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PHYSICAL AND MATHEMATICAL MODELLING TO AID SCALE-UP OF LIQUID CHROMATOGRAPHY

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SUMMARY

A review of previous work indicates that the mathematical modelling of adsorption rate processes is well established and provides a basis for predictive methods for scale-up. Small-scale experiments to provide isotherm and kinetic data for code prediction purposes are described and pilot-scale equipment to provide results for code predictions are outlined. Predictions of the performance of a packed-bed adsorption column using numerical methods incorporated in the FACSIMILE code show good agreement with results from an analytic solution, and with the experimental data of Chase for affinity adsorption of lysozyme on Blue Sepharose CL-6B. This is part of a programme aimed at validating the FACSIMILE code for application to the design, performance prediction, optimization and scale-up of industrial adsorption and chromatography equipment.

INTRODUCTION

There is considerable industrial interest in the scale-up of adsorption and chromatographic techniques for the recovery, separation and purification of biochemical components from liquid feedstocks. This leads to a requirement for computer methods for the design, performance prediction and optimization of adsorption equipment. Before general application of such computer programs, it is necessary that predictions from codes be validated against relevant experimental and operational data, to give confidence in application of the codes to scale-up.

In this paper, previous work on the mathematical modelling of adsorption rate processes is briefly reviewed, and details are given of the computer code FACSIMILE, which is being developed for the prediction of such processes, in particular for scale-up and performance studies. Complementary to the mathematical modelling work, small-scale experiments to provide adsorption isotherm and kinetic data for use in making predictions with the FACSIMILE code, and pilot-scale equipment to provide experimental results to check the code predictions, are described.

Comparisons are given between FACSIMILE predictions for the mathematical modelling of a packed-bed adsorption column and results from the analytic solution that can be derived in the case of no axial diffusion, and with experimental data from the literature for the adsorption of lysozyme on Sepharose CL-6B–Cibacron Blue affinity adsorbent in a packed column.

PREVIOUS WORK

Useful reviews of the rate theories of adsorption are given by Yang and Tsao[1], Vermeulen *et al.*[2] and Ruthven[3].

For a packed-bed column, the mass balance for the mobile phase can be written as

$$D \cdot \frac{\partial^2 c}{\partial z^2} - V \cdot \frac{\partial c}{\partial z} - M = \frac{\partial c}{\partial t} \tag{1}$$

where D is the axial dispersion coefficient, V is the linear velocity, c is the solute concentration in the fluid stream, M is the rate of interface mass transfer, z is the axial co-ordinate, and t is time. Differences in rate theory models are mainly due to the variation in the rate equations for interface mass transfer or for the specification of M in eqn. 1. The rate of interface mass transfer may be formulated for (i) fluid film diffusion rate controlling, (ii) surface adsorption reaction rate controlling, and (iii) particle and/or pore diffusion rates controlling; the various mass transfer steps are depicted in Fig. 1.

For film diffusion controlling, Furnas[4] has given solutions with the assumptions of plug flow and linear isotherm, and Michaels[5] obtained the exact solution for a range of favourable equilibrium. Thomas[6] has given analytical solutions for surface adsorption reaction rate controlling for fixed-bed ion exchange, neglecting axial dispersion.

When the particle and/or pore diffusion rate is controlling, two types of approach have been used. These are: (i) the homogeneous solid model and (ii) the porous particle model. The homogeneous solid model treats the particle as a homogeneous matrix, irrespective of its porous structure. A number of workers have obtained analytical solutions by assuming a homogeneous model: Rosen[7,8] and Tien and Thodos[9], based on linear isotherms; and Cooper[10] and Ozil and Bonnetain[11], based on irreversible isotherms. More recently, Rice[12] has given analytical solutions for batch, packed-tube and radial flow adsorbers by assuming a linear isotherm, together with experimental data to validate the predictions for batch and packed-tube systems. Numerical results have been obtained by Tien and Thodos[13], Ying and Weber[14] and Weber and Liu[15], by assuming Freundlich isotherms; and by Westmark[16], for a linear isotherm.

Due to its realistic description of the porous feature of the packing used, the porous particle model has received considerable attention. Kasten *et al.*[17] obtained an analytical solution by assuming a linear isotherm, as did Masamume and Smith[18–20] for cases with pore diffusion and surface adsorption resistances considered simultaneously, but neglecting axial dispersion. Analytical solutions for irreversible isotherms have been obtained by Weber and Chakravorti[21] and by McKay and Allen[22]. Numerical solutions have been obtained for non-linear isotherm systems by Lee and Weber[23,24] and by Meyer and Weber[25]. Fleck *et al.*[26] provide numerical solutions for fixed-bed adsorption or ion exchange for Langmuir and Freundlich

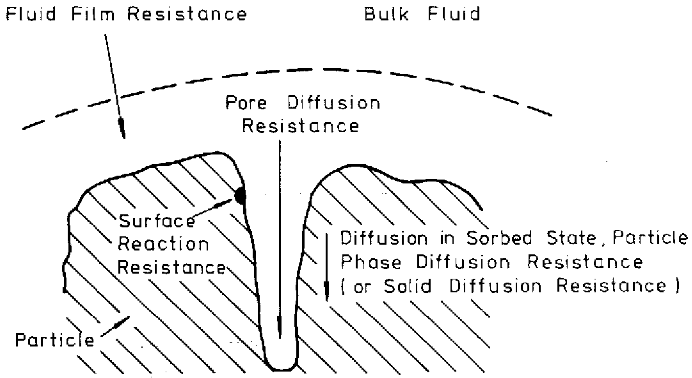

Fig. 1. The physical nature and location of individual steps in mass transfer of a solute from a fluid to a solid particle.

isotherms. Other numerical solutions have been given by Neretnieks[27], Liapis and Rippin[28], Svedberg[29], Costa and Rodrigues[30], Raghaven and Ruthven[31], Leyva-Ramos and Geankoplis[32], Mehrotra and Tien[33] and Rasmuson[34].

