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Martin-Synge algorithm for the solution of equilibrium-dispersive model of liquid chromatography

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ABSTRACT

An alternative method, called the Martin-Synge algorithm, is introduced to calculate numerical solutions of the equilibrium-dispersive (ED) model. The developed algorithm is based on the earlier work of Friday and Levan [1] and on the continuous plate model of Martin and Synge [2]. The column is divided evenly into a series of virtual vessels in which a simplified mass balance equation is solved accurately by the Runge-Kutta-Fehlberg method and the elution profile is given by the numerical solution for the last vessel. The dispersion of the compound during the elution process is controlled by adjusting the number of virtual vessels into which the column is divided. Solving the ED model under linear conditions with this method gives exactly the same profile as the analytical solution of the Martin-Synge plate model. The Martin-Synge method gives better results than the Rouchon method (1) when the isotherms involved are sigmoidal or anti-Langmuir; and, more importantly, (2) in the case of multi-component problems. Finally, the Martin-Synge method proves to be more robust and faster than the OCFE method that, until now, was considered to be one of the most robust and accurate algorithms. The developed algorithm was used for the calculation of the coefficients of the isotherm of butyl benzoate by the inverse method, using a simplex optimization algorithm.

1. Introduction

Several differential models describe the migration of sample zones along chromatographic columns [3]. These models have different degree of complexity. The most complex general rate model [4–7], considers all the processes taking place in the mobile phase, in the pores, and on the surface of the stationary phase. This model provides the most detailed information on the chromatographic processes. On the other hand, the simplest ideal model [8–10] does not consider any kinetic process causing band broadening. It just informs on the effects of the thermodynamic process on the evolution of band profiles. The equilibrium-dispersive (ED) model is a good compromise for the optimization of chromatographic processes. In the ED model [3], it is assumed that: (1) the mass transfer kinetics is fast and the mobile and the stationary phases are constantly in equilibrium, (2) band dispersion takes place in the column through axial dispersion and nonequilibrium effects (mass transfer resistances and finite adsorption-desorption kinetics) and their contributions can be lumped together in an apparent axial dispersion coefficient, D_a. The ED model has no closed-form analytical solution in most cases. Although it has some approximate solutions, their validity is limited (see Chapter 10.2 of Ref. [3]). In most cases of practical interest, numerical solutions are needed.

A variety of methods are available to derive numerical solutions of Eq. (3) (see later), including finite-difference and finite-element methods. The principle of the finite difference methods consists of replacing the continuous plane (z, t) by the grid obtained by dividing the space and time into a number of small, equal segments and replacing the differential terms by the corresponding finite difference terms. Many combinations of these various finite differences can be used for each term of the mass balance equation and a partial differential equation can be approximated by many different finite-difference schemes. It is essential that the numerical errors made during the calculations be controlled and there are two different approaches for the calculation of numerical solutions of the mass balance equation. First, it can be directly solved by setting the integration increments to minimize the error made [11,12]. Second, the space and time increments can be set on such a way that the numerical error simulates the band dispersion in the column, as is done in Rouchon [13,14] and Craig [15,16] algorithms. The finite difference methods give fast solutions that are easy to use for the solution of the mass balance

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equation of single compounds. However, the accuracy of the band profiles calculated by finite difference methods is poor in the case of multi component mixtures. In these cases, the apparent dispersion coefficient can be estimated precisely only for one compound. Then, the time and space increments of the numerical solution cannot simulate the dispersion of the other components. The discrepancy increases with increasing number of components and with increasing difference between the retention factors of these compounds. The over- or underestimation of the apparent dispersion may have serious impact on the estimates of isotherm parameters with the inverse method and on the optimization of separations.

In contrast with finite difference schemes, the time and space domains in the finite element methods are divided into subdomains, commonly referred to as finite elements. The unknown function is represented within each element by an interpolating polynomial which is continuous and has continuous derivatives to a specified order, within the element [17]. There are several finite element methods. The one most frequently used in chromatography is orthogonal collocation on finite elements (OCFE). The calculation of numerical solutions of partial differential equations with an OCFE method was widely discussed in the fundamental book of Villadsen and Michelsen [18]. This method was successfully applied to the modeling of many different separation and reaction processes in chemical engineering. The method of orthogonal collocation on finite element was initially applied to the solution of the ED model by Ma and Guiochon [19]. The numerical solutions of the systems of partial differential equations of chromatography calculated by OCFE are more accurate than those obtained with finite difference methods, but these calculations take much more time [3].

Friday and Levan [1] investigated theoretically the condensation of benzene and water in adsorption beds during their thermal regeneration. As Martin and Synge [2] did earlier for the modeling of liquid chromatography, the authors modeled the packed bed as a number of well-mixed tanks in series. A numerical solution of the model was obtained by using backward differences for the discretization of the partial differential equations in the axial direction, in order to conserve mass and energy, providing ordinary differential equations (ODEs) for each stage. These ODEs were solved by the fourth-order Runge-Kutta method [20]. Later, different authors used the same procedure for modeling processes in adsorption bed [21,22]. Although this procedure is capable for the simulation of convection-diffusion problems, neither of these groups investigated the number of stages necessary to correctly estimate the effects of diffusion and mass transfer. Recently, Katsuo et al. [23] and Cornel et al. [24] used the same approach for the simulation of simulated moving bed chromatography [23] and of high-performance liquid chromatography [24]. Although these authors analyzed the numerical error of the calculation, they did not determine the exact number of stages required for an accurate simulation of dispersion in the column.

The aim of this work is to investigate the applicability of the method introduced by Friday and Levan [1] to calculate solutions of the mass balance equation of liquid chromatography. Since this approach is analogous to the Martin and Synge plate model, the method is named the Martin-Synge algorithm. In this work, this method will be compared with the most frequently used finite difference (Rouchon) and finite element (OFCE) methods. Our goal was also to show that the Martin-Synge algorithm can perform satisfactorily under conditions when other methods are either unstable or require special attention to implement. The developed algorithm is applied to the determination of the isotherm parameters of butyl benzoate by the inverse method.

2. Theory

2.1. Martin-Synge plate model

The Martin and Synge plate model [2] is a continuous plate model. It assumes that the column is equivalent to a series of continuous flow mixers. Mobile phase is transferred from one vessel to the next as new mobile phase is added into the first vessel. Hence, the mobile phase flows continuously and the volume of mobile and stationary phases in each mixer remain constant. The model assumes also that, at the beginning of the experiment, the first plate only is loaded with the sample and that there are no sample components in the other plates. The elution profile given by this model is

$$c[t] = \frac{1}{\tau} e^{\frac{t}{\tau}} \left(\frac{t}{\tau}\right)^{(N-1)} \frac{1}{(N-1)!} \tag{1}$$

where c is the concentration of the eluted compound, N is the number of vessels, later called theoretical plates, and τ is the residence time of the compound in a vessel.

$$\tau = \frac{L\ (1+k)}{u_0 N} \tag{2}$$

In this equation, L is the column length, k is the retention factor, and u_0 is the linear velocity of the mobile phase.

