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# Optimisation of frontal chromatography by partial loading

PHILIPPE DANTIGNY, YUYAN WANG, JOHN HUBBLE and JOHN A. HOWELL*

*School of Chemical Engineering, University of Bath, Claverton Down, Bath BA2 7AY (UK)*

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ABSTRACT

   Quantitative assessment of adsorbate losses during washing is used to provide the basis for a new approach to optimising the performance of packed-bed adsorption chromatography. This paper presents this new approach, and shows, through simulating the performance of the adsorption and washing processes how it can be used with a variety of performance criteria. These include: maximum use of column capacity, minimum product loss and maximum process throughput. The results show that for product loss to be minimised, it is advantageous to stop adsorption before column breakthrough is detected, in order to leave unused capacity capable of scavenging unadsorbed material and product eluted during the washing process. The effect of changes in axial dispersion, length of column loading, inherent adsorbent capacity and adsorption rate or mass transfer are analysed and discussed with respect to optimising the point at which washing is started. It is shown that the application of the new approach can improve column performance significantly and minimise waste without any serious consequence on column capacity utilisation and process throughput.

INTRODUCTION

   In any of the current methods of adsorption chromatography used in biotechnology, including ion-exchange, reversed-phase and affinity interactions, it is the typical operating procedure to load a bed until close to breakthrough. This is defined as the first detectable quantity of product in the column effluent. The column is then washed to remove impurities from the bed beyond the minimum point of the column monitor. If the contaminant does not adsorb to the affinity packing but simply diffuse into the pores, Arnold *et al.* [1] indicate that a maximum of three bed volumes of washing solution can be required. In other cases, Arve and Liapis [2] indicate that up to eight bed volumes can be required. It is recognised [3–5] that the washing procedure may cause valuable products to be lost, but as yet there is no quantitative method for assessing wastage continuously. As a consequence, alternative operating protocols for minimising product loss have yet to be developed.
   Before optimisation is considered, it is necessary to define the objectives of the adsorption operation so that a rational operating procedure can be defined. Chase [5], in suggesting that the first objective in these processes is the achievement of maximum product purity, discussed the first and second stages of the process as adsorption followed by washing to reduce the level of contaminants in the bed to a predetermined level. There are other possible objectives which may be achievable simultaneously with

the first [*i.e.*, (1) maximisation of product bound; (2) minimisation of product loss; (3) minimisation of process time; and (4) maximisation of process productivity]. The weight of these objectives will depend on the relative costs of the raw materials, column operation and the product value. The controllable variable is the flow-rate which Lowe and Dean [6] suggested should be kept slow to ensure the attainment of equilibrium in the bed. So far most research has focused on the objectives of improving product purity and maximising bed capacity during the adsorption phase.

This paper focuses on the sources of product loss and shows a new approach by which this can be minimised whilst maintaining a high column utilisation efficiency. The approach requires the determination of the position of the saturation front within the bed, defined as the leading edge of the adsorbate-saturated region within the column. As this cannot easily be experimentally determined at present, the current work uses simulation to determine the best strategy assuming the saturation point can be localised or predicted. It is shown that the benefits of operating in the new fashion are considerable and thus it is highly desirable to find ways of experimentally locating the saturation front. A possible method which has been assumed to be applicable is the detection of the thermal changes due to the liberation of the enthalpy of adsorption [7,8]. It is suggested that this might be detected as saturation is nearly complete (say >95% complete).

It turns out that it is necessary to stop adsorption when the saturation front remains well within the column. The exact position depends on several process parameters which also must be determined.

This work presents the results of simulations of bed performance showing the effects of different operating protocols on product loss, overall productivity, process time and utilisation of bed capacity.

METHODS

*Model*

Modern methods of adsorption operations include the use of fluidised beds [9–11], where axial dispersion may be higher than is usual in fixed-bed operation. Accordingly, the effect of axial dispersion is included specifically in the formulation and evaluated as one of the parameters influencing the process.

The equations are [12–14]

$$D_{\mathrm{L}} \frac{\partial^2 c}{\partial x^2} - u \frac{\partial c}{\partial x} - \frac{\partial c}{\partial t} - \left(\frac{1 - \varepsilon}{\varepsilon}\right) \frac{\partial q}{\partial t} = 0 \tag{1}$$

$$\frac{\partial q}{\partial t} = k_1 c (q_{\mathrm{m}} - q) - k_2 q \tag{2}$$

The boundary conditions are

$$uc - D_{\mathrm{L}} \frac{\partial c}{\partial x} = c_0 u A(t) \bigg|_{x=0} \tag{3}$$

$$\frac{\partial c}{\partial x} = 0 \bigg|_{x=1} \tag{4}$$

where

$$A(t) = 1 \text{ if } 0 \leqslant t < t_{ws} \tag{5}$$

$$A(t) = 0 \text{ if } t \geqslant t_{ws}$$

Using the following dimensionless groups

$$C = \frac{c}{c_0}; \; Q = \frac{q}{q_m}; \; \theta = \frac{ut}{l}; \; z = \frac{x}{l}$$

$$Pe = \frac{ul}{D_L}; \; B = \left(\frac{1-\varepsilon}{\varepsilon}\right)\frac{q_m}{c_0}; \; k_A = \frac{k_1 c_0 l}{u}; \; k_B = \frac{k_2 l}{u}$$