Simplified models have also been used effectively where the assumption is made that the solid adsorbent matrix is homogeneous, not only in structure but also in concentration, which is then represented by the mean concentration within the particle. The interface mass transfer equations then become simple functions of time and position only, and are no longer controlled by the momentary rate of particle diffusion, which is dependent on the shape of the unsteady concentration profile within the particle. Yang and Tsao[1] categorize the various simplified rate equations into three types: (i) the kinetic rate expression type; (ii) the linear driving force type; and (iii) miscellaneous, including constant pattern behaviour.

For the kinetic rate expression models, the adsorption process is treated as a reversible or irreversible chemical reaction. Analytical solutions for this case have been given by Thomas[6,35]. Other solutions have been presented by Heister and Vermeulen[36], Goldstein[37], Lapidus and Amundson[38] and Dranoff and Lapidus[39]. Chase[40,41] neglecting axial dispersion, has adapted Thomas' solution to the prediction of the performance of preparative affinity separation for biological macromolecules in packed columns for a favourable isotherm of the Langmuir type.

In the linear driving force model, the rate of interface mass transfer is assumed to be proportional to the distance the system is from equilibrium. Linear driving force models have been developed by Heister and Vermeulen[36], Heister *et al.*[42], Chen *et al.*[43] and Hashimoto *et al.*[44,45], covering linear, Langmuir and Freundlich isotherms. Hsieh *et al.*[46] give details of a method for prediction of multi-component liquid phase adsorption in a fixed bed, by assuming a Langmuir isotherm and the linear driving force approximation. Garg and Ruthven[47], Peel and Benedek[48], Yoshida *et al.*[49] and Leaver[50] have studied the use of linear driving force approximations for intraparticle diffusion mass transfer.

It is often observed in frontal analysis column operation with very favourable isotherm systems, that the shape of the wave front becomes essentially time independent, or column length independent after a certain distance from the entrance. Yang and Tsao[1] point out that this behaviour was first noted by Bohart and Adams[51], Wicke[52], Sillen[53] and Sillen *et al.*[54]. Hall *et al.*[55], assuming Langmuir isotherms, give numerical solutions for fixed-bed adsorption under constant pattern conditions taking into account both solid diffusion and pore diffusion. Katoh *et al.*[56] have developed numerical methods of prediction of breakthrough curves and elution profiles for packed-bed affinity chromatography columns for constant pattern conditions and the Freundlich isotherm.

The review shows that the mathematical modelling of adsorption rates processes is well established and provides a basis for the application of the FACSIMILE code to different problems.

Any mathematical model that is proposed has to be evaluated by comparing its predictions with experimental results. For application of the models in codes such as FACSIMILE, specific information on equilibrium and kinetics are required either from the literature or from small-scale experiments. The section below outlines some of the experiments that can be used to generate useful data, and includes some preliminary results. The following section then details the testing of FACSIMILE. This testing includes the use of data from the literature.

SMALL-SCALE EXPERIMENTS TO PROVIDE EQUILIBRIUM AND KINETIC DATA AND PILOT-SCALE EXPERIMENTS FOR CODE VALIDATION

There are two types of experiments that are concerned with the modelling of any adsorption process. The first investigates the equilibrium situation, usually expressed in terms of adsorption isotherms, and the second investigates the time course of the approach to equilibrium; the kinetics. A programme of experimental work is in progress, aimed at providing a wide range of data to validate the FACSIMILE code. The particular system under study is the adsorption of aspartic acid onto an ion exchanger. Duolite A162; some of the experimental details are given below.

Measurement of adsorption isotherms

Adsorption isotherms were generated by contacting solutions of different concentrations of aspartic acid with known weights of adsorbent, at a constant temperature, until equilibrium was attained. The amount of material adsorbed, the capacity, is plotted against the equilibrium solution concentration, as shown in Fig. 2. This was a typical result and shows the isotherms following a characteristic Langmuir-type pattern, which can also be modelled by a forward and reverse reaction model[40]. The isotherm shape illustrates that the experimental system under investigation shows consistency with the model used by Chase[40]. This is important, because checking the validity of a particular proposed model is a significant part in the overall process of mathematical modelling.

Kinetics of adsorption

There are several possible rate-limiting steps in any adsorption process, arising from the resistances to the transport of material from the bulk liquid to the interior of the adsorbent particles, as shown in Fig. 1. The kinetics of these steps can be measured in several ways, the simplest of which is to monitor the uptake of adsorbate in a stirred cell, illustrated in Fig. 3. The result from this is shown in Fig. 4. Providing

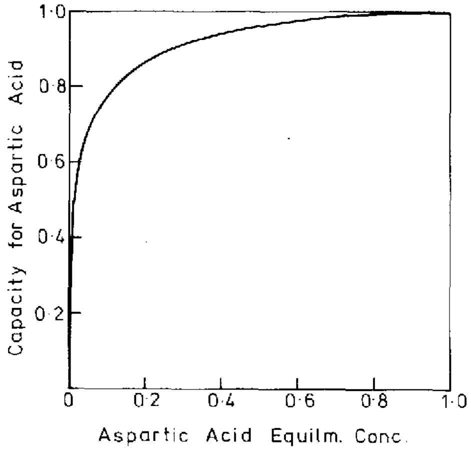

Fig. 2. Dimensionless adsorption isotherm for aspartic acid onto Duolite A162.

the agitation is sufficient; no significant concentration gradients arise in the bulk liquid, thereby negating the effects of that particular resistance and thus slightly simplifying the process description.

Most adsorption processes are performed in columns and although a stirred cell provides useful information, experiments examining column operations are necessary. The simplest apparatus for doing this is shown in Fig. 5, where the column output is monitored in response to either step or pulse changes in input conditions.