2.2. Equilibrium-dispersive model

It was shown that, when the mass transfer kinetics is fast or when the dispersion coefficient of the solute can be calculated accurately, the differential mass balance of the solute [25–27] can be written as:

$$\frac{\partial c(z,t)}{\partial t} + F\frac{\partial q(z,t)}{\partial t} + u\frac{\partial c(z,t)}{\partial z} = D_\mathrm{a}\frac{\partial^2 c(z,t)}{\partial z^2} \tag{3}$$

where q and c are the stationary and the mobile phase concentrations of the compound, respectively, t is the time, z the distance along the column, u the linear velocity, and $F = (1-\varepsilon)/\varepsilon$ is the phase ratio, with ε the total column porosity of the column. q is related to c through the isotherm equation, $q = f(c)$. Eq. (3) is a local equation, and valid everywhere in the column.

The apparent dispersion coefficient, D_a, is given by:

$$D_\mathrm{a} = u\frac{H}{2} \tag{4}$$

where H is the apparent height equivalent to a theoretical plate (HETP), obtained experimentally. This approximation allows the equilibrium-dispersive model to correctly take into account the influence of the column efficiency on the profile of elution bands.

2.3. Martin-Synge algorithm for the solution of mass balance equation

Just as in the original Martin and Synge plate model [2] and in the work of Friday and Levan [1], the column is divided evenly into a series of continuous flow mixers. In each vessel, the following non-linear differential equation is solved accurately:

$$\frac{\mathrm{d}\, c_m[t]}{\mathrm{d}\, t} + F\frac{\mathrm{d}\, q_m[t]}{\mathrm{d}\, t} + u\frac{c_m[t] - c_{m-1}[t]}{\Delta z} = 0 \tag{5}$$

The initial condition is $c_m[t=0] = c0_m$. In this equation, m is the rank of the vessel. Assuming that the column is divided into M vessels, we have $1 \le m \le M$. Δz is the length of the vessel in which the equation is solved ($\Delta z = L/M$). c_m and c_{m-1} are the concentration profiles of the solute in the mth and $(m-1)$th vessels. Accordingly, c_0 is the injection concentration and c_M is the elution profile of the solute.

At a given time, the Taylor series expansion of the solute concentration in the $(m-1)$th vessel

$$c_{m-1} = c_m - \Delta z \left.\frac{\partial c}{\partial z}\right|_z + \frac{\Delta z^2}{2}\left.\frac{\partial^2 c}{\partial z^2}\right|_z - \frac{\Delta z^3}{6}\left.\frac{\partial^3 c}{\partial z^3}\right|_z + \cdots \quad (6)$$

where $z = m\,\Delta z$. We can truncate this series after the second order term in Δz and use this approximation during the solution of the differential equation:

$$c_{m-1} \approx c_m - \Delta z \left.\frac{\partial c}{\partial z}\right|_z + \frac{\Delta z^2}{2}\left.\frac{\partial^2 c}{\partial z^2}\right|_z \quad (7)$$

This equation is approximate, hence erroneous, due to the truncation. Because the order of this truncation error is Δz^3, $O(\Delta z^3)$, it can be neglected in most cases, since the values of the Δz-s, which are equal to the HETP (see later), are small, even in the case of preparative columns.

Eq. (7) can be rearranged to calculate the backward difference quotient of the concentration in space.

$$\frac{c_m - c_{m-1}}{\Delta z} \approx \left.\frac{\partial c}{\partial z}\right|_z - \frac{\Delta z}{2}\left.\frac{\partial^2 c}{\partial z^2}\right|_z \quad (8)$$

Then, this backward different quotient can be substituted into Eq. (5) which can be rearranged as follows

$$\left.\frac{\partial c}{\partial t}\right|_z + F\left.\frac{\partial q}{\partial t}\right|_z + u\left.\frac{\partial c}{\partial z}\right|_z \approx u\frac{\Delta z}{2}\left.\frac{\partial^2 c}{\partial z^2}\right|_z \quad (9)$$

By comparing Eqs. (3) and (9), we conclude that the previous equation can be approximated by the latter one if $D_a = u(\Delta z/2)$. In Eq. (4) it was shown that, according to the ED model, the apparent dispersion coefficient, D_a, is equal to $u(H/2)$. Thus, Eqs. (3) is equivalent to the equation of the ED model if $\Delta z = H$, or in other words, if the number of slices into which the column is divided is equal to the number of its theoretical plates. Accordingly

$$\Delta z = \frac{L}{N} \quad (10)$$

where L is the length of the column, and N the number of theoretical plates.

3. Experimental

3.1. Instrumentation and materials

The experiments were carried out using a HP 1090 Series II liquid chromatograph (Hewlett Packard, now Agilent Technologies, Palo Alto, CA), equipped with a multisolvent delivery system, an automatic injector, a column thermostat, a DAD detector, and a HP Chemstation data aquisition system. Band profiles of butyl benzoate were recorded at 290 nm. The volume of the system from the gradient pump to the detector is 0.63 mL while that from the injector to the detector is 0.033 mL.

The column used during the experiments was a 150 mm × 4.6 mm Luna C18 (Phenomenex, Torrance, CA, USA) column packed with 5 μm particles. The total porosity of this column was 0.620. A 65:35 methanol–water mixture was used as the eluent, at a flow rate of 1 mL/min. The components of the mobile phase were purchased from Fisher Scientific (Fair Lawn, NJ, USA), the butyl benzoate solution was from Sigma-Aldrich (St. Louis, MO, USA).

3.2. Computation

3.2.1. Solution of the mass balance equation

The solution of the mass balance equation using the newly developed method was performed using a software written in house in the C++ language, using the GNU Scientific Library (GSL) [28]. The simplified algorithm is illustrated in Figure 1. The column was evenly divided into N virtual parts, representing the cascade of vessels of the Martin-Synge plate model. In each virtual vessel, Eq. (5) was solved by the embedded Runge-Kutta-Fehlberg (RKF45) ODE solver routine provided by the GSL (see Chap. 25 of Ref. [28]). The embedded RKF45 method is one of the adaptive Runge-Kutta methods. It produces an estimate of the local truncation error of a single Runge-Kutta step. This error estimate is then used to control the stepsize and through it the numerical error of the calculation. In the RKF method any accuracy goal can be set arbitrarily and the calculation of the "exact" solution of Eq. (3) can be achieved by setting the error to be very small. During our calculations, the error was set at 1×10^{-8}.

