

Comparison of the various kinetic models of non-linear chromatography

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ABSTRACT

It is not possible to separate simply the influences of a slow mass transfer kinetics and of a slow kinetics of adsorption–desorption on the elution profile of a component. Four kinetic models of chromatography are studied: (i) the Thomas or reaction model, which assumes Langmuir kinetics of adsorption–desorption and no axial dispersion; (ii) the reaction-dispersive model, which uses the same Langmuir kinetics as the Thomas model but assumes a finite axial dispersion; (iii) a transport model, which uses the linear solid film driving force model to account for a slow kinetics of mass transfer and assumes no axial dispersion; and (iv) a transport-dispersive model, using the same mass transfer kinetics as the transport model and assumes finite axial dispersion. The analytical solution of the Thomas model can be fitted, with an accuracy which exceeds the precision of experimental measurements, on bands calculated using either one of the other three kinetic models of chromatography. Thus, the Thomas model, which assumes a slow adsorption–desorption kinetics and infinitely fast mass transfer kinetics, accounts very well for profiles calculated with a model making the reverse assumption. However, the values of the lumped kinetic coefficient obtained by curve fitting depend on the sample amount. Thus, the examination of an elution profile and its fitting to a model do not permit an easy solution of the inverse problem of chromatography.

INTRODUCTION

A number of different kinetic models have been introduced in linear chromatography [1–4]. Closed-form solutions for these models or their solutions in the Laplace domain have been derived, the general equations of chromatography being greatly simplified by the assumption of a linear isotherm. It has been shown that, provided the number of transfer units is not very small, the results of all these models are equivalent and that their solution is well approximated by a Gaussian profile [4–7]. Further, this common result is equivalent to the results of the equilibrium-dispersive model [1,8,9] and of the plate theory [5,10], provided that the proper apparent number of transfer units be used.

The elution profile of a component is the distribution of the residence times of its molecules. As for all distributions, a variance can be defined for the elution profile. Glueckauf [7] showed that a contribution to this variance can be calculated for each independent source of band broadening and that these contributions are simply additive. Van Deemter *et al.* [5] also established this rule of additivity. They simplified the analytical solution of Lapidus and Amundson [1] in the case of a non-equilibrium model of linear chromatography and showed that, if the rate-controlling step of the mass transfer kinetics in the chromatographic column is not very slow, this solution can be reduced to a Gaussian profile. By comparing their simplified solution with that of the plate theory [10], they derived a landmark relationship between the height equivalent to a theoretical plate of the plate model, the axial dispersion coefficient and the lumped mass transfer coefficient of their linear driving force model.

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Using a completely different approach, the moment analysis, Kucera [2] and Kubin [3] demonstrated also the additivity of the different contributions to band broadening. This demonstration is based on the solution of the general rate model of linear chromatography in the Laplace domain. The solution cannot be inverted into the time domain, but the moments of the distribution in the time domain can be calculated. Giddings [6], using the rate theory, derived the same additivity rule. The most general analysis of the dependence of the height equivalent to a theoretical plate in linear chromatography on the experimental conditions is due to Horvath and Lin [11]. Contributions for all the known contributions to the mass transfer resistance have been discussed.

In the course of these investigations, several general kinetic models have been used. These models can be extended to non-linear chromatography, where the isotherm is no longer linear. The purpose of this work is a comparison between the results given by these different models in non-linear chromatography and the search for whether, and under which conditions, they could be equivalent, as they are in linear chromatography.

THEORY

Chromatography is a complex combination of phenomena, involving the dynamic transfer, under conditions which are often close to equilibrium but never achieve it, of a pulse of a mixture of components along a column. In this study, however, we consider only the simplest possible case, the migration of a pulse of a pure compound. The column is packed with porous particles between which flows a mobile phase in which the component is soluble. The component has free access to the inside of the porous particles. During its migration, the component experiences transfer between the mobile phase and the surface of an adsorbent. The band profile depends on the equilibrium isotherm and on the different phenomena which act to broaden the band, axial dispersion, diffusion across the mobile phase stream, resistance to mass transfer across the external film around the particles, intraparticle diffusion and kinetics of adsorption-desorption.

Different chromatographic models attempt to model the band migration in different ways. They

can be grouped in two classes of models. The general rate models consider a more or less complex array of kinetic equations and make a detailed analysis of the various steps involved in the chromatographic process. The lumped rate models consider only one kinetic process, regarded as the rate-controlling step, or at most a few such processes, and they lump in the rate constant the contributions of the kinetics of the other processes.

General rate model

A general rate model of chromatography uses two mass balance equations, one in the mobile phase outside the particle and the other in the stagnant mobile phase inside a particle, and two kinetic equations, one relating the two mobile phase concentrations (mass transfer kinetics) and the other relating the stagnant mobile phase and the stationary phase concentrations (kinetics of adsorption-desorption).