Pilot-scale experiments

Small-scale experiments provide a means of characterizing the adsorbent

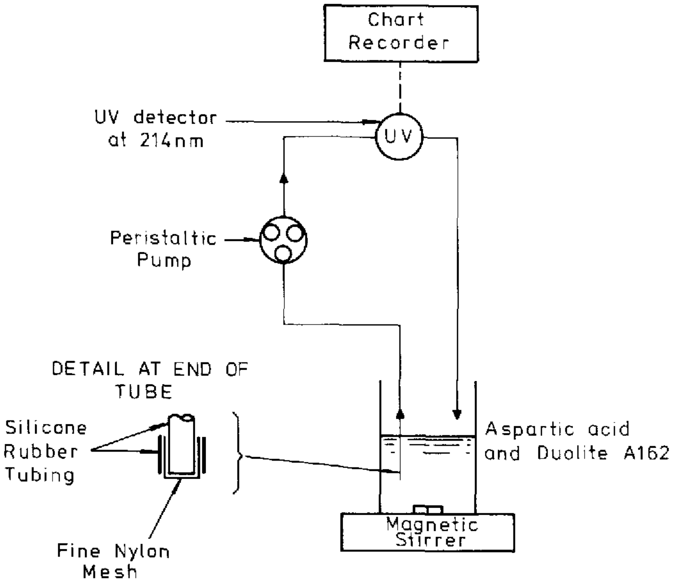

Fig. 3. Diagram of apparatus for stirred cell experiments.

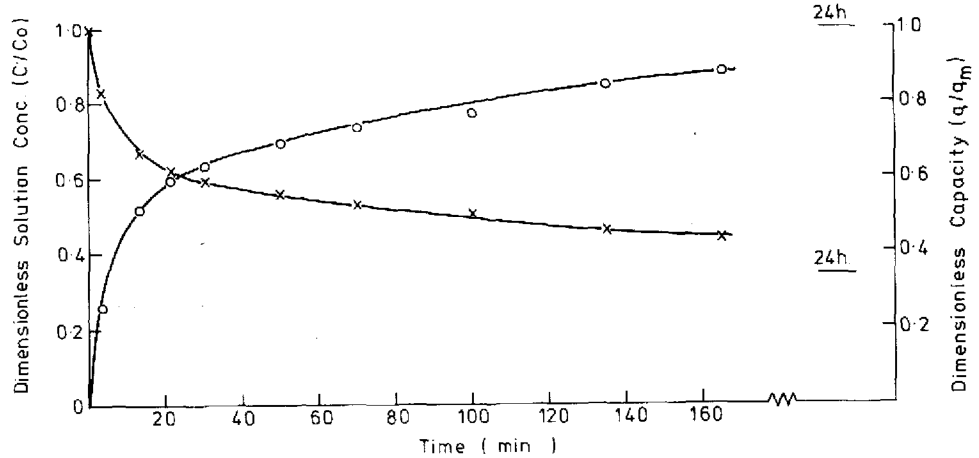

Fig. 4. Kinetics of aspartic acid adsorption, in a stirred cell: C_0 = initial solution concentration; q_m = capacity at equilibrium.

within a limited microenvironment and the results will be applicable to any scale of operation, to a certain extent. Regardless of scale, the adsorbent will always be operating in a microenvironment so, provided that these conditions are known, the adsorbent performance can be predicted from the results of small-scale experiments. The major differences in scale-up are the hydrodynamic variations that arise from poor distribution, and pilot-scale equipment is under construction (Fig. 6) to evaluate these effects. This pilot-scale equipment will also be used to validate computer predictions of scale-up, based on results from the small-scale experiments.

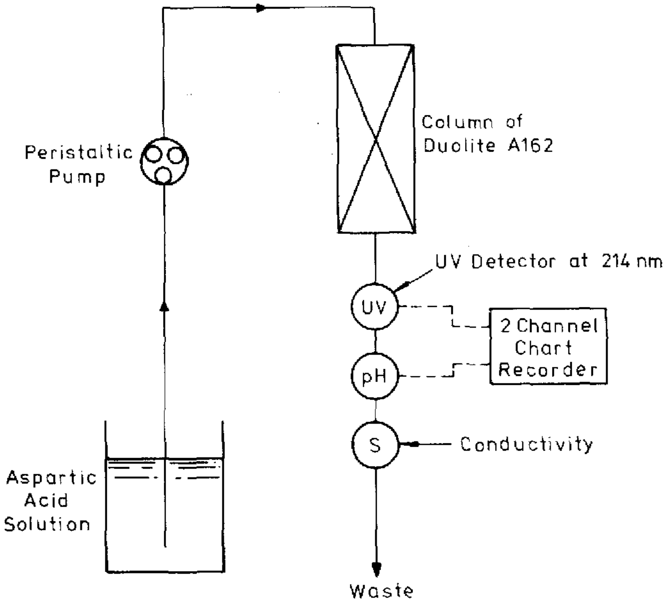

Fig. 5. Diagram of apparatus for column experiments.

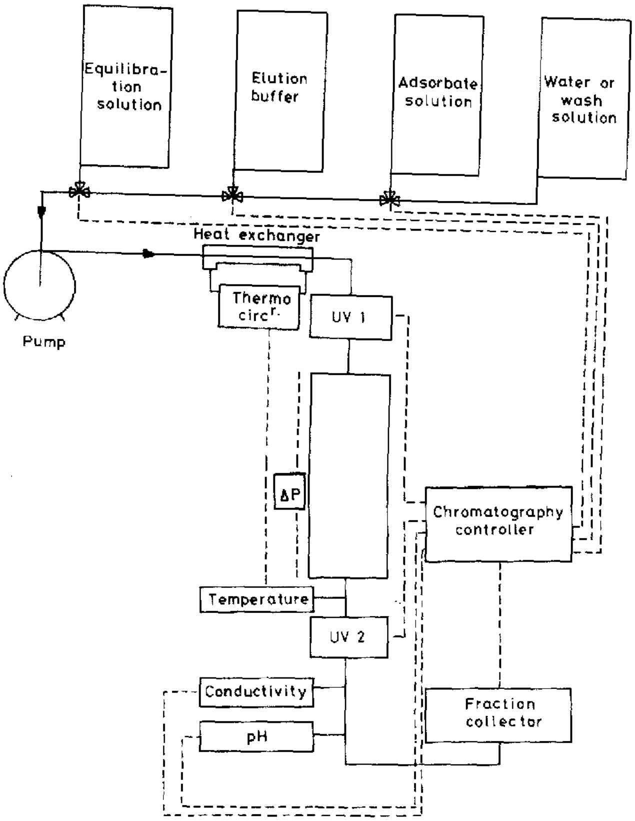

Fig. 6. Adsorption column performance rig (schematic).

