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Selection of competitive adsorption model for modelling displacement chromatography

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ABSTRACT

The influence of the model used to describe the basic competitive interactions between a stationary phase and migrating solutes was investigated to simulate reversed-phase displacement chromatography. Experimental separations of catechol–resorcinol mixtures using phenol as the displacer were compared with numerical simulations. The competitive Langmuir model, the LeVan–Vermeulen model and the quadratic model were chosen to describe the competitive adsorption equilibria. These models were related either to their non-competitive parameters or to their competitive parameters. A novel simplified experimental procedure is proposed to obtain competitive parameters for a binary mixture. The chromatographic process is described by the equilibrium-dispersive model and the calculations were performed by using a finite difference method. The results demonstrated that competitive isotherm equations with numerically fitted parameters do not lead to a good description of a displacement separation process. On the other hand, the LeVan–Vermeulen isotherm, with non-competitive Langmuir parameters, was found to be a relevant choice to the experimental conditions involved.

INTRODUCTION

Rapid and economical preparative separations of biochemical components from complex mixtures are nowadays an important challenge in the pharmaceutical and biotechnological industries. Among all the available techniques to achieve this goal, preparative liquid chromatography has proved to be an effective and promising tool. However, this technique has to be considered as completely different from the uncertain semi-empirical extrapolation of the chromatographic results. Regarded as a science in its own right, this preparative technique appears to be a difficult-to-design means of purification. Therefore, numerical modelling is a useful tool to help in understanding it. This strategy has reduced the use of experimentation where too many parameters impede an easy and correct interpretation. Besides an accurate theoretical knowledge, numerical modelling will lead to a better use of chromatographic columns, resulting in marked increases in productivity and yield [1].

All the physical phenomena encountered in chromatographic separation may be classified into two categories: the transient flow of solutes in granular media and the basic thermodynamic interactions between these migrating solutes and the stationary phase. The modelling of the former has long been the subject of many studies (for a review, see ref. 2). Different ways are proposed for describing the fluid flowing through the porous media, and the models vary from the simplest, such as the equilibrium-dispersive model, to very sophisticated, involving external and internal mass transfer resistances, radial velocity profiles, etc. Most of these models, combined with robust numerical algorithms, have proved to be very efficient tools for the

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design of most chromatographic bioseparations in downstream processing. However, they remain useless unless they are fed with the appropriate equations describing the equilibria between the solutes and the stationary phase. This description, especially in the high concentration range, suffers from a lack of a theoretical basis, as it has not been extensively studied [3].

At high product concentrations, these basic interactions are very non-linear owing to the saturation of the support and to the concept of competition for adsorption sites that derives from it. This non-linearity and these competition effects may be of crucial importance and their influence in the modelling of the chromatographic process may exceed greatly any one of the other physical phenomena, such as the mass transfer resistances, especially when using modern HPLC columns, which are expected to be very efficient. This is why the correct choice of a model accounting for these basic interactions, even coupled with a rather simple description of the chromatographic process, deserves special attention. This tendency is nowadays observed in the scientific literature where the use of the well known competitive Langmuir isotherm appears unsuitable in too many situations [4].

As already stated in a previous paper [3], some workers have attempted to account for these various non-linear phenomena and have presented new models or adaptations of older concepts. We must emphasize, however, that only a few studies have dealt with the performances of these descriptions, especially when considering their use in dynamic simulations of a given chromatographic process. We shall consider, for instance, the work of Golshan-Shirazi *et al.* [5] and that of Jacobson *et al.* [6], but these two studies were restricted to the simulation of the elution mode in mass overload conditions.

In this paper, our purpose is to point out the difficulty of selecting a model for competitive adsorption equilibria to describe reversed-phase preparative separations. To illustrate this we chose the displacement process. This chromatographic mode was defined by Tiselius as early as 1943 [7], then fell into disuse till Horváth [8] reintroduced it in the 1980s. This is an efficient separation method that involves to a great extent all the competition phenomena for adsorption sites and therefore constitutes a good field of experimentation for testing competitive equilibria modelling. Few previous studies have undertaken the same approach but the studies by Frenz and Horváth [9] and Katti and Guiochon [10] should be mentioned.

In this study we considered an academic case, that is, the separation of common compounds such as resorcinol and catechol using phenol as the displacer. This experimental work was stimulated by that of Frenz and Horváth [9]. Three models of competitive adsorption, *i.e.*, the classical competitive Langmuir isotherm, the LeVan–Vermeulen isotherm and the quadratic isotherm, were considered and compared on the basis of either their own theoretical foundation or the choice of their parameters.

DISPLACEMENT CHROMATOGRAPHY

An outline of the principle of this chromatographic mode is necessary for familiarization with its characteristic aspects that differ from those of isocratic preparative elution. The general article by Horváth [8] covers relevant historical, experimental and theoretical studies related to this subject.

Before carrying out the separation, the chromatographic column is first equilibrated with a carrier whose affinity for the stationary phase is negligible. The mixture containing the products to be separated is then introduced, immediately followed by the feed of a solution containing the displacer. This latter is chosen in such a way that it presents an affinity for the stationary phase higher than that of the components to be separated.

When the feed mixture is introduced, a first separation process occurs in the frontal mode. Then, owing to the action of the following displacer and to competition phenomena, the components organize themselves into separated zones. Under appropriate conditions, a steady state is achieved: the components migrate, in a purified and sometimes concentrated state, at a fixed and identical velocity in the form of adjacent square waves (isotachic displacement). Fi-

nally, each component leaves the column in an order imposed by its respective affinity for the stationary phase. When all the components have been collected, the displacer must be desorbed and the column re-equilibrated with the carrier.

MODELLING SINGLE-COMPONENT ADSORPTION EQUILIBRIA

Adsorption isotherm

The amount of product adsorbed at equilibrium, per unit mass or volume of adsorbent, is essentially dependent on the concentration of this product itself in the mobile phase. This function, termed here a single-component adsorption isotherm, is the mathematical expression describing quantitatively, at a constant temperature, the relationship between these two quantities. When several components are present, interference and competition phenomena for adsorption sites occur and lead to a more complex mathematical formulation of the equilibrium. Therefore, these isotherms, termed here competitive isotherms, attempt to express relationships between the amount of one component adsorbed and the concentrations of all other constituents, either in solution or already adsorbed.

Langmuir isotherm

The simplest theoretical model and the most widely used in liquid chromatography was first developed by Langmuir [11]. It describes the adsorption of one component adsorbed as a monolayer. It was originally derived from simple kinetic considerations of gas or vapour adsorption phenomena. It may also be obtained by thermodynamic considerations that additionally lead to a more precise definition of its characteristic constants [12]. Its basic hypotheses are as follows: molecules are adsorbed on a fixed number of well localized sites; each site may accept only one molecule in such a way that they form a monolayer; all sites are energetically equivalent; there is no interaction between adsorbed molecules; and local equilibrium is assumed between the liquid phase and the support, with the equation

$$q = \frac{aC}{1 + bC} \tag{1}$$

where a and b are characteristic constants and C and q are the liquid phase and adsorbed product concentrations, respectively.

Bi-Langmuir isotherm

As indicated previously, the Langmuir adsorption isotherm is very simple, and its basic hypotheses stress its limitations. As a consequence, it may be unsuitable, especially when energetic heterogeneity of sites is present [12]. To complete the description of adsorption phenomena by taking into account the occurrence of two categories of independent and non-cooperative sites, the bi-Langmuir isotherm was derived [13–15]. This frequently used model [16–18] is expressed as follows:

$$q = \frac{aC}{1 + bC} + \frac{dC}{1 + eC} \tag{2}$$

where a, b, d and e are constants obtained by parametric identification.

MODELLING MULTI-COMPONENT ADSORPTION EQUILIBRIA

Description of the problem

The modelling of preparative separations does not simply require the precise knowledge of the specific interactions occurring between each of the encountered components and the chromatographic stationary phase. The more or less accurate understanding of the competitive equilibria involved between these mixed components and the adsorption sites is also of major importance. Numerous, and often complicated, the models have attempted to give a mathematical description of these interference and competition phenomena [3]. In addition to the arduous theoretical problems raised by this understanding of the different thermodynamic mechanisms, we would point out the difficulty in obtaining experimentally the numerical parameters of these theoretical models elaborated more or less rigorously. Among all the proposed models described in the literature, we have chosen three of them, because of the simplicity of their equations, of

their theoretical development, whose validity is suited to the experimental conditions we shall consider in our study, and also because of their widespread use. These three models are the competitive Langmuir isotherm, the quadratic isotherm and the LeVan–Vermeulen isotherm.

It is worth noting that these three competitive models have the advantage of being related either to the parameters of the individual Langmuir isotherms of each component or to correcting factors associated with the non-competitive Langmuir isotherm parameters. Within the framework of this study, we shall also consider these models as empirical equations in which all coefficients, without exception, will be obtained by parametric identification from experimental competitive adsorption data.

Competitive Langmuir isotherm

The extension of the basic Langmuir model [11] to the description of competitive adsorption phenomena was first proposed by Schwab [19], Butler and Ockrent [20] and Markham and Benton [21]. This modified model is based on the same hypotheses as for the initial one and is formulated as follows:

$$q_i = \frac{a_i C_i}{1 + \sum_{j=1}^{M} b_j C_j} \tag{3}$$

where a_i and b_i are drawn from the corresponding single Langmuir isotherms and M is the total number of components.