Eqns. 1–4 become

$$\frac{1}{Pe}\frac{\partial^2 C}{\partial z^2} - \frac{\partial C}{\partial z} - \frac{\partial C}{\partial \theta} - B\frac{\partial Q}{\partial \theta} = 0 \tag{6}$$

$$\frac{dQ}{d\theta} = k_A C(1 - Q) - k_B Q \tag{7}$$

with the boundary conditions

$$\frac{dc}{dz} = Pe[C - A(\theta)]\bigg|_{z=0} \tag{8}$$

$$\frac{dC}{dz} = 0\bigg|_{z=1} \tag{9}$$

The two-dimensional block pulse function (BPF) method has been used to transform eqns. 6–9 into non-linear algebraic recursive equations (see Appendix). A Fortran program has been coded on a PC apricot XEN-i 286/45 in order to solve the latter equations. The bed was divided into twenty identical sections, therefore simulation results were available every 0.05 step.

*Comparison of operational protocols*

The traditional operating procedure is to load the bed before the concentration of adsorbate in the effluent reaches 1, 5 or 10% of its value in the feed [14–17]. For the simulations of the traditional procedure, the washing starts when $C = 0.05$ at the outlet (Fig. 1).

The partial-loading approach requires the position of the breakthrough front to be determined within the bed. It is assumed that the adsorption wave can be thermally detected with certainty when $C = 0.95$ (Fig. 1). This approach allows the column feed to be controlled such that different levels of bed utilisation are achieved. For example, $Z^* = 0.5$ means that the washing starts when the adsorption front reaches the middle of the column (say $C = 0.95$ at $z = 0.5$).
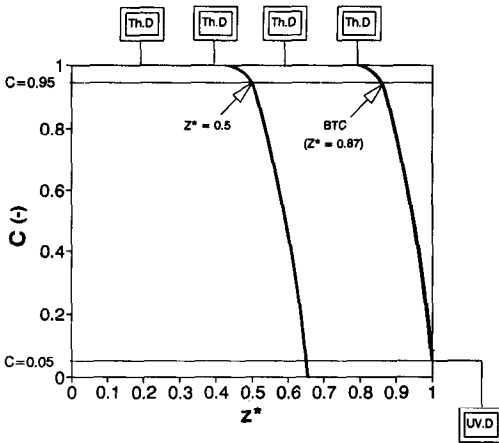
Fig. 1. Adsorption waves within the bed at the end of loading, without axial dispersion, exhibiting the differences between the partial loading approach ($Z^* = 0.5$) and the traditional procedure [Breakthrough curve (BTC)]. Th. D. = Thermal detector; UV. D. = UV detector.
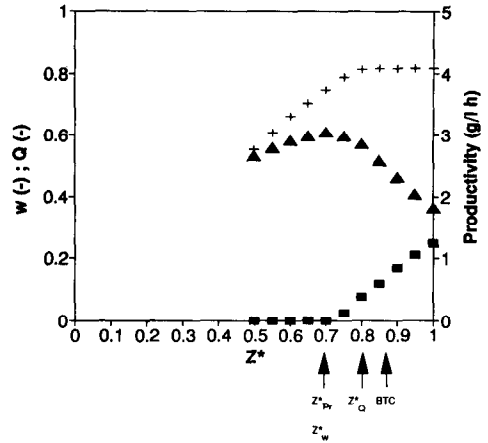
Fig. 2. Product loss ($w$), use of the column ($Q$) and productivity ($Pr$) after washing *vs.* position of the saturation front at the beginning of washing ($Z^*$) for no axial mixing: $1/Pe = 0$; $B = 16.64$; $k_A = 9.38$; $k_B = 0.232$; $(+)$ $Q$, ($\blacksquare$) $w$, ($\blacktriangle$) $Pr$.

In practical systems washing continues beyond the minimum detection point of the column monitor, but for simulations the washing volume has been chosen equal to ten bed volumes to ensure high purity of the product. The influence of the washing volume is not considered here.

The model applies to a single-component system, but it will also be possible to extend the analysis to non-interacting multicomponent systems by introducing different parameters for each component.

*Simulation plan*

The effect of axial dispersion, the capacity of the column and the kinetic constants ($k_1$ and $k_2$) on the results obtained with the different techniques was studied by varying the dimensionless groups in which each of these parameters appears (*i.e.*, varying the Peclet number, $B$, $k_A$ and $k_B$ shows the variation of each of the first four parameters).

A set of matrix parameters for lysozyme on Blue Sepharose as used for affinity adsorption [18,19] has been taken: $c_0 = 10^{-3}$ g/cm$^3$; $q_m = 1.2 \cdot 10^{-2}$ g/cm$^3$; $k_1 = 20.2$ cm$^3$/gs; $k_2 = 5 \cdot 10^{-4}$ s$^{-1}$; $l = 10.4$ cm; $u = 224$ $\mu$m/s.