External mass balance equation. The differential mass balance equation of the solute in the stream of mobile phase around the particles can be written as

$$u \cdot \frac{\partial C}{\partial z} + \frac{\partial C}{\partial t} + F \cdot \frac{\partial \bar{C}_s}{\partial t} = D_L \cdot \frac{\partial^2 C}{\partial z^2} \quad (1)$$

where u is the mobile phase linear velocity, $F = (1 - \epsilon_e)/\epsilon_e$ is the phase ratio, ϵ_e is the external porosity of the column, D_L is the axial dispersion coefficient, C is the mobile phase concentration in the interparticle stream, \bar{C}_s is the stationary phase concentration averaged over the entire particles and $\partial \bar{C}_s / \partial t$ is the rate of adsorption averaged over an entire particle. For a spherical particle,

$$\bar{C}_s = \frac{3}{R_p^3} \int_0^{R_p} r^2 C_s dr \quad (2)$$

where R_p is the particle radius. For a spherical particle, we have

$$\frac{\partial \bar{C}_s}{\partial t} = \frac{3}{R_p} \cdot N_0 \quad (3)$$

where N_0 is the mass flux of solute from the bulk solution through the external surface of the particle. The boundary condition at the external particle surface is given by

$$N_0 = D_p \cdot \frac{\partial C_p}{\partial r} \Big|_{r=R_p} = k_f(C - C_p \Big|_{r=R_p}) \quad (4a)$$

where k_f is the external mass transfer coefficient.

The Danckwerts-type initial and boundary conditions in the mobile phase are given by

$$C(z, 0) = 0 \quad (4b)$$

$$\frac{\partial C}{\partial z} \Big|_{z=L} = 0 \quad (4c)$$

$$uC(0, t) = uC_0(t) + D_L \cdot \frac{\partial C}{\partial z} \Big|_{z=0} \quad (4d)$$

Intraparticle mass balance equation. The differential mass balance equation of the solute in the particle yields

$$\varepsilon_p \cdot \frac{\partial C_p}{\partial t} + (1 - \varepsilon_p) \frac{\partial C_s}{\partial t} = D_p \left(\frac{\partial^2 C_p}{\partial r^2} + \frac{2}{r} \cdot \frac{\partial C_p}{\partial r} \right) \quad (5)$$

where ε_p is the internal porosity of the packed bed, D_p is the diffusion coefficient of the solute inside the pores of the particles and C_p and C_s are the solute concentrations in the solution inside the pores and in the stationary phase, respectively. The boundary conditions for the particle is the symmetrical condition

$$\frac{\partial C_p}{\partial r} \Big|_{r=0} = 0 \quad (6a)$$

The initial condition is

$$C_p = C_p(r, 0) \text{ at } t = 0 \quad (6b)$$

For a pulse injection, we have

$$C(0, t) = C_0 \text{ for } 0 \leq t \leq t_p \quad (7a)$$

$$C(0, t) = 0 \text{ for } t_p \leq t \quad (7b)$$

Kinetic equation. If we may assume that the kinetics of adsorption-desorption are infinitely fast, the concentrations of the solute in the mobile phase contained in the pores and in the stationary phase are related through the equilibrium isotherm, $C_s = f(C_p)$. If these kinetics are slow, they are related through the kinetic equation. For example, for a linear isotherm and slow kinetics of adsorption-desorption with a first-order rate, we have

$$\frac{\partial C_s}{\partial t} = k_{ads}(C_p - C_p^*) = k_{ads}(C_p - C_s/K_a) \quad (8)$$

where k_{ads} and K_a are the adsorption rate constant and the adsorption equilibrium constant (Henry constant), respectively, and C_p^* is the liquid concentration in equilibrium with the stationary phase concentration, $C_p^* = C_s/K_a$.

Solution of the general rate model. Kubin [3] and Kucera [2] derived in the Laplace domain the analytical solution of the system of eqns. 1-8 of the general rate model of linear chromatography just presented. This solution cannot be inverted in the time domain, but they could derive from it the moments of the retention time distribution which constitute the elution band profile. More recently, Lenhoff [4] calculated the elution band profile in the time domain by numerical evaluation of the inverse Laplace transform.

General rate models coupled to a non-linear isotherm have been studied in detail by Wang and co-workers [12-14], using the method of orthogonal collocation for the numerical calculation of solutions. The general rate model considering an infinite rate of adsorption-desorption and a non-linear isotherm was solved numerically by Yu and Wang [12] and by Lee *et al.* [13]. Later, this model was extended to the case of slow adsorption-desorption, possibly involving also reactions in the mobile or stationary phases, with a slow reaction rate [14]. Lin and Ma [15] solved numerically, by orthogonal collocation, a simpler pore diffusion model, considering only intraparticle diffusion and axial dispersion, ignoring the diffusion through the external film around the particles, but including the influence of non-uniform particle size by taking the particle size distribution into account.

Lumped model of chromatography

The general rate model of chromatography just discussed is a complete and correct model of the chromatographic process. It accounts for all the known contributions, whether of thermodynamic or kinetic origins, to the elution band profile. Unfortunately, the prediction of the band profiles in any real case requires the prior knowledge, determination or evaluation of a number of parameters (*e.g.*, isotherm coefficients, rate constants, mass transfer coefficients). Accordingly, the optimization of the experimental conditions for maximum production rate (let alone for minimum production cost!) becomes extremely complex when using this

model. To simplify the solution of the problem of non-linear chromatography, several simpler kinetic models have been introduced. These models are extensions of models which were successfully used in linear chromatography.

