D \left(\frac{\partial^2 C}{\partial z^2} \right)_j^n &= \frac{\tau^2}{6} \left(\frac{\partial^3 C}{\partial z^3} + F \cdot \frac{\partial^3 C}{\partial t^3} \right)_j^n + \\ &+ \frac{uh^2}{6} \left(\frac{\partial^3 C}{\partial z^3} \right)_j^n + \frac{\tau}{2} \left[\left(\frac{\partial^2 C}{\partial t^2} + F \cdot \frac{\partial^2 q}{\partial t^2} \right) - u^2 \cdot \frac{\partial^2 C}{\partial z^2} \right]_j^n \end{aligned} \quad (48)$$

The numerical error contains two parts. The first part contains the first two terms of the right-hand side of eqn. 48 and is of second order [$O(h^2 + \tau^2)$]. The last term of eqn. 48 is of first order in τ . Hence, in the non-equilibrium case, the Lax–Wendroff procedure introduces a first-order error. The third term of eqn. 48 is equal to

$$\frac{\tau}{2} \cdot \frac{\partial}{\partial z} [K(q - f)] \quad (49)$$

It is obvious that when the system approaches equilibrium, this last term becomes zero. An apparent diffusion term appears, much as with the characteristic procedure. There is an important difference, however. With the characteristic procedure, the apparent diffusion coefficient depends only on the integration increments and on the differential of the isotherm (eqn. 29). If a proper set of values is chosen for these increments, in order to simulate the elution profile of a band with a column having a certain finite efficiency, the apparent column efficiency for other compounds having a different retention will be fixed. This efficiency varies rapidly with the retention (*i.e.*, with k'_0). Thus, although it is possible to simulate properly the elution of a binary mixture with a relative retention close to unity, the procedure cannot be applied to multicomponent

mixtures or to gradient elution. In contrast, the use of a kinetic model and of the Lax-Wendroff calculation procedure permits the simulation of the migration of a multicomponent band in gradient elution, while keeping the column efficiency of each component constant and equal to the required value, or varying it as needed, during an experiment.

RESULTS AND DISCUSSION

Numerical simulations were performed for the different cases discussed above, varying the values of the space and time increments of the integration, in order to test the validity of our theoretical analysis of the error problem. The results of these calculations are reported in Figs. 1-12. In Fig. 1, two chromatograms are shown, calculated by integration of eqn. 1, performed using the characteristic method and two different values of the space increment, for the same value of the time increment. A linear isotherm was used. A Gaussian band profile should be obtained. This is the result given by the calculation. The effect of doubling the space increment is important and corresponds to a two-fold reduction of the apparent column efficiency. This phenomenon has been used to advantage in our recent work^{3,9-12}. Fig. 2 shows the effect of the same change in the space increment when a non-linear isotherm is used,

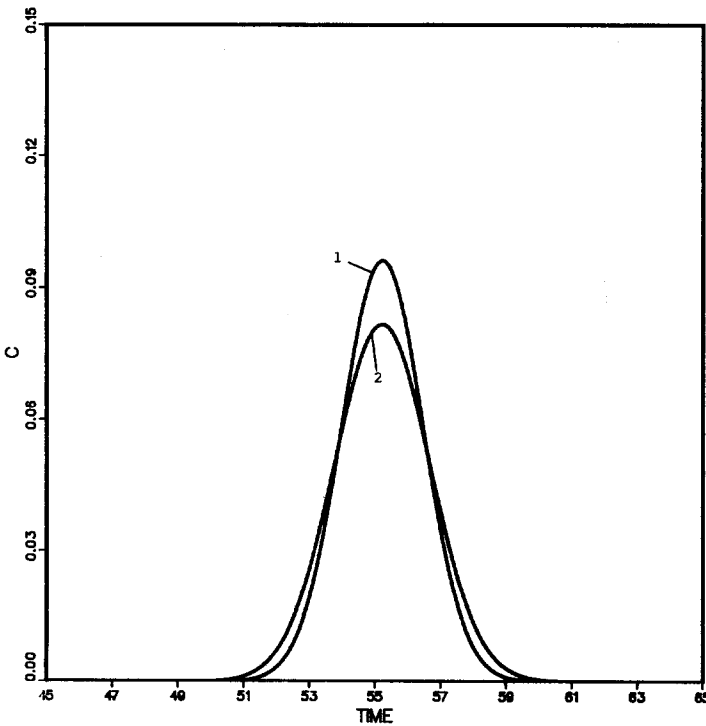


Fig. 1. Profiles obtained as solution of eqn. 1 using the characteristic method and the first type difference equation. Linear isotherm; column length, 5 cm; linear flow velocity, 0.25 cm/s; constant time increment, $\tau = 0.05$ s. Profile 1, $h = 0.0005$ cm; profile 2, $h = 0.001$ cm.