Other physical parameters have been taken from Onwuasoanya [20] to describe a matrix with particularly high axial dispersion: $D_L = 0.0233$. The voidage was $\varepsilon = 0.589$.

As the model includes mass transport limitations in the adsorption and desorption rate terms, the identification of the parameters of the model is easy. The experimental procedure to determine the parameters $q_m$, $k_1$ and $k_2$ was described previously by Chase [14]. Nevertheless, further work is now proceeding using a distributed parameter model to isolate the mass transport effects, in order to assess specifically the influence of the flow-rate on productivity.

The values of the dimensionless groups from the above parameters are: $1/Pe =$ 0.1; $B = 16.6$; $k_A = 9.38$; $k_B = 0.232$.

## RESULTS

Each of the Figs. 2–6 shows three variables ($w$, $Q$ and $Pr$) obtained at the end of the washing stage. The curves show the evolution of each of the variables as a function of $Z^*$.

*Basic case*
Firstly, axial dispersion is assumed negligible. The shape of adsorption waves within the bed, at the beginning of washing, is shown in Fig. 1. When breakthrough is detected, it is shown in Fig. 1 that $C = 0.95$ at $Z^* = 0.87$. Hence, $Z^* = 0.87$ refers to the traditional procedure (BTC) (Fig. 2).

A considerable fraction of the product loaded is lost ($w = 0.16$) by applying the traditional protocol in this case. The loss of product arises from both unadsorbed product and bound product. Because the elution phenomena also occur during the washing stage, only 81% of the maximum capacity of the column can be attained at the end of washing (Fig. 2).

If the goal of the process is the maximisation of the product bound, the traditional method is convenient, but it is also possible to use the partial loading approach. By loading the bed until $Z^* = 0.8$, the same amount of product is bound at the end of the washing, whereas the amount of product loaded is less. In that case, the loading time is shorter, thus reducing the overall time of the process and minimising the loss of product to $w = 0.08$. The time which can be saved by partially loading the column may be valuable if the loading time represents a significant fraction of the overall processing time. In any case, it is pointless to continue loading beyond the time at which the front reaches $Z_Q^*$.

Assuming a constant linear velocity with no axial dispersion, the product bound at the end of washing should be proportional to the fraction of the column loaded until product is lost at the outlet ($Z^* = 0.70$). In fact, the relation between $Q$ and $Z^*$ is not rigorously proportional (Fig. 2) due to the remaining product in solution at the end of washing. The average concentration of the product in solution after the washing is negligible compared to the concentration of product bound, but varies in a range 0.06–0.10 for $Z^*$ from 0.50 to 0.70. For $Z^*$ greater than 0.70, $C = 0.10$.

If the goal of the process is the minimisation of product losses, the partial loading approach is valuable compared to the traditional one. The loss is reduced from 16 to 0% by loading the bed until $Z^* = 0.70$ (Table I).

Productivity is the main criterion chosen to evaluate the relative worth of different operating conditions as it is the one most nearly related to the value of the process. The above two other criteria are noted because they have been used by laboratory workers, or by manufacturers, as prime measures of process worth. It may well be desirable to have higher column utilisation by developing more effective packing. However, for a given packing, it is not the fractional utilisation of the column which counts, but the productivity per unit time. Without a detailed cost analysis an optimum productivity cannot be totally defined. The expression for productivity (see nomenclature) has been arbitrarily constructed and includes elements for the costs of
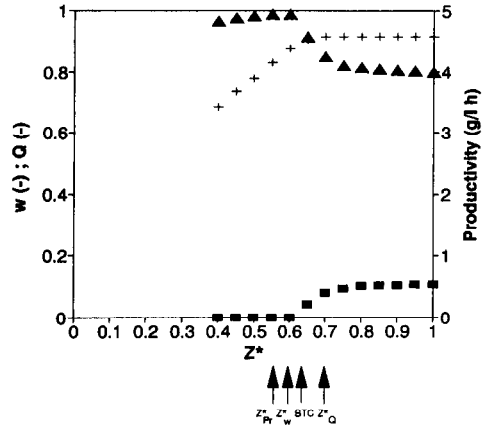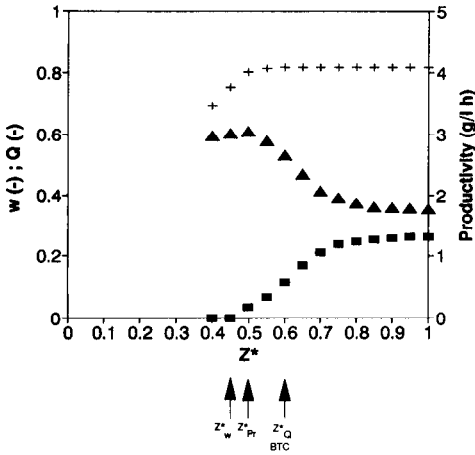
Fig. 3. Product loss ($w$), use of the column ($Q$) and productivity ($Pr$) after washing *vs.* position of the saturation front at the beginning of washing ($Z^*$) for the basic case: $1/Pe = 0.1$; $B = 16.64$; $k_A = 9.38$; $k_B = 0.232$; ($+$) $Q$, ($\blacksquare$) $w$, ($\blacktriangle$) $Pr$.