Thomas model. The simplest lumped model is due to Thomas [16]. Like the ideal model, the Thomas model ignores the axial dispersion (*i.e.*, $D_L = 0$ in eqn. 1) and the mass transfer kinetics. It could be called a reaction model. It assumes, however, that the rates of adsorption and desorption are finite and given by the second-order Langmuir kinetics:

$$\frac{\partial C_s}{\partial t} = k_a(q_s - C_s)C - k_d C_s \quad (9)$$

where k_a and k_d are the rate constants of adsorption and desorption, respectively, and q_s is the specific saturation capacity of the adsorbent, or amount needed to form a saturated monolayer. Because of the difference between the kinetic models used, there is no reason for k_{ads} (eqn. 8) to be equivalent to k_a (eqn. 9). As we assume that the mass transfer kinetics are very fast, C (eqn. 1) and C_p (eqn. 5) are equivalent. Thomas derived a closed-form solution for his model in the case of a step function input, *i.e.*, for the frontal analysis problem [16]. Later, Goldstein [17] derived an analytical solution of the Thomas model in the case of a pulse injection of any width, finite or not. More recently, Wade *et al.* [18] studied the solution of the Dirac problem, in which case the input function is an impulse or rectangular pulse of infinitely narrow width. They found that this problem has a solution simpler than Goldstein's, and compared it with experimental results obtained in affinity chromatography, a mode of separation in which the effects of a slow adsorption-desorption kinetics may often offset the effects of both axial dispersion and the resistances to mass transfer.

In the case of an impulse input, the solution given by Wade *et al.* [18] can be written as [19]

$$\frac{C}{C_0} = \frac{1 - e^{-N_{rea}L\tau}}{k'_0 N_{rea} L \tau} \cdot \frac{N_{rea} \sqrt{\frac{1}{\tau}} I_1(2N_{rea} \sqrt{\tau}) e^{-N_{rea}(\tau+1)}}{1 - T(N_{rea}, N_{rea}\tau)(1 - e^{-N_{rea}L\tau})} \quad (10a)$$

or

$$\frac{C}{C_{di,0}} = \frac{1 - e^{-N_{rea}L\tau}}{N_{rea} L \tau} \cdot \frac{N_{rea} \sqrt{\frac{1}{\tau}} I_1(2N_{rea} \sqrt{\tau}) e^{-N_{rea}(\tau+1)}}{1 - T(N_{rea}, N_{rea}\tau)(1 - e^{-N_{rea}L\tau})} \quad (10b)$$

where $\tau = (t - t_0)/(t_{R,0} - t_0)$ is a dimensionless time, $C_0 = A_p/t_0 = n/\varepsilon SL$ and $C_{di,0}$ is a reference, dimensionless concentration obtained by dividing the amount injected by the product of the column hold-up volume and the retention factor of the component studied at infinite dilution, also equal to the ratio of the area of the input profile to the net retention time at infinite dilution [$C_{di,0} = n/\varepsilon SL k'_0 = A_p/k'_0 t_0 = C_p t_p/(t_{R,0} - t_0) = C_p \tau_0$]. n (mol) is the amount of solute injected, S and L are the column cross-section area and length, respectively, $A_p = C_p t_p$ is the area (conservative) of the rectangular pulse of solute injected, C_p being the solute concentration, and t_p the time width. In eqns. 10, $I_1(x)$ is the first-order modified Bessel function of the first kind, and $T(u,v)$ is a Bessel function integral [17-19]. Eqn. 10b is convenient as it gives a normalized profile depending only on two parameters, and we see that the dimensionless elution profile (*i.e.*, the plot of $C/C_{di,0}$ versus τ) depends only on two parameters, the loading factor, L_f [19], and the reaction (or adsorption-desorption) number of transfer units, $N_{rea} = k'_0 k_d L/u$. If the pulse width is finite, the solution derived by Goldstein [17] applies, and it depends on one additional parameter, the reduced injection pulse width, $\tau_0 = t_p/(t_{R,0} - t_0)$.

Reaction-dispersive model. More recently, an extension of the Thomas model, the reaction-dispersive model of chromatography, has been suggested [19]. In this model, we use a single mass balance equation and a kinetic equation. The mass balance equation is written as

$$u \cdot \frac{\partial C}{\partial z} + \frac{\partial C}{\partial t} + F \cdot \frac{\partial C_s}{\partial t} = D_a \cdot \frac{\partial^2 C}{\partial z^2} \quad (11)$$

where C and C_s are the concentrations of the component in the mobile and stationary phases, respectively, and D_a is the apparent dispersion coefficient, related to the axial dispersion coefficient, D , and to the lumped mass transfer coefficient, k_f . Any proper kinetic equation can be used in this model. For the sake of comparison with the Thomas model, we may assume the Langmuir kinetic equation, eqn. 9. The model has no analytical solution. A numerical solution can be obtained easily, using the finite difference method [19,20]. The solutions of the reaction-dispersive model for a narrow injection pulse depend on three parameters, the loading factor, L_f , and two kinetic parameters, the reaction

number of transfer units, $N_{\text{rea}} = k'_0 k_a L/u$, and the dispersion number of transfer units, $N_{\text{Disp}} = Lu/2D_a$. When $D_a = 0$, the reaction-dispersive model reduces to the Thomas model and the solution is obtained using either the Goldstein (finite pulse width) or the Wade *et al.* (impulse) solution.