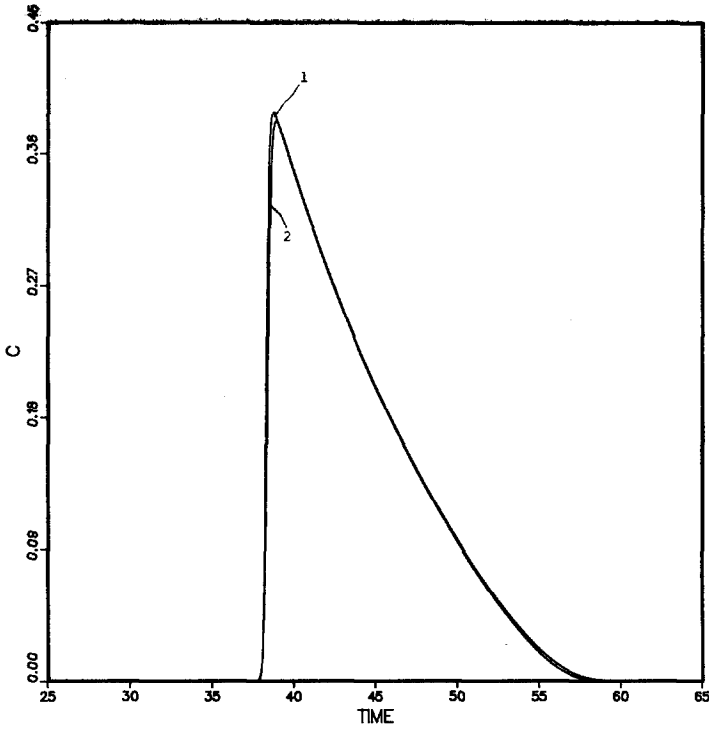


Fig. 2. Same as Fig. 1, except non-linear isotherm and sample size 100 times larger.

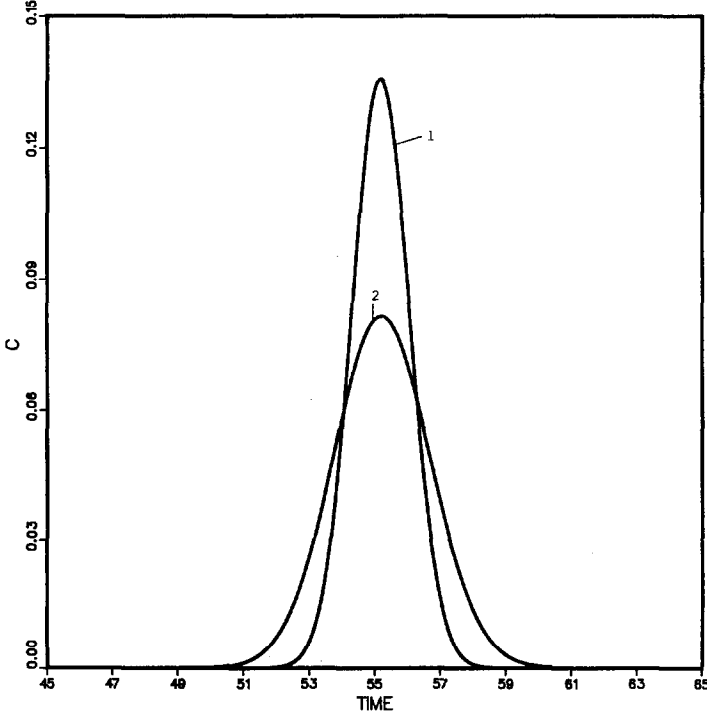


Fig. 3. Same as Fig. 1, except constant space increment, $h = 0.001$ cm. Profile 1, $\tau = 0.025$ s; profile 2, $\tau = 0.05$ s.