Fig. 4. Product loss ($w$), use of the column ($Q$) and productivity ($Pr$) after washing *vs.* position of the saturation front at the beginning of washing ($Z^*$) for the case of high column capacity: $1/Pe = 0.1$; $B = 83.2$; $k_A = 9.38$; $k_B = 0.232$; ($+$) $Q$, ($\blacksquare$) $w$, ($\blacktriangle$) $Pr$.



Fig. 5. Product loss ($w$), use of the column ($Q$) and productivity ($Pr$) after washing *vs.* position of the saturation front at the beginning of washing ($Z^*$) for the case of fast adsorption: $1/Pe = 0.1$; $B = 16.64$; $k_A = 46.9$; $k_B = 0.232$; ($+$) $Q$, ($\blacksquare$) $w$, ($\blacktriangle$) $Pr$.
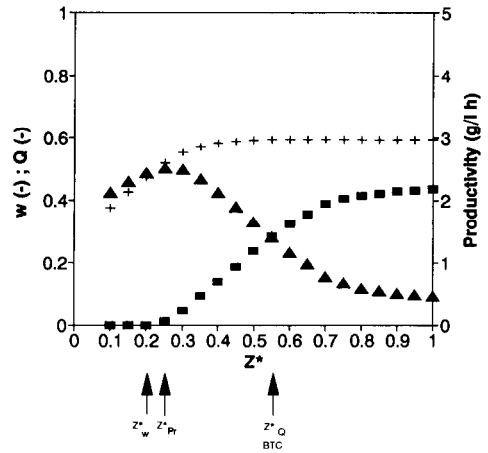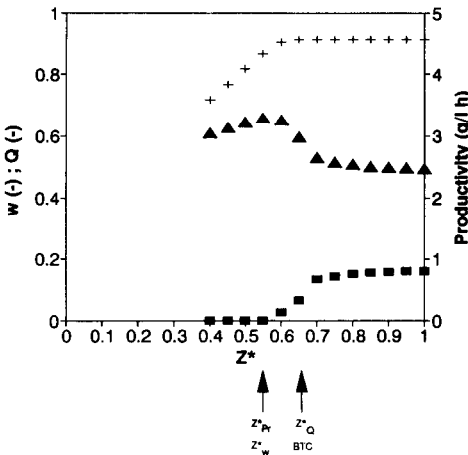
Fig. 6. Product loss ($w$), use of the column ($Q$) and productivity ($Pr$) after washing *vs.* position of the saturation front at the beginning of washing ($Z^*$) for the case of fast desorption: $1/Pe = 0.1$; $B = 16.64$; $k_A = 9.38$; $k_B = 1.16$; ($+$) $Q$, ($\blacksquare$) $w$, ($\blacktriangle$) $Pr$.

TABLE I

INFLUENCE OF THE DIMENSIONLESS GROUPS ($Pe$, $B$, $k_A$ AND $k_B$) ON THE PRODUCT LOSS ($w$), THE TOTAL PROCESS TIME ($\theta_{tot}$), THE USE OF THE CAPACITY OF THE COLUMN ($Q$) AND THE OVERALL PRODUCTIVITY ($Pr$) OBTAINED BY THE PARTIAL LOADING APPROACH ($Z_w^*$, $Z_{Pr}^*$ AND $Z_Q^*$) AND BY TRADITIONAL PROCEDURE (BTC)

| Parameters of the model | | | | Simulation results | | | | |
|---|---|---|---|---|---|---|---|---|
| $1/Pe$ | $B$ | $k_A$ | $k_B$ | $Z^*$ | $w$ | $\theta_{tot}$ | $Q$ | $Pr$ |
| 0 | 16.64 | 9.38 | 0.232 | $Z_w^* = 0.70$ | 0 | 22.7 | 0.74 | 3.03 |
| | | | | $Z_{Pr}^* = 0.70$ | 0 | 22.7 | 0.74 | 3.03 |
| | | | | $Z_Q^* = 0.80$ | 0.08 | 24.5 | 0.81 | 2.83 |
| | | | | (BTC) 0.87 | 0.16 | 26 | 0.81 | 2.45 |
| 0.1 | 16.64 | 9.38 | 0.232 | $Z_w^* = 0.45$ | 0 | 22.6 | 0.75 | 2.99 |
| | | | | $Z_{Pr}^* = 0.50$ | 0.03 | 23.5 | 0.79 | 3.03 |
| | | | | $Z_Q^* = 0.60$ | 0.11 | 25 | 0.81 | 2.63 |
| | | | | (BTC) 0.60 | 0.11 | 25 | 0.81 | 2.63 |
| 0.1 | 83.2 | 9.38 | 0.232 | $Z_{Pr}^* = 0.58$ | 0 | 80.2 | 0.85 | 4.95 |
| | | | | $Z_w^* = 0.60$ | 0 | 82 | 0.87 | 4.92 |
| | | | | (BTC) 0.62 | 0.02 | 84 | 0.88 | 4.72 |
| | | | | $Z_Q^* = 0.70$ | 0.10 | 91 | 0.91 | 4.24 |
| 0.1 | 16.64 | 46.9 | 0.232 | $Z_w^* = 0.57$ | 0 | 24.9 | 0.88 | 3.24 |
| | | | | $Z_{Pr}^* = 0.57$ | 0 | 24.9 | 0.88 | 3.24 |
| | | | | $Z_Q^* = 0.62$ | 0.05 | 25.8 | 0.91 | 2.88 |
| | | | | (BTC) 0.62 | 0.05 | 25.8 | 0.91 | 2.88 |
| 0.1 | 16.64 | 9.38 | 1.16 | $Z_w^* = 0.20$ | 0 | 18 | 0.47 | 2.43 |
| | | | | $Z_{Pr}^* = 0.25$ | 0.02 | 18.8 | 0.51 | 2.48 |
| | | | | $Z_Q^* = 0.55$ | 0.30 | 25.5 | 0.59 | 1.42 |
| | | | | (BTC) 0.55 | 0.30 | 25.5 | 0.59 | 1.42 |