PREDICTION OF PACKED-BED COLUMN PERFORMANCE

With information available on the equilibrium and kinetic characteristics from small-scale experiments, it is possible to predict the performance of adsorption processes using the FACSIMILE code. This code has been developed at Harwell. Computer models using FACSIMILE for general prediction of adsorption and chromatographic systems are being written. There is particular emphasis on writing models suitable for predicting scale-up. The code solves the mass balance and mass transfer rate equations for a given adsorption system with specified initial conditions. The numerical methods used in FACSIMILE are outlined here, with reference to the prediction of packed-bed adsorption column performance, and predictions are compared with the experimental data of Chase[40] for an affinity chromatography application.

The FACSIMILE program

FACSIMILE is a computer program designed for solving ordinary differential equations such as those which arise from problems involving mass action kinetics. The equations are described to FASCIMILE in a high-level language. To solve a particular system, a program is written in the FACSIMILE data language. This program should specify all the rate equations for a system. A particular problem is solved by supplying FACSIMILE with this program and with the values for all the parameters for the particular problem.

Because of the power of the FACSIMILE data language, almost any model for a particular system can be described to FACSIMILE. The kernel of FACSIMILE is the Harwell Library subroutine DC03AD. This is a routine for solving sets of stiff ordinary differential equations. The class of stiff differential equations includes those which arise from reaction kinetics where there are processes proceeding at different rates. DC03AD uses a numerical method, which is efficient at solving such equations. From experience of solving real problems, the routine has been found to be robust and reliable. FACSIMILE is written in Fortran 77 and can be run on any computer with a good Fortran 77 compiler. FACSIMILE is described in a Harwell report[57].

The experimental data

This work takes data from experiments conducted by Chase[40]. Chase measured the adsorption of lysozyme in a 0.05 *M* Tris–HCl buffer at pH 7.2 onto Cibacron Blue supported on Sepharose CL-6B. For each experiment, Chase has supplied the values of adsorbate concentration at the outlet of the column against time, *i.e.* values on the breakthrough curve. The results given here are in two sets. In the first set, the only difference between the experiments was the length of the column. The second set of data contains values from an experiment that used a lower fluid speed than the first set of experiments.

The mathematical model

Chase[40] suggested a set of equations to describe this system. The equations are of the form described in eqn. 1. The system is modelled as a reversible mass transfer reaction in which the free adsorbate becomes bound to the adsorbent. The forward rate of the reaction is proportional to the amount of free adsorbate multiplied by the amount of adsorbent free to bind with the adsorbate. The reverse rate is proportional to the amount of adsorbate bound to the adsorbent, *i.e.*

$$C \underset{K_2}{\overset{K_1(Q_m - q)}{\rightleftharpoons}} Q \tag{2}$$

where C is the free adsorbate, Q is the bound adsorbate, Q_m is the maximum capacity of the adsorbent and K_1 and K_2 are constants.

The solution of free adsorbate flows down the column, of length L, with speed V; V is sometimes called the interstitial velocity. The free adsorbate also diffuses through the solution with coefficient D. The differential equations suggested by Chase are expressed here, using the symbols t for time and z for distance down the column; $c(z,t)$ is used for the concentration of free adsorbate, as a function of distance and time, and $q(z,t)$ is used for the concentration of bound adsorbate, also as a function of distance and time. The differential equations are

$$\frac{\partial c}{\partial t} = D\frac{\partial^2 c}{\partial z^2} - V\frac{\partial c}{\partial z} - K_1 c\,(Q_m - q) + K_2 q \tag{3}$$

$$\frac{\partial q}{\partial t} = K_1 c(Q_m - q) - K_2 q \tag{4}$$

One of the boundary conditions for c is that before the process starts, at time $t = 0$, the value of c is zero all along the column except at the inlet, *i.e.*

$$c(z,0) = \begin{cases} 0, & z > 0 \\ C_0, & z = 0 \end{cases}$$

Another boundary condition is that, at all times, the value of c at the inlet is C_0 so $c(0,t) = C_0$, $t \geqslant 0$. In the case of diffusion, $D \neq 0$, another condition is needed; it is assumed that at any particular value of t, t_1 say, there is some large value of z, z_1 say, such that for all values of $z > z_1$, $c(z,t_1) = 0$.

The boundary condition for q is that at time $t = 0$, $q = 0$ all along the column, *i.e.* $q(z,0) = 0$, $z \geqslant 0$.

These equations assume that the adsorbate in solution is well mixed radially. The fluid speed V is the true fluid speed, not the superficial speed. So V can be expressed as:

$$V = \frac{\text{fluid volume entering the column in unit time}}{\text{cross-section area of column} \times \text{porosity}}$$

The concentrations c, q, C_0 and Q_m are measured in moles of adsorbate divided by the volume of fluid containing that amount of adsorbate.

Thomas' analytic solution

If the assumption is made that diffusion is zero, there is an analytical solution for these equations with these boundary conditions. The results in this section include a comparison between the predictions from FACSIMILE and the predictions from Thomas' solution using the same parameters. This analytic solution is quoted in Appendix 1.