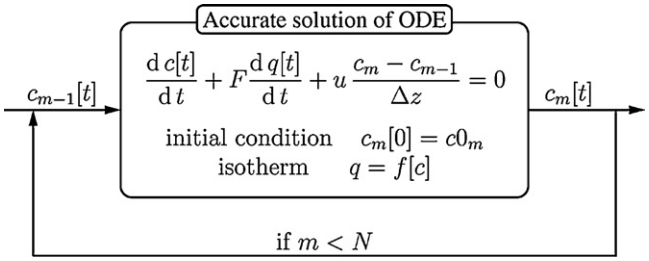

Fig. 1. Simplified algorithm of the solution of equilibrium-dispersive model by Martin-Synge method.

In order to calculate the solution, the RKF45 ODE solver needs the derivatives of the concentrations (dc/dt) for each compound. In the case of a single component problem, Eq. (5) was simply rearranged for (dc/dt), which could be introduced in the source code easily. In the case of a competitive multi-component problem, a mass balance equation like Eq. (5) was written for each component and the equation system obtained was solved for dc_A/dt, dc_B/dt, dc_C/dt, and so on. The results were then introduced in the RKF45 ODE solver algorithm. The solution for a given plate was the "inlet profile" for the next plate. A spline was fitted for each inlet profile by a cubic spline interpolation with natural boundary conditions (see Chap. 26 of Ref. [28]), thus the ODE solver was able to handle them as continuous functions. The solution of the last plate was the elution profile. It was saved for data processing. The source code of the program was compiled by g++ shipped by GNU Compiler Collection ver. 4.4.2. The O1 optimization level used during the compilation turns on the most common forms of optimization that do not require any speed-space tradeoffs. The calculations were performed on a Pentium IV computer (2.80 GHz) running GNU Linux operating system (blackPanther OS).

The injection profile has a most significant effect on the shape and position of the profile of the elution band calculated and also on the accuracy of the inverse method. During the model calculations (see Figs. 1–6), a rectangular injection profile was used. However the inverse method requires that the injection profiles be as accurate as possible, in order to minimize the calculation error. In this study, injection profiles were recorded by injecting the compound again after replacing the column with a zero-volume connector. For the calculation of the band profiles of butyl benzoate, a cubic spline was fitted on the recorded injection profile, providing the real injection profile to the Martin-Synge algorithm (see Appendix A).

To solve the mass balance equation by the Rouchon and the OCFE methods, we used the Chromatographic Column ver. 2.03 software [29]. This software was written especially for the calculation of preparative separations. With this program, the equilibrium-dispersive and the transport-dispersive models can be solved using the Rouchon and the OCFE methods, as well. This program permits also the derivation of estimates of the parameters

of single-component and multicomponent isotherm models. In the Chromatographic Column software, the VODE solver [30] is implemented for the solution of differential equations with the OCFE algorithm. The VODE solver automatically controls the integration time interval to fulfill the requirement of accuracy of the calculation. However, the number of the subdomains, *NS*, and the number of internal collocation points, $N(k)$ have to be chosen individually for any specific problem. In the Chromatographic Column software, $N(k)$ was set to be three. The Chromatographic Column program is a free software that can be used for any purpose. This free software has several restriction: it solves chromatographic models assuming the same efficiency (the same number of theoretical plates) for each component, it has a restricted possibility for the estimation of the model parameters and for the optimization of chromatographic separations. However, for the purpose of this work, these restrictions are not important.

3.2.2. Simplex method for isotherm determination

The inverse method for the determination of isotherm parameters from an overloaded band profile was carried out using the Simplex algorithm of Nelder and Mead [31] implemented in GSL (see Chap. 35 of Ref. [28]). With the simplex algorithm, the sum of the squares of the relative differences (SSRD) between the recorded and the calculated data was minimized. A spline was fitted to the chromatogram calculated from the actual isotherm parameters, then the concentration values of this data set was calculated at the time points of the measured band profile. The SSRD was calculated on the basis of these points. The minimization was stopped when the overall size of the simplex decreased below 10^{-6}.

4. Results and discussion

4.1. Analytical solution of the model for linear case

Under linear conditions, Eq. (5) simplifies to the following form:

$$(1+k)\frac{\mathrm{d}\,c_m[t]}{\mathrm{d}\,t} + u\frac{c_m[t]-c_{m-1}[t]}{H} = 0 \tag{11}$$

where k is the retention factor of the solute. An analytical solution of this equation is easily derived in the Laplace domain, in which case, the Laplace transform of the concentration profile in the mth vessel, $\mathcal{C}_m[s]$, is given by

$$\mathcal{C}_m[s] = \mathcal{C}_{m-1}[s]\frac{1}{1+(H/u)(1+k)s} \tag{12}$$

The Laplace-transform of the injection profile, $\mathcal{L}\{c_0[t]\}$, is $\mathcal{C}_0 = c_{\mathrm{inj}}$ or $c_{\mathrm{inj}}(1-e^{-st_{\mathrm{inj}}})/s$ in the case of a Dirac-pulse injection and also in the case of a t_{inj} long rectangular injection, if c_{inj} is the injected concentration of the solute. The concentration profiles at the last vessel, i.e., the elution profiles in the Laplace and the time domains in the case of the injection of Dirac impulses are

$$\mathcal{C}_N[s] = \frac{c_{\mathrm{inj}}}{\left[1+\frac{H}{u}(1+k)s\right]^N} \tag{13}$$

and

$$c[t] = \frac{c_{\mathrm{inj}}}{t\,(N-1)!}\exp\left(-\frac{u\,t}{H(1+k)}\right)\left(\frac{u\,t}{H(1+k)}\right)^N \tag{14}$$

Note that Eq. (14) is equivalent to the peak profile provided by the Martin and Synge plate model. In the case of a rectangular injection, the elution profile in the Laplace and the time domains are

$$\mathcal{C}_N[s] = \frac{1-e^{-s\,t_{\mathrm{inj}}}}{s}\frac{c_{\mathrm{inj}}}{\left[1+(H/u)(1+k)s\right]^N} \tag{15}$$

and

$$c[t] = c_{\mathrm{inj}}\left[1-e^{-p_1}\sum_{r=0}^{N-1}\frac{p_1^r}{r!}+\mathcal{H}[t-t_{\mathrm{inj}}]\cdot\left(e^{-p_2}\sum_{r=0}^{N-1}\frac{p_2^r}{r!}-1\right)\right] \tag{16}$$

where $p_1 = (t\,u)/(H(1+k))$, $p_2 = ((t-t_{\mathrm{inj}})\,u)/(H(1+k))$, and $\mathcal{H}[x]$ is the Heaviside step function [32], which is unity if $x \geq 0$ and is zero otherwise. The area and the first two normalized moments of Eq. (16) are:

$$\mu_0 = c_{\mathrm{inj}}\,t_{\mathrm{inj}} \tag{17}$$

$$\mu_1 = L\frac{(1+k)}{u} + \frac{t_{\mathrm{inj}}}{2} \tag{18}$$

$$\mu_2 = \frac{L^2}{N}\left[\frac{(1+k)}{u}\right]^2 + \frac{t_{\mathrm{inj}}^2}{12} \tag{19}$$

Eqs. (13)–(19) do not provide any new results and we conclude that the model derived in this work is equivalent to both the equilibrium-dispersive and the Martin-Synge plate models.