Transport and transport-dispersive models. Instead of assuming slow kinetics of adsorption-desorption and very fast kinetics of mass transfer, we may as well assume very fast kinetics of adsorption-desorption and slow kinetics of mass transfer. An attractive kinetic model of chromatography combines a mass balance equation (eqn. 11) and the kinetic equation of the solid film linear driving force model [21,22]. Now, we have the following system:

$$u \cdot \frac{\partial C}{\partial z} + \frac{\partial C}{\partial t} + F \cdot \frac{\partial C_s}{\partial t} = D_L \cdot \frac{\partial^2 C}{\partial z^2} \quad (12a)$$

$$\frac{\partial C_s}{\partial t} = k_f (q^* - C_s) \quad (12b)$$

where k_f is the lumped mass transfer coefficient and q^* is the stationary phase concentration in equilibrium with the local mobile phase concentration, as given by the isotherm equation. The analytical solution of this model in the case of a linear isotherm has been derived [1,5]. In the case of a non-linear isotherm, numerical solutions have been obtained using a finite difference procedure [20,23,24]. In this case, the band profile depends on L_f , N_{Disp} and another kinetic parameter, the number of transfer units, $N_m = k'_0 St$, where St is the Stanton number, $St = k_f L/u_0$. If we assume $D_L = 0$ in eqn. 12a, we have a transport model, and the band profile depends only on L_f and N_m . If D_L is different from 0, we have a transport-dispersive model.

Thus, we have a series of similar models, which differ essentially by the nature of the step in the global mass transfer which is considered as the slowest and may control the entire kinetics of the chromatographic process and depending on whether the axial dispersion is neglected or not. We now compare the solutions of these models for a non-linear isotherm.

RESULTS AND DISCUSSION

In all the cases discussed here, we have assumed in the calculations a narrow injection plug width, 20 μl ,

so we can compare directly the profiles obtained by numerical integration and by the Wade *et al.* [18] equation. For wider injection plugs, the Goldstein equation [17] could also be used, but it requires the evaluation of four Bessel function integrals instead of one, rendering the numerical calculation as complex and possibly slower than straightforward numerical integration of the system of partial differential equations.

Comparison between the Thomas model and the reaction-dispersive model

In Fig. 1, we compare two band profiles corresponding to the same experimental conditions with a loading factor $L_f = 1\%$ and obtained as analytical solution of the Thomas model (dotted line) and numerical solution of the reaction-dispersive model

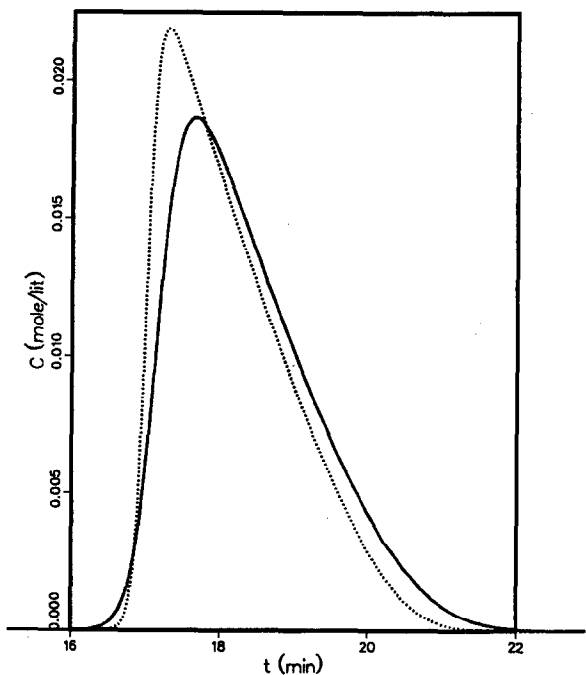


Fig. 1. Comparison between the numerical solution of the reaction-dispersive model of chromatography (solid line) and the analytical solution of the Thomas model (dotted line). Values of parameters; loading factor, $L_f = 1\%$; retention factor, $k'_0 = 5$; Thomas number, $N_{\text{rea}} = k'_0 k_a L/u = 2000$; corrected efficiency, for the reaction-dispersive model:

$$2N_{\text{Disp}} \left(\frac{k'_0}{1+k'_0} \right)^2 = P_{e,z} \left(\frac{k'_0}{1+k'_0} \right)^2 = \frac{Lu}{D_a} \left(\frac{k'_0}{1+k'_0} \right)^2 = 2000,$$

for the Thomas model, $N_{\text{Disp}} = \infty$.

(solid line). The dimensionless number characterizing the kinetics of adsorption-desorption or number of reaction units, N_{rea} , is equal to 2000. The dimensionless number characterizing the axial dispersion in the reaction-dispersive model is

$$2N_{\text{Disp}} \left(\frac{k'_0}{1+k'_0} \right)^2 = Pe \left(\frac{k'_0}{1+k'_0} \right)^2 = 2000 \quad (13)$$

with $Pe = uL/D_a$. As expected, the two band profiles are different, as the reaction-dispersive model takes into account the axial dispersion (axial diffusion and mass transfer kinetics) whose effects have been neglected in the Thomas model.

It is interesting to examine now whether it would be possible to lump together the two main contributions to band broadening, the adsorption-desorption kinetics and the axial dispersion. If this is possible, we could fit a solution of the Thomas model on the solid line in Fig. 1. Of course, the values of the kinetic parameters leading to the best fit would be different from those corresponding to the strict Thomas model. We call $N_{\text{rea}}^{\text{app}}$ this apparent value of the number of reaction units which corresponds to an apparent rate parameter and includes the effects of both slow adsorption-desorption and finite axial dispersion.

The calculations were carried out using a three-dimensional simplex algorithm with k'_0 , L_f and $N_{\text{rea}}^{\text{app}}$ as the parameters, and fitting the Wade *et al.* [18] equation for the Thomas model (eqn. 10a) to the profile calculated by numerical integration of the reaction-dispersive model. In the modified simplex approach used [25-27], a method of successive estimation of the three parameters (k'_0 , L_f and N_{rea}) was designed. The band profile computed with the Thomas model from a set of values of the three parameters is compared with the profile generated by the other model by calculating a score measuring the degree of similarity between the two profiles. Then, an algorithm generates a new set of parameters leading to a new profile. The simplex algorithm assures convergence of the similarity between the profiles and selects the best set.