Solving the model using FACSIMILE

FACSIMILE provides a tool for solving the above equations without needing to assume $D = 0$. Chase assumed that diffusion was negligible and, using this assumption, the differential equations were solved using FACSIMILE and using Thomas' solution. This allowed comparison between the answers gained from using FACSIMILE, the experimental data and the analytical solution. The following describes some results which can be deduced from assuming that, in the case of negligible diffusion, the concentration has a constant pattern. These results were used to speed up the calculations performed by FACSIMILE without forcing FACSIMILE to produce a solution with a constant pattern.

The constant pattern assumption

Away from the column inlet, Thomas' solution is similar to a wave moving down the column at fixed speed. This is known as a constant pattern.

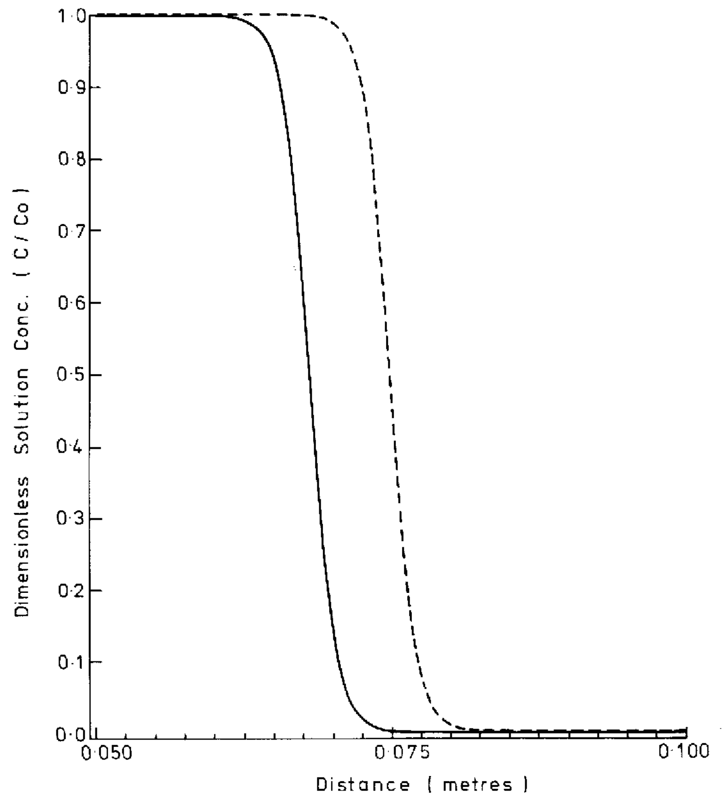

Fig. 7. Results assuming a constant pattern (Thomas' solution) for two different times.

Fig. 7 shows Thomas' solution plotted as concentration against distance at two different times during the experiment. As illustrated in Fig. 7, along the section of column between the column inlet and one end of the wave-front the concentration of free adsorbate is constant. Equally, from the other end of the wave-front to the column outlet the concentration is also zero. Therefore, at any particular time, only a section of the column needs to be modelled in detail. This section is called here a grid. The grid needs to be long enough to include all of the wave-front. It also needs to move so as to include all of the wave-front at any given time.

Appendix 2 considers the constant pattern assumption. In it, is the derivation for the speed of the wave-front, by assuming a constant pattern. This speed is:

$$U = \frac{VC_0}{C_0 + Q_0} \tag{5}$$

where Q_0 is defined by:

$$Q_0 = \frac{C_0 Q_m}{K_2/K_1 + C_0} \tag{6}$$

The same section also derives an expression for l, the length of grid needed to model the wave-front.

The equations used within the grid

The next task is to decide how to model the section of column covered by the grid. The grid is divided into a one-dimensional set of cells. In each cell, the mass transfer reaction between the free adsorbate and the bound adsorbate are provided to FACSIMILE. The flow of solution through the grid and diffusion along the grid are modelled by transfer of species between neighbouring cells. If there are n cells, then, using c_i and q_i for the concentrations of free and bound adsorbate in cell i, the ordinary differential equations for each cell are:

$$\frac{\mathrm{d}c_i}{\mathrm{d}t} = \frac{D}{h^2}(c_{i-1} + c_{i+1} - 2c_i) - \frac{V}{h}(c_{i-1} - c_i) - K_1c_i(Q_\mathrm{m} - q_i) + K_2q_i \quad (7)$$

and

$$\frac{\mathrm{d}q_i}{\mathrm{d}t} = K_1c_i(Q_\mathrm{m} - q_i) - K_2q_i \quad (8)$$

for $1 \leqslant i \leqslant n$ and where c_0, c_{n+1}, q_0 and q_{n+1} are defined by $c_0 = C_0$, $c_{n+1} = 0$, $q_0 = 0$ and $q_{n+1} = 0$.

Note that a central difference is used for the diffusion term and a backward difference is used for the advection term. This makes the method stable. This form of discretization ensures local conservation of adsorbate. In other words, the equations, which are solved using FACSIMILE, ensure that the difference between the amount of adsorbate entering a section of column and the amount leaving that section is equal to the increase in adsorbate in that section of column.

Integrating the equations

The model works in two phases. In the first phase, the grid is stationary with one end at the inlet of the column. The differential equations within the grid are then integrated until the concentrations of free adsorbate in the cells at the centre of the grid have reached half of their equilibrium values. By this stage, the value of the concentrations in the cells adjacent to the column inlet should have reached their equilibrium values. The constant pattern assumption is now valid and, in phase two, the integration continues with the grid moving along the column at a fixed speed until it has passed the end of the column. This means that the speed of the free adsorbate relative to the grid is $V - U$ and the bound adsorbate is moving in the opposite direction at speed U relative to the grid. There are no special boundary conditions at the end of the column and so the same equations can be solved while the grid passes over the end of the column.