Quadratic isotherm

From statistical thermodynamic considerations, it has been shown that competitive adsorption isotherms may be formulated as the ratio of two polynomials of the same degree [22]. The competitive Langmuir isotherm is, for instance, the ratio of two polynomials of degree one. Better accuracy is expected when using two polynomials of degree two. Lin *et al.* [22], Zhu *et al.* [4] and Poppe [23] have used this type of isotherm, termed quadratic isotherms.

This competitive model modifies the Langmuir isotherm by assuming that the adsorption and desorption rates of each component are linear functions of the adsorbed solute and of the dissolved solute concentrations, respectively. This assumption enables one to account for molecular interactions in the two phases [22]. This isotherm is expressed here for two components:

$$q_1 = \frac{a_1 C_1 + a_{12} C_1 C_2}{1 + b_1 C_1 + b_2 C_2 + b_{12} C_1 C_2} \tag{4a}$$

$$q_2 = \frac{a_2 C_2 + a_{21} C_1 C_2}{1 + b_1 C_1 + b_2 C_2 + b_{21} C_1 C_2} \tag{4b}$$

where only the a_i and b_i are obtained from single-component Langmuir isotherms. The other parameters are correction terms.

LeVan–Vermeulen isotherm

We have also considered the use of a model based on rigorous theoretical considerations. This LeVan–Vermeulen model is derived from the I.A.S. theory (ideal adsorbed solution) and predicts in a non-intuitive manner the equilibrium relationships of solute mixtures only from data derived from single adsorption isotherms.

The I.A.S. theory, first developed by Myers and Prausnitz [24] for gaseous mixtures, is a very elaborate theory, based, as for the Langmuir model, on the concept of ideal behaviour of components in both the mobile and stationary phases. The theory has been extended to liquid–solid equilibria and applied by Radke and Prausnitz [25], Jossens *et al.* [26] and Fritz and Schluender [27]. The results may be very satisfactory in certain cases but, as emphasized by McKay and Duri [28], the mathematical complexity of the procedure, especially for more than two-component mixtures, has restricted its use among workers. Nevertheless, it must be mentioned that Golshan-Shirazi *et al.* [5] and Golshan-Shirazi and Guiochon [29] have to some extent re-established this theory by using in their numerical simulations the LeVan–Vermeulen isotherm [30], which is perhaps the simplest isotherm derived from the I.A.S. theory. Antia and Horváth [31] have also used this model to study in displacement chromatography the isotachic behaviour of components exhibiting single crossing isotherms.

The LeVan–Vermeulen model, derived from the Langmuir isotherm, has been considered in our simulations of displacement chromatography. In the case of a three-component mixture, it is written as follows:

$$q_i = \frac{b_i q_s C_i}{1 + \sum_{j=1}^{3} b_i C_i} + C_i \cdot \frac{\partial q_s}{\partial C_i} \ln\left(1 + \sum_{j=1}^{3} b_i C_i\right) \quad (5)$$

When the saturation capacities are different for each component, and when considering the two-term expansion of the LeVan–Vermeulen isotherm, always derived from the Langmuir model, q_s represents the following function [5]:

$$q_s = \frac{\sum_{j=1}^{3} q_{s,i} b_i C_i}{\sum_{j=1}^{3} b_i C_i} \quad (6)$$

where $q_{s,i} = (a_i/b_i)$ is the specific saturation capacity of the column with respect to solute i, and where the a_i and b_i are the single-component Langmuir isotherm parameters.

NUMERICAL MODEL

Within the framework of this study, we chose to use the equilibrium-dispersive model based on continuity equations whose numerical solution is achieved by the R.G.S. method (from the name of its authors, Rouchon and Golshan-Shirazi), which is a particular finite difference algorithm, used in numerous studies [32,33]. The simulation program was written in FORTRAN. A description of the model and its numerical solution have been presented previously [34].

EXPERIMENTAL

Chemicals

Catechol was purchased from Sigma (St. Louis, MO, USA) and resorcinol from Fluka (Buchs, Switzerland). Other chemicals [phenol (Rectapur), methanol (Normapur), orthophosphoric acid (Rectapur) and carbon tetrachloride and triethylamine (for HPLC analysis)] were purchased from Prolabo (Paris, France). Ultrapure water was obtained with a Milli-Q reagent water system (Millipore, Bedford, MA, USA).

Columns

Two 5-μm Nucleosil C_{18} columns (250 × 4.6 mm I.D.) (Touzart et Matignon, Vitry sur Seine, France) were used. Frontal analysis and displacement chromatographic separations were performed with the same column to ensure reliable equilibrium data characterizing the column and the chemicals. Conventionally, a microcolumn is used to obtain equilibrium data, in order to avoid excessive product consumption, but may lead to errors when actual separations are carried out and simulated in a larger column, with of course a similar stationary phase [5]. The uncertain column-to-column reproducibility may be prejudicial to simulation accuracy. HPLC analysis of the collected fractions was performed with the other column.

The column efficiency may be estimated from the Knox equation [35]:

$$h = \frac{2}{v} + v^{1/3} + \frac{v}{10} \quad (7)$$

where h is the reduced plate height ($h = H/d_p$) and v is the reduced mobile phase velocity ($v = ud_p/D_m$), d_p being the average particle diameter and D_m the molecular diffusion coefficient of the product considered; u will be taken as equal to 0.028 cm/s for frontal analysis and displacement separations and a similar diffusion coefficient (equal to 10^{-5} cm^2/s) was taken for all the small organic compounds studied in this work.

The reduced mobile phase velocity is then equal to 1.4, which corresponds to nearly 0.5 times the theoretical optimum value of this velocity ($v_{opt} = 2.71$) leading to the smallest H for the operating conditions under consideration. In this case the calculated H value is 14 μm for all products, which gives a number of theoretical plates for the column of 17 850. This corresponds to 71 420 theoretical plates per meter and indicates the very high efficiency of these columns. The columns were also experimentally tested for their efficiency by elution chromatography, and yielded the same good results.

Apparatus

A schematic diagram of the experimental apparatus used for frontal analysis and displacement separations is presented in Fig. 1. This set-up is based directly on that one of Jacobson *et al.* [36] used for measurements of competitive isotherms. It consists of a Model 420 HPLC pump (Kontron, Zurich, Switzerland) equipped with a micro-head allowing flow-rates as low as 10 μl/min. This pump was connected to an injection system composed of two sampling valves (Model 7010; Rheodyne, Cotati, CA, USA). Tubing to the two valves was fitted in such a way as to avoid significant dead volumes. The two Rheodyne loop volumes were adjusted from 5 to 10 ml by substitution. The valves were connected to the Nucleosil C_{18} column (250 × 4.6 mm I.D.) described earlier. The column effluent was monitored by a differential refractometer and its signal was recorded and processed by a data acquisition software (BOREAL; Prolabo, Paris, France). The column temperature was controlled in an oven (Sup-R5, Stabitherm; Prolabo).

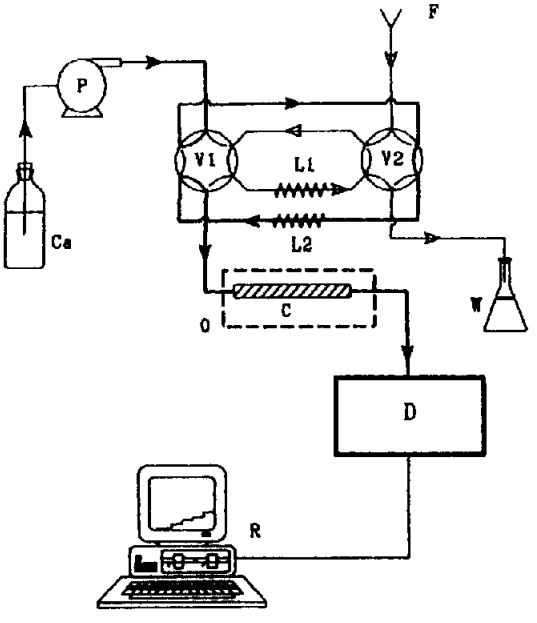

Fig. 1. Schematic diagram of the apparatus used either to perform displacement separations or to measure single-component and competitive isotherms by frontal chromatography. C = Adsorption column; Ca = carrier; D = detector; F = feed load; L1, L2 = stainless-steel sample loops; O = oven; P = pump; R = recorder; V1, V2 = sampling valves; W = waste.

Measurement of hold-up volumes

The hold-up or dead volume of the tubing (without the column) was calculated from tracer experiments, to be 0.160 ml for our set-up (Fig. 1).

The dead volume of the column itself was measured by the gravimetric method, first suggested by Riedo and Kováts [37] and used by Jacobson *et al.* [6], Frenz and Horváth [9] and Huang and Horváth [38]. With water as the carrier, the use of this method is relevant [39]. The measured hold-up volume (V_{Φ_m}) was then equal to 2.949 ml, which led to a total porosity (ε) of the column equal to 0.71.

Frontal analysis

Frontal analysis was carried out on the experimental unit shown in Fig. 1. This method was chosen as the best practical approach to obtain the single-component isotherms for resorcinol, catechol and phenol and also for the resorcinol–catechol competitive isotherm. Because of the size of the column, consumption of products is not negligible and could be a major drawback in certain situations [6].