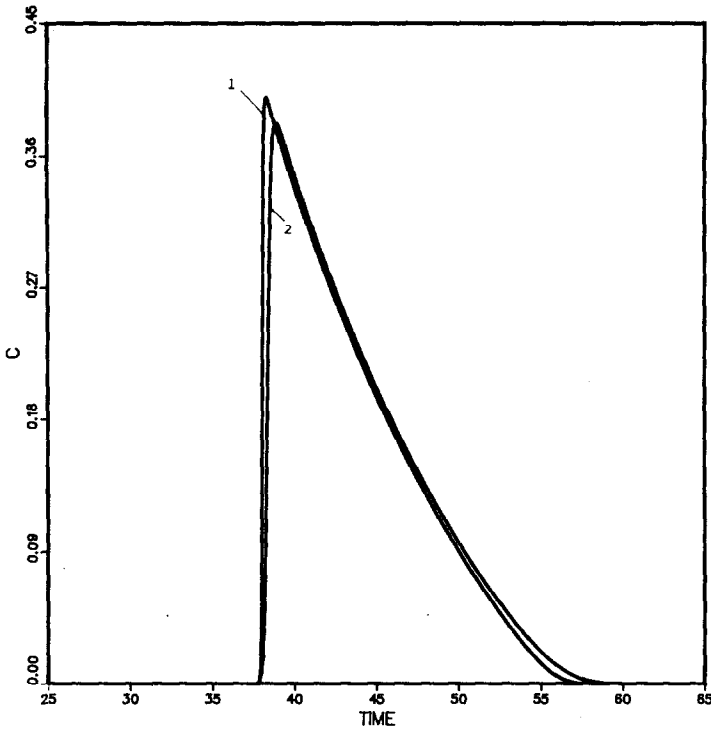


Fig. 4. Same as Fig. 3, except non-linear isotherm and sample size 100 times larger.

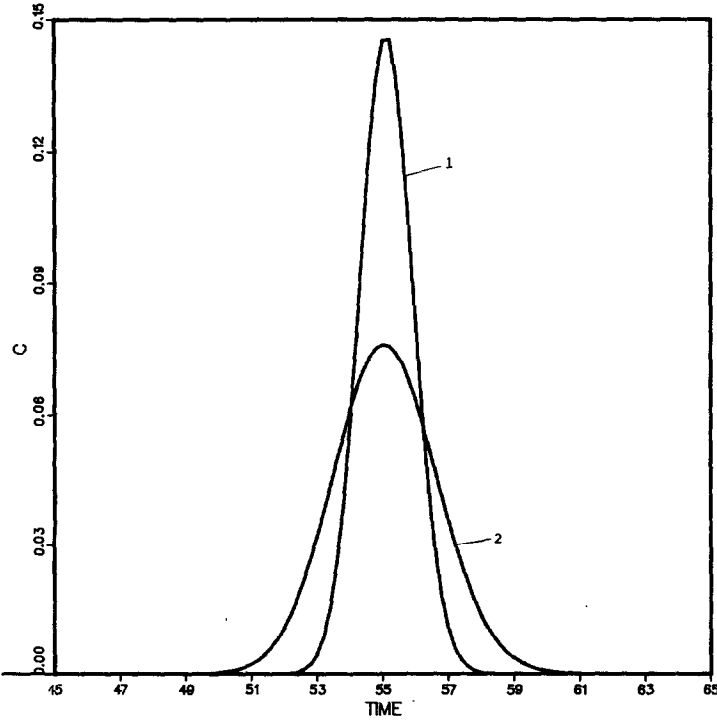


Fig. 5. Same as Fig. 1, except second difference type. Constant time increment, $\tau = 0.01$ s. Profile 1, $h = 0.0025$ cm; profile 2, $h = 0.005$ cm.