If there is no diffusion, the length used for the grid is the minimum required, calculated using the constant pattern assumption. If the diffusion is small but not zero, the same method works but diffusion means that the wave-fronts for the concentrations of free and bound adsorbate broaden slowly as they move down the column. So the grid length is chosen to be larger than the minimum required. If diffusion is large, the grid covers the entire column and never needs to move.

Note that the results of the constant pattern assumption were only used to find values for the grid length and speed. The equations are still solved properly on the grid and the assumptions can be checked as the calculation proceeds. The moving grid is just used to speed-up FACSIMILE's calculations, it does not affect the answers. The same answers could be obtained using a grid which covered the entire column and which had more cells so that the size of each cell was the same.

Results for the first set of experiments

Fig. 8 plots the breakthrough curves for the first set of experiments. These are on five columns of different length, with all other parameters the same. The parameters are: $Q_m = 8.75 \cdot 10^{-4}$ mol/l, $K_1 = 2.86 \cdot 10^2$ l/(mol s), $K_2 = 5.0 \cdot 10^{-4}$/s, $C_0 = 7.1 \cdot 10^{-6}$ mol/l, $V = 2.24 \cdot 10^{-4}$ m/s, $D = 0$ m^2/s. The column lengths were 14, 41, 66, 104 and 161 mm.

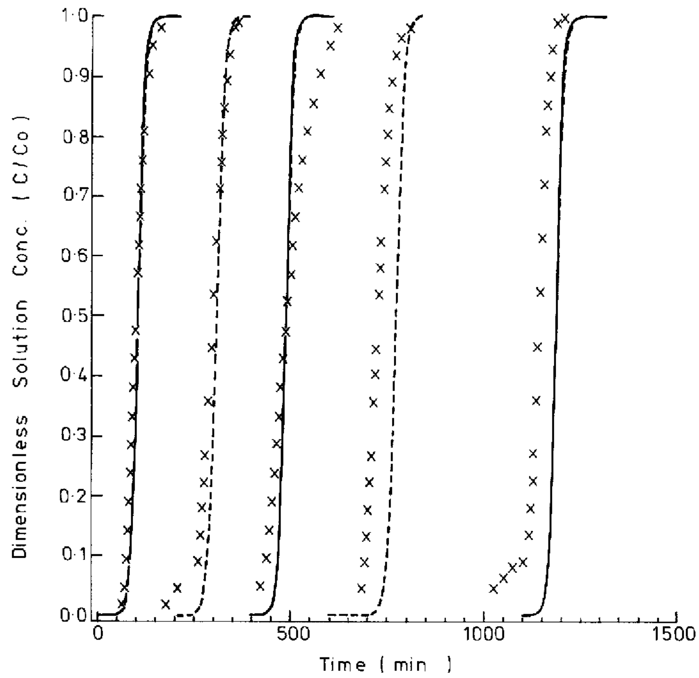

Fig. 8. Breakthrough curves for five columns of different length. (——) Thomas' solution, (--------) FACSIMILE, (×) experimental data.

The five dashed lines are predictions gained from FACSIMILE for the five different column lengths. The leftmost line is for the 14-mm column and the lines are in order of column length. The three solid lines are the analytical results from Thomas' solution for the first, third and fifth columns. The five sets of crosses are the experimental results on the breakthrough curves. FACSIMILE's results agree very well with Thomas' solution and are similar to the experimental results. The fact that results gained from using FACSIMILE are very close to those gained from Thomas' solution means that in this case, where diffusion is ignored, FACSIMILE is certainly solving the equations accurately. This gives confidence in FACSIMILE's predictions in cases where Thomas' solution does not hold.

The predicted breakthrough curves are very sensitive to the parameters used in the calculation. Fig. 9 gives the same results calculated using a value for the adsorbent capacity about 4% smaller than that suggested by Chase. This new value of Q_m is $8.45 \cdot 10^{-4}$ mol/l. The predicted curves fit the experimental results more closely and it is unlikely that the capacity is known to within 4%.

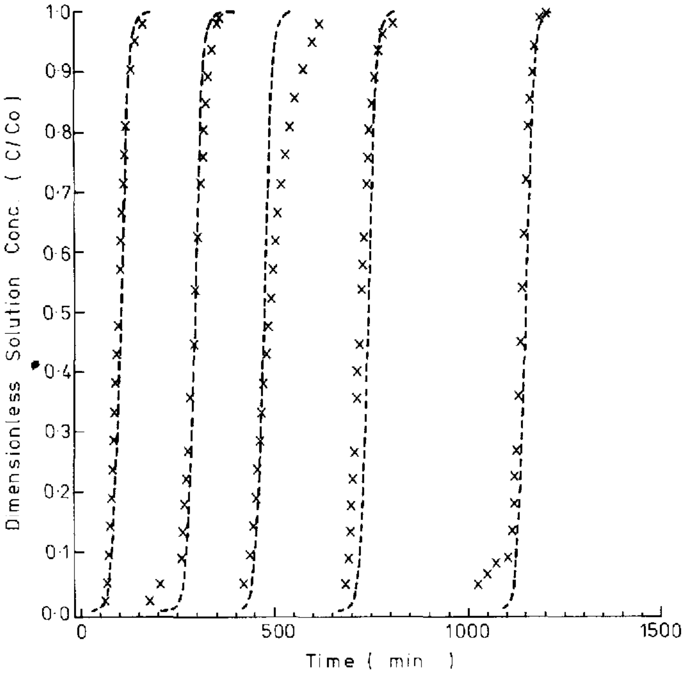

Fig. 9. Breakthrough curves for five columns of different length. Examination of parameter sensitivity of Q_m. (------) FACSIMILE, (×) experimental data.

Results from the second set of data

The second set of data comes from an experiment where the fluid speed was $4.62 \cdot 10^{-5}$ m/s and the column length (L) was 0.032 m. This was modelled using FACSIMILE and Chase's suggested values for the other parameters. These parameters are $Q_m = 8.75 \cdot 10^{-4}$ mol/l, $K_1 = 2.86 \cdot 10^2$ l/(mol s), $K_2 = 5.0 \cdot 10^{-4}$/s, $C_0 = 7.1 \cdot 10^{-6}$ mol/l, $D = 0$ m²/s.The experimental data are the crosses on Fig. 10 and the prediction for these parameter values is the dashed line.