For single-component isotherm measurement, the procedure was as follows [38]. The column was first equilibrated at 30°C with degassed ultrapure water as the mobile phase. The room temperature was also maintained at 30°C so as to allow thermally equilibrated products to be injected. The flow-rate was 0.200 ml/min. The switching valves were arranged in such a way that the mobile phase flowed through the second injection loop (circuit in thick lines in Fig. 1) while the first loop being filled, with a syringe, with a solution of the lowest product concentration. After the column had been equilibrated, the two Rheodyne valves were manually switched to apply, at the column entrance, the concentration step of the solution contained in the first loop. Frontal analysis then occurred, while the second loop was filled with a solution of product of a higher concentration than the first injected solution. When the signal of the first step was detected at the column outlet, the two

valves were rotated again. This procedure allows gradual saturation of the column with solutions of increasing concentration, sequentially introduced into the column. Finally, after the last step had been monitored, the column was washed with methanol–water mixture (50:50) and then re-equilibrated with the neat mobile phase for other measurements.

Adsorption isotherms were then calculated from the typical curve showing successive steps that have been monitored and by using a simple and accurate method based on mass balance, proposed by Jacobson *et al.* [6] and termed M.M.B. (method of mass balance). The concentration of the adsorbed compound on the stationary phase, q_i, in equilibrium with its mobile phase concentration was calculated with the following relationship:

$$q_i = [(C_i - C_{i-1})(V_{r,i} - V_D)/V_{\Phi_s}] + q_{i-1} \quad (8)$$

where C_{i-1} and C_i are the mobile phase concentrations of component i at the beginning and the end of the frontal development respectively, and q_{i-1} and q_i are the adsorbed phase concentration in equilibrium with C_{i-1} and C_i, respectively. $V_{r,i}$ is the retention volume of the concentration step corresponding to C_i, V_D is the system dead volume and V_{Φ_s} is the volume of stationary phase [38].

For competitive isotherm measurement, it is customary to operate frontal analysis in the same way as described above, by injecting mixtures of increasing concentration, with differing ratios between the various components [4,36,40–42]. Several methods are then possible for processing the results [41], but all of them require either very accurate HPLC analyses of each component concentration in all the steps, or the handling of the arduous theory of Helfferich and Klein [43].

Within the scope of this work we propose a different experimental procedure, restricted to binary mixtures. In this method, only one concentration step of the binary mixture is injected at the column entrance. During their migration, the two solutes will classify themselves as a function of their affinity for the stationary phase. Two transitions are then observed. The first is constituted by the less retained component, in a pure state, and the second by the initial mixture. After washing and re-equilibration of the column, the experiment is repeated with binary mixtures of different product ratios. Then only the monitoring of the column effluent is required to obtain the breakthrough volumes of each step.

The novelty of our approach lies in the fact that the concentration of the first step is no longer measured by HPLC but is simply estimated by the following reasoning: if the formation of the first plateau is considered to be very rapid (with regard to the total time of the frontal analysis) we may assume, for this first plateau, constituted by the pure, less retained component, that we are dealing with a simple frontal analysis of a single component. The knowledge of the single isotherm of this component, the column length and the residence time of this plateau allows a very simple determination of the concentration of this plateau to be made. By referring to the papers by Ma and Guiochon [42,44], our procedure is justified for two reasons: first, our column is characterized by a very high efficiency, and therefore may be not so different from an ideal one; and second, from Ma and Guiochon's work, the time needed for the formation and stabilization of the first front has been estimated as less than 4% of the total duration of the analysis.

Finally, our method, based only on the M.M.B. and simple experiments, may be of great interest as it can be applied to any binary system for which frontal chromatographic data can be obtained. Therefore, it is not restricted to systems whose single components exhibit Langmuir adsorption behaviour.

Displacement experiments

The set-up in Fig. 1 was also used to effect displacement separations. As mentioned previously, the column was first equilibrated with the carrier (degassed pure water). The column temperature was maintained at 30°C and the flow-rate was 0.200 ml/min. The resorcinol–catechol mixture that filled the second loop was then introduced into the column by rotating the two Rheodyne valves. After the desired volume of feed had flowed into the column, the displacing solution (phenol) contained in the first loop was

pumped to the column entrance by re-switching the two valves. Fractions of 100 μl were then manually collected throughout the emergence of the feed components. For all these experiments, the injection time of the feed containing resorcinol and catechol was 120 s. The displacer was 80 g/l of phenol in pure water, and four different mixtures corresponding to 40, 50, 60 and 70 g/l each of catechol and resorcinol were injected.

Analysis of collected fractions

Fractions collected during the displacement chromatographic runs were analysed by isocratic HPLC. First, each fraction was diluted sixfold and analysed on the previously described Nucleosil C_{18} column. The pump and the oven were the same as those used for the displacement experiments. A conventional Model 7125 sampling valve (Rheodyne) with a 20-μl sample loop was used to inject the diluted samples. The column effluent was monitored at 290 nm with a UV detector (Model 481; Waters, Milford, MA, USA). The signal was recorded by the BOREAL software already mentioned.

The temperature was 50°C and the flow-rate 0.800 ml/min. The mobile phase consisted of 10% (v/v) methanol, 0.5% orthophosphoric acid and 0.5% triethylamine in ultra-pure water [9]. This eluent was sonicated with a Vibra cell (Bioblock Scientifics, Illkirch, France).

RESULTS AND DISCUSSION

Displacement operating conditions

Experimental determination of single-component isotherms of each product (resorcinol, catechol and phenol) is justified for many reasons. First, this preliminary study allows one to characterize the kind of interaction each product has with the stationary phase and indicates the best suited model to its mathematical description. As we shall see later, this will be of major importance in the case of phenol. Second, this study allows the determination of the appropriate operating conditions for a displacement to occur and concentrations for separated products, in the case of an ideal displacement, to be predicted. Finally, this will make it possible to evaluate the error made when modelling displacement separations with single-component isotherm parameters, an evaluation that has seldom been reported in the literature.

Fig. 2 shows the single-component adsorption isotherms of resorcinol, catechol and phenol for a wide range of concentration. These curves are concave towards the abscissa; this is a necessary condition for carrying out a displacement separation, as stated by Hagdahl *et al.* [45] and Tiselius [7].

The choice of the displacer and its operating concentration is one of the most critical design parameters for obtaining a good separation efficiency. As expected [9], phenol is an adequate displacer, because its adsorption isotherm overlies the isotherms of all feed components to be displaced. An 80 g/l phenol concentration allows the operating line to intersect all the feed single-component isotherms, and thus permits a separation to occur.

Single-component isotherm

Our experimental results show that adsorption of catechol and resorcinol is perfectly well described by the Langmuir model. Concerning the adsorption of phenol, several models have been

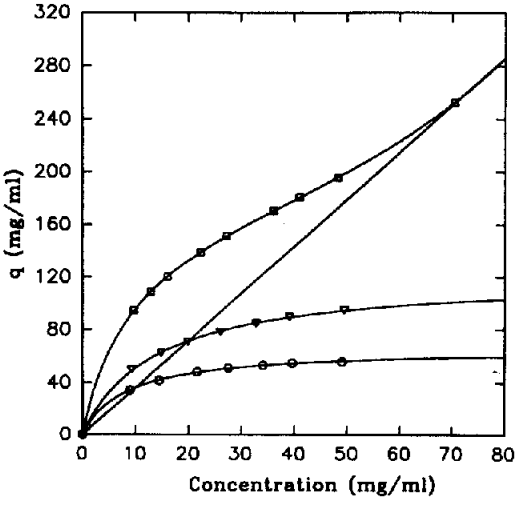

Fig. 2. Operating line for an 80 g/l phenol concentration and single adsorption isotherms for (○) resorcinol, (▽) catechol and (□) phenol measured on a 5-μm Nucleosil C_{18} column (250 × 4.6 mm I.D.) at 30°C; mobile phase, water, flow-rate, 0.2 ml/min.

TABLE I

NON-COMPETITIVE LANGMUIR ISOTHERM PARAMETERS FOR RESORCINOL AND CATECHOL

The mean relative error is the sum of the relative differences between the calculated and the experimental concentrations divided by the number of data.

Product	a	b (l/g)	$q_{s,i}$ (g/l)	k'_i	Mean relative error (%)
Resorcinol	7.937	0.120	66.08	10.45	0.69
Catechol	8.810	0.073	120.68	11.90	0.66

tested, the Langmuir, the bi-Langmuir, the Freundlich and the Langmuir–Freundlich models; it appeared that the bi-Langmuir isotherm gave the best fit. The values derived for the isotherm parameters of each product are summarized in Tables I and II. A few comments about these results are of great interest for analysing precisely the adsorption behaviour of each product.

First, considering phenol, it could be considered surprising to obtain a negative value for the parameter e in the bi-Langmuir model (see eqn. 2). This coefficient is theoretically the ratio of the adsorption rate constant to the desorption rate constant of the component concerned on one category of sites on the stationary phase. Nevertheless, when operating parametric identification on the experimental curve, two distinct phenomena, the gradual saturation of the stationary phase and solute–solute interactions between adsorbed solutes, are included in this numerical e Langmuir parameter [3]. In our case, and considering the second category of adsorption sites, we note that the complexity of the system encountered cannot be correctly, *e.g.*, physically, described by this second term of the bi-Langmuir isotherm. When fitting the experimental adsorption data of another compound, *i.e.*, 2-phenylethanol, to the bi-Langmuir model, Fallah and Guiochon [46] encountered the same problems, and preferred to use a linear function associated with the Langmuir model instead of two Langmuir equations. They specified that actually, because of the lack of physico-chemical measurements, no adequate explanation can account for such behaviour where a column seems to have an infinite saturation capacity.

