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Determination of the single component and competitive adsorption isotherms of the 1-indanol enantiomers by the inverse method

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Abstract

The inverse method of isotherm determination consists in calculating the numerical values of the coefficients of an isotherm model that give a set of chromatographic profiles in best possible agreement with the set of experimental profiles available. This method was applied to determine the adsorption isotherms of the 1-indanol enantiomers on a cellulose tribenzoate chiral stationary phase. Both single-component and competitive isotherms were determined by using no more than one or two overloaded band profiles. The isotherms determined from the overloaded band profiles agreed extremely well with the isotherms determined by frontal analysis. Several isotherm models were used and tested. The best-fit isotherm was selected by means of statistical evaluation of the results. The results show that the adsorption is best characterized with a model describing heterogeneous adsorption with bimodal adsorption energy distribution.

Keywords: Adsorption isotherms; Inverse method of isotherm determination; Chiral stationary phases, LC; 1-Indanol; Cellulose tribenzoate

1. Introduction

The production of pure enantiomers is one of the major fields of application of preparative chromatography in the pharmaceutical industry. These separations must be carried out on chiral stationary phases (CSP) which often have a relatively low saturation capacity. So, these separations are usually executed under strongly nonlinear conditions. Accordingly, the accurate determination of the equilibrium isotherms of the two enantiomers on a CSP is of fundamental importance to do computer-assisted optimization or scaling up of the process.

Several dynamic methods are available to determine equilibrium isotherms by chromatography. The most common methods are the frontal analysis (FA), the elution by characteristic point (ECP), the frontal analysis by characteristic point (FACP), and the perturbation (injection on a plateau, PM) methods [1]. FA is the most popular method, because of

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its high accuracy. It requires, however, a large amount of compounds and it is time consuming because FA demands that several dozens of equilibrium isotherm data points be collected, data points covering a sufficiently wide concentration range. However, FA can be applied to the determination of competitive isotherm data of binary or ternary mixtures, as well as to that of single components [2,3]. The ECP method derives the isotherm data from the diffuse part of the elution chromatogram of a single, large-size pulse. Unfortunately, ECP cannot be applied to determine competitive isotherms, and, even for single-component isotherms, it should only be used with columns of high efficiency [4].

The inverse method of isotherm determination was developed recently [5–7]. It derives the isotherm from overloaded band profiles of the pure compound or of the components of mixtures. The equilibrium isotherms are determined by numerically integrating a proper model of nonlinear chromatography and by tuning the values of the isotherm parameters to minimize the difference between the calculated and the measured band profiles. The inverse method has been applied in several simulated moving bed separations to determine nonlinear equilibrium isotherms [8–10]. Recent comparisons of the frontal analysis and the inverse methods determined that the inverse method gives rather accurate estimates of the competitive isotherm parameters up to the maximum elution concentration of the overloaded bands. It is only moderately accurate from the maximum elution concentration up to the injected concentration [11]. Another comparison between single component isotherms obtained with frontal analysis, perturbation on plateau and the inverse method confirmed that the single-component isotherms determined with the three methods are very close to each other [12].

The aim of the present study is to show that the inverse method is an attractive alternative for the determination of both single component and competitive isotherms. With the inverse method, one can determine the numerical parameters of rather complex isotherm models. The equilibrium isotherms of 1-indanol isomers on a cellulose tribenzoate stationary phase were studied recently by frontal analysis [13,14]. We use here the overloaded elution band profiles of the pure enantiomers and of the racemic mixture to derive the isotherm parameters.

2. Theory

The inverse method of isotherm determination estimates the isotherm parameters through the following steps. First, an isotherm model is selected and initial estimates are determined for its numerical parameters. These initial estimates can be helped by the results of an analytical injection. Then, overloaded band profiles are calculated with the a properly chosen model of nonlinear chromatography. The measured and calculated band profiles are compared by evaluating the following objective function:

$$\min \sum_i r_i^2 = \min \sum_i (C_i^{\mathrm{sim}} - C_i^{\mathrm{meas}})^2 \tag{1}$$

where C_i^{sim} and C_i^{meas} are the calculated and the measured concentrations at point i and r_i is their difference. Finally, the isotherm parameters are changed to minimize the objective function, using an optimization routine. The equilibrium-dispersive model of chromatography can be employed for the modeling of many nonlinear separations [1]. In this model we assume constant equilibrium between the stationary and the mobile phases and use an apparent dispersion term to account for the band-broadening effects of both axial dispersion and the finite rate of the mass transfer kinetics. The following mass balance equation is written for each component of the sample:

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

where C_i and q_i are the concentrations of component i in the mobile and the stationary phases, respectively; z is the length, t the time, u the mobile phase linear velocity, and F the phase ratio, with $F = (1 - \varepsilon_{\mathrm{t}})/\varepsilon_{\mathrm{t}}$, where ε_{t} is the total porosity of the column. D_{a} is the apparent dispersion coefficient that can be calculated from the number of theoretical plates (N) determined by an analytical injection:

$$D_{\mathrm{a}} = \frac{uL}{2N} \tag{3}$$

where L is the column length.

The initial condition $C_i(z,\ 0) = 0$ states that at $t = 0$ the column is equilibrated with the pure mobile

phase. The Danckwerts boundary conditions describe the feed flux at the column inlet and outlet, respectively:

$$uC_i^0 = uC_i(0,t) - D_a \frac{\partial C_i(z,t)}{\partial z}\Big|_{z=0} \quad (4)$$

$$D_a \frac{\partial C_i(z,t)}{\partial z}\Big|_{z=L} = 0 \quad (5)$$

Because the chromatographic columns used in actual practice are of high efficiency, the classical Danckwerts boundary conditions can be written simply for each component as:

$$C_i(0,t) = C_i^0 \quad 0 < t \leq t_p \quad (6)$$

where t_p is the injection time. Accordingly, as a first approach, we may assume that the sample is introduced into the column as a rectangular pulse of length t_p. In most practical applications, however, this assumption is unrealistic and cannot be used. The real inlet profile should be determined and used in the model, particularly when the injection time is not very small compared to the retention time [15].

The system of mass balance equations with the proper isotherm equations is to be integrated numerically to obtain the concentration profiles at the column outlet.

3. Experimental

An Agilent 1090 liquid chromatography system (Agilent Technologies, Palo Alto, CA, USA), equipped with a multisolvent delivery system, an automatic injector with a 25-μl sample loop, a column thermostat, a diode array detector, and a computer data station, was used for all experiments. The mobile phase was a solution of *n*-hexane and 2-propanol (92.5:7.5, v/v). Hexane and 2-propanol were HPLC grade solvents from Fisher Scientific (Fair Lawn, NJ, USA). 1,3,5-tri-*tert*.-butylbenzene (TTB), used as the nonretained marker, and the racemic 1-indanol were purchased from Aldrich (Milwaukee, WI, USA). The pure *R*-1-indanol and *S*-1-indanol, also from Aldrich, were previously purified in our laboratory.