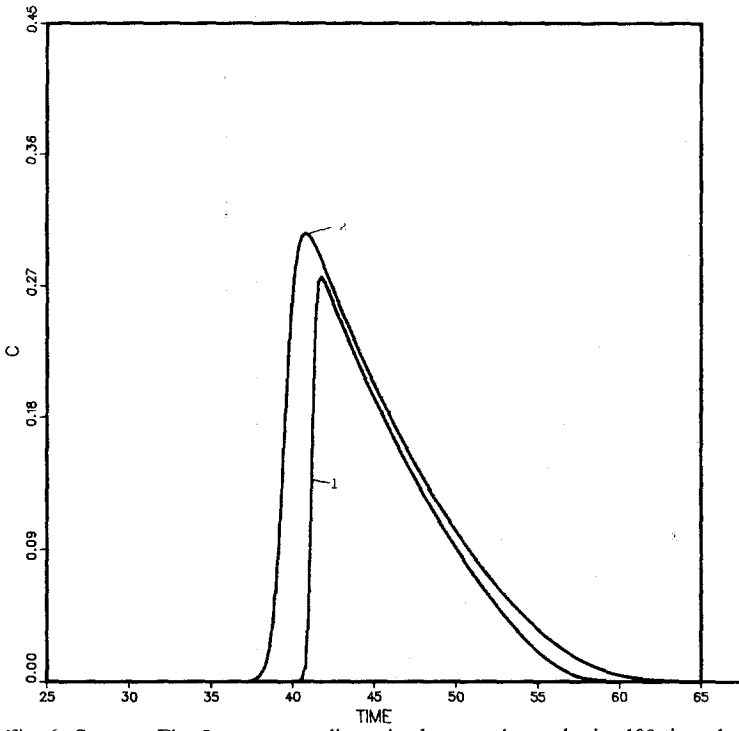


Fig. 6. Same as Fig. 5, except non-linear isotherm and sample size 100 times larger.

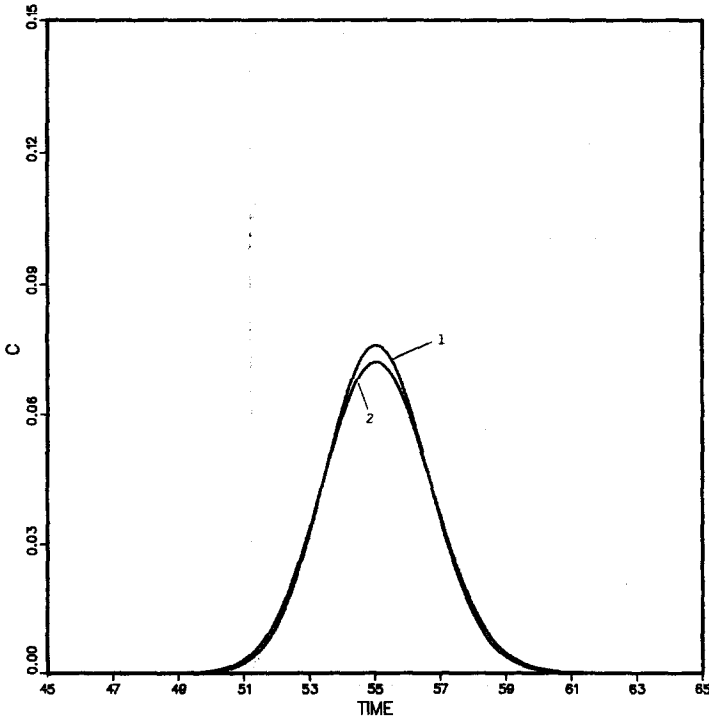


Fig. 7. Same as Fig. 5, except constant space increment, $h = 0.005$ cm. Profile 1, $\tau = 0.005$ s; profile 2, $\tau = 0.01$ s.

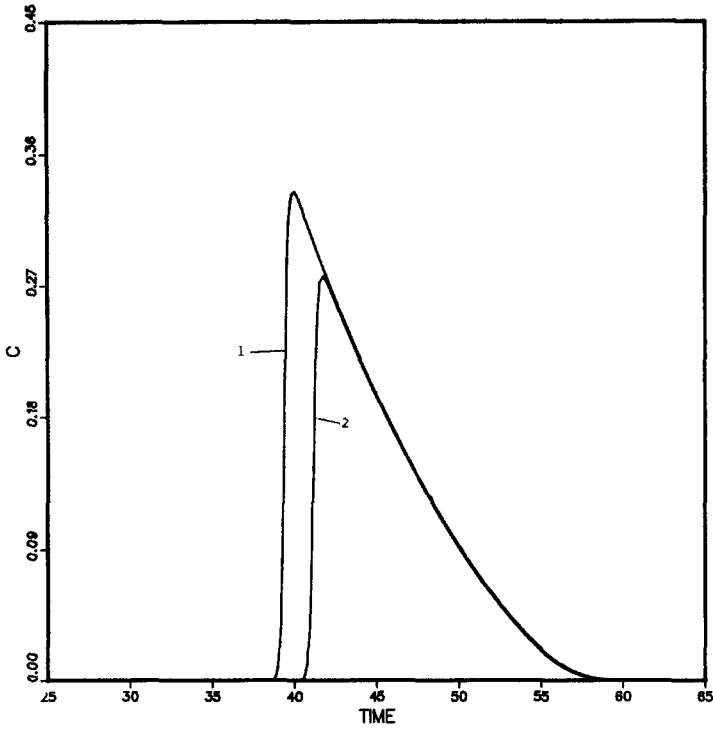


Fig. 8. Same as Fig. 7, except non-linear isotherm and sample size 100 times larger.