TABLE II

NON-COMPETITIVE BI-LANGMUIR ISOTHERM PARAMETERS FOR PHENOL

Parameter	Value
a_3	18.218
b_3 (l/g)	0.108
d_3	0.7613
e_3 (l/g)	−0.0069
Mean relative error (%)	0.15

Nevertheless, we shall assume, in the concentration range under study, that the adsorption of phenol is well described by a "bi-Langmuir" model where the adsorption on the first category of sites is very well accounted for by a Langmuir isotherm and where the adsorption on the second category of sites is only numerically described by an empirical fitted function. This hypothesis, even though open to criticism, will not handicap our conclusions on separation modelling, as we shall see further, and will be of great use in handling our simulations.

Concerning now resorcinol and catechol, we have compared their respective retention factors (k'_i), obtained from either analytical elution experiments, and the Langmuir model:

$$k'_i = \frac{t_R - t_{R_0}}{t_{R_0}} = F \cdot \frac{\partial q_i}{\partial C_i} = Fa_i \qquad (9)$$

where F is the phase ratio and a_i the coefficient of the Langmuir isotherm that represents its slope at the origin. t_{R_0} is the residence time of an unretained component and t_R the retention time of the studied product under analytical conditions.

We have observed, as was done by Frenz and Horváth [9] and Golshan-Shirazi *et al.* [5], that the Langmuir model always underestimates this retention factor (see Table I). For these solutes in the low concentration range, Frenz and Horváth [9] came to the conclusion that the adsorption behaviour was more complex than

that given by the Langmuir isotherm. Nevertheless, the Langmuir isotherm describes very well the adsorption of the desired components in the high concentration range, which is of much greater interest when considering the simulation of a separation process based on the non-linearity of solute adsorption isotherms.

Competitive isotherms related to the individual isotherm parameters

For the sake of simplicity, when considering the modelling of displacement separations, or other preparative separation modes, it seems very attractive to use the non-competitive parameters from the single-component isotherms, more especially as the classical description we obtained for these single-component adsorptions (Langmuir or bi-Langmuir isotherms) allows us to choose two models which are easy to handle, the competitive Langmuir and the LeVan–Vermeulen isotherms.

As we have seen in the previous section, phenol is adsorbed on two categories of sites. We have assumed that only the first category of sites, which is well described by the Langmuir model (coefficients a and b in eqn. 2), is subject to competitive adsorption with resorcinol and catechol, while phenol is adsorbed alone on the second category of sites, this adsorption being described by the second term in the equation of the bi-Langmuir model (the "empirical" Langmuir function). The opposite hypothesis, catechol and resorcinol adsorbing on the second category of sites, and no longer on the first, was tested in our simulations and led to very bad results (not shown).

The phenol adsorption, partly described by an empirical fitting, may be considered as a real drawback, as we lose the physical understanding of the parameters. Nevertheless, although its adsorption is of crucial importance for displacement phenomena, it only interferes with resorcinol and catechol in a narrow zone, located near the displacer front, while competition between catechol and resorcinol, that ensures the occurrence of an efficient displacement train, is much more involved in space and time. Therefore, this empirical fitting for phenol was deemed acceptable for this work.

Competitive Langmuir isotherm. Fig. 3 shows simulations of displacement separations for the resorcinol–catechol mixture in a 1:1 ratio. These chromatograms were calculated by using the competitive Langmuir isotherm related to the non-competitive parameters of each compound. They are compared with experiments done at four different loading factors concerning the resorcinol–catechol mixture. The loading factor is the ratio of the amount of injected product to the saturation capacity of the column for this considered product [47] and is expressed as follows:

$$Lf_i = \frac{C_{i,0} V_{\text{inj}} b_i}{(1-\varepsilon) S L a_i} \tag{10}$$

where $C_{i,0}$ is the initial concentration of the injected product at the entrance of the column, V_{inj} the injection volume, ε the total porosity, S the column cross-sectional area and L its length; a_i and b_i are the parameters of the single Langmuir isotherm for component i.

Whatever the loading factor, it is obvious that no simulation accounts properly for the experimental results (see Fig. 3). Indeed, whereas all experiments achieve a more or less effective separation by displacement, simulations are only suitable in predicting the residence time of phenol but do not describe any separation between catechol and resorcinol.

We may conclude that the competitive Langmuir model, used with parameters drawn from single-component Langmuir isotherms, is really unsatisfactory. This conclusion is not surprising and has already been pointed out by other workers [29,48,49], and an attempt to explain this fact will be given below.

It must be remembered that the competitive Langmuir model, derived from the classical Langmuir model, is based on the same simplifying hypotheses, *i.e.*, an ideal behaviour of solutes in both stationary and mobile phases, without any molecular interactions between them. Golshan-Shirazi and Guiochon [29] and Jacobson *et al.* [18] specified that such ideal conditions are only seldom found, as for instance in the case of an enantiomer mixture separation. It must also be added that the competitive Langmuir

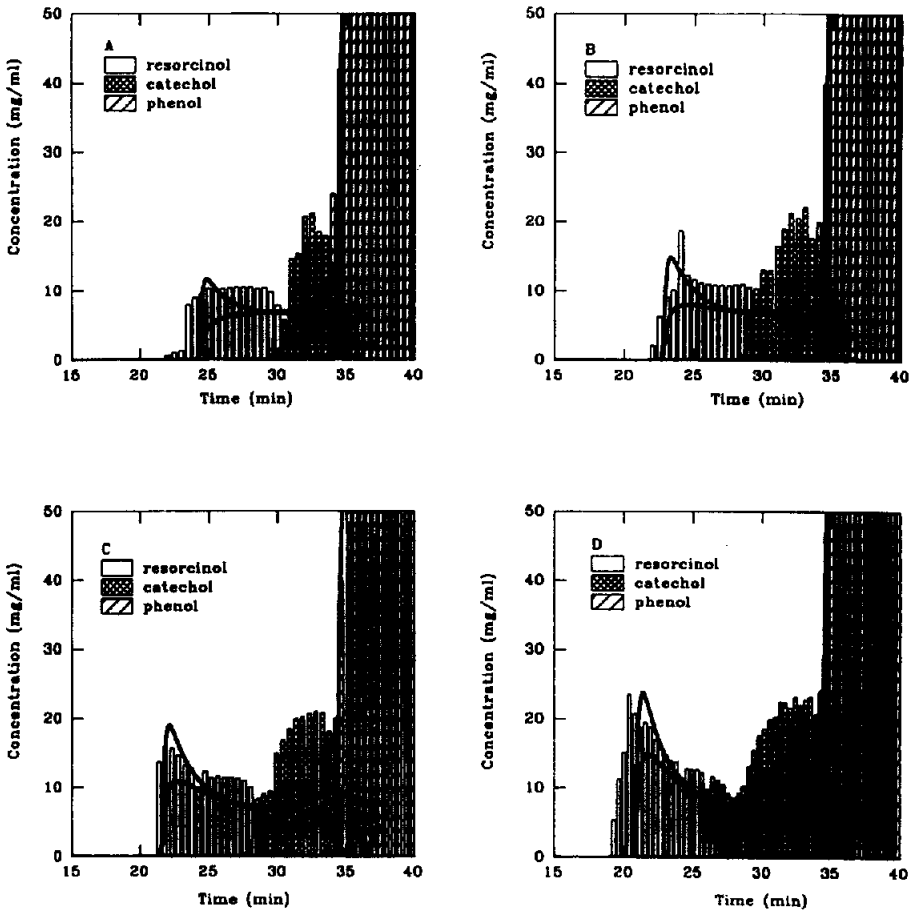

Fig. 3. Reversed-phase displacement chromatograms of a 1:1 binary mixture of resorcinol and catechol using phenol as displacer. Comparison between the band profiles (lines) calculated by using the competitive Langmuir isotherm with non-competitive parameters and the experimental data (bars). Conditions: column, 5-μm Nucleosil C_{18} (250 × 4.6 mm I.D.); phase ratio, 0.4; mobile phase, water; flow-rate, 0.2 ml/min; temperature, 30°C; V_{inj}, 0.4 ml; displacer, 80 g/l phenol in water. (A) $Lf_{res} = 20.1\%$, $Lf_{cat} = 11\%$; (B) $Lf_{res} = 25.1\%$, $Lf_{cat} = 13.7\%$; (C) $Lf_{res} = 30.1\%$, $Lf_{cat} = 16.5\%$; (D) $Lf_{res} = 35.1\%$, $Lf_{cat} = 19.2\%$.

isotherm violates the Gibbs' relationship [12] and therefore becomes thermodynamically inconsistent as soon as the saturation capacities (a_i/b_i) are different for all components [50,51]. The assumption of identical saturation capacities for products of different molecular sizes is very unrealistic because each molecule occupies on the surface of the support a space essentially dependent on its size, its three-dimensional conformation and other characteristics that cannot be applied to other molecules except in the case of enantiomers [18]. In this work, the competitive Langmuir model has been used more like a numerical description where saturation capacities may be different for every molecule than a rigorous description of the relevant thermodynamic or mechanistic phenomena encountered during the adsorption process. Besides, because of its simple and easy to handle formulation, this model remains one of the most commonly employed in the literature [10,52].

In addition, we also stress another failing of this competitive model that concerns the description of the selectivity, a parameter characterizing, for a given binary mixture of known composition, the ability of the stationary phase to

induce different migration velocities for each component and therefore its ability to separate this mixture. Selectivity is defined as follows:

$$\alpha = (q_i/C_i)/(q_j/C_j) \quad (11)$$

The competitive Langmuir isotherm predicts a constant selectivity for two components, whatever their respective concentrations, and does not take into account the influence of other components. In the present instance, it corresponds to the ratio of the initial slopes of single-component isotherms. This contradicts experimental results when the saturation capacities of the concerned products are different, and especially when the saturation capacity of the less retained component is the largest [29]. All these remarks question the validity of this model, and explain that its use, when intense competition for adsorption sites occurs, is not satisfactory. Hence a more elaborate model, such as the LeVan–Vermeulen isotherm, must be considered.