A 20 × 1-cm stainless steel column packed with Chiracel OB (cellulose tribenzoate coated on a silica support; Daicel, Tokyo, Japan) was used for all the measurements. The column was packed in house. The average particle size of the packing material was 20 μm. The total porosity, measured by injecting TTB, was $\varepsilon_t = 0.705$. The efficiency of the column at a flow-rate of 2.5 ml/min was about $N = 1200$ theoretical plates.

4. Calculations

The concentration profile of the two components is derived from the original chromatograms (absorbance versus time) through a calibration. Since enantiomers have identical UV response factors, the detected absorbance signal of either enantiomer or the racemic mixture can easily be transformed into a concentration profile with a simple step.

For the calculation of the individual profiles, the system of two partial differential equations is solved using a finite difference scheme written for Eq. (2) with $D_a = 0$ (ideal model). The values of the time and length increments of the integration are chosen such as that the numerical dispersion will exactly be equal to the desired apparent dispersion [16]. For the numerical integration, a modified Rouchon (finite difference) algorithm was used, which ignores the empty sections of the (z, t) plane and thus significantly speeds up the calculations [17].

5. Results and discussion

5.1. Inlet profile

The inlet concentration profile has a major effect on the band profile. The inlet profile constitutes the boundary condition of the differential mass balance equation, thus it should be accurately known. Ideally, the shape of the inlet profile should be a rectangle but, in practice, significant deviations from this profile are almost always observed [15]. In the capillaries connecting the injection port and the column, dispersion takes place, thus the inlet concentration profile is not a sharp pulse. If the isotherm is Langmuirian, the extra-column dispersion increases the spread of the recorded band profile. The true inlet profile can be determined by injecting a sample with the column removed from the system and replaced by a zero-volume connector.

Probably the simplest model to account for the extra-column band broadening—in the case of an infinitesimally narrow impulse injection—is the exponentially modified Gaussian (EMG) function. That model is a convolution of a Gaussian peak and an exponential decay function. The former contribution describes the band broadening in the connecting tubes, while the latter models the mixer-type extra volumes [18]. When the ideal inlet profile is a wide rectangular pulse, the true inlet concentration can be modeled by the convolution of the EMG function and a rectangular pulse of length t_p. The resulting profile is:

$$C(t) = \frac{1}{2a}\left\{\operatorname{erfc}\frac{m-t}{\sqrt{2}\sigma} - \operatorname{erfc}\frac{t_p+m-t}{\sqrt{2}\sigma} + \exp\left(\frac{\sigma^2}{2\tau^2}+\frac{m-t}{\tau}\right) \times\left[e^{t_p/\tau}\operatorname{erfc}\left(\frac{\sigma}{\sqrt{2}\tau}+\frac{t_p+m-t}{\sqrt{2}\sigma}\right) - \operatorname{erfc}\left(\frac{\sigma}{\sqrt{2}\tau}+\frac{m-t}{\sqrt{2}\sigma}\right)\right]\right\} \quad (7)$$

where m is the residence time in the connecting tube, σ is the Gaussian band width and τ is the time constant of the mixer-type extra-column volume.

The measured inlet concentration profile for a 1-min injection is reported in Fig. 1 (symbols). The fitted model described in Eq. (1) (solid lines) follows remarkably well the measured concentration profile with the parameters: $t_p = 1.00$ min, $m = 0.1195$ min, $\sigma = 0.007778$ min, $\tau = 0.05696$ min. This inlet profile was used in all band profile calculations with properly changing the value of t_p.

The numerical values of the parameters of the inlet function strongly depend on the flow-rate.

5.2. Single component data

Single-component isotherms were determined by applying the inverse method to the overloaded band profiles of the pure enantiomers. The isotherms determined via this method were compared to the experimental results of frontal analysis.

5.2.1. Frontal analysis

The single-component and competitive adsorption

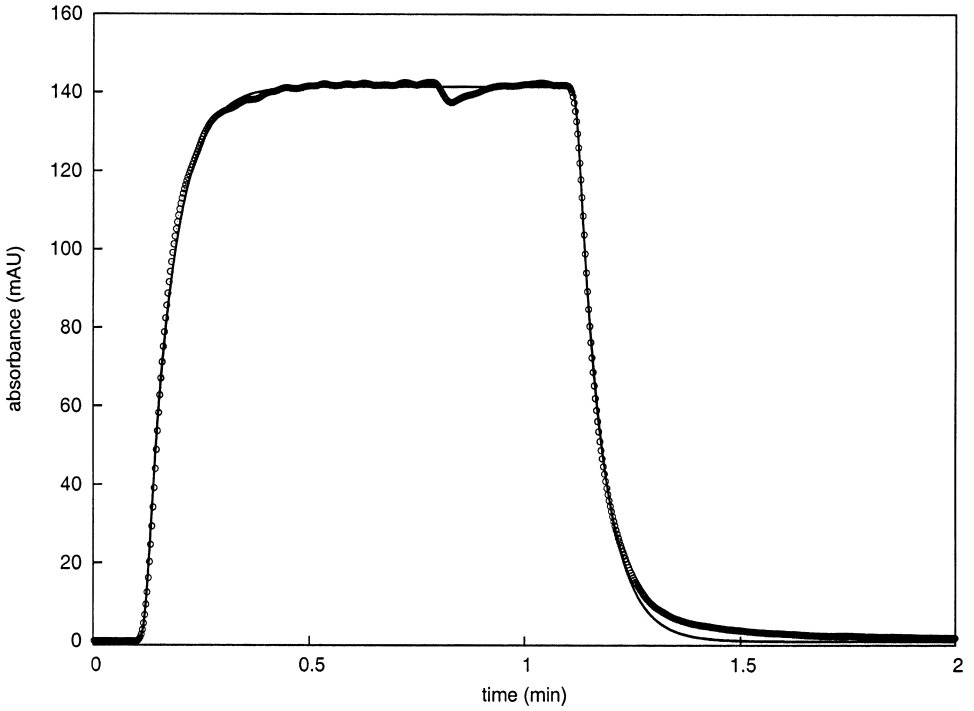

Fig. 1. Plot of the inlet concentration profile.

isotherms of 1-indanol has been previously determined by frontal analysis and are reported elsewhere [13]. Here we use these data as a reference to validate the results obtained by the inverse method. The results obtained with three different isotherm models are summarized here.

The Langmuir isotherm is the most common model to describe nonlinear adsorption, although it is assumed to be a model too simple to account for the adsorption on chiral stationary phases. The Langmuir isotherm corresponds to a homogeneous adsorption kinetics and is given as:

$$q = \frac{q_s bC}{1 + bC} \tag{8}$$

where q_s is the saturation capacity and b is the equilibrium constant or distribution coefficient.

Adsorption isotherms measured on heterogeneous surfaces often follow the Tóth model [19] that differs from the Langmuir isotherm only by an exponent. The role of the exponent is to take into account the heterogeneity of the distribution of the sorption energies.

The Tóth isotherm is written as:

$$q = \frac{q_s bC}{[1 + (bC)^{\nu}]^{1/\nu}} \tag{9}$$

where q_s is the saturation capacity, b is the equilibrium constant, and ν is the heterogeneity parameter. When the heterogeneity parameter is $\nu = 1$, the Tóth model becomes identical to the Langmuir isotherm. The smaller the value of ν, the more disperse the energy distribution is. The Tóth isotherm corresponds to a unimodal adsorption energy distribution.