From the experimental data, the breakthrough curve appears broader than that predicted using these parameter values. Also, the breakthrough occurs earlier than predicted. A second model was run using parameters chosen to fit the experimental data more closely.

To make the breakthrough occur at the correct time, the speed of the wavefront needs to be increased. This can be done either by altering the fluid speed V or

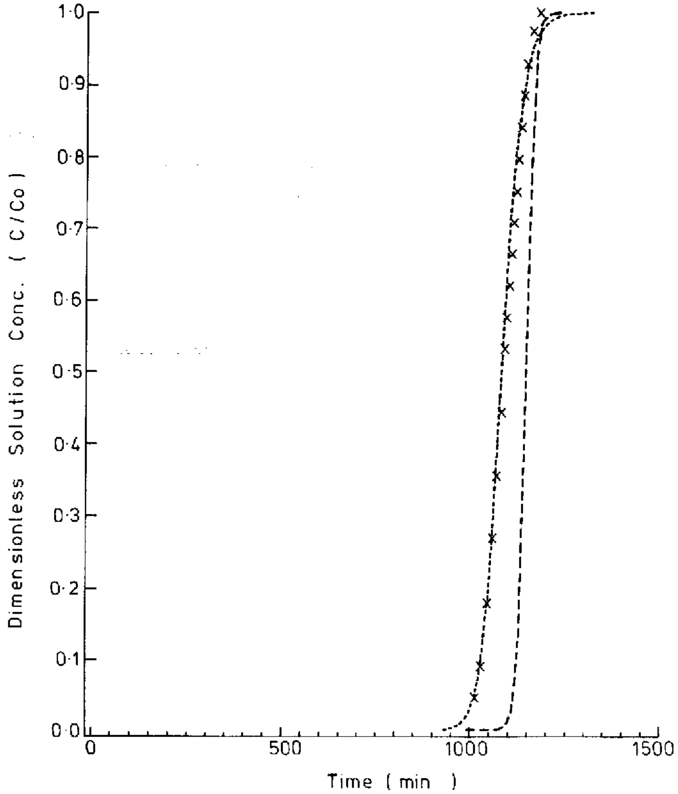

Fig. 10. Breakthrough curve for column of length 0.032 m. (– – –) FACSIMILE prediction, (×) experimental data, (---------) FACSIMILE prediction, but including diffusion.

the bed capacity Q_m, depending on which value was measured more accurately. In this case, V was altered to $4.89 \cdot 10^{-5}$ m/s.

To broaden the breakthrough curve, a diffusion coefficient D of $3 \cdot 10^{-8}$ m^2/s was used. This is reasonable as a value to include both the effect of diffusion through the solute and the increased dispersion caused by the adsorbent around which the solute flows.

The prediction gained using FACSIMILE with this altered set of parameters is the dotted line in Fig. 10.

CONCLUSION

It has been shown that the FACSIMILE computer code accurately solves the mathematical model used to describe the affinity adsorption process. Although in the example the model incorporated a simplified kinetic rate equation, FACSIMILE has the potential to predict a wide range of adsorption and chromatography systems for performance, optimization and design purposes. This includes the potential to solve more-complex mass transfer rate models, which include dispersion, coupled with the ability to cover the whole process cycle: adsorption, washing, elution and regeneration. To gain physical understanding of the relevant adsorption process and to gain accuracy of prediction, it is desirable to provide information on isotherms and kinetics from small-scale experiments of the type described in this paper. The comparison of the FACSIMILE predictions with the affinity adsorption data gives a first check of the code, but further comparison with data from small-scale rigs, and industrial equipment, will validate the code to give confidence in the application to scale-up of adsorption and chromatographic processes.

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APPENDIX 1 — THOMAS' SOLUTION

If the assumption is made that axial diffusion is zero, the mathematical equations for this system become:

$$\frac{\partial c}{\partial t} = -V\frac{\partial c}{\partial z} - K_1 c(Q_m - q) + K_2 q \qquad \text{(A1)}$$

$$\frac{\partial q}{\partial t} = K_1 c(Q_m - q) - K_2 q \qquad \text{(A2)}$$

There is an analytic solution to these equations, which was quoted by Thomas[53]. The solution is quoted here using the notation of this paper, which is different from Thomas' original notation. The solution for the concentration of C at time t and position z is given by:

$$\frac{c(x,y)}{C_0} = \frac{I_0(2\sqrt{ABxy}) + \varphi(\alpha y,\beta x)}{I_0(2\sqrt{ABxy}) + \varphi(\alpha y,\beta x) + \varphi(Bx,Ay)} \quad \text{for } x \geqslant 0,\ y \geqslant 0 \qquad \text{(A3)}$$

As before, z is the position along the column; $z = 0$ at the inlet. t is the time measured from when the solution entered the column. At a particular position z and a particular time t, x is the time it would take an unadsorbed component of the solution to reach the current position after entering the column. y is the difference between the current time and the time at which an unadsorbed component would have reached the current position. Thus x and y are: $x = z/V$ and $y = t - z/V$. y less than zero means that an unadsorbed component would not yet have reached the current position, so $y < 0 \Rightarrow c(x,y) = 0$.

x is always positive for positions within the column. The constants A, B, α and β are defined thus: $A = K_2$, $B = K_1Q_m$, $\alpha = K_1C_0 + K_2$, $\beta = \frac{K_2K_1Q_m}{K_1C_0 + K_2}$. The function I_0 is the zeroth-order imaginary Bessel function.