LeVan–Vermeulen isotherm. The LeVan–Vermeulen isotherm, derived from the Langmuir model, is also related to the non-competitive Langmuir parameters of each product. This model is more rigorous than the previous one because it makes use of conventional thermodynamic principles, such as the Gibbs' relationship, and can take into account the different saturation capacities of components, without problems of inconsistency. It is based, however, on simplifying hypotheses such as the ideal behaviour of solutes in both the stationary and mobile phases, a constant activity coefficient of these solutes and the absence of any molecular interaction between them [5]. Few studies have used this model to simulate separations [5,29] and our present work aims to complete these previous studies and to check the suitability of this model for our operating conditions.

Fig. 4 shows the same experimental displacement separations as in Fig. 3 and the corresponding simulations performed with the LeVan–Vermeulen model. Phenol competitive adsorption is described by this LeVan–Vermeulen isotherm plus the "empirical Langmuir" function which remained unaffected. We may note, in every situation, the very good agreement of the modelling with the actual separations. However, some mixing zones, appearing in experimental chromatograms between phenol and catechol, are not at all predicted by the calculated displacements. One explanation may be drawn from the influence of the dead volume between the column outlet and the sample collector, where hydrodynamic dispersion may degrade the separation. However, this is surely not the only reason. One may also put forward the poor and not well understood description of basic interaction phenomena with the stationary phase at low product concentrations, as previously stated for the general description of the Langmuir model. Nevertheless, one must admit the essentially good description of experimental results with this LeVan–Vermeulen model.

This model was then demonstrated to be effective for our operating conditions where products exhibit very different saturation capacities (66.08 g/l for resorcinol and 120.68 g/l for catechol), and are injected at high concentrations. Hence this difference in saturation capacities strongly influences the separation process and may be accurately taken into account by the LeVan–Vermeulen model [4,5]. In addition, as already stated by Golshan-Shirazi *et al.* [5], we can point out that the LeVan–Vermeulen model predicts a better displacement effect than that predicted by the competitive Langmuir model (see Fig. 3) when the more retained component of the binary mixture (here catechol) has the highest saturation capacity.

To complete these comments about this model, some useful information may be found in Fig. 5, which shows the competitive LeVan–Vermeulen isotherms of the two products, resorcinol and catechol, in a 1:1 ratio, and also the evolution in their selectivity. These curves are plotted as a function of the loading factor of resorcinol. The non-linearity of these isotherms is strongly marked, especially for resorcinol, which very quickly reaches it maximum concentration on the stationary phase. Resorcinol, because of strong competition for adsorption sites, cannot reach its saturation capacity on the stationary phase ($q_{s,r} = 66.08$ g/l, calculated per unit volume of particle skeleton) and its maximum adsorbed concentration is only 23 g/l. In addition, after

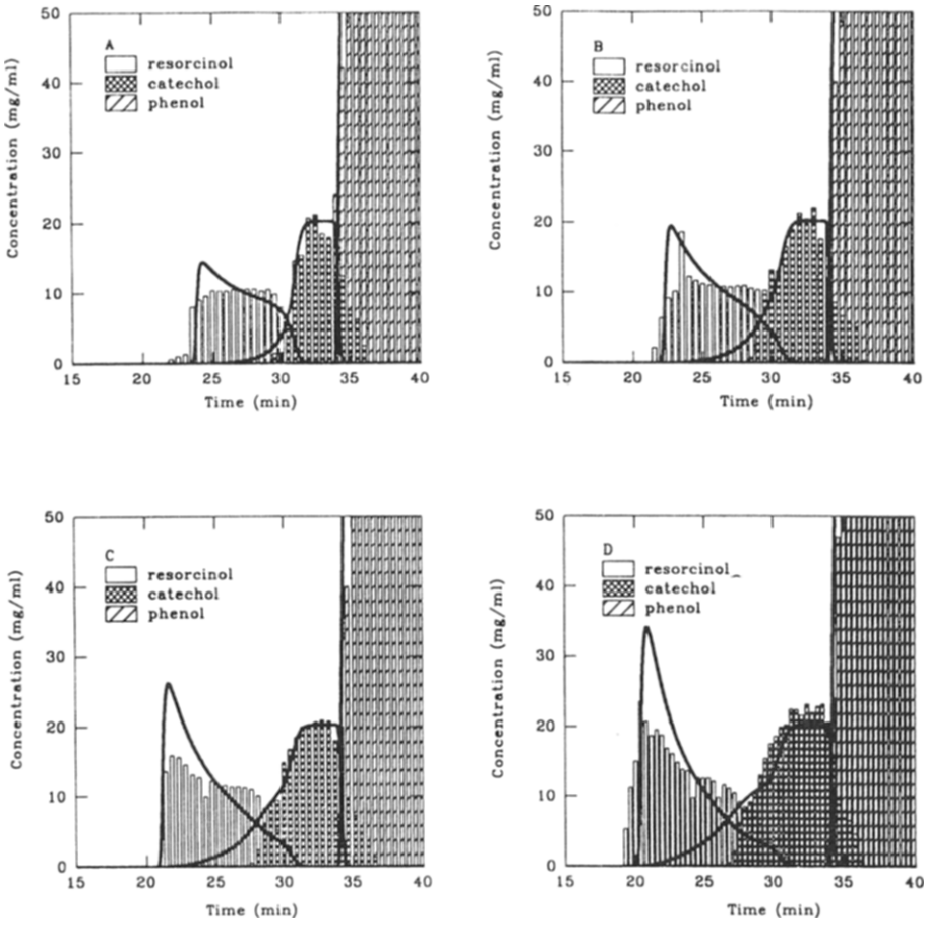

Fig. 4. Reversed-phase displacement chromatograms of a 1:1 binary mixture of resorcinol and catechol using phenol as displacer. Comparison between the band profiles (lines) calculated by using the two-term expansion LeVan–Vermeulen isotherm with non-competitive parameters and the experimental data (bars). Experimental conditions as in Fig. 4.

reaching 8% of the resorcinol loading factor, the adsorbed resorcinol concentration gradually decreases, these molecules being displaced by catechol molecules more strongly bound to the stationary phase. These latter will reach their saturation capacity only for very high loading factors because they have first to displace the adsorbed resorcinol molecules.

We observe also a continuous increase in the selectivity. This last effect is very important because it indicates that weakly resolved mixtures on an analytical scale may, under certain conditions, be separated easily on a preparative scale, and that selectivity inversions may be observed [5]. Finally, let us stress the value of this study for the LeVan–Vermeulen model, that has qualities and characteristics in common with the stoichiometric displacement model (S.D.M.) used in ion-exchange chromatography [34].

Quadratic isotherm: three floating parameters. The case of the quadratic isotherm we consider now is somewhat peculiar as this model mixes the non-competitive parameters from the single Langmuir isotherm of each component with extra correction coefficients derived from competitive experimental data. Hence great accuracy in the description of displacement effects is expected with the use of such a model, accuracy that has to justify the amount of extra experimental work required to obtain these specific competitive parameters.

From a practical point of view, we restricted

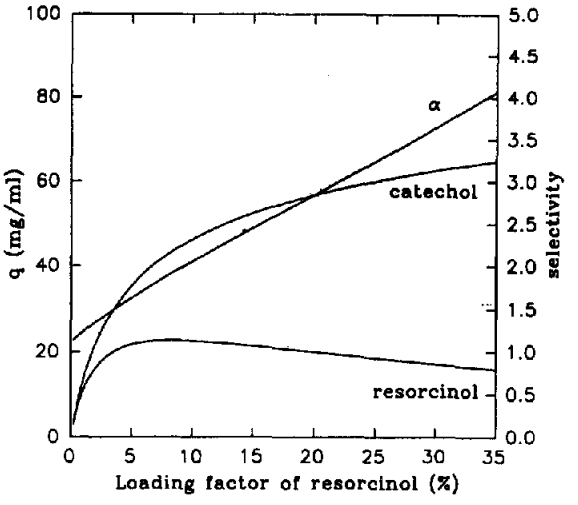

Fig. 5. Selectivity and LeVan–Vermeulen competitive isotherms with non-competitive parameters for a 1:1 binary mixture of resorcinol and catechol. Conditions: column, 5-μm Nucleosil C_{18} (250 × 4.6 mm I.D.) at 30°C; mobile phase, water.

our study to the determination of correction coefficients related only to the two products to be separated, *i.e.*, resorcinol and catechol, and we considered that the non-competitive parameters of the displacer bi-Langmuir isotherm were accurate enough. This approach may be justified in the case of displacement separations. Indeed, the displacer, *i.e.*, phenol, exerts a great influence on resorcinol and catechol but, as already stated, this influence is restricted to a narrow zone of the column, located near the displacer front. In contrast, resorcinol and catechol maintain a strong mutual competition in a broad zone. To simulate this kind of separation process it seemed to us more relevant to describe separately these competition phenomena without involving phenol and its correction factors. The experimental determination of competitive data was therefore done in an easy manner.