The result of this exercise is shown in Fig. 2, for various values of the loading factor, $L_f = 1, 5, 10$ and 20%. There is excellent agreement between the two curves. In all instances an excellent fit was achieved. The best values of the three parameters are

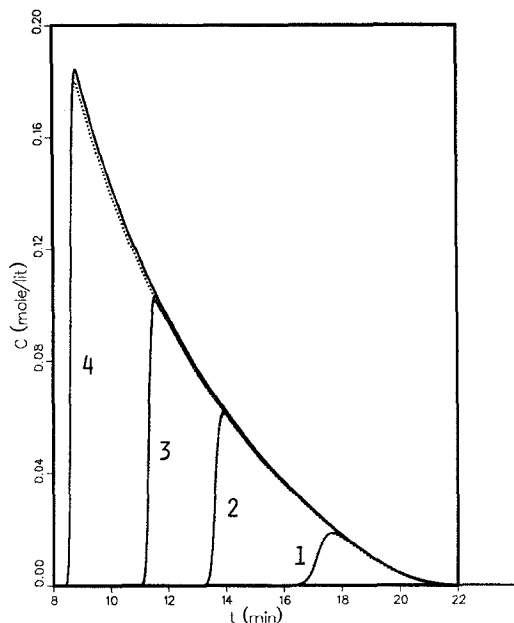


Fig. 2. Same as Fig. 1, except that the parameters of the Thomas model were obtained by a best fit of eqn. 10a to the numerical solution of the reaction-dispersive model (see Table I). Value of the loading factor, L_f : (1) 1%; (2) 5%; (3) 10%; (4) 20%.

given in Table I. There is excellent agreement between the "true" values of the retention and the loading factors used for the numerical calculation of the solutions of the reaction-dispersive model and the "best-fit" values derived from the fitting of the

TABLE I

BEST PARAMETERS OBTAINED BY FITTING BAND PROFILES CALCULATED WITH THE REACTION-DISPERSIVE MODEL^a TO THE THOMAS MODEL^b

k'_0	L_f (%)	k'_0^c	L_f^c	$N_{\text{rea}}^{\text{app}c}$
5	1	4.994	0.98	954
5	5	4.992	4.91	865
1	5	0.993	4.93	865
20	5	19.98	4.92	865
5	10	4.986	9.81	798
5	20	4.968	19.54	690

^a Parameters of the generated profiles: $2[k'_0/(1+k'_0)]^2 N_{\text{Disp}} = 2000$, $N_{\text{rea}} = k'_0 k_d L/u = 2000$. Hence, $N_{\text{rea}}^{\text{app}} = 1000$.

^b Parameter of the Thomas model: $N_{\text{Disp}} = \infty$.

^c Best values of, the parameters obtained by curve fitting.

Thomas model to these profiles. The relative differences between the true and the calculated values of the loading factor and the retention factors are constant and close to 2 and 0.5%, respectively. As they are constant, they are probably due to the fitting process itself. This agreement is better than what can be expected when actual experimental data are fitted to a correct model. In a case like that, no model error can be detected. On the other hand, as expected, the value of N_{rea}^{app} is smaller than N_{rea} . This theoretical result is supported by data published by Lucy *et al.* [28]. They recorded experimental band profiles at increasing sample sizes for a series of compounds and fitted them to the Thomas model. They found that the best values obtained for the retention factor, k'_0 , and the column saturation capacity are nearly independent of the sample size while the kinetic parameter is concentration dependent, which is in agreement with our results.

The variances of the various contributions to band broadening in linear chromatography are additive. Thus, in linear chromatography we may write

$$H = H_{Disp} + H_{m,t} + H_{react}$$

or

$$\frac{1}{N_{rea}^{0,app}} = \frac{1}{2} \left(\frac{1+k'_0}{k'_0} \right)^2 \frac{1}{N_{Disp}} + \frac{1}{N_m} + \frac{1}{N_{rea}} \quad (14)$$

where $N_{rea}^{0,app}$ is the apparent number of reaction transfer units and H , H_{Disp} , $H_{m,t}$ and H_{react} are the total height equivalent to a theoretical plate of the column and the contributions of the axial dispersion, the mass transfer kinetics and the adsorption-desorption kinetics, respectively. According to eqn. 14, the apparent number of transfer units in linear chromatography as derived from the reaction-dispersive model (eqns. 1-7) would be $N_{rea}^{0,app} = 1000$. The data in Table I suggest that N_{rea}^{app} is not constant in non-linear chromatography, but decrease with increasing value of the loading factor.

Attempts were also made to fit the Thomas model to solutions of the reaction-dispersive model corresponding to lower values of the loading factor, *e.g.*, 0.2% or less. The agreement between the two profiles (not shown) becomes increasingly less satisfactory with decreasing values of the loading factor. Also, the value of the loading factor obtained by curve fitting was increasingly more different from

the value used in the numerical calculation. The same problem was already observed by Lucy *et al.* [28] when attempting to fit experimental band profiles on the Thomas model at low values of the loading factor. Obviously, at high loading factors, the influence of the thermodynamics on the band profiles is major and the kinetic influence moderate, unless the rates are very slow. When the loading factor is small, chromatography is becoming linear and the band broadening contributions of kinetic origin are dominant. The fitting procedure then fails to determine the correct value of the loading factor. We conclude that, if isotherm parameters are to be determined by fitting an experimental profile to a model, the best results will be obtained when using a large sample size and strong column overload.