When enantiomers are separated on a chiral stationary phase, we expect the stationary phase to be heterogeneous, with a bimodal energy distribution. The biLangmuir isotherm model assumes that the surface of the chiral stationary phase contains two different types of sites, the nonselective and the enantioselective sites. Nonselective sites retain both enantiomers with the same adsorption energy, whereas the enantioselective sites interact differently with these two enantiomers, binding them with different energy (and/or, possibly, a different saturation capacity). This isotherm model is written as:

$$q = \frac{q_{ns} b_{ns} C}{1 + b_{ns} C} + \frac{q_s b_s C}{1 + b_s C} \tag{10}$$

where b_{ns} is the equilibrium constant for the adsorption on the nonselective sites, b_s the equilibrium constant for the adsorption on the enantioselective sites, q_{ns} the saturation capacity of the nonselective sites and q_s the saturation capacity of the enantioselective sites.

The results of fitting the three isotherm models to the experimental frontal analysis data are summarized in Table 1. To rank the isotherm models, we compare the fitting errors of each model. The final sum of squares of the residuals (FSSR) is the variance of the fitting errors, therefore a Fisher test can be applied to determine whether or not the difference in the FSSRs is statistically significant [11].

The frontal analysis was carried out at 19 concentrations; the isotherm models have two to four parameters, thus the Fisher ratio is calculated with 15–17 degrees of freedom. In that range, the critical Fisher ratio is 2.3 at $\alpha = 0.05$. The analysis of the final sum of squares of the residuals (FSSR) shows that—as expected—the models that describe adsorption on heterogeneous surfaces outperform the Langmuir model, yielding a significantly better fit. Out of the two heterogeneous models, the biLangmuir isotherm fits better, confirming that adsorption takes place on two different types of sites. In the case of the R-1-indanol, the biLangmuir model fits only a little better than the Tóth isotherm, the difference

Table 1
Single-component isotherm parameters determined by fitting the isotherm equations to the frontal analysis data

	R-1-Indanol	*S*-1-Indanol
Langmuir		
q_s (g/l)	60.00	47.63
b (l/g)	4.469×10^{-2}	9.114×10^{-2}
FSSR	8.54×10^{-3}	5.25×10^{-2}
Tóth		
q_s (g/l)	146.5	144.6
b (l/g)	1.965×10^{-2}	3.886×10^{-2}
n	0.6528	0.5119
FSSR	8.73×10^{-4}	2.76×10^{-3}
biLangmuir		
q_{ns} (g/l)	71.76	90.40
b_{ns} (l/g)	3.335×10^{-2}	1.960×10^{-2}
q_s (g/l)	0.4916	8.844
b_s (L/g)	0.9957	0.3536
FSSR	8.244×10^{-4}	1.34×10^{-4}

between the two models is not significant. On the other hand, for the *S*-1-indanol, the biLangmuir isotherm fits significantly better than the Tóth isotherm.

5.2.2. The inverse method

The inverse method requires a single overloaded band profile for the isotherm determination. With pure samples, the injection of a sample of sufficient volume, with the highest possible concentration is preferred—usually limited by the solubility of the sample in the solvent—in order to have reliable isotherm data over a wide concentration range. Overloaded band profiles were recorded by injecting 46.26 mg *R*-1-indanol and 53.01 mg *S*-1-indanol in nearly saturated solutions.

As with the frontal analysis data, the Langmuir, the Tóth, and the biLangmuir isotherms were fitted by the inverse method. The numerical results are summarized in Table 2. The results obtained with the inverse method show the same trend as the frontal analysis data: the heterogeneous models fit better than the Langmuir isotherm. Out of the two heterogeneous model, the biLangmuir model outperforms the Tóth model confirming again the bimodal adsorption energy distribution. The band profile used for fitting contains about 800 points in the nonzero concentration range. In that range of degrees of freedom, the critical Fisher ratio is 1.12 at $\alpha = 0.05$. Thus the FSSR values in Table 2 indicate that the Tóth isotherm fits significantly better than the Langmuir isotherm and the biLangmuir model fits significantly better than the Tóth model, for either enantiomer.

Table 2
Single-component isotherm parameters determined by the inverse method

	R-1-Indanol	*S*-1-Indanol
Langmuir		
q_s (g/l)	68.88	50.76
b (l/g)	3.704×10^{-2}	6.934×10^{-2}
FSSR	75.35	473.9
Tóth		
q_s (g/l)	123.9	124.1
b (l/g)	2.337×10^{-2}	4.106×10^{-2}
n	0.6933	0.5302
FSSR	25.78	172.1
biLangmuir		
q_{ns} (g/l)	109.23	85.85
b_{ns} (l/g)	1.101×10^{-2}	1.809×10^{-2}
q_s (g/l)	14.88	9.097
b_s (l/g)	0.1055	0.3704
FSSR	15.77	67.47

The numerical values of the isotherm parameters determined via frontal analysis and the inverse method are very close. Only one major difference can be observed when one compares the data of Tables 1 and 2: frontal analysis underestimates the amount of selective sites in the case of *R*-1-indanol. We recall, however, that the data obtained for the enantioselective sites are more prone to be less precisely measured because there are many more nonselective sites on a chiral surface than there are enantioselective sites [11].

In Fig. 2, the biLangmuir isotherms determined with the inverse method for 1-indanol are plotted (solid lines). As a reference, the frontal analysis data are also shown (symbols). We can see that the two methods give remarkably similar results.

The measured and calculated overloaded band profiles of *R*-1-indanol are overlaid in Fig. 3. The main figure shows that, for the largest sample size, the band profile calculated with the biLangmuir isotherm obtained with the inverse method follows very closely the experimental band profile. The diffuse rear part of the band profile calculated with the frontal analysis isotherm data differs slightly from the experimental profile. To check whether the isotherm determined with the inverse method properly models the adsorption over the whole concentration range, a band profile corresponding to a five times smaller sample size was also calculated and compared with the experimental data (see insert in Fig. 3). The agreement is very good again. The chromatogram calculated with the isotherm obtained by the inverse method estimates the shape and the retention time of the peak better than the one derived from the frontal analysis data.

The measured and the calculated band profiles of *S*-1-indanol are compared in Fig. 4. For both the large and the moderate sample sizes, the agreement between the experimental and the calculated band profiles is remarkable.