the resin, of the product and of the equipment. This can be modified if different relative costs need to be used. It does allow the concept that the true optimum will differ from that chosen either on grounds of wastage of product or of resin cost alone. By loading the column until $Z^* = 0.70$, this criterion is increased by 24% when compared to the traditional protocol (Table I).

*Influence of the Peclet number*

   $1/Pe = 0.1$ + reference for $B$, $k_A$, $k_B$

   To increase the accuracy of the model, axial dispersion is now accounted for, using a Peclet number of 10 ($1/Pe = 0.1$). The adsorption wave broadens and the breaktime is now equal to fifteen compared to sixteen when axial dispersion was assumed negligible (Table I). The decrease of the breaktime with decreasing Peclet number has been also reported by Raghaven and Ruthven [21]. The detection of the breakthrough at the outlet might correspond to a detection of the adsorption front at $Z^* = 0.60$.

   The traditional method maximises the bound product. It is shown in Table I that axial dispersion has no influence on the maximum amount of product which can be

bound. Due to early breakthrough, unused capacity has been left in the lower area of the column. During the washing, the desorbed material of the upper region has been trapped in the lower, thus reducing the product loss to $w = 0.11$.

Due to axial dispersion, the product bound at the end of washing is not proportional to $Z^*$ (Fig. 3). A great decrease of the product bound is observed with decreasing $Z^*$ from $Z^* = 0.50$. It is shown that the maximum productivity can be achieved by loading the column until $Z_{Pr}^* = 0.50$; in that case little product is lost ($w = 0.03$). The productivity obtained loading until $Z_w^*$ is nearly the same as until $Z_{Pr}^*$, suggesting that, unless the product is very expensive, there is little benefit in loading until $Z_w^*$ or $Z_{Pr}^*$.

It is shown in Table I that the productivity can be maintained at 3.03 g/lh by using a partial-loading approach. Contrarily, productivity is greatly dependent on the Peclet number when using the traditional protocol. The productivity is increased only by 15% with the partial-loading approach, compared to 24% in the previous case. This result indicates that partial-loading is more valuable when axial dispersion is negligible, for example when high flow-rates can be used.

For small Peclet numbers (less than 50), the fraction of the column loaded must be evaluated from the loading time instead of $Z^*$. For example, a great decrease of $Z_w^*$ is shown in Table I with decreasing the Peclet number, whereas the loading time remains nearly constant. This result shows that the amount of product which must be loaded for optimising the process is in fact slightly dependent on the Peclet number.

*Influence of the capacity of the column*

$$B = 83.2 + \text{reference for } 1/Pe, \, k_A, \, k_B$$

To show the influence of an increase in the capacity of the column, the effect of a five-fold increase in $q_m$ has been studied. The results show that maximum working capacity of the column is higher ($Q = 0.91$) than previously ($Q = 0.81$). The average concentration of the product in solution after washing is higher than the previous example (0.14–0.28 compared to 0.06–0.10), thus allowing a greater fraction of the capacity of the column to be used.

The maximum working capacity is obtained by loading the column until $Z^* = 0.70$. This occurs when 50% of the inlet concentration of adsorbate is detected at the outlet. Hence, the maximum working capacity is not obtained by using the traditional protocol, which is described by a lower value of $Z^*$ (Table I). Surprisingly enough, the partial-loading approach should allow a larger loading time than the traditional procedure if the goal is the maximisation of the product bound. However, the productivity obtained loading until $Z_Q^*$ can be improved because 10% of the product loaded is lost during the washing.

This can be achieved for example by using the traditional technique. However, a very low concentration of the product in the effluent must be detected in order to stop the loading period. Otherwise, the productivity may decrease significantly as indicated by the shape of the curve productivity *vs.* $Z^*$ shown in Fig. 4. Generally, it is seen that the productivity obtained with the traditional technique is located in the region of steep decrease of the curve as mentioned above.

Increasing $B$ (*e.g.*, by having better adsorbent capacity), increases operation time

of the column. The optimal productivity is marginally higher ($+5\%$) with the new approach because overall productivity becomes less sensitive to the exact value of $Z^*$. Maximum productivity is only about 60% more with a column capacity increased by 500% (Table I).