Similarly, if we change the retention factor, from 5 to 20 or 1 (results not shown), while keeping the

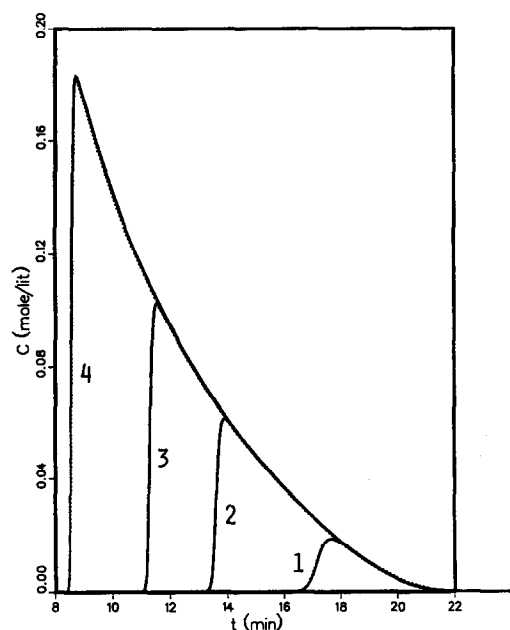


Fig. 3. Comparison between a profile obtained as numerical solution of the transport model of chromatography (solid line) and a profile given by the analytical solution of the Thomas model (dotted line). Experimental conditions for the linear driving force model: loading factor, $L_f = 1\%$; limit retention factor, $k'_0 = 5$; number of mass transfer stages, $N_m = k'_0 k_t L/u = 1000$; coefficient of axial dispersion, $D_L = 0$, $N_{Disp} = \infty$. The parameters of the Thomas model were obtained by fitting eqn. 10a to the profile obtained by numerical integration of the linear driving force model (see coefficients in Table II). Values of the loading factor, L_f : (1) 1%; (2) 5%; (3) 10%; (4) 20%.

other parameters constant, we can also achieve an excellent fit. The values of the parameters obtained by this curve fitting are also reported in Table I. The change in k'_0 does not have any effect on the best values of either L_t or $N_{\text{rea}}^{\text{app}}$. This was expected as the retention factor has no influence on the dimensionless profile of the band [19].

Comparison between the Thomas model and the transport model

In Fig. 3 we compare two series of band profiles. The first (solid lines) are calculated using the solid film linear driving force model kinetic equation (eqn. 12b) and the mass balance of the ideal model (eqn. 12a with $D_L = 0$, transport model). These calculations were performed assuming a number of transfer units, $N_m = k'_0 k_t L/u$, equal to 1000. The second series of profiles (dotted lines) were calculated using the equation derived by Wade *et al.* [18] as solution of the Thomas model (eqn. 10a). The three coefficients of these Thomas profiles are selected so as to minimize the difference between the two profiles, using a simplex program. The corresponding parameters of the Thomas model are compared in Table II with the parameters used in the calculation of the profiles with the linear driving force model. A similar comparison is shown in Fig. 4. In this case, however, the calculated profile was obtained with the transport-dispersive model (eqns. 12a and 12b), with a number of transfer units, N_m ,

TABLE II
BEST PARAMETERS OBTAINED BY FITTING THE BAND PROFILES CALCULATED WITH THE TRANSPORT^a AND TRANSPORT-DISPERSIVE MODELS^b TO THE THOMAS MODEL^c

k'_0	L_t (%)	k'_0 ^d	L_t ^d	$N_{\text{rea}}^{\text{app}}$ ^d
5	1	5.0	0.991	954 ^a
5	5	4.996	4.952	886 ^a
5	5	4.998	4.87	823 ^b
5	10	4.993	9.91	828 ^a
5	20	4.995	19.82	727 ^a

^a Parameters of the generated profiles: $N_{\text{Disp}} = \infty$ and $N_m = k'_0 k_t L/u = 1000$. Hence $N_{\text{rea}}^{\text{app}} = 1000$.

^b Parameters of the generated profiles: $2[k'_0/(1+k'_0)]^2 N_{\text{Disp}} = 2000$ and $N_m = k'_0 k_t L/u = 2000$. Hence $N_{\text{rea}}^{\text{app}} = 1000$.

^c Parameter of the Thomas model: $N_{\text{Disp}} = \infty$.

^d Best values of the parameters obtained by curve fitting.

equal to 2000, and a finite coefficient of axial dispersion, such that

$$\frac{uL}{D_L} \left(\frac{k'_0}{1+k'_0} \right)^2 = 2N_{\text{Disp}} \left(\frac{k'_0}{1+k'_0} \right)^2 = 2000$$

Thus, in linear chromatography the column efficiency and the band profiles would be the same as for the conditions selected for Fig. 3 (see eqn. 14, which gives $N_{\text{rea}}^{\text{app}} = 1000$).