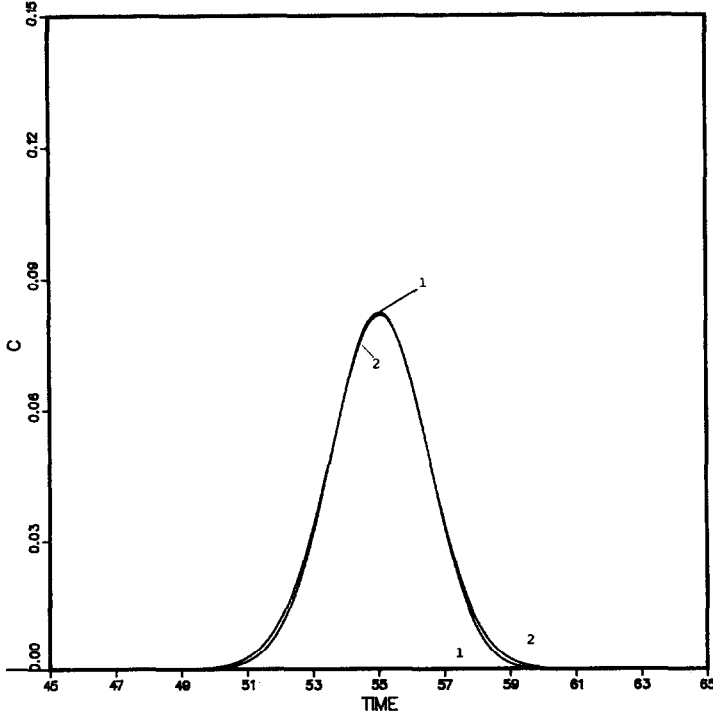


Fig. 9. Profiles obtained as solutions of eqn. 33, using the Lax-Wendroff procedure. Linear isotherm. Column length, 5 cm; linear flow velocity, 0.25 cm/s; mass transfer coefficient, $K = 60 \text{ s}^{-1}$; axial dispersion coefficient, $D = 0.00011 \text{ cm}^2 \text{ s}^{-1}$; constant time increment, $\tau = 0.005 \text{ s}$. Space increment: profile 1, $h = 0.0025 \text{ cm}$; profile 2, $h = 0.005 \text{ cm}$.

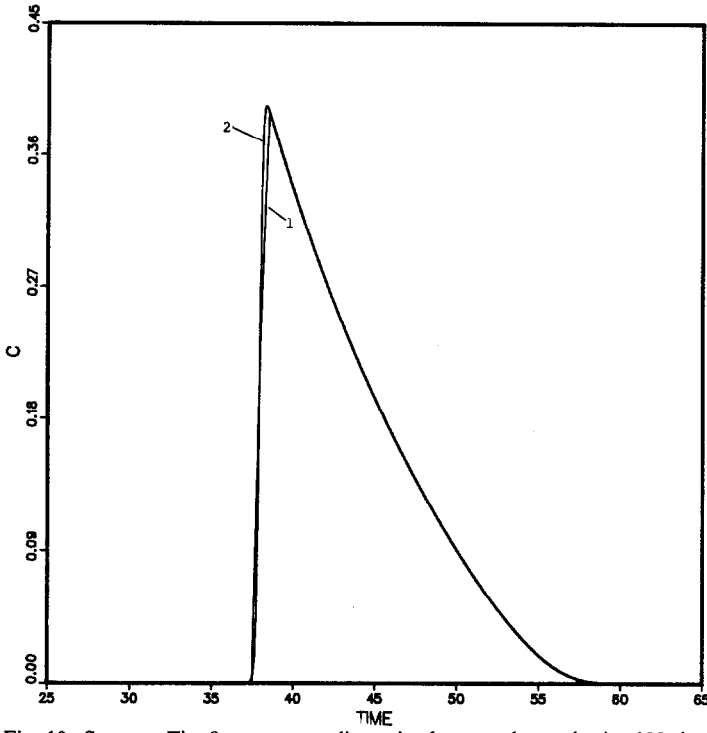


Fig. 10. Same as Fig. 9, except non-linear isotherm and sample size 100 times larger.