The productivity decreases slightly from $Z^* = 0.50$ with decreasing $Z^*$. Because adsorption time dominates processing time, the decrease of the product bound is balanced by the reduction of the processing time. In that case, it is possible to stop adsorption earlier than $Z^*_{Pr}$ without significant loss of productivity. This facility may be useful when the exact position of the adsorption front cannot be accurately determined. It should be possible to load the bed until $Z^*_{Pr}$ ($\pm 0.05\ Z^*$ units) without any significant effect on productivity.

*Influence of kinetic constants*

"On" constant: $k_1$.

$$k_A = 46.9 + \text{reference for } 1/Pe, B, k_B$$

To show the influence of an increase in the value of $k_1$, $k_A$ has increased five fold. Because the value of the velocity has been kept constant, an increase in $k_1$ means an improvement in the strength of the interaction between the product and the binding site. The average concentration of the product in solution after washing is less than $C = 0.10$. The useful capacity of the column has a greater value ($Q = 0.91$) than for $k_A = 9.38$ ($Q = 0.81$) due to a more favourable shape of the adsorption isotherm.

Less product can be eluted during washing, and the product loss falls to only 5% when the traditional technique is used (Table I). It is shown in Fig. 5 that the product loss rapidly increases up to $w = 0.14$ with increasing $Z^*$ from 0.57 to 0.70. The new approach increases the productivity by 13%, at the same time no product is lost by loading the bed until $Z^* = 0.57$.

"Off" constant: $k_2$.

$$k_B = 1.16 + \text{reference for } 1/Pe, B, k_A$$

To show the influence of an increase in $k_2$, $k_B$ has increased five fold. An increase of $k_2$ means a decrease of the strength of the interaction. Hence, the amount of product eluted during washing is large; under these conditions, the concentration of the product in solution after washing can reach $C = 0.20$. Only 60% of the theoretical capacity of the column can be utilised by using the traditional procedure, highlighting the influence of $k_B$ on the process throughput.

Product loss appears during washing for loading over $Z^* = 0.20$ (Fig. 6). During washing, 30% of the product loaded is wasted by using the traditional technique. Sufficient capacity in the lower region of the column must be left in order to adsorb the material which desorbs in the upper area. By loading the columns until $Z^* = 0.25$, the productivity is maximised and the product lost is reduced to only 2% (Table I).

When $k_B$ is increased by 500%, the maximum productivity decreases by 18% and the productivity obtained using the traditional method decreases by 46%. In repetitive operation, one of the major effects of an increased number of cycles is an increased

non-specific adsorption and thus a decrease in the maximum capacity of the column. It may also result in a lower affinity of the remaining active sites for the adsorbate [5,22], described here as a decrease of $k_2$. The above effects result in a decrease of productivity. Thus, if the adsorbent needs to be replaced when the productivity falls below a critical value, this will take longer with the new approach. Therefore, the new approach permits larger number of cycles in repetitive operation, further increasing productivity.

CONCLUSIONS

A partial-loading approach has been studied with a model of adsorption chromatography, the central concept being to stop the adsorption before the breakthrough is detected at the outlet. The Peclet number, the maximum capacity of the column, and the kinetic constants have all been assessed with respect to: product loss, the use of column capacity and productivity. A systematic investigation of the effects of these parameters has been made using four dimensionless groups: $Pe$, $B$, $k_A$ and $k_B$. Compared to the traditional procedure, the new approach allows product losses to be reduced without important decrease in bound material, hence increasing the process throughput. By stopping adsorption before all capacity is saturated, unbound product and also material removed in the upper region of the column during washing can be readsorbed in the lower regions of the column. The benefits of the partial-loading approach is most clearly demonstrated when the capacity of the column is low or when the interaction between the product and the binding site is weak. Under these conditions the productivity of the process can be increased by 75% using the partial-loading approach.

SYMBOLS

| | | |
|---|---|---|
| $a_{ij}$ | Element of matrix $\alpha$ | |
| $A$ | Heaviside function of eqn. 5 | |
| $B$ | Dimensionless group of eqn. 5 | |
| $c$ | Concentration of product in solution | $g/cm^3$ |
| $c_0$ | Initial concentration of product | $g/cm^3$ |
| $C$ | Dimensionless concentration of product in solution; $C = c/c_0$ | |
| $C(\theta)$ | Vector of liquid-phase dimensionless concentration at time $\theta$, $i$th element of which refers to the concentration at $i$th stage of the column | |
| $D_L$ | Axial diffusivity | $cm^2/s$ |
| $E$ | Constant matrix defined in eqn. A18 | |
| $F$ | BPF parameter matrix defined in eqn. A3 | |
| $G$ | Function defined by eqn. A13 or A30 | |
| $h_{ij}$ | Two-dimensional block pulse function defined in eqn. A1 | |
| $H_m$ | One-dimensional BPF vector for time $\theta$ | |
| $H_n$ | One-dimensional BPF vector for distance $z$ | |
| $I$ | Unit matrix with order $n$ | |
| $J$ | Function defined in eqn. A29 | |
| $k_A$ | Dimensionless group of eqn. 6 | |
| $k_B$ | Dimensionless group of eqn. 6 | |

| $k_1$ | Forward rate constant | $cm^3/gs$ |
|---|---|---|
| $k_2$ | Backward rate constant | $s^{-1}$ |
| $l$ | Length of the column | cm |
| $m$ | Integer step of $\theta$ | |
| $n$ | Integer step of $z$ | |
| $P_m$ | Operational matrix for variable $\theta$ defined in eqn. A9 | |
| $P_n$ | Operational matrix for variable $z$ defined in eqn. A10 | |
| $Pe$ | Peclet number | |