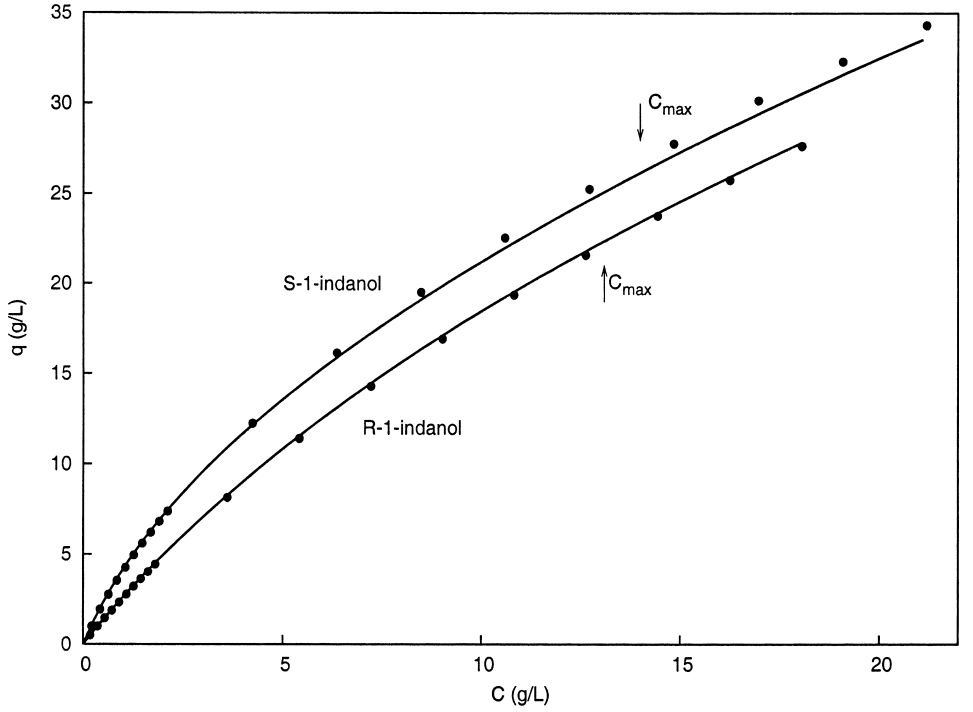

Fig. 2. Comparison of the single-component biLangmuir isotherms obtained by the inverse method (lines) and the experimental results of frontal analysis (symbols). C_{max} indicates the maximum elution concentration in the band profile used for the inverse method.

5.2.3. Simultaneous fitting of two single-component chromatograms

As all the calculations of the inverse method, as described earlier, confirm that the adsorption data of the 1-indanol enantiomers on the Chiralsel OB CSP are best fitted by an isotherm model corresponding to a bimodal adsorption energy distribution, we further focused our attention on the isotherm models of this category.

The separate handling of the isotherm data of the two enantiomers resulted in slightly different saturation capacities and equilibrium constants for the Langmuir contribution corresponding to the lowest energy, nonselective sites. By processing simultaneously the high concentration band profiles of the two enantiomers, we can restrict the biLangmuir isotherm model by requiring identical saturation capacities and equilibrium constants on the nonselective sites. Furthermore, we require—for the sake of thermodynamical consistency—identical saturation capacities on the enantioselective sites. Accordingly, the biLangmuir model takes the following form:

$$q_{\mathrm{R}} = \frac{q_{\mathrm{ns}} b_{\mathrm{ns}} C_R}{1 + b_{\mathrm{ns}} C_R} + \frac{q_{\mathrm{s}} b_{\mathrm{s},R} C_R}{1 + b_{\mathrm{s},R} C_R} \tag{11}$$

$$q_{\mathrm{S}} = \frac{q_{\mathrm{ns}} b_{\mathrm{ns}} C_S}{1 + b_{\mathrm{ns}} C_S} + \frac{q_{\mathrm{s}} b_{\mathrm{s},S} C_S}{1 + b_{\mathrm{s},S} C_S} \tag{12}$$

where subscripts R and S indicate R- and S-1-indanol. The first column of Table 3 summarizes the results of the isotherm determinations made with the inverse method, using simultaneously the band profiles of the two pure enantiomers.

The biLangmuir isotherm assumes that the adsorption energy is constant for either the nonselective sites or the enantioselective sites while it is in fact dispersed around its average value. As the Langmuir model of homogeneous surfaces is extended to a two-site biLangmuir model, so can the Tóth equation of unimodal energy distribution be extended to a bimodal distribution when we compose as follows an

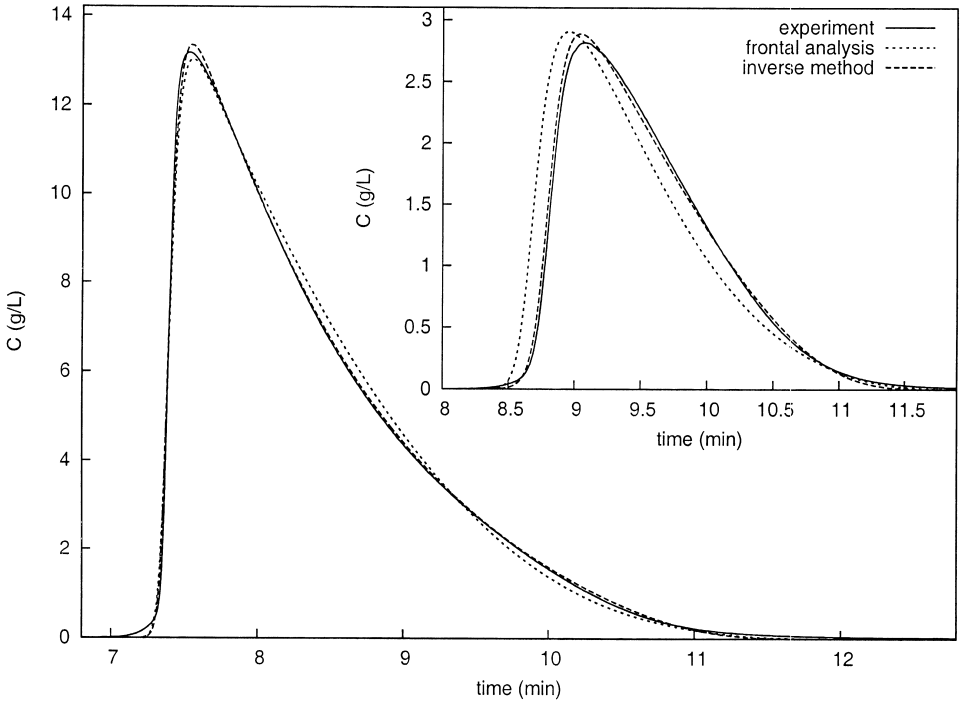

Fig. 3. Simulated (using the biLangmuir model) and experimental chromatograms recorded with injecting 46.25 and 9.251 mg (insert) *R*-1-indanol. The isotherm was determined from the band profile obtained when injecting 46.25 mg of the pure isomer.

isotherm equation containing two Tóthian terms:

$$q = \frac{q_{ns} b_{ns} C}{[1 + (b_{ns} C)^{\nu_{ns}}]^{1/\nu_{ns}}} + \frac{q_s b_s C}{[1 + (b_s C)^{\nu_s}]^{1/\nu_s}} \qquad (13)$$

where ν_{ns} and ν_s are the heterogeneity parameters for the nonselective and the enantioselective sites, respectively. Note that this isotherm thermodynamically consistent only if $\nu_s = \nu_{ns}$.