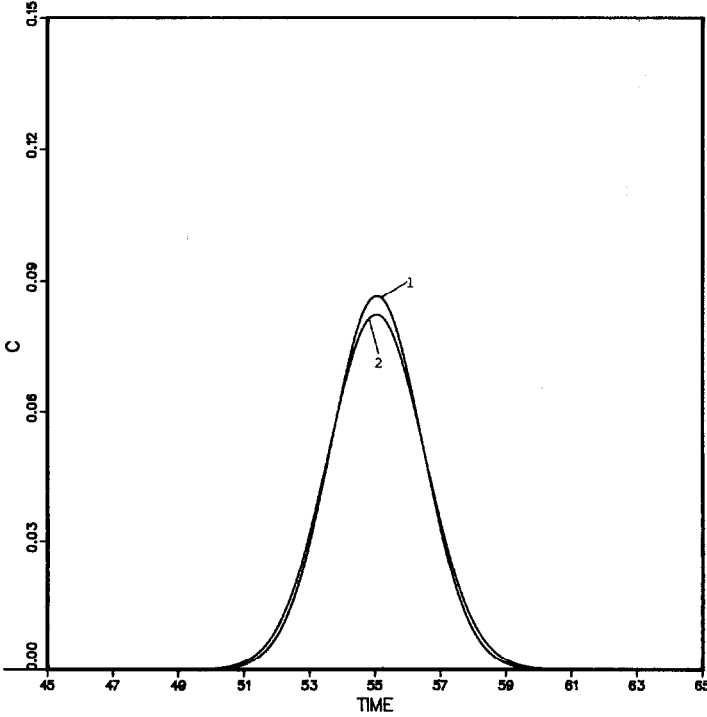


Fig. 11. Same as Fig. 9, except constant space increment, $h = 0.005$. Time increment: profile 1, $\tau = 0.0025$ s; profile 2, $\tau = 0.005$ s.

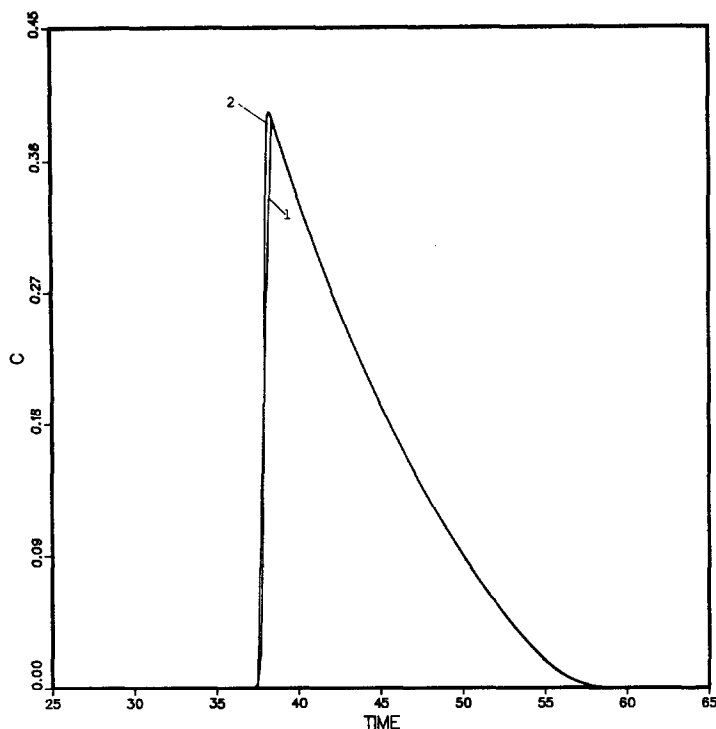


Fig. 12. Same as Fig. 11, except non-linear isotherm and sample size 100 times larger.

with a large sample size. Then the effect is small, which is in agreement with the fact that the influence of the column efficiency on the band profile is small at high loading factors¹².