Figs. 3 and 4 show that the band profiles obtained with the transport and the transport-dispersive models can be fitted accurately enough to the Thomas model. The data in Table II show a very small error, of the order of 0.1%, for the retention factor, k'_0 . For the loading factor, the error is *ca.* 1%. Both errors are independent of the loading factor. On the other hand, the value obtained for $N_{\text{rea}}^{\text{app}}$ is not constant. It is significantly lower than 1000 and it decreases with increasing loading factor, whereas in

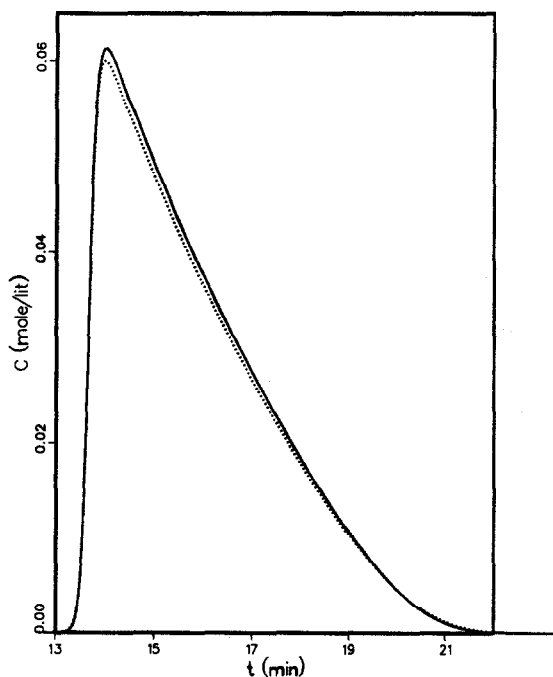


Fig. 4. Comparison between a profile obtained as numerical solution of the transport-dispersive model of chromatography (solid line) and a profile given by the analytical solution of the Thomas model (dotted line). Same conditions as in Fig. 3 for $L_t = 5\%$, except $N_m = k'_0 k_t L/u = 2000$, and $2N_{\text{Disp}}[k'_0/(1+k'_0)]^2 = 2000$. In linear chromatography, the overall band broadening would be the same in Figs. 3 and 4.

linear chromatography, and from eqn. 14, this value would be 1000 for Figs. 3 and 4.

We conclude from this comparison that it is possible to fit experimental data to any of the simple kinetic models. Different models will give approximately the same values for the limit retention factor at infinite dilution, k'_0 , and for the loading factor, L_f . However, the lumped kinetic parameters derived in the process will not remain constant. These parameters appear to be concentration dependent and to decrease with increasing concentration or sample size. In the following, we discuss the fundamental reason why the rate constant determined by fitting an experimental profile to a lumped kinetic model is concentration dependent.

Dependence of the lumped kinetic coefficients on the sample size

The dependence of the apparent kinetic parameter on the concentration was discussed by Rhee and Amundson [29] in an analysis of the properties of the shock layer in frontal analysis. We know that the ideal model predicts a concentration shock whenever the equilibrium isotherm is not linear [30]. The shock takes place on the band front in the case of a convex upward isotherm, the most frequent in liquid chromatography. This is due to the fact that, in the ideal model, each concentration propagates at its own velocity, related to the slope of the isotherm for the concentration considered. This velocity increases with increasing concentration for a convex upward isotherm. The faster high concentrations cannot pass the slower low concentrations and a concentration discontinuity or shock appears instead [30,31]. For an actual column, however, a concentration shock is impossible. This corresponds to an infinitely steep concentration gradient, generating an infinite mass flux by diffusion. A very steep front appears instead, the shock layer.

If we assume [29] the existence of a shock layer (region of very rapid variation of the concentration with the position in the column), write the mass balance equation and assume a linear driving force model for the kinetic equation of chromatography (eqns. 12a and 12b), it is possible to derive, by combination of the mass balance and the kinetic equation, the following relationship:

$$-\frac{\lambda}{PeSt} \frac{\partial^2 C}{\partial \eta^2} + \left[\frac{1}{Pe} + \frac{\lambda(1-\lambda)}{St} \right] \frac{\partial C}{\partial \eta} = F\lambda f(C; C^f, C^i) \quad (15)$$

where λ is the migration velocity of the shock layer:

$$\lambda = \frac{1}{1 + F\Delta q/\Delta C} \quad (16)$$

F is the phase ratio, Δq and ΔC are the amplitude of the concentration change (*i.e.*, shock) in the stationary and mobile phases, respectively, and η is a new variable:

$$\eta = x - \lambda t_d \quad (17)$$

with $x = z/L$ and $t_d = ut/L$, dimensionless variables, and the function f is given by

$$f(C; C^f, C^i) = \frac{\Delta q}{\Delta C} (C - C^f) - q(C^i) + q(C^f) \quad (18)$$

where C^i and C^f are the initial and final concentrations of the breakthrough curve and $\Delta C = C^f - C^i$.

Rhee and Amundson [29] showed that the velocity of the shock layer is the same as the velocity predicted for the shock in the ideal model. It is independent of the values of the axial dispersion coefficient and the kinetic coefficients. Thus, the elution of the mid-point of the breakthrough curve is independent of all kinetic influence and depends only on the thermodynamics. As can be seen, the axial dispersion term, Pe , and the mass transfer resistance term, St , have equivalent roles in eqn. 15. Their individual contributions add in the first-order differential term. In addition, however, there is a coupled, second-order differential term. In the practice of chromatography, both the Peclet and Stanton numbers are large. Hence the first term in the left-hand side of eqn. 15 is very small and can be neglected. The effects of the axial dispersion and the kinetics of mass transfer resistances are additive. The band profiles calculated by the equilibrium-dispersive model (infinitely fast mass transfer kinetics but finite axial dispersion) and the solid film driving force model are the same, provided the axial Peclet number of the kinetic model is replaced in the equilibrium-dispersive model with an apparent Peclet number related to the Peclet and Stanton numbers of the linear driving force model by

$$\frac{1}{Pe_{app}} = \frac{1}{Pe} + \frac{\lambda(1-\lambda)}{St} \quad (19a)$$

or

$$H = \frac{2D_L}{u} + 2 \left(\frac{K}{1+K} \right)^2 \frac{u}{Kk_f} \quad (19b)$$

where $K = F(\Delta q/\Delta C)$ is the slope of the chord, which is concentration dependent.