APPENDIX 2 —RESULTS FROM ASSUMING A CONSTANT PATTERN

In general, the concentration of adsorbate in solution is a function of both time and position along the column. The constant pattern means that this function can be expressed as a function of one variable whose argument is $z - Ut$, *i.e.* $c(z,t) \approx f(z - Ut)$, for some function f and some constant U. U is the speed of the wave-front and f is its shape.

Let the cross-section area of the fluid be A, then the amount of free adsorbate which flows into the column in time δt is $C_0VA\delta t$. In time δt, the extra adsorbate goes into increasing the nett amount of free adsorbate in the column, *i.e.* moving the wave-front of c down the column, and into increasing the amount of adsorbate bound to the adsorbent, *i.e.* moving the wave-front of q down the column. These two increases require an increase in total adsorbate of $\delta zA(C_0 + Q_0)$. The increase of total adsorbate in the column must equal the amount of free adsorbate flowing into the column; thus the speed of the wave front is:

$$U = \frac{\delta z}{\delta t} = \frac{VC_0}{C_0 + Q_0}$$

Consider the concentration of the adsorbate bound to the adsorbent. At equilibrium, for any part of the column, the concentration of the free adsorbate is C_0, the concentration at the inlet. So the concentration of bound adsorbate can be obtained from the isotherm. Let Q_0 be the equilibrium value of the concentration of the bound adsorbate, then:

$$Q_0 = \frac{C_0Q_m}{K_2/K_1 + C_0}$$

Next, the assumption is made that the bound adsorbate also moves at a fixed speed and also has a fixed shape. The speeds of the two wave-fronts must then be the same for otherwise one would get completely ahead of the other. So, after a long time, at some point along the column, either the concentration of the free adsorbate would be at its equilibrium value while the concentration of the bound adsorbate was still zero or the concentration of the bound adsorbate would be at its equilibrium value while the concentration of the free adsorbate was still zero. Neither of these is possible, so assuming that both wave-fronts move at fixed speeds means that they must both move at the same speed. So, the further assumption is made that there exists a function g such that $q(z,t) \approx g(z - Ut)$. This value of U is the speed at which the grid should move once the solution has reached the constant pattern stage.

Using the value for U eqns. A1 and A2 can be rewritten in terms of f. Let $\zeta = z - Ut$, then:

$$\frac{\partial c}{\partial t} = -U\frac{\mathrm{d}f}{\mathrm{d}\zeta}$$

$$\frac{\partial c}{\partial z} = \frac{\mathrm{d}f}{\mathrm{d}\zeta}$$

and

$$\frac{\partial q}{\partial t} = -U\frac{\mathrm{d}g}{\mathrm{d}\zeta}$$

These turn eqns. A1 and A2 into:

$$-(V - U)\frac{\mathrm{d}f}{\mathrm{d}\zeta} - K_1 f(Q_\mathrm{m} - g) + K_2 g = 0$$

$$U\frac{\mathrm{d}g}{\mathrm{d}\zeta} + K_1 f(Q_\mathrm{m} - g) - K_2 g = 0$$

Addition of these equations gives:

$$(V - U)\frac{\mathrm{d}f}{\mathrm{d}\zeta} = U\frac{\mathrm{d}g}{\mathrm{d}\zeta}$$

For $\zeta \ll 0, f = C_0$ and $g = Q_0$, so by integration

$$(V - U)(f - C_0) = U(g - Q_0)$$

Note that

$$\frac{U}{(V - U)}Q_0 = \left(\frac{VC_0}{C_0 + Q_0}\right)\left(\frac{VQ_0}{C_0 + Q_0}\right)^{-1} Q_0 = C_0$$

Thus, g can be expressed in terms of f:

$$g(\zeta) = \frac{Q_0}{C_0}f(\zeta)$$

This gives an ordinary differential equation for f:

$$(V - U)\frac{\mathrm{d}f}{\mathrm{d}\zeta} = K_1 f\left(Q_\mathrm{m} - \frac{Q_0}{C_0}f\right) + K_2\frac{Q_0}{C_0}f$$

The solution to this is:

$$f(\zeta) = \frac{C_0}{(1 + \mathrm{e}^{(\zeta - \zeta_0)C_0K_1/U})}$$

and therefore the equation for g is:

$$g(\zeta) = \frac{Q_0}{(1 + e^{(\zeta-\zeta_0)C_0K_1/U})}$$

The value of ζ_0 is determined by the equation:

$$z - Ut = \zeta = \zeta_0 \Rightarrow \frac{c}{C_0} = \frac{1}{2}$$

Note that $\zeta \to -\infty \Rightarrow f \to C_0$ and $\zeta \to \infty \Rightarrow f \to 0$, and similarly for g.

These formulae for the shapes of the wave-fronts make it possible to calculate the length of grid needed to model the system.

To use such a grid assumes that along all of the column, from the column inlet to one end of the grid, both the concentration of free adsorbate and the concentration of bound adsorbate are practically at their equilibrium values. It also assumes that from the other end of the grid to the column outlet both of these concentrations are practically zero. To find the grid length, some ratio R is needed which specifies how closely these assumptions are met. The first requirement is that between the grid and the inlet, the error in c from its correct value of C_0 is less than R, *i.e.*

$$\frac{C_0 - c}{C_0} < R$$

The other requirement is that between the end of the grid and the outlet, the error in assuming $c = 0$ is:

$$\frac{c}{C_0} < R$$

Having decided upon some small number for R which is small compared to one, 0.0001 is a reasonable value, the minimum value required for the grid length l is given by:

$$l \approx -2\ln(R)\frac{U}{C_0K_1}$$

It is interesting to look at the width of the breakthrough curve. This can be taken to be the time interval for the value of c at the outlet of the column to rise from C_0R to $C_0(1 - R)$. This time interval is given by:

$$\frac{l}{U} = \frac{-2\ln(\mathrm{R})}{C_0K_1}$$

Thus, given the assumptions made about a constant pattern, the width of the breakthrough curve is independent of both the speed of fluid flowing through the column and the capacity of the adsorbent.

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