Figs. 3 and 4 show similar chromatograms, obtained by changing the time increment, while keeping the space increment constant, which is the reverse of what was done in Figs. 1 and 2. The results obtained are very similar to those obtained in the previous case, as predicted by our discussion of eqn. 19.

Figs. 5–8 show chromatograms obtained under nearly the same conditions as those in Figs. 1–4, but with the second difference method described here. The results obtained under linear conditions are satisfactory, and are as predicted by eqn. 27. The effect of the choice of the space increment on the efficiency of the peak obtained is important (Fig. 5), while the effect of the choice of the time increment is nearly negligible (Fig. 7). In contrast, the results obtained under non-linear conditions are poor: it is seen in Figs. 6 and 8 that the mass is not even conserved! This method should certainly be avoided, although it gives profiles that look realistic.

Figs. 9–12 show chromatograms obtained by solving eqn. 34 using the Lax–Wendroff method. The equilibrium isotherm is again linear in Figs. 9 and 11, and two different values of the space increment were used with the same value of the time increment for Fig. 9, the opposite, two different values of the time increment with the same space increment for Fig. 11. In both instances the two profiles are extremely close, almost impossible to differentiate in most of the concentration range. Finally,

Figs. 10 and 12 show the solutions obtained under non-linear conditions, with two different values of the space increment (Fig. 10) for the same time increment, or two different values of the time increment for the same space increment. The differences between the two profiles on either Fig. 10 or Fig. 12 are very small, comparable to the differences between the two profiles shown in Figs. 2 and 4.

There are differences between the two basic approaches studied here, the characteristic and the Lax–Wendroff methods, regarding the stability of the numerical solutions. Oscillations easily take place, especially with the Lax–Wendroff scheme, if the integration increments are not properly chosen. Hence a direct comparison between the results obtained by the two methods is difficult and must be limited to a narrow range of values of τ and h . Depending on the nature of the problem studied, the first type difference method^{2,3,7,9–12} or the Lax–Wendroff method^{6,15} will be chosen.

ACKNOWLEDGEMENTS

This work was supported in part by Grant CHE-8715211 from the National Science Foundation and by the cooperative agreement between the University of Tennessee and Oak Ridge National Laboratory.

REFERENCES

- 1 P. C. Haarhoff and H. J. Van der Linde, *Anal. Chem.*, 38 (1966) 573.
- 2 P. Rouchon, M. Schonauer, P. Valentin and G. Guiochon, *Sep. Sci. Technol.*, 22 (1987) 1793.
- 3 G. Guiochon, S. Golshan-Shirazi and A. Jaulmes, *Anal. Chem.*, 60 (1988) 1856.
- 4 H. C. Thomas, *J. Am. Chem. Soc.*, 66 (1944) 1664.
- 5 L. Lapidus and N. L. Amundson, *J. Phys. Chem.*, 56 (1952) 984.
- 6 B. C. Lin, S. Golshan-Shirazi and G. Guiochon, *J. Phys. Chem.*, 93 (1989) 3343.
- 7 B. C. Lin and G. Guiochon, *Sep. Sci. Technol.*, 24 (1988) 31.
- 8 B. C. Lin, S. Golshan-Shirazi, Z. Ma and G. Guiochon, *Anal. Chem.*, 60 (1988) 2647.
- 9 G. Guiochon and S. Ghodbane, *J. Phys. Chem.*, 92 (1988) 3682.
- 10 S. Golshan-Shirazi and G. Guiochon, *J. Chromatogr.*, 461 (1989) 1.
- 11 A. Katti and G. Guiochon, *J. Chromatogr.*, 449 (1988) 25.
- 12 S. Golshan-Shirazi and G. Guiochon, *Anal. Chem.*, 60 (1988) 2364.
- 13 S. Goldstein, *Proc. R. Soc. London, Ser. A*, 219 (1953) 151.
- 14 J. L. Wade, A. Bergold and P. W. Carr, *Anal. Chem.*, 59 (1987) 1286.
- 15 B. C. Lin, Z. Ma and G. Guiochon, *Sep. Sci. Technol.*, in press.
- 16 R. D. Richtmyer and K. W. Morton, *Difference Methods for Initial-Value Problems*, Interscience, New York, 2nd ed., 1967.
- 17 P. C. Haarhof and H. J. Van der Linde, *Anal. Chem.*, 38 (1966) 573.
- 18 M. Goedert and G. Guiochon, *J. Chromatogr. Sci.*, 11 (1973) 326.