4.2. Comparison of the Martin-Synge method and the Rouchon algorithm

The Rouchon algorithm is a finite difference method in which the spatial derivative in Eq. (5) is replaced with a forward finite difference while the time derivative is replaced by a backward finite difference. The algorithm can be used successfully to calculate numerical solutions of the mass balance equation of single compounds having isotherms for which the slope decreases monotonically (typically, Langmuir-type isotherms). However, the program crashes easily during the calculation of solutions of the mass balance equation of compounds having a BET or an anti-Langmuir isotherm when the solute concentration is high. The slope of anti-Langmuir isotherms increases monotonically until it reaches infinity for a particular concentration. BET isotherms may have one or more inflection points, so their slopes do not vary monotonically but increase in some concentration regions and decrease in others. The BET isotherm may be represented by the following equation:

$$q = \frac{qs\,bs\,c}{(1-bl\,c)(1-bl\,c+bs\,c)} \tag{20}$$

where qs is the saturation capacity of the stationary phase, q and c are the concentrations of the solute on the stationary and in the mobile phases, bs and bl are equilibrium constants of adsorption on the surface of the stationary phase and on the adsorbed layer of solutes. If bl is equal to bs, the BET isotherm reduces to an anti-Langmuir isotherm. Both the BET and the anti-Langmuir isotherms have a point of discontinuity at $c = 1/bl$.

Profiles calculated with the Rouchon method are shown in Fig. 2, for a BET isotherm (qs = 100 mg/l, bs = 0.3 l/mg, bl = 0.08 l/mg). This profile cannot be interpreted above a critical concentration. At the same time, the Martin-Synge algorithm calculates correct peak profiles even when the injected concentrations exceeds $1/bl$, the point of discontinuity of the isotherm, as seen in Fig. 2. However, it is important to note that the Rouchon method is much faster than the continuous plate method. While it took only ~40 s to calculate the peaks of Fig. 2 (N = 10,000), it took slightly more than five minutes with the Martin-Synge method. The relative difference between the calculation times decreases with decreasing number of theoretical plates (e.g., the run times are 2 s vs. 5 s at N = 1000).

The Rouchon algorithm crashes when the Courant-Friedrich-Lewy stability condition (see Chap. 10.3 of Ref. [3]) fails, which it does with anti-Langmuir, BET, or other sigmoidal isotherms, when if the injected concentration is too high. For the Rouchon algorithm,

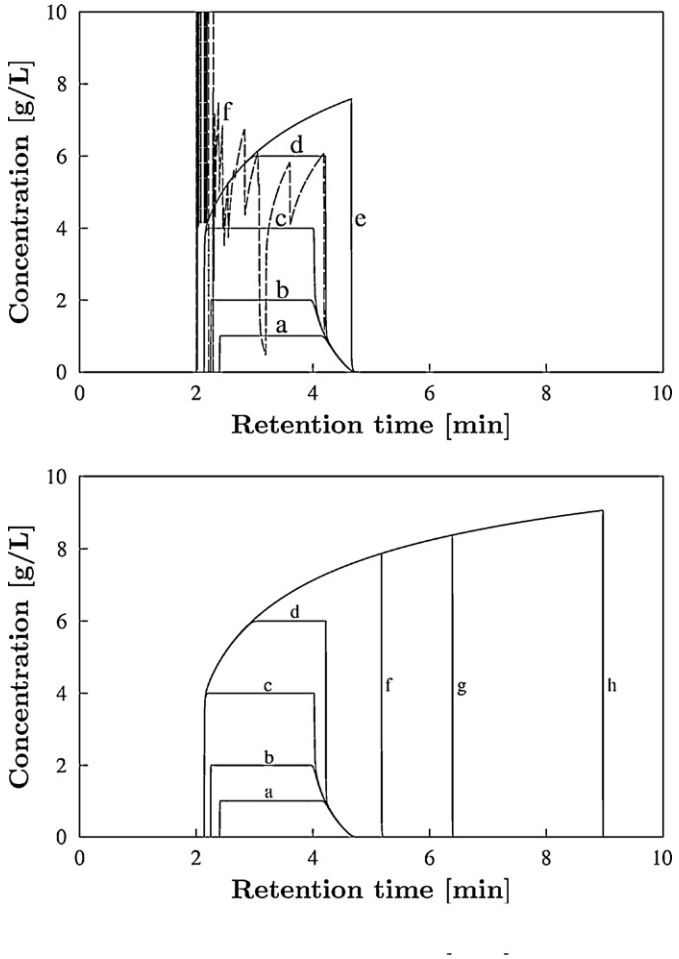

Fig. 2. Comparison of band profiles of a compound having BET isotherm [see Eq. (20)] calculated by Rouchon method (top), and Martin-Synge method (bottom). Injected concentrations: (a) 1 g/l, (b) 2 g/l, (c) 4 g/l, (d) 6 g/l, (e) 8 g/l, (f) 10 g/l, (g) 15 g/l, and (h) 25 g/l. Column: 100 mm × 2.1 mm, eluent flow rate: 1 ml/min, injection time: 2 min, total porosity: 0.769, number of theoretical plates: 10,000, isotherm parameters: qs = 100 g/L, bs = 0.3 L/g, bl = 0.08 L/g.

the Courant-Friedrich-Lewy stability condition requires that the Courant number be higher than or equal to one.

$$a = \frac{\Delta t \ u}{\Delta z \ (1+k)} \geq 1 \tag{21}$$

where a is the Courant number, k the retention factor of the solute, and Δt and Δz the time and space increments of the numerical calculation, respectively. Since the retention factor of a compound having anti-Langmuir or a BET isotherm increases with increasing liquid phase concentration, there will always be an injection concentration above which the Courant number will become smaller than unity. Eq. (21) shows that the stability of the Rouchon method can be improved by either decreasing Δz or increasing Δt. However, the Rouchon method gives an exact solution only if

$$\Delta z = \frac{H}{a_0 - 1} \tag{22}$$

and

$$\Delta t = \frac{a_0 \ \Delta z \ (1+k_{\text{lin}})}{u} \tag{23}$$

where H is the height equivalent to a theoretical plate, k_{lin} the retention factor of the solute under linear conditions, and a_0 the initial Courant number that is chosen to perform the calculation.