$Pr$ Productivity of the process; $Pr = 3.6 \cdot 10^6 \left[ q - c_0(\theta_{tot} - 10)w \dfrac{1 - \varepsilon}{\varepsilon} \right] \dfrac{1}{t}$ g/lh

| $q$ | Solid-phase concentration of product | $g/cm^3$ |
|---|---|---|
| $q_m$ | Maximum capacity of the column | $g/cm^3$ |
| $Q$ | Dimensionless solid-phase concentration of product; $Q = q/q_m$ | |
| $Q(\theta)$ | Vector of solid-phase dimensionless concentration at time $\theta$, $i$th element of which refers to the concentration at $i$th stage of the column | |
| $t$ | Time | s |
| $T$ | Largest value of $t$ | s |
| $t_{ws}$ | Washing start time | s |
| $u$ | Velocity | cm/s |
| $w$ | Product lost/product loaded | |
| $x$ | Axial position along the column | cm |
| $z$ | Dimensionless distance | |
| $Z$ | Largest value of $z$ | |
| $Z^*$ | Distance reached by the adsorption front at the beginning of washing | |
| $Z_{Pr}^*$ | Value of $Z^*$ which maximises $Pr$ | |
| $Z_Q^*$ | Smallest value of $Z^*$ which maximises $Q$ | |
| $Z_w^*$ | Highest value of $Z^*$ with $w = 0$ | |
| $\alpha$ | Matrix defined in eqn. A28 | |
| $\varepsilon$ | Voidage | |
| $\theta$ | Dimensionless time | |
| $\theta_{tot}$ | Dimensionless process time | |
| $\theta_{ws}$ | Dimensionless washing start time | |

APPENDIX

A two-dimensional block pulse function (BPF) is defined below

$$h_{ij}(z,t) = \left\{ \begin{array}{l} 1, \dfrac{(j - 1)Z}{n} < z \leqslant \dfrac{jZ}{n}; \dfrac{(i - 1)T}{m} < t \leqslant \dfrac{iT}{m} \\ 0, \text{else} \end{array} \right\} \quad \text{(A1)}$$

A function $f(z,t)$ absolutely integrable in the region $t \in (0,T)$ and $z \in (0,Z)$ can be approximated as

$$f(z,t) = \sum_{i=1}^{m} \sum_{j=1}^{n} f_{ij} h_{ij}(z,t) = H_m^T(t) \, F H_n(z) \tag{A2}$$

where

$$F = [f_{ij}]_{m \times n} \tag{A3}$$

$$f_{ij} = \frac{m \, n}{T \, Z} \int_{\frac{(j-1)Z}{n}}^{\frac{jZ}{n}} \int_{\frac{(i-1)T}{m}}^{\frac{iT}{m}} f(z,t) \, dt dz \tag{A4}$$

$$H_m(t) = \begin{bmatrix} h_1(t) \\ \dots \\ h_m(t) \end{bmatrix} \tag{A5}$$

$$H_n(z) = \begin{bmatrix} h_1(z) \\ \dots \\ h_n(z) \end{bmatrix} \tag{A6}$$

Applying the integration theorem [15] to eqn. A2

$$\int_0^z \int_0^t f(z,t) \, dt dz = H_m^T(t) \, P_m^T \, F \, P_n \, H_n(z) \tag{A7}$$

$$\int_z^1 \int_0^t f(z,t) = H_m^T(t) \, P_m^T \, F \, P_n^T \, H_n(z) \tag{A8}$$

where

$$P_m = \frac{T}{m} \begin{bmatrix} \frac{1}{2} & 1 & \dots & \dots & 1 \\ 0 & \frac{1}{2} & 1 & \dots & 1 \\ \dots & \dots & \dots & \dots & \dots \\ 0 & \dots & \dots & \dots & \frac{1}{2} \end{bmatrix}_{m \times m} \quad ; \quad P_n = \frac{Z}{n} \begin{bmatrix} \frac{1}{2} & 1 & \dots & \dots & \dots \\ 0 & \frac{1}{2} & 1 & \dots & 1 \\ \dots & \dots & \dots & \dots & \dots \\ 0 & \dots & \dots & 0 & \frac{1}{2} \end{bmatrix}_{n \times n} \tag{A9} \tag{A10}$$