This important result demonstrates that, in non-linear as in linear chromatography, the effects of axial dispersion and mass transfer resistances are additive. Since λ and K are concentration dependent, however, the apparent axial dispersion term also depends on the concentration. This makes the situation much more complex in non-linear than in linear chromatography.

We have shown above that the additivity of the contributions of the axial dispersion and the mass transfer resistances valid in linear chromatography also holds in non-linear chromatography, but the retention factor, k'_0 should be replaced with the slope of the chord, $F(\Delta q/\Delta C)$. In linear chromatography, this slope is equal to k'_0 and eqn. 19 becomes

$$\frac{1}{Pe_{app}} = \frac{1}{Pe} + \frac{k'_0}{(1 + k'_0)^2 St} \quad (20a)$$

or

$$H = \frac{2D_L}{u} + \frac{2k'_0 u}{(1 + k'_0)^2 k_f} \quad (20b)$$

Eqn. 20, which is valid only for linear chromatography, is exactly the result obtained by Van Deemter *et al.* [5].

The previous analysis applies to the combination of a finite axial dispersion and slow mass transfer kinetics, which can be accounted for using the solid film linear driving force model. When the mass transfer kinetics are fast but the kinetics of adsorption-desorption are slow and can be accounted for by the Langmuir model (eqn. 9), we can let $b = k_a/k_d$ and rewrite the second-order Langmuir kinetics as

$$\begin{aligned} \frac{\partial C_s}{\partial t} &= k_d[bCq_s - C_s(1 + bC)] = k_d(1 + bC) \\ &\quad \left[\frac{bCq_s}{1 + bC} - C_s \right] \\ &= k_d(1 + bC)(q^* - C_s) \end{aligned} \quad (21)$$

where q^* is the stationary phase concentration in equilibrium with the mobile phase concentration C . For a linear isotherm (*i.e.*, $bC \rightarrow 0$), eqn. 21 is exactly the solid film linear driving force model (eqn.

8), with $k_f = k_d$. These two models are identical in linear chromatography. Eqn. 21 shows that, with a non-linear isotherm, the Langmuir kinetic model can still be written under the general form of the solid film linear driving force model, but with a kinetic coefficient

$$k_f = k_d(1 + bC) \quad (22a)$$

or, conversely, a linear driving force model can be written under the general form of the Langmuir kinetic model, but with a rate constant

$$k_d = \frac{k_f}{1 + bC} \quad (22b)$$

In both instances, however, the new rate constant is concentration dependent. This is why when a band profile is simulated using the transport model (*i.e.*, $D = 0$ and solid film linear driving force kinetics), the profile can be fitted to the Thomas model ($D = 0$ and Langmuir kinetics). However, the parameters supplied by the regression, k_d and N_{rea}^{app} , are concentration dependent and decrease with increasing concentration.

The equivalence between the kinetic equations of the Langmuir model (eqn. 9) and the linear driving force model (eqn. 12) has been shown previously by Hiester and Vermeulen [32] in the case of the breakthrough curve (Riemann problem). They also showed that the equivalent rate parameter is concentration dependent. Arnold and Blanch [33] suggested that, when slow mass transfer kinetics and slow adsorption-desorption kinetics coexist, the solution of the Thomas model can still be applied. In this instance, however, the apparent number of reaction units used should be related to the numbers of reaction units and mass transfer units by

$$\frac{1}{N_{rea}^{app}} = \frac{1}{N_{rea}} + \frac{1}{N_m} \quad (23)$$

As in non-linear chromatography N_m depends on the concentration, the apparent number of transfer units also depends on the concentration. The concentration dependence of the kinetic parameter is more consequential in frontal analysis and in displacement chromatography where the variation of concentration is much more important. The maximum concentration of a band in elution chromatography is smaller than the step height in the other two

methods. Hence the profile of an elution band calculated without accounting for the concentration dependence of the kinetic parameter is close to the actual band profile, especially when the column efficiency is significant [34].

All these results explain why we can fit band profiles calculated with a model to the formalism of another model and determine satisfactory values for the parameters of this other model. It explains also why, in this instance, the kinetic parameter of the other model depends on the concentration range of the band, *i.e.*, on the sample size.

CONCLUSIONS

Experimental band profiles acquired in non-linear chromatography can be fitted to many different models. The values supplied by the curve-fitting procedure for the thermodynamic parameters, the limit retention factor, k'_0 , and the loading factor, L_f , are accurate with all models. The differences between the values derived from different models are probably not significant, but less than the experimental error. On the other hand, the lumped kinetic coefficient is concentration dependent. The values obtained differ, depending on the model used and on the loading factor corresponding to the experiment.

In a further paper we shall consider the dependence of the kinetic parameters on the concentration range studied and on the column efficiency [34], and investigate the differences between the various models at very low column efficiency.

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