We applied the inverse method with this new model, using simultaneously the band profiles of the two pure enantiomers to determine the isotherm parameters of the biTóth model. The results of the isotherm determination with the biTóth model are summarized in the second column of Table 3. The heterogeneity parameters are $\nu_{ns} = 0.77$ and $\nu_s = 0.84$ indicating that the nonselective sites possess a more broadly dispersed energy distribution than the enantioselective sites. The goodness of the fit is remarkably better than that obtained with the biLangmuir model.

In Fig. 5 we compare the experimental and the calculated band profiles. For both enantiomers, an excellent fit is observed. The biTóth isotherms of the two enantiomers are plotted in Fig. 6. The agreement with the experimentally determined frontal analysis data (symbols) is excellent, except at high concentrations for *S*-1-indanol, in which case, this agreement is only good.

The fitting of the biTóth model to the frontal analysis data failed. The nonlinear fit converged to sets of parameters that have no physical meaning (e.g., heterogeneity parameters larger than one, or enormous saturation capacity). We believe that this failure can be attributed to the fact that the biTóth isotherm contains seven parameters to be fitted and any small error in the 19 data pairs measured by frontal analysis can have a huge effect on the numerical parameters of an isotherm with so many variables. On the other hand, we used the inverse method with more than 800 data points per peak.

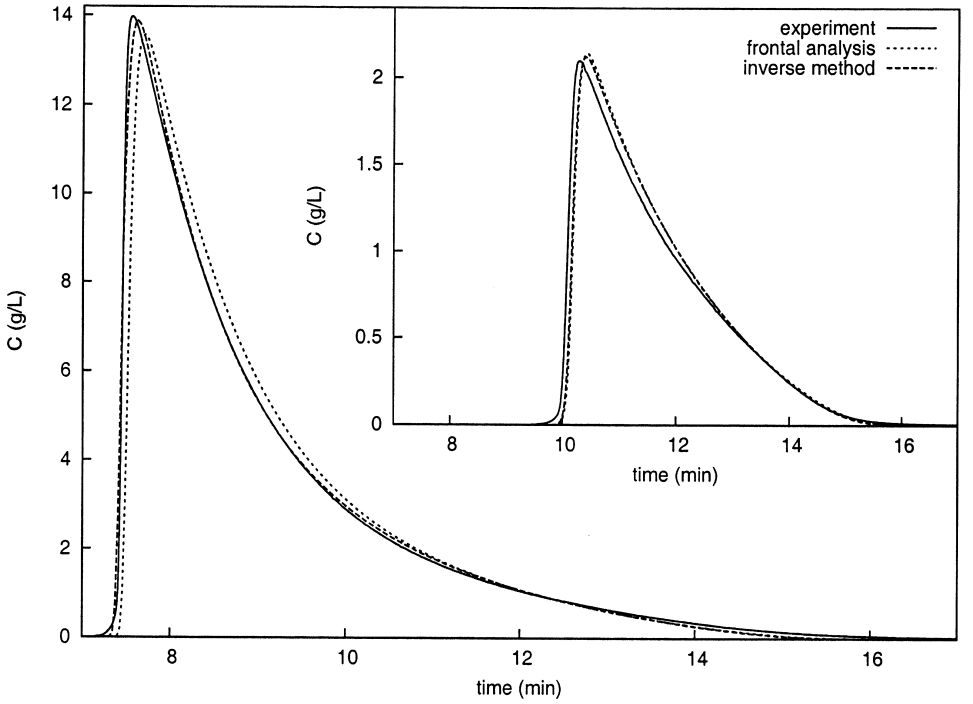

Fig. 4. Simulated (using the biLangmuir model) and experimental chromatograms recorded with injecting 53.01 and 10.60 mg (insert) *S*-1-indanol. The isotherm was determined from the band profile obtained when injecting 53.01 mg of the pure isomer.

5.3. Competitive data

5.3.1. Frontal analysis

The competitive isotherms of the 1-indanol isomers were determined by frontal analysis [13]. The results of fitting the competitive Langmuir, the biLangmuir, and the Tóth models to the experimental FA data are summarized in Table 4. As it was the case with the single component data, the Langmuir isotherm failed correctly to model the adsorption data of the 1-indanol isomers. Out of the heterogeneous models, the biLangmuir model gives a significantly better fit than the competitive Tóth isotherm.

Table 3
Single-component isotherm parameters determined by the inverse method using simultaneously the overloaded band profiles of the two pure enantiomers

	biLangmuir	biTóth
q_{ns} (g/l)	78.51	149.6
b_{ns} (l/g)	0.01924	0.00959
q_s (g/l)	12.44	15.08
$b_{s,R}$ (l/g)	0.08196	0.09783
$b_{s,S}$ (l/g)	0.2463	0.2490
n_{ns}	–	0.7687
n_s	–	0.8381
FSSR	233.6	133.2

The competitive biLangmuir isotherm has the same parameters as the biLangmuir isotherms of Eqs. (11) and (12). The difference is that the stationary phase concentration depends on the mobile phase concentrations of both enantiomers that compete for adsorption.

$$q_i = \frac{q_{ns} b_{ns} C_i}{1 + b_{ns}(C_1 + C_2)} + \frac{q_s b_i C_i}{1 + b_1 C_1 + b_2 C_2} \qquad (14)$$

With a similar reasoning, the competitive biTóth isotherm is written as:

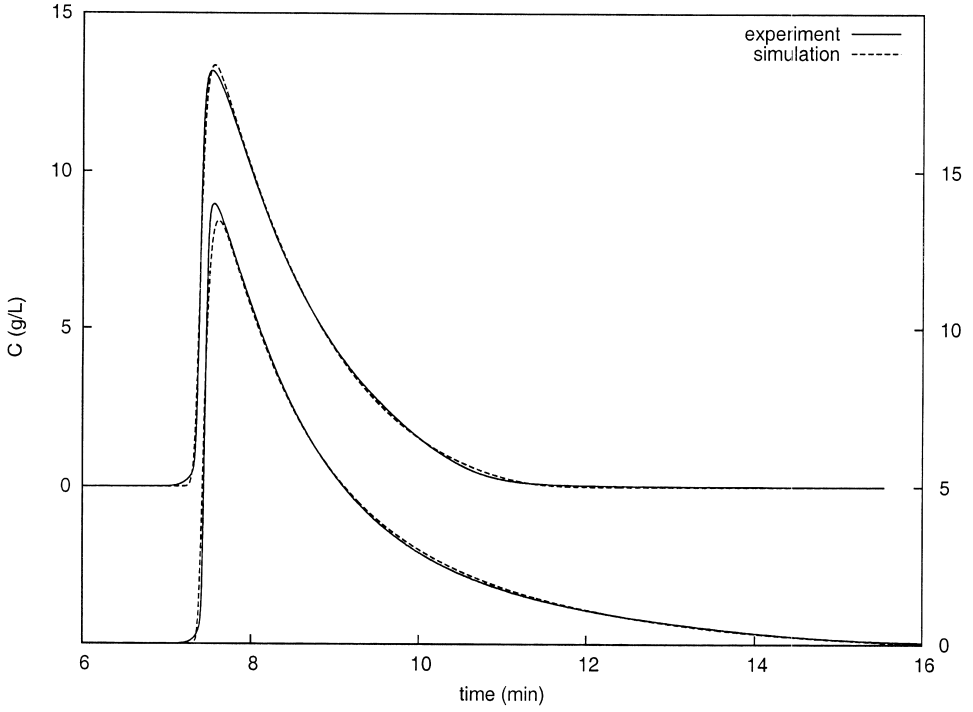

Fig. 5. Comparison of the single-component experimental overloaded band profiles of *R*-1-indanol (top) and *S*-1-indanol (bottom) and the calculated ones obtained with the best-fit biTóth isotherm.