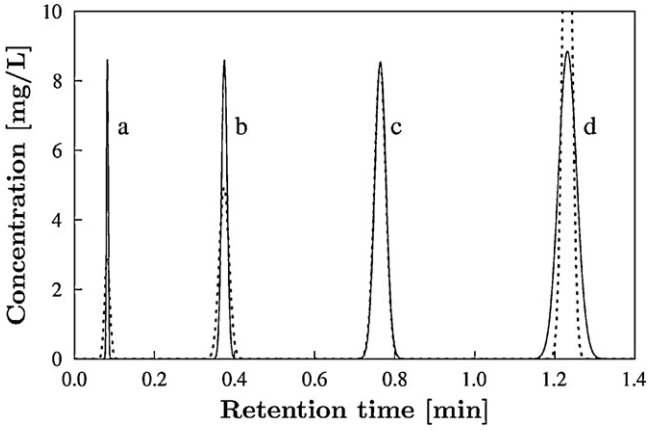

Fig. 3. Chromatogram of a quarternary mixture calculated with the Martin-Synge (solid line) and the Rouchon (dotted line) algorithms under linear conditions. Column: 100 × 2.1 mm, eluent flow rate: 1 ml/min, injection time: 0.005 min, total porosity: 0.7, number of theoretical plates: 3000, retention factors: (a) 0.3, (b) 5.1, (c) 11.6, and (d) 19.3. The numbers of theoretical plates derived from the first and second moments of the elution peaks calculated with the Martin-Synge algorithm are: (a) 3000, (b) 2999, (c) 3000, and (d) 3000. These numbers derived similarly from the peaks calculated with the Rouchon method are: (a) 165, (b) 955, (c) 2930, and (d) 11,800.

Eqs. (22) and (23) suggest that the stability of the Rouchon method can be increased only if an initially high Courant number is chosen. However, if the mobile phase concentration of the solute is close to the discontinuity of the isotherm, k increases so rapidly that an extremely high value of a_0 should be chosen in order to keep the method stable. This can lead to an increase of the calculation time by several orders of magnitude. In addition, high a_0 values can result in too small values of Δz and Δt, which can cause rounding-up problems, hence errors, if the analyst is not careful enough.

It may seem contradictory that the Martin-Synge algorithm does not crash for injection concentrations that exceed the point of discontinuity of the isotherm ($1/bl$). However, an isotherm shows the relationship between the equilibrium concentrations of a compound in the liquid and the solid phases. Actually, to reach the critical equilibrium concentration of the solute in the liquid phase ($1/bl$), one should inject an infinite amount of solute to reach the infinite concentration of the compound in the adsorbed phase. The injection of any sample having a finite concentration results in an equilibrium concentration in the liquid phase that is smaller (or even much smaller) than $1/bl$.

As mentioned previously, the Rouchon method is poorly accurate in multi-component chromatography because it must use the same apparent dispersion coefficient for all the components, so an accurate estimate can be obtained only for one of them. In contrast, the Martin-Synge method does not suffer from this inconvenient. As shown in Fig. 3, the numbers of theoretical plates of the peaks of four different compounds having a wide range of retention factors (k = 0.3, 5.1, 11.6, 19.3) do not change when their profiles are calculated with the Martin-Synge method while they vary significantly when the Rouchon method is used. Note that, even though the importance of the calculation errors made may differ widely, all the classical finite difference methods (e.g the Craig method) have similar limitations for the chromatograms calculated in multi-component cases, regardless of the scheme selected for the discretization of the derivatives (backward-forward, forward-backward, etc.).

Fig. 4 shows the chromatogram calculated with the Martin-Synge algorithm for a mixture of four components, two of which have competitive Langmuir -BET isotherms, when the injected concentrations are well in the non-linear range. The competitive

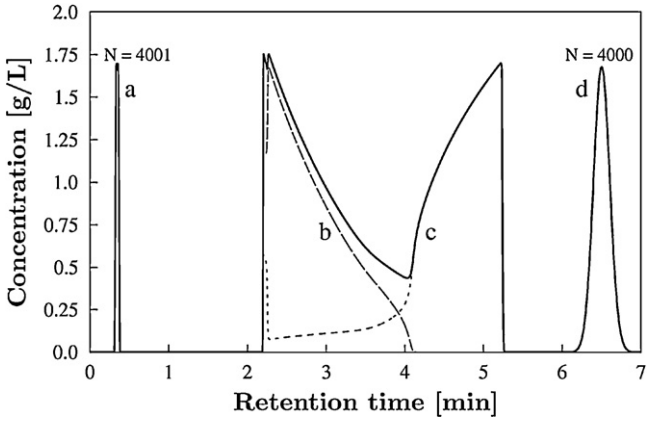

Fig. 4. Chromatogram of a quaternary mixture calculated by Martin-Synge method. Compound a and d have linear (k = 0.3, 25.7), compound b and c have competitive Langmuir (b) and BET (c) isotherms [see Eqs. (24) and (25)]. Column: 100 × 2.1 mm, eluent flow rate: 1 ml/min, injection time: 0.05 min, total porosity: 0.7, number of theoretical plates: 4000, isotherm parameters: qs_A = 150 g/L, qs_B = 100 g/L, bs_A = 0.28 L/g, bs_B = 0.35 L/g, bl_B = 0.18 L/g.

isotherms used were as follows:

$$q_A = \frac{qs_A\, bs_A\, c_A}{1 + bs_A\, c_A + bs_B\, c_B} \tag{24}$$

$$q_B = \frac{qs_B\, bs_B\, c_B}{(1 - bl_B\, c_B)(1 - bl_B\, c_B + bs_B c_B + bs_A\, c_A)} \tag{25}$$

As seen in Fig. 4, the computation process remains stable when the sample contains two components with competitive isotherms, one of them with having a BET isotherm, under nonlinear conditions. Thus, the Martin-Synge method should be favored for the calculation of band profiles of mixtures of compounds having anti-Langmuir, S-Shaped, or otherwise complex isotherms or when multi-component chromatograms must calculated. In any other cases, the Rouchon algorithm should be preferred to the Martin-Synge method due to its greater speed of calculation. However, chromatographers who use the former model for band profile calculations must know its serious limitations.