The problem previously encountered that arises yet again is to handle components with different adsorption models. Indeed, we use the competitive quadratic isotherm for resorcinol and catechol on the one hand, and the bi-Langmuir model characterizing the phenol adsorption on the other. To take into account the competitive influence of phenol on the adsorption of resorcinol and catechol, we modified in an intuitive manner the quadratic isotherm of these two components in the same way as the competitive Langmuir isotherm is derived from the single Langmuir isotherm. We obtained the following equations, simpler but more empirical than those derived from a quadratic model involving three components:

$$q_1 = \frac{a_1 C_1 + a_{12} C_1 C_2}{a + b_1 C_1 + b_2 C_2 + b_{12} C_1 C_2 + b_3 C_3} \quad (12a)$$

$$q_2 = \frac{a_2 C_2 + a_{21} C_1 C_2}{1 + b_1 C_1 + b_2 C_2 + b_{21} C_1 C_2 + b_3 C_3} \quad (12b)$$

where the subscripts 1 and 2 refer to resorcinol and catechol, respectively, and the coefficient b_3 is the b parameter from the Langmuir model (see eqn. 2) accounting for the adsorption of phenol on the same sites as the other two components. Let us specify again that concerning phenol, an empirical function is always associated with this Langmuir model to obtain the "semi-empirical" bi-Langmuir model introduced previously. The competitive adsorption of phenol with the other two components has been accounted for by a conventional competitive Langmuir isotherm associated with the unaffected empirical function. The latter remained unaffected because it only describes the non-competitive adsorption of phenol on specific adsorption sites.

The quadratic isotherm coefficients a_{12}, a_{21} and b_{12} were obtained by a numerical fitting of a set of competitive isotherm data. The other parameters a_i and b_i (see eqns. 12a and b) are the non-competitive Langmuir parameters. The coefficient b_{12} is set equal to b_{21} as stated by Lin *et al.* [22]. Results are summarized in Table III.

Fig. 6 shows the close agreement between the experimental displacement separations and their numerical simulations obtained with the equilibrium-dispersive model associated with the quadratic isotherms. However, a mixing zone between resorcinol and catechol, experimentally observed and also visible in the LeVan–Vermeulen-calculated profiles, is not present in the theoretical profiles presented in Fig. 6. The occurrence of a plateau for resorcinol is better

TABLE III

COMPETITIVE ISOTHERM PARAMETERS FOR THE RESORCINOL–CATECHOL MIXTURE: SUMMARY OF RESULTS

Competitive isotherm model	Parameters		Mean relative error (%)
	Resorcinol	Catechol	
Competitive Langmuir	$a_1 = 5.156$	$a_2 = 11.456$	17.50
(best-fit parameters)	$b_1 = 0.0748$ l/g	$b_2 = 0.1055$ l/g	
LeVan–Vermeulen	$a_1 = 10.746$	$a_2 = 11.3811$	10.09
(best-fit parameters)	$b_1 = 0.160$ l/g	$b_2 = 0.0989$ l/g	
Quadratic isotherm	$a_1 = 7.937$	$a_2 = 8.810$	
(three floating parameters)	$b_1 = 0.120$ l/g	$b_2 = 0.073$ l/g	8.53
	$a_{12} = -0.0622$	$a_{21} = 0.2047$	
	$b_{12} = 0.0017$ g/l	$b_{21} = b_{12}$	
Quadratic isotherm	$a_1 = 4.7253$	$a_2 = 6.476$	
(seven floating parameters)	$b_1 = 0.0358$ l/g	$b_2 = 0.0408$ l/g	4.21
	$a_{12} = -0.0537$	$a_{21} = 0.0291$	
	$b_{12} = 0.00075$ l/g	$b_{21} = b_{12}$	

accounted for in the present case than with the simulations using the LeVan–Vermeulen isotherm (see Fig. 4). Therefore, we may conclude that this quadratic model shows greater displacement effects than does the LeVan–Vermeulen model.

Fig. 7 shows the quadratic isotherms of resorcinol and catechol with a constant concentration ratio chosen as 1:1, and the evolution of their selectivity α plotted as a function of the loading factor of resorcinol. The preceding remarks about a large displacing effect may be recognized in the value of the selectivity that is always greater than that derived from the LeVan–Vermeulen model (see Fig. 5). Moreover, the increase in selectivity with increasing loading factor, observed with both the LeVan–Vermeulen and the quadratic isotherms, is much more sensitive with the latter.

Models of numerical adaptation

In this last approach, the previously mentioned models are now considered as empirical equations where all coefficients without exception are given by a parametric identification from experimental competitive adsorption data. It must be recalled that many studies have already used this concept, *e.g.*, by Jacobson *et al.* [36] and Jacobson and Frenz [41], who determined in this way the coefficients of the competitive Langmuir isotherm, Zhu *et al.* [4], who numerically identified the coefficients of the quadratic isotherm of the Fowler, Langmuir and LeVan–Vermeulen competitive models, Golshan–Shirazi *et al.* [5], who studied the LeVan–Vermeulen model, and Lin *et al.* [22], who obtained the seven floating parameters of the quadratic isotherm.

Concerning the quantitative description of the basic interaction and competitive adsorption phenomena on the stationary phase, a better accuracy is expected from this empirical approach than from that obtained with models related to non-competitive parameters, with or without correction factors [4,36]. Our study aims to show if, in the framework of our experimental displacements, other coefficients applied to the same models can lead to a better description of the separation process than that simulated by these models with their originally planned coefficients. We should mention also that modelling isotherms in a wide range of concentration, which is necessary for displacement simulations, raises some additional difficulties, as even the mobile phase concentration is no longer ideal in this instance. This can explain the agreement between calculated and experimental profiles

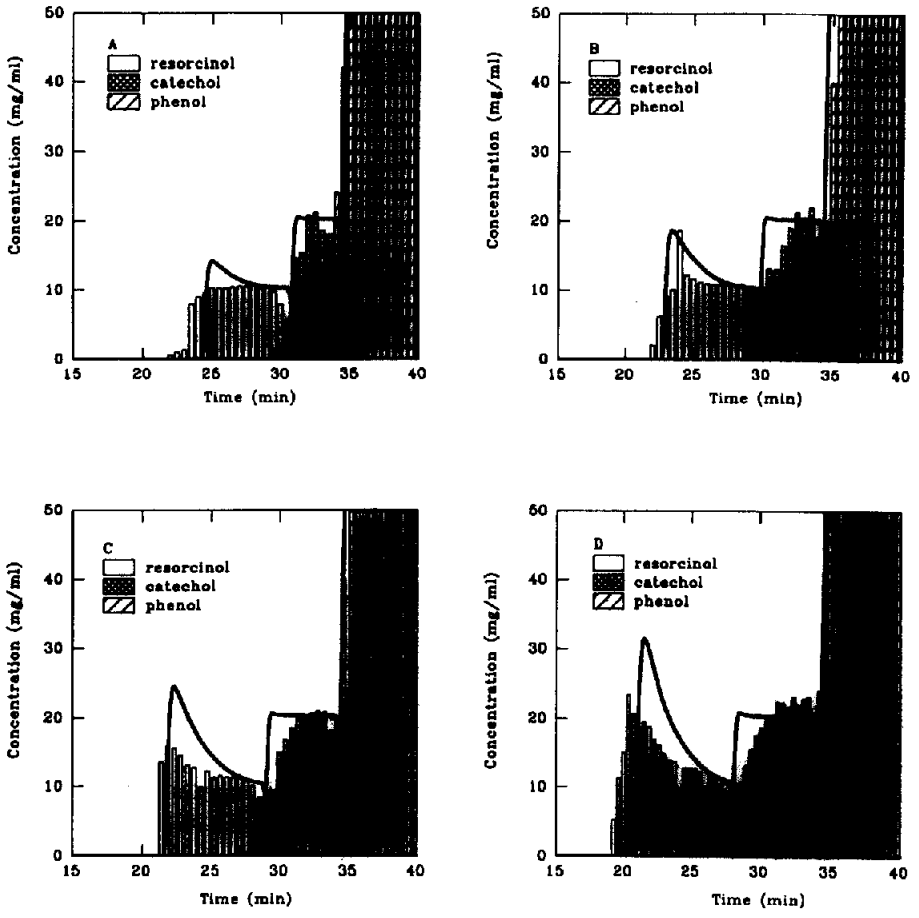

Fig. 6. Reversed-phase displacement chromatograms of a 1:1 binary mixture of resorcinol and catechol using phenol as displacer. Comparison between the band profiles (lines) calculated by using the quadratic isotherm with three floating parameters and the experimental data (bars). Experimental conditions as in Fig. 4.

being less good than in other studies dealing with elution chromatography.

As done previously, only the competitive parameters for resorcinol and catechol will be identified, and the original parameters for the phenol isotherm will again be considered as sufficiently accurate.

Competitive Langmuir isotherm. We have seen in a previous section that the competitive Langmuir isotherm related to non-competitive parameters was not at all satisfactory in describing displacement separations. This model is now considered as an empirical model for resorcinol and catechol.