$$q_i = \frac{q_{ns} b_{ns} C_i}{[1 + (b_{ns} C_1 + b_{ns} C_2)^{\nu_{ns}}]^{1/\nu_{ns}}} + \frac{q_s b_i C_i}{[1 + (b_1 C_1 + b_2 C_2)^{\nu_s}]^{1/\nu_s}} \quad (15)$$

The competitive biTóth model differs from the competitive biLangmuir model by the exponents that account for the surface heterogeneity.

5.3.2. Inverse method

For the isotherm determination by the inverse method, the injection of a large sample is preferred. When a binary mixture is injected, however, resolution decreases with increasing sample size. The imperfect resolution between the bands is expected to cause uncertainty, especially in the case of the less retained enantiomer as the diffuse tail of its band cannot be observed at all. As a compromise, we followed the strategy of fitting the isotherm parameters by simultaneously using two chromatograms: one at a rather high sample load and another one at a moderate sample size that results in touching bands.

Fig. 7 shows the result of fitting the biLangmuir model simultaneously to two chromatograms of the racemic mixture. The biLangmuir isotherm determined this way is plotted in Fig. 8 with the frontal analysis data. The numerical values of the isotherm are summarized in Table 5. We can see in Fig. 7 that the diffuse part of the band obtained when injecting 50.7-mg sample is well accounted for by the isotherm model, but that the fit is less satisfactory at the moderate, 10.14-mg, sample size. On the other hand, the competitive biTóth isotherm model gives a significantly better representation of the experimental data. The bands of both the large and the moderate sample sizes fit much better (see Fig. 9). The competitive biTóth isotherm is plotted in Fig. 10. A comparison with the frontal analysis data confirms again that the isotherms of the more retained enantiomer match perfectly. The match of the isotherms of the less retained enantiomer is remarkable.

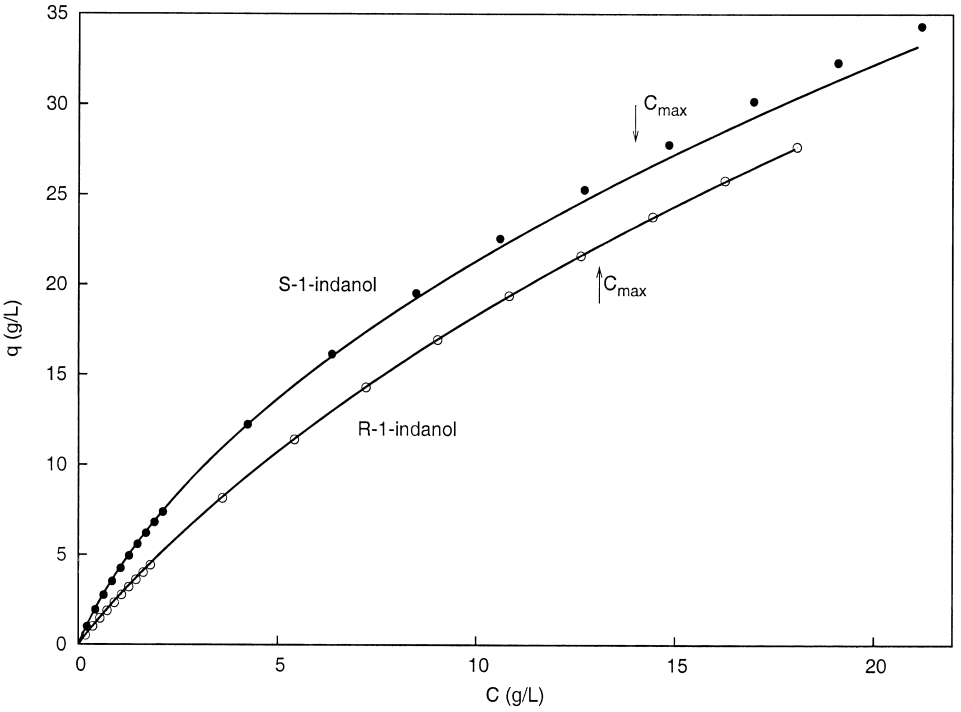

Fig. 6. Comparison of the single-component biTóth isotherms determined by the inverse method (lines) and the experimental results of frontal analysis (symbols).

Table 4
Competitive isotherm parameters determined by fitting the isotherm equations to the frontal analysis data

Langmuir	
q_s (g/l)	50.23
b_1 (l/g)	0.05718
b_2 (l/g)	0.0901
FSSR	0.111
Tóth	
q_s (g/l)	95.58
b_1 (l/g)	0.03257
b_2 (l/g)	0.05130
n	0.6892
FSSR	0.0926
biLangmuir	
q_{ns} (g/l)	100.46
b_{ns} (l/g)	0.01549
q_s (g/l)	11.02
$b_{s,R}$ (l/g)	0.1161
$b_{s,S}$ (l/g)	0.3163
FSSR	0.00146

The adsorption energy distribution corresponding to the Tóth isotherm is a unimodal distribution that is slightly skewed towards the smaller energy values. The adsorption equilibrium constant b, and the adsorption energy E can be related as [20]:

$$b = k_0 \, e^{E/RT} \tag{16}$$

where k_0 is a pre-exponential constant, R is the ideal gas constant and T the column temperature.

The equilibrium constant corresponding to the average adsorption energy is:

$$\bar{b} = k_0 \, e^{\bar{E}/RT} \tag{17}$$

Thus, when we introduce $\kappa = (b/\bar{b})^{\nu}$, we obtain:

$$\kappa^{1/\nu} = b/\bar{b} = e^{(E-\bar{E})/RT} \tag{18}$$

The distribution of the adsorption energies is simplest to express through the distribution of the equilibrium constants by means of the normalized equilibrium constant κ:

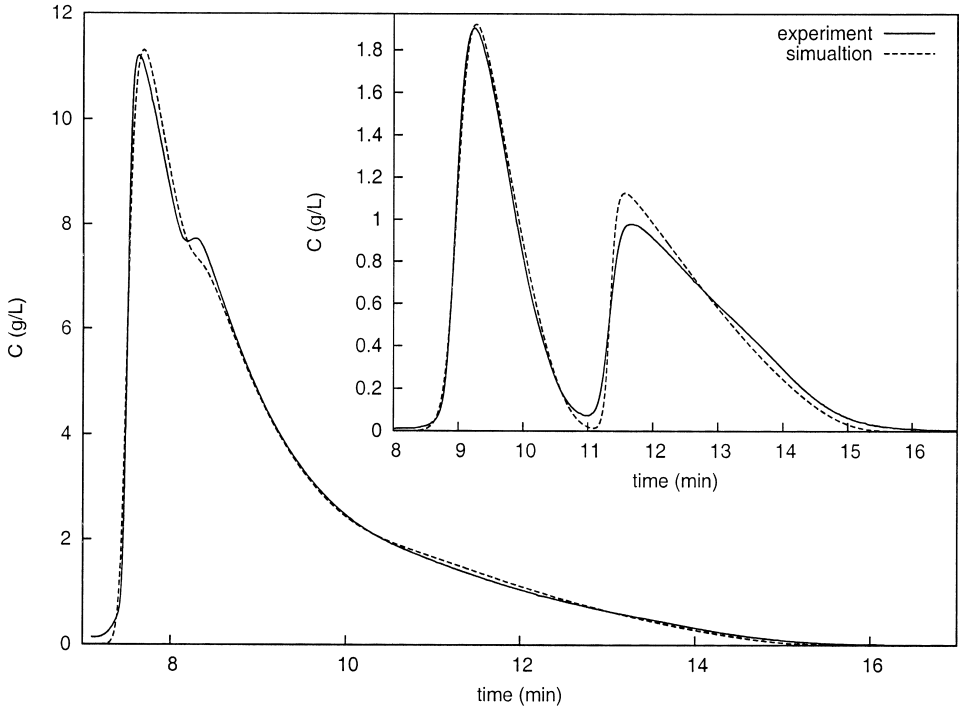

Fig. 7. Simultaneous fitting of the competitive biLangmuir model to a large (50.7 mg) and a moderate (10.14 mg) injection of the racemic mixture.

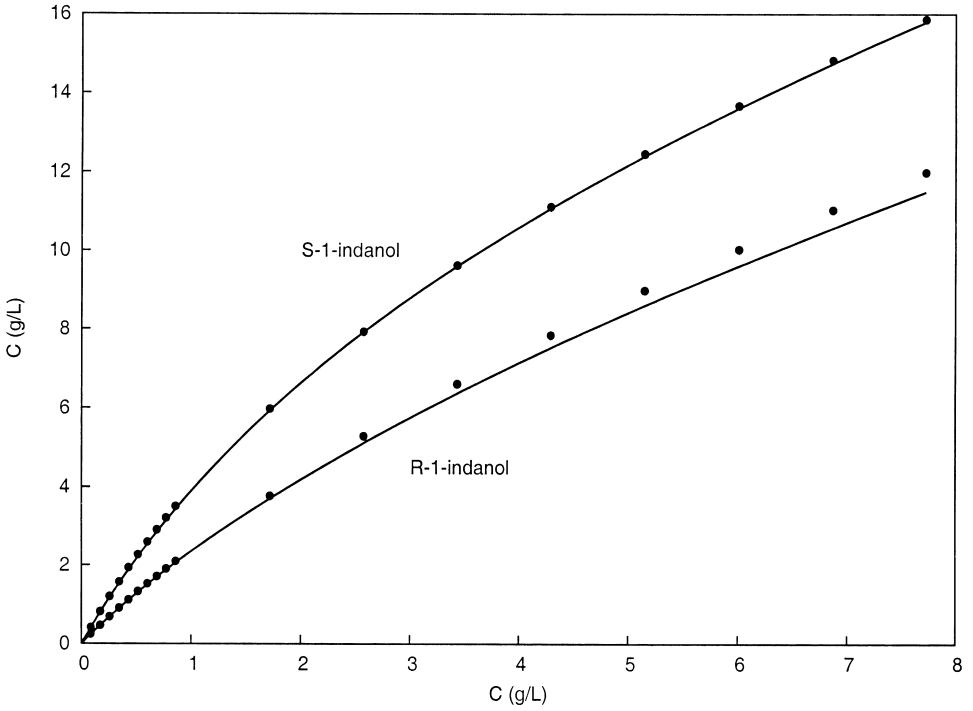

Fig. 8. Comparison of the competitive biLangmuir isotherms obtained by the inverse method (lines) and the experimental results of frontal analysis (symbols).

Table 5
Competitive isotherm parameters determined by the inverse method

	biLangmuir	biTóth
q_{ns} (g/l)	135.2	170.31
b_{ns} (l/g)	0.00900	0.01026
n_{ns}	–	0.706
q_s (g/l)	14.75	11.36
$b_{s,R}$ (l/g)	0.1067	0.09583
$b_{s,S}$ (l/g)	0.2484	0.2974
n_s	–	0.931
FSSR	187.1	65.46

$$f(\kappa) = \frac{\sin(\gamma/\nu)}{\pi RT(\kappa^2 + 2\kappa\cos(\pi\nu) + 1)^{1/2\nu}} \quad (19)$$

where γ is given by

$$\gamma = \arccos\frac{\kappa\cos(\pi\nu) + 1}{(\kappa^2 + 2\kappa\cos(\pi\nu) + 1)^{1/2}} \quad (20)$$

The distribution of the equilibrium constants on a logarithmic scale—which is identical to the distribution of the adsorption energies on a linear scale—is plotted in Fig. 11 for the competitive biTóth isotherm. As $\nu_{ns} < \nu_s$, the spread of the adsorption energies is larger on the nonselective sites. This means that, on the enantioselective sites, the adsorption can be characterized with a narrower energy range. These results agree well with studies of the adsorption energy distribution with the expectation maximization method [21].

6. Conclusions

Our results indicate, first, that the inverse method offers an attractive approach to determine single-component and competitive adsorption isotherms quickly, with a minimum use of sample and solvent. Isotherms can be determined with a different combinations of overloaded elution bands. For the determination of single component isotherms, an injection of a very large sample is preferred, because