4.3. Comparison of the OCFE and the Martin-Synge algorithms

The OCFE method is considered to be one of the most accurate and robust method for the solution of mass balance equations in chromatography. The idea of the OCFE method is to divide the normalized space coordinate in the interval [0,1] into NS subdomains (elements). These elements can have different length, however, when solving chromatography separations, all the elements are assumed to have equal size. In each kth element, $N(k)$ internal collocation points are defined and the solution is approximated by Lagrange polynomial of degree $(N(k)+2)$. The overall solution is obtained by joining the solutions in each element. The details of the discretization of the spatial derivatives following the orthogonal collocation method were explained among others in [33]. The ED model [Eq. (3)] was solved with an OCFE method assuming Danckwerts [3] boundary conditions:

$$u\, c_0 - u\, c_{z=0} = -D_a \left.\frac{\partial c}{\partial z}\right|_{z=0} \tag{26}$$

$$\left.\frac{\partial c}{\partial z}\right|_{z=L} = 0 \tag{27}$$

The solution calculated can be regarded as the "real" solution when: (1) increasing the number of subdomains or of internal collocation points above a certain value has practically no effect on the solution obtained, (2) the mass balance is fulfilled. From our experience, it is appropriate, for the solutions of chromatographic separation processes for which the isotherm model is described by a convex upward isotherm (e.g, a Langmuir or a Jovanovič isotherm), to choose a number of collocation points, $N(k)$, in each subdomain equal to 3. In the Chromatographic Column ver. 2.03 used for our OCFE calculations., three internal collocation points were used. In this case the number of subdomains should typically be set close to 10% of the number of theoretical plates of the column in order to obtain an "accurate" solution. However, when the isotherm can generate extremely steep shocks, a larger number of subdomains is required while for problems generating elution band profile that are quasi Gaussian, the number of subdomains used may be smaller.

The rules given above regarding the choice of NS and $N(k)$ do not apply for isotherms that are expressed by mathematical formulae similar to that of the anti-Langmuir model, for example the BET model, Eq. (20), or for competitive model expressed by Eqs. (24) and (25). Then, the OCFE method converges toward a real solution only if the solute concentration in the mobile phase entering into the column is less than the critical concentration:

$$c = \frac{1}{bl} \tag{28}$$

When the inlet concentration is larger than $1/bl$, the OCFE method generally fails. An example of the behavior of the OCFE method when the condition in Eq. (25) is not fulfilled, is presented in Figs. 5 and 6 where it is compared with the solution provided by the Martin-Synge algorithm.

Fig. 5 shows that the OCFE band profiles of a given compound that were shown in Fig. 2 as calculated with the Martin-Synge algorithm is distorted at high sample size even if the number of subdomains applied is a tenth of the number of theoretical plates of the column. The area of the peaks in Fig. 5 are constant and proportional to the injected amount. Fig. 5 shows that the profile converges toward the one calculated by the Martin-Synge method when the number of subdomains increases above $N/10$ and reaches it with a number of subdomains equal to $0.30N$. Unfortunately, increasing the number of subdomains causes a large increase of the calculation time. While it took 27 s with 100 subdomains, it takes 2.25 min with 300 subdomains on the PC configuration used. For the sake of comparison, the same calculation took only five seconds with the Martin-Synge algorithm.

Fig. 6 shows that the choice of the number of subdomains is still more important for the calculation of the band profiles of two compounds having one a Langmuir, the other a BET isotherm,

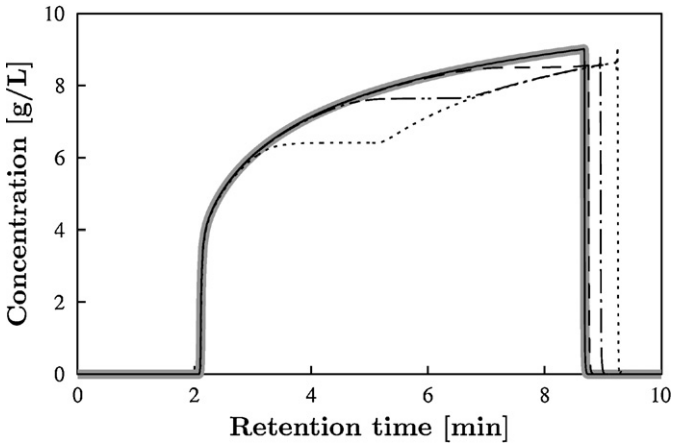

Fig. 5. Band profile of a compound having BET isotherm calculated by OCFE (black lines) and Martin-Synge (thick gray line) methods. Number of subdomains: 100 (dotted line), 150 (dot-dashed line), 200 (dashed line), and 300 (solid line). Number of theoretical plates: 1000. For all the remaining parameters, see Fig. 2.