First, it must be pointed out that the parametric identification used in this study led to a set of coefficients predicted with a high mean relative error (see Table III). This strong discrepancy (17.5%) highlights a poor fit of the competitive equilibrium data, and may justify the rejection of the competitive Langmuir isotherm. However, a closer study may moderate this statement. Indeed, most of the competitive frontal chromatograms were obtained with resorcinol and catechol mixtures whose total concentrations were below 80 g/l. Under these conditions we have observed that the competitive Langmuir model gave a better fit with experimental data (within a 10% mean deviation). On the other hand, when the column was more loaded, the observed deviation was larger. Relative deviations of more than 100% have been found, especially for

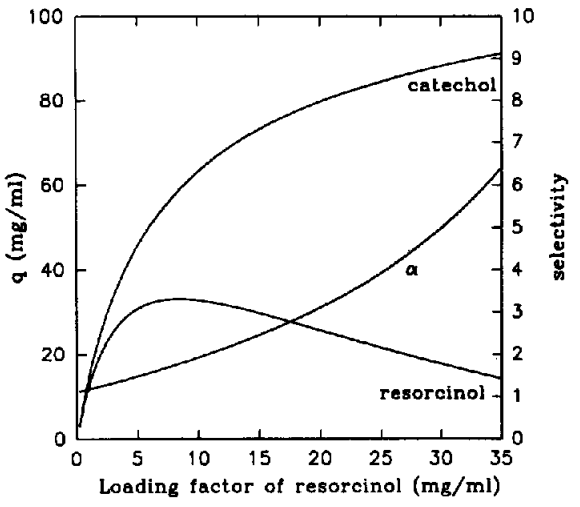

Fig. 7. Selectivity and quadratic isotherms with three floating parameters for a 1:1 binary mixture of resorcinol and catechol. Conditions: column, 5-μm Nucleosil C_{18} (250 × 4.6 mm I.D.) at 30°C; mobile phase, water.

resorcinol, whose calculated adsorbed concentration was always over-evaluated. We may conclude that, when a high limiting value of the loading factor is exceeded, the competitive Langmuir model is no longer able to account accurately for competitive adsorption of resorcinol and catechol, therefore leading to a restricted range of validity for this model. The high mean deviation is mainly due to the contribution of high concentrations and this does not exclude the use of the model in a lower concentration range.

This is illustrated in Fig. 8, where calculated displacement separations are compared with the corresponding experimental data and where a good agreement between the theoretical and actual profiles is observed. Indeed, although the initial operating conditions are not so appropriate for the use of this model (products are injected in 1:1 ratio, at concentrations higher than 40 g/l), the two products rapidly achieve a dilution that enables this model to be correct.

One can easily see that the simulations in Fig. 8 are totally different from those performed with the same competitive Langmuir model (see Fig. 2), but related to non-competitive parameters. However, this numerically adapted model still predicts a constant selectivity, independent of product concentrations, and is still as thermodynamically inconsistent as the original Langmuir model. Besides, in both models, the saturation capacities of each product are more or less similar (66.08 g/l before with non-competitive parameters and 68.93 g/l now for resorcinol, 120 g/l before and 108.58 g/l now for catechol). Therefore, it is very surprising to obtain a very poor description of the separation in one case and a fairly satisfactory one in the other.

Finally, as an attempt to understand this result, we may consider the influence of the relative retention factor of resorcinol with respect to catechol ($\alpha' = a_2/a_1$), which was studied by Ghodbane and Guiochon [53]. They observed that, when considering preparative chromatography, the larger this parameter is, the larger are the displacement effects, leading to increased yields and productivities. In our case its value is 2.22 for the numerically adapted competitive Langmuir model against a value near unity ($\alpha' = 1.11$) for the original competitive Langmuir model. This difference is certainly the explanation for the very different simulation results.

To conclude this section on the competitive Langmuir model, we must note that for two major reasons its use will nevertheless be restricted to special cases. First, as we have already mentioned, its poor description of the competitive adsorption phenomena in the high concentration range may be a real drawback in many instances.

Second, and this remark applies to all other numerically adapted models, it cannot predict suitably a totally developed displacement separation. Indeed, in the ideal case, the conventional theory of displacement enables one to predict very easily the concentrations of each product in the isotachic displacement train by the use of single-component isotherms and also the operating line. When applying this theory to the single isotherms shown in Fig. 2, it leads to the isotachic concentrations of 10.15 and 20.03 g/l for resorcinol and catechol, respectively. When using the numerically adapted Langmuir model, it is not possible to account correctly for non-competitive adsorption; indeed, we obviously do not obtain the actual single adsorption isotherm when the concentration of other components tend to zero in the equation. This is why it

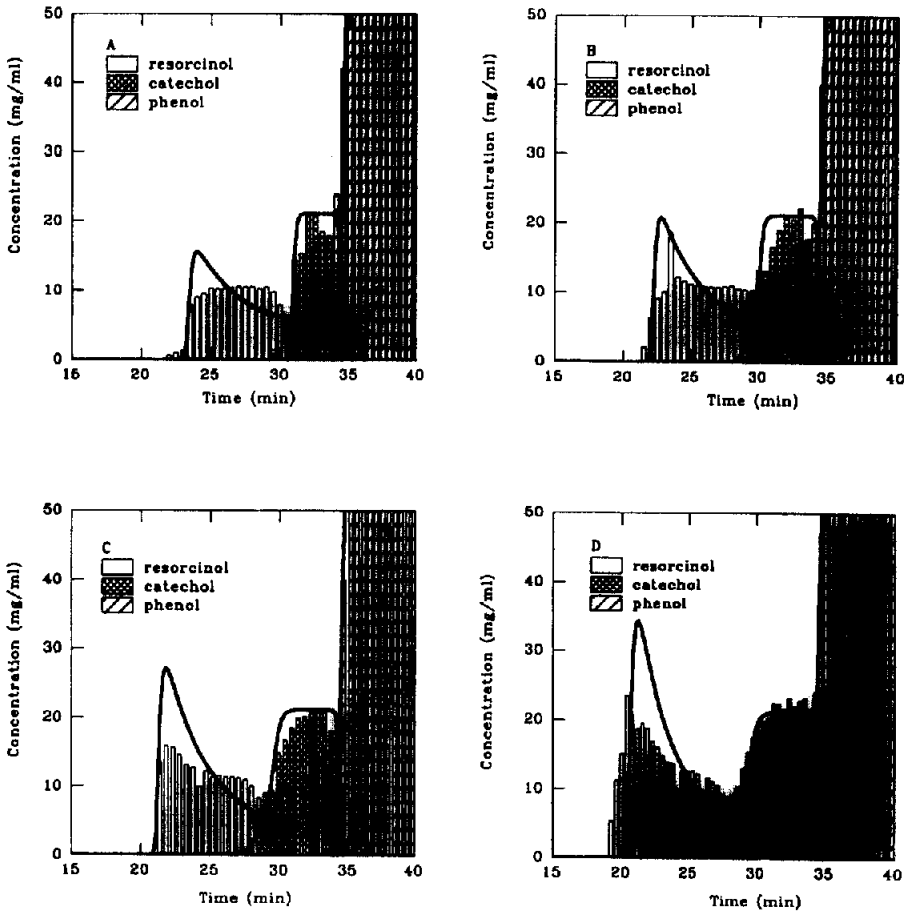

Fig. 8. Reversed-phase displacement chromatograms of a 1:1 binary mixture of resorcinol and catechol using phenol as displacer. Comparison between the band profiles (lines) calculated by using the competitive Langmuir isotherm with competitive parameters and the experimental data (bars). Experimental conditions as in Fig. 4.

cannot describe the situation where the product is migrating separately from the other one (as, for instance, when the displacement train is near to establishment). Concerning now the isotachic concentrations, we calculate with this competitive equation values of 5.90 and 20.87 g/l for resorcinol and catechol, respectively. This explains, for resorcinol, why the simulated starting plateau concentration (see Fig. 8) is much lower than the experimental value. This last conclusion may doom to failure the use of numerically adapted models to describe any developed displacement separations.

LeVan–Vermeulen isotherm and quadratic isotherm. Four parameters are now to be determined for the LeVan–Vermeulen model and seven floating parameters for the quadratic model, the coefficient b_{12} always being taken to be equal to b_{21} as stated by Lin *et al.* [22]. The results are summarized in Table III. The seven-parameter quadratic isotherm leads to the lowest mean relative deviation (4.21%) and *a priori* augurs well for the following simulations done with this model.

Figs. 9 and 10 show the results of simulations with the LeVan–Vermeulen model and the quadratic model, respectively. One can observe that these two last models, in their numerically adapted version, do not account adequately for the experimental results. For instance, the LeVan–Vermeulen model overestimates the concentration plateau for each product to be separated. Indeed, when considering the previous remark in the above section about the competi-