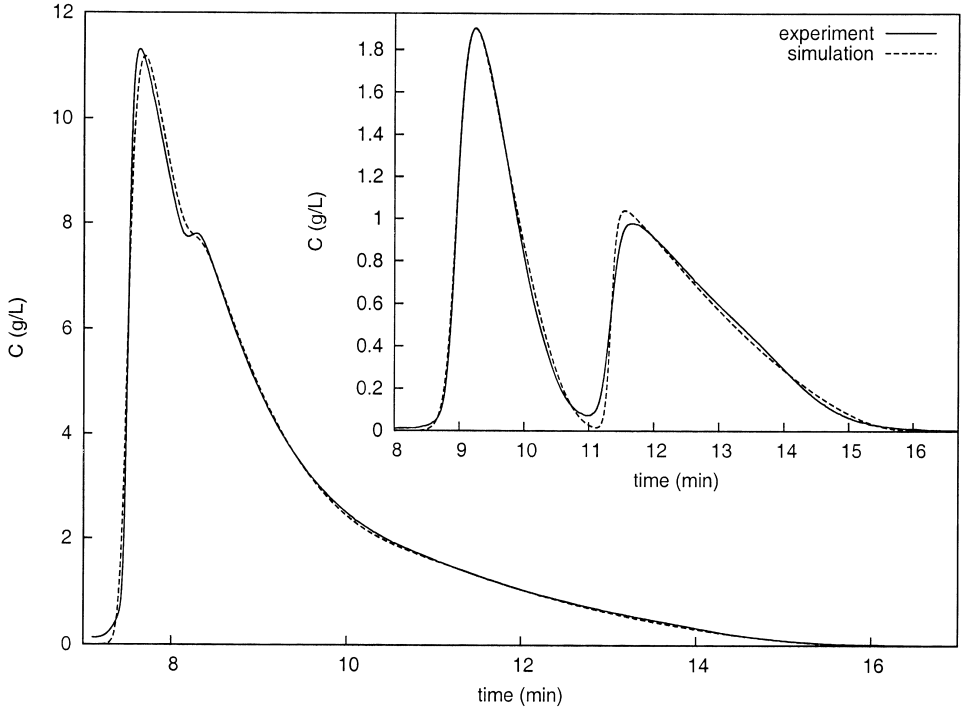

Fig. 9. Simultaneous fitting the competitive biTóth model to a large (50.7 mg) and a moderate (10.14 mg) injection of the racemic mixture.

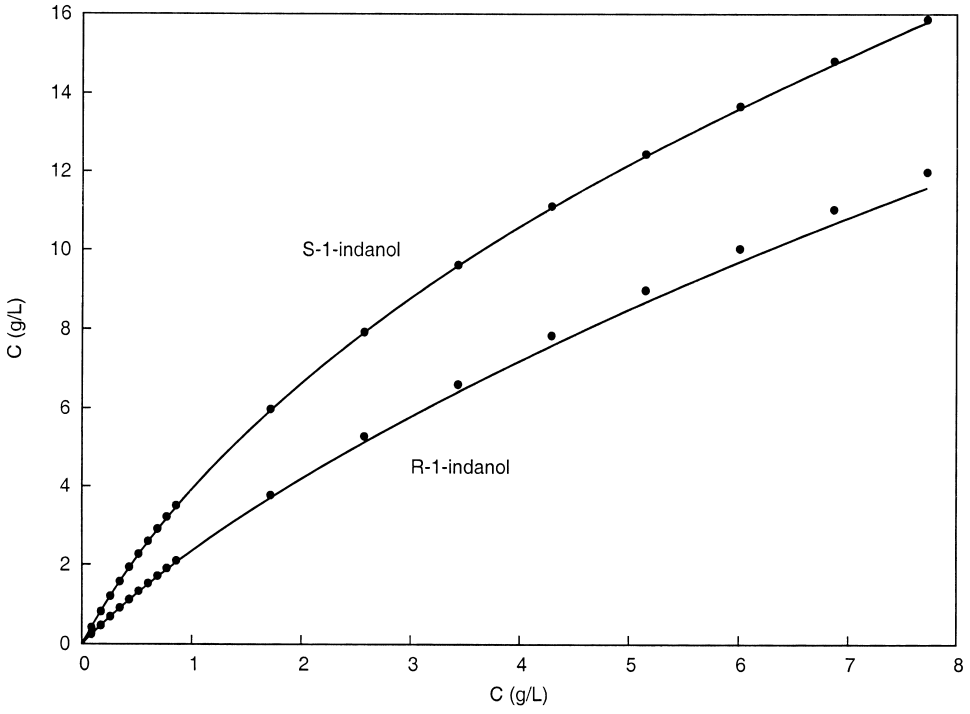

Fig. 10. Comparison of the competitive biTóth isotherms obtained by the inverse method (lines) and the experimental results of frontal analysis (symbols).

in order to determine isotherm parameters that are valid over a large concentration range, large elution concentration is required. For the determination of competitive isotherms, a single injection of a large amount of the racemic mixture may be insufficient if peak resolution is completely lost due to column overload. We propose that in that case the simultaneous fit of the bands of a rather large sample and of a moderately large sample—showing good resolution or touching bands separation—is to be carried out to derive the isotherm parameters.

The single component and competitive isotherms determined by the inverse method agree well with those determined with the well established frontal analysis. This agreement validates the data obtained with this novel approach.

For the adsorption of 1-indanol on celluloze tribenzoate, the biTóth model seems to be the most appropriate model to account for the band profiles recorded. This isotherm model exhibits a bimodal adsorption energy distribution, like the biLangmuir isotherm model, but it takes into account the dispersion of the adsorption energies around their average values. The heterogeneity parameters of the biTóth isotherm evince that the nonselective sites are more heterogeneous than the enantioselective ones. The enantiomers interact with the selective site with more unique energies, whereas several different interactions with the nonselective sites are possible.

Acknowledgements

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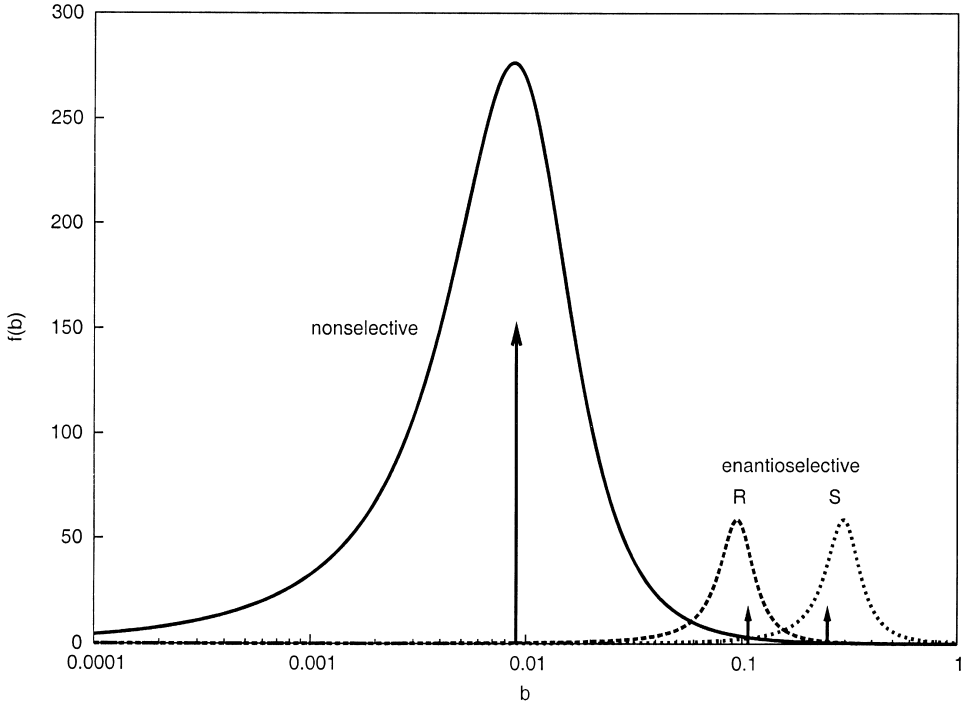

Fig. 11. Distribution of the equilibrium constants of adsorption calculated by means of the biTóth model. The arrows indicate the equilibrium constants derived from the competitive biLangmuir isotherm.

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