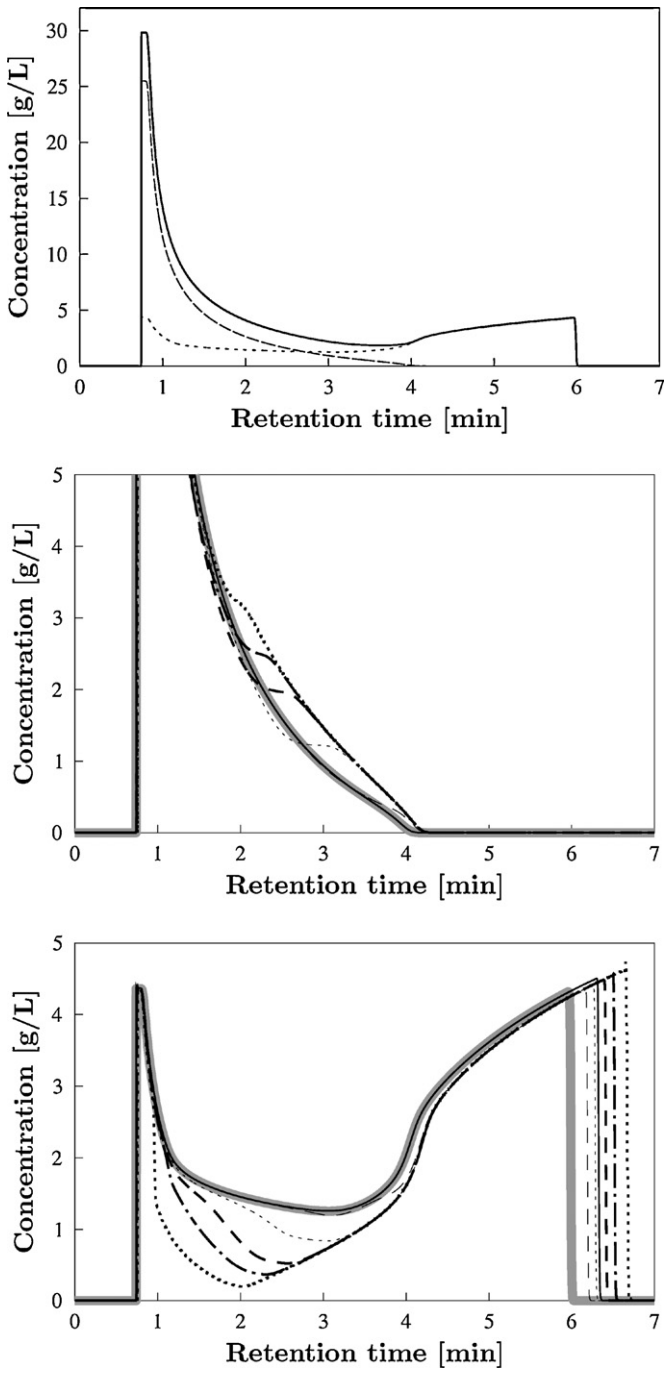

Fig. 6. Chromatogram of two competing compounds with Langmuir (dashed line) and BET (dotted line) isotherms calculated by Martin-Synge method (top), the peak profile of the compound having Langmuir isotherm (middle), and that of the compound with BET isotherm (bottom) calculated by OCFE (black lines, see later) and Martin-Synge (thick gray line) methods. Injected concentration: 25, injection time: 0.05 min, isotherm parameters: qs_A = 150 g/L, qs_B = 150 g/L, bs_A = 0.28 L/g, bs_B = 0.25 L/g, bl_B = 0.10 L/g, number of theoretical plates: 1000, number of subdomains: 100 (black dotted line), 150 (black dot-dashed line), 200 (black dashed line), 300 (thin black dotted line), 500 (thin black dot-dashed line), and 1000 (black solid line). For all the remaining parameters see Fig. 2.

and experiencing competitive behavior under nonlinear conditions. The peaks calculated with the OFCE and the Martin-Synge methods differ significantly, especially for the compound with the BET isotherm. As the number of subdomains increases from 10% to 100% of the number of theoretical plates, the results of the OCFE calculations converge toward the results of the Martin-Synge method. Finally, the peak profiles of the compound having a Langmuir isotherm calculated by the two methods match each other perfectly well. However, in the case of the other compound (BET isotherm) a perfect match could not be reached since the area of this compound increases significantly with increasing number of subdomains. Table 1 reports the peak areas of the two compounds calculated by the OCFE method with different numbers of subdomains. It shows clearly how the peak area of the compound having a Langmuir isotherm remains stable and accurate while that of the other compound increases by 11% when the number of subdomains is increased from 100 to 1000. In contrast, the areas of both peaks calculated with the Martin-Synge method were constant. It must be mentioned, that the OCFE method with three internal collocation points could not calculate the chromatograms under the experimental conditions selected for Fig. 4. This chromatogram could be calculated only after increasing of the number of collocation points in the subdomains or manipulating the distribution of the subdomain sizes. Whenever the peak area for the second component increases with increasing number of subdomains, it means that the OCFE method is failing.

Table 1
Peak area of two competing compounds calculated by OCFE method at different number of subdomains (N.o. SD). For details, see Fig. 6.

N.o. SD	Langmuir	BET
100	12.50	12.54
150	12.50	12.57
200	12.50	12.61
300	12.50	12.70
500	12.50	12.94
1000	12.50	13.97

The unexpected behavior of the OCFE method when it is used to calculate elution band profiles for compounds having BET isotherms is related to the problems of fulfilling the mass balance at the column inlet for concentrations greater than the critical concentration. The classical OCFE cannot handle physical conditions under which the surface concentration cannot increase to infinity for a finite solute mass introduced into the column. It seems that coupling the OCFE method with a procedure that would control the mass balance at the column inlet ought to improve the efficiency of the OCFE method. This complex mathematical problem is, however, out of the scope of this paper.

The OCFE and the Martin-Synge algorithms were compared in the case of low efficiency columns (N = 100). The results were almost identical, since only a negligible difference could be observed between the two chromatograms. The source of this slight difference was that the boundary conditions implemented in the two methods were slightly different. The Danckwerts condition is used in the Chromatographic Column software while the Martin-Synge algorithm uses open-open boundary conditions. The choice of the different boundary conditions can cause slight differences in the first and second moments of the peaks if N is really small (see Chapter 6.2 of Ref. [3]). However, for practical values of N, the differences caused by the use of different boundary conditions is unobservable. Results comparing the Martin-Synge and the OCFE algorithms in the case of N = 100 are not presented here.

In conclusion, even though the OCFE method is generally robust and accurate, it can fail for isotherm models for which the surface concentration can, at least in theory, increase to infinity. At the same time the Martin-Synge algorithm can solve easily, quickly, and accurately such type of problems.

4.4. The Inverse method of isotherm determination

The Martin-Synge algorithm can be used for the calculation of the isotherm parameters of a compound by the inverse method

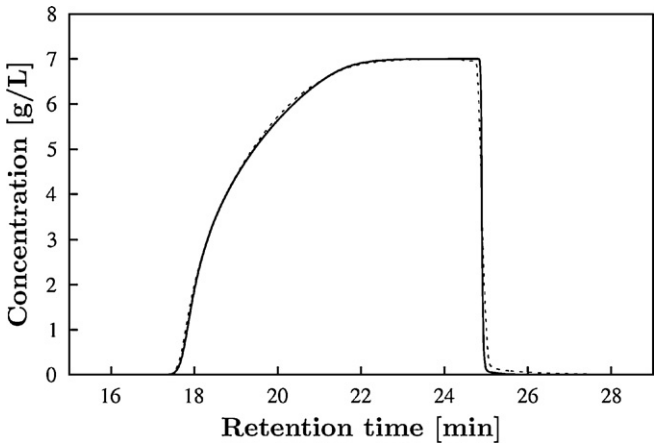

Fig. 7. Overloaded band profile of butyl benzoate for the determination of isotherm parameters by inverse method (dotted line). The solid line represents the resulting band profile of fitting by inverse method. Solute concentration: 7 g/L, 6 min wide rectangular injection.

[34], in the same way as the Rouchon, the Craig or the OFCE methods were used successfully [35–38]. The inverse method requires (1) the record of at least one overloaded band profile of the compound injected, preferably one at modest, the other at the highest possible concentration.; (2) the transformation, by suitable calibration of the recorded signal into a total concentration profile; (3) a program that determines the best values of the parameters of an isotherm model by minimizing the difference between the calculated and the experimental profiles. Fig. 7 shows such an overloaded band profile for butyl benzoate. The injected concentration was 7 g/L, equal to the solubility of butyl benzoate in the eluent used (for more details on the experimental conditions, see Experimental section). The coefficients of the BET isotherm [Eq. (20)] determined by the inverse method are the following: qs = 198.7 g/L, bs = 0.0842 L/g, bl = 0.0395 L/g. Fig. 7 compares calculated and recorded profiles and illustrates the remarkable agreement. Note, that the values found in this work are close to those determined by Gritti et al. [39] for the same compound in the same system (qs = 164.1 g/L, bs = 0.098 L/g, bl = 0.0396 L/g). Considering that the authors used a different column and recorded the chromatogram at a different temperature, the differences between the numerical values of the coefficients are negligible.