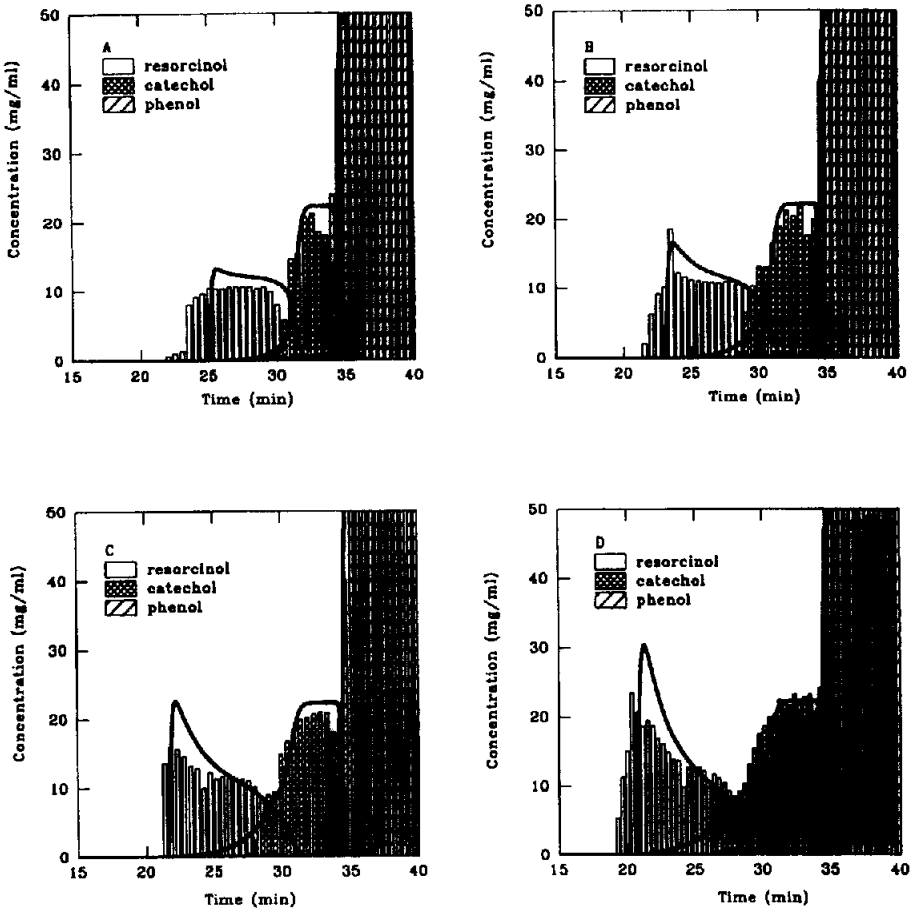

Fig. 9. Reversed-phase displacement chromatograms of a 1:1 binary mixture of resorcinol and catechol using phenol as displacer. Comparison between the band profiles (lines) calculated by using the two-term expansion LeVan–Vermeulen isotherm with competitive parameters and the experimental data (bars). Experimental conditions as in Fig. 4.

tive Langmuir model, the isotachic concentrations calculated with this LeVan–Vermeulen isotherm are 12.52 and 22.05 g/l for resorcinol and catechol, respectively, instead of the calculated values of 10.15 and 20.03 g/l according to the theory of displacement chromatography. Finally, simulations with the quadratic isotherm considered as an empirical model are the worst ones, although this model gave the best fit of the competitive adsorption experimental data (4.21% mean relative deviation).

We can therefore conclude that a competitive adsorption model, when considered as a numerical empirical equation, is not appropriate to describe the evolution of a separation process. This kind of model, which may prove to be very effective in describing competitive adsorption isotherms, could be very unsuitable when implemented in a simulation program for chromatographic separations. Indeed, after injection of products and after most of the separation process has occurred, there is no reason to consider models describing solute adsorption with competitive parameters, because products are now isolated. The use of these numerical equations will only be suitable when products remain mixed to a certain extent.

CONCLUSIONS

This work has attempted to establish a comparison between different competitive isotherms in accordance with an original criterion, more demanding than the conventional one that con-

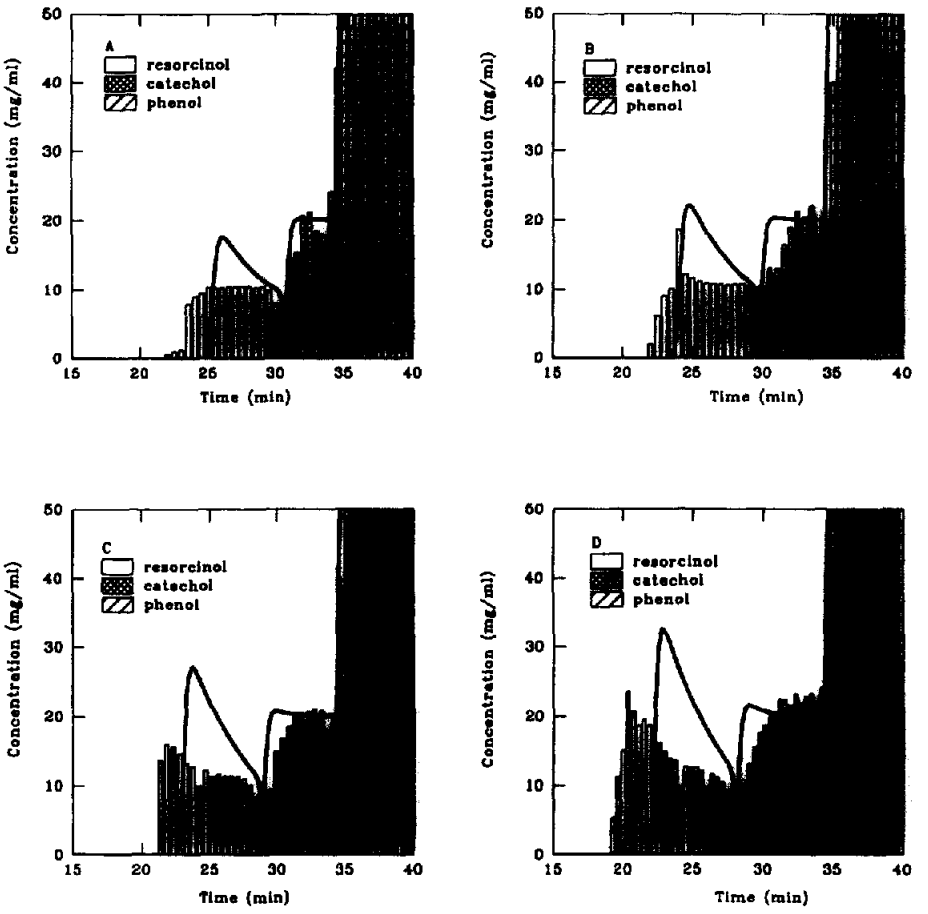

Fig. 10. Reversed-phase displacement chromatograms of a 1:1 binary mixture of resorcinol and catechol using phenol as displacer. Comparison between the band profiles (lines) calculated by using the quadratic isotherm with seven floating parameters and the experimental data (bars). Experimental conditions as in Fig. 4.

sists only in the ability of the isotherm equation to fit any set of experimental data points evaluated from competitive frontal analysis. Indeed, we have preferred to use a "dynamic" criterion which implies the implementation of the adsorption isotherm in a numerical program simulating displacement separations. This evaluation *in situ* is, in our opinion, an effective way to improve the understanding of the chromatographic process and to point out general problems directly related to the concept of separation and to the transient phenomena encountered during chromatographic separations. Three competitive adsorption models have been studied: the competitive Langmuir model, the LeVan–Vermeulen model and the quadratic model.

During the past 10 years, experimental methods for obtaining competitive adsorption data have been simplified, and no longer need such tedious experiments. Nevertheless, obtaining data from single-isotherm measurements remains the simplest way [4]. Besides, in spite of the relatively good agreement of the competitive Langmuir isotherm related to competitive parameters with the experimental results, we have emphasized the limited value of competitive models considered as empirical equations in the simulation of displacement separations. This questions the usefulness of performing specific experiments to obtain these competitive parameters. Perhaps the best solution is to keep non-competitive parameters and to associate them with correction

coefficients as previously seen in the case of the quadratic isotherm with three floating parameters, or to find a numerical function describing the evolution of these correction factors with the concentration of solutes in the mobile phase. Theoretical research is also perhaps necessary to find new models or to adapt the old ones.

These conclusions have been drawn from a study that was focused on displacement separations and one may ask whether they will remain valid for other chromatographic modes, such as overloaded elution. In our opinion, in so far as a preparative separation is concerned, that means that concentrated solutions are injected, and in so far as an efficient separation process will inevitably progress from a zone of high competition for adsorption sites, to a zone of single adsorption (the aim is, of course, to obtain separated bands of migrating solutes throughout the column), all our conclusions may probably become generalized.

SYMBOLS

a_i Constant in Langmuir isotherm for component i
b_i Adsorption equilibrium constant for component i (m^3/kmol)
C_i Concentration of component i in the mobile phase (kmol/m^3)
$C_{i,0}$ Concentration of component i at the column entrance (kmol/m^3)
d_p Particle diameter (m)
$D_{i,m}$ Molecular diffusion coefficient of component i in the mobile phase (m^2/s)
F Phase ratio of the column packing $[=(1-\varepsilon)/\varepsilon]$
H Height equivalent to a theoretical plate (HETP) (m)
h Reduced plate height $(=H/d_p)$
k_i' Capacity factor for component i
L Column length (m)
M Number of components
N Number of theoretical plates $(=L/H)$
q_i Concentration of component i adsorbed on the stationary phase (calculated per unit volume of particle skeleton) (kmol/m^3)
q_s Function used for the LeVan–Vermeulen isotherm (see eqn. 6) (kmol/m^3)
$q_{s,i}$ Specific saturation value of stationary phase concentration for component i (kmol/m^3)
S Column cross-sectional area (m^2)
t Time coordinate (s)
t_R Retention time of the considered component (s)
t_{R_0} Residence time of an unretained component (s)
t_0 Beginning of a frontal analysis or a displacement chromatography (s)
u Interstitial fluid velocity (m/s)
V_D System dead volume (m^3)
V_{inj} Volume of feed injection (m^3)
V_{Φ_m} Column dead volume (m^3)
V_{Φ_s} Volume of stationary phase (m^3)
$V_{r,i}$ Retention volume of the C_i concentration step (m^3)
z Axial coordinate (m)

Greek letters

α Selectivity $[=(q_i/C_i)/(q_j/C_j)]$
α' Relative retention factor
ε Total porosity of the column packing
υ Reduced mobile phase velocity $(=ud_p/D_m)$
υ_{opt} Optimum reduced mobile phase velocity

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