Using the isotherm parameters, the elution band profiles of butyl benzoate were calculated for different injection profiles. The results are summarized in Figs. 8–10. Even if two of the injection profiles

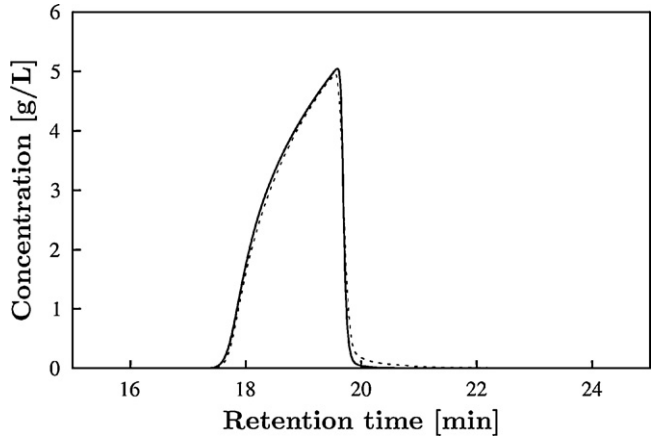

Fig. 8. Measured (dotted line) and calculated (solid line) elution profile of butyl benzoate. Solute concentration: 7 g/L, injection time: 1 min.

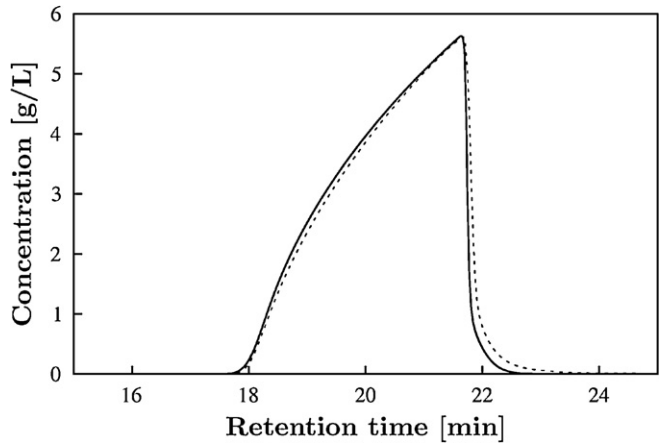

Fig. 9. Measured (dotted line) and calculated (solid line) elution profile of butyl benzoate. Triangle injection: 0 to 7 g/L from 0 to 2 min, then 7 to 0 g/L from 2 to 4 min.

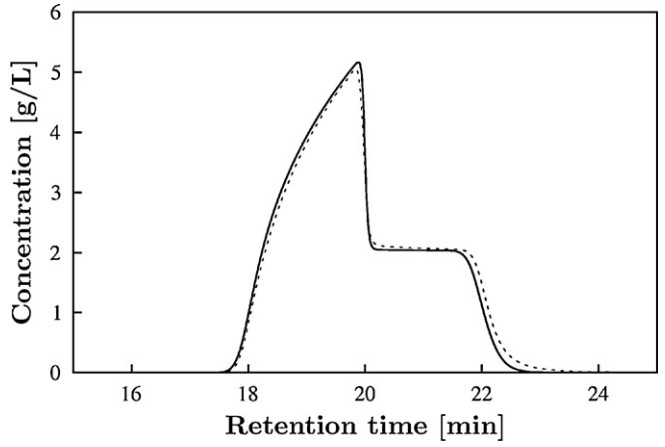

Fig. 10. Measured (dotted line) and calculated (solid line) elution profile of butyl benzoate. Injection: 0 to 3.5 g/L from 0 to 0.25 min, 7 g/L from 0.25 to 1 min, 2.1 g/L from 1 to 4 min.

do not have any practical importance, they can be used for a fair test of whether isotherms determined by the inverse method properly describe solute retention. It can be concluded that the peak profiles calculated with the isotherm obtained by the inverse method provide satisfactory estimates of the shape and the position of the band of butyl benzoate.

5. Conclusions

The results of our work confirm the usefulness of an alternative method for the calculation of numerical solutions of the equilibrium-dispersive model. The Martin-Synge algorithm is robust and fast; it permits the successful calculations of the elution band profiles of single compounds and of mixtures of several components having different types of isotherms, particularly complex isotherms. Although, several different algorithms are available to solve the ED model, such as the Rouchon and the OCFE algorithms, the Martin-Synge method that we have developed is a favorable alternative to these other methods, due to its robustness, its accuracy and its speed of calculations.

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Appendix A.

The algorithm developed for the solution of the mass balance equation (Fig. 1) can be implemented easily in the software Mathematica (Wolfram Research). For example, in the case of a binary mixture, with both compounds having Langmuir isotherms, the solution is written as:

```
qA[t_] := (qsA bsA cA[t])/(1 + bsA cA[t] + bsB cB[t])
qB[t_] := (qsB bsB cB[t])/(1 + bsA cA[t] + bsB cB[t])
c0A[t_] := cinjA UnitStep[t] UnitStep[-t + tinj]
c0B[t_] := cinjB UnitStep[t] UnitStep[-t + tinj]
Do[
  sol = NDSolve[{cA'[t] + f qA'[t] + u (cA[t] - c0A[t])/dz == 0,
  cB'[t] + f qB'[t] + u0 (cB[t] - c0B[t])/dz == 0,
  cA[0] == 0, cB[0] == 0}, {cA,cB}, {t, 0, tmax},
  WorkingPrecision ->12, PrecisionGoal ->10, AccuracyGoal ->10,
  MaxSteps ->Infinity];
  c0A[t_] := Evaluate[cA[t]/.sol],
  c0B[t_] := Evaluate[cB[t]/.sol],
  {i, 1, n}]
```

After defining the phase ratio (f), the linear velocity (u), the isotherm parameters (qsA, qsB, bsA, bsB), the injection duration (tinj) and its concentration (cinjA, cinjB), the height of a theoretical plate (dz), the time of calculation (tmax), and the number of theoretical plates (n), this code can be run in Mathematica (it was tested with ver. 6 and 7). The resulting peak profiles (c0A[t] and c0B[t]) are then plotted, integrated, and analyzed in any way desired. The numerical error of the calculation can be decreased or increased with the WorkingPrecision, PrecisionGoal, AccuracyGoal options. Due to the ODE solver algorithms being implemented in Mathematica, it is possible that in the case when competitive isotherms are needed, the initial concentration of the compounds (cA[0], cB[0]) must be set at a value larger than zero (e.g. 10^{-30}). We also need to mention that the solution of the mass balance equation with Mathematica is very time consuming in multicomponent cases.

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