By integrating eqn. 6 with respect to $z$, we have

$$\int_0^z \frac{\partial C}{\partial \theta} \, dz = \frac{1}{Pe} \frac{\partial C(z,\theta)}{\partial z} - C(z,\theta) -$$

$$\int_0^z G(z,\theta) \, dz - \frac{1}{Pe} \frac{\partial C(0,\theta)}{\partial z} + C(0,\theta) \tag{A11}$$

$$\int\limits_{z}^{1}\int\limits_{0}^{z} \frac{\partial C}{\partial\theta}\,\mathrm{d}z\mathrm{d}z = \frac{1}{Pe}[C(1,\theta) - C(z,\theta)] - \int\limits_{z}^{1} C(z,\theta)\mathrm{d}z -$$

$$\int\limits_{z}^{1}\int\limits_{0}^{z} G(z,\theta)\mathrm{d}z\mathrm{d}z + \int\limits_{z}^{1}\left[-\frac{1}{Pe}\frac{\partial C(0,\theta)}{\partial z} + C(0,\theta)\right]\mathrm{d}z \qquad \text{(A12)}$$

where

$$G = B[k_A C(1 - Q) - k_B Q] \qquad \text{(A13)}$$

From the boundary conditions, eqn. 8, we obtain

$$-\frac{1}{Pe}\frac{\partial C(0,\theta)}{\partial z} + C(0,\theta) = A(\theta) \qquad \text{(A14)}$$

Substituting eqns. A14 and 9 into eqn. A11

$$C(1,\theta) = A(\theta) - \int\limits_{0}^{1}\left[G(z,\theta) + \frac{\partial C}{\partial\theta}\right]\mathrm{d}z \qquad \text{(A15)}$$

Substituting eqn. A14 and eqn. A15 into eqn. A12

$$\int\limits_{z}^{1}\int\limits_{0}^{z} \frac{\partial C}{\partial\theta}\,\mathrm{d}z\mathrm{d}z = \frac{1}{Pe}\left\{A(\theta) - \int\limits_{0}^{1}\left[G(z,\theta) + \frac{\partial C}{\partial\theta}\right]\mathrm{d}z - C(z,\theta)\right\} -$$

$$\int\limits_{z}^{1} C(z,\theta)\mathrm{d}z - \int\limits_{z}^{1}\int\limits_{0}^{z} G(z,\theta)\mathrm{d}z\mathrm{d}z + \int\limits_{z}^{1} A(\theta)\mathrm{d}z \qquad \text{(A16)}$$

Applying the integration theorem to eqn. A16 we obtain

$$\frac{\mathrm{d}\vec{C}(\theta)}{\mathrm{d}\theta} P_n P_n^T H_n(z) = \frac{A(\theta)}{Pe} E^T H_n(z) - \frac{1}{Pe} \vec{C}(\theta) H_n(z) -$$

$$\left[\vec{G}(\theta) + \frac{\mathrm{d}\vec{C}(\theta)}{\mathrm{d}\theta}\right]\frac{1}{nPe} EE^T H_n(z) - \vec{C}(\theta) P_n^T H_n(z) -$$

$$\vec{G}(\theta) P_n P_n^T H_n(z) + A(\theta) E^T P_n^T H_n(z) \qquad \text{(A17)}$$

where

$$E = \begin{bmatrix} 1 \\ 1 \\ \cdots \\ 1 \end{bmatrix} \qquad \text{(A18)}$$

Equating the coefficients $h_i(z)$, eqn. A17 gives

$$\frac{d\vec{C}(\theta)}{d\theta} P_n P_n^T = \frac{A(\theta)}{Pe} E^T - \frac{1}{Pe} \vec{C}(\theta) - \frac{1}{Pe}\left[\vec{G}(\theta) + \frac{d\vec{C}(\theta)}{d\theta}\right]\frac{1}{n} EE^T H_n(z) -$$

$$\vec{C}(\theta) P_n^T - \vec{G}(\theta) P_n P_n^T + A(\theta) E^T P_n^T \qquad (A19)$$

Eventually, after some manipulations, eqn. A19 becomes

$$\frac{d\vec{C}}{d\theta} = (A(\theta) E^T - \vec{C})\left(\frac{1}{Pe} + P_n^T\right)\left[P_n P_n^T + \frac{1}{nPe} EE^T\right]^{-1} - \vec{G} \qquad (A20)$$

Applying the product theorem [16] to eqn. 7, we have on the other hand

$$\frac{d\vec{Q}(\theta)}{d\theta} H_n(z) = k_A[\vec{C}(\theta) H_n(z) - C\vec{Q}(\theta) H_n(z)] - k_B \vec{Q}(\theta) H_n(z) \qquad (A21)$$

where

$$C\vec{Q}(\theta) = \begin{bmatrix} c_1(\theta) \times q_1(\theta) \\ \dots \\ c_n(\theta) \times q_n(\theta) \end{bmatrix} \qquad (A22)$$

Equating the coefficients $h_i(z)$, eqn. A21 gives

$$\frac{d\vec{Q}(\theta)}{d\theta} = k_A[\vec{C}(\theta) - C\vec{Q}(\theta)] - k_B \vec{Q}(\theta) \qquad (A23)$$

From initial conditions we have

$$\vec{C}(\theta) = \vec{Q}(\theta) = 0\bigg|_{\theta = 0} \qquad (A24)$$

Eqns. A20, A23 and A24 can be rewritten as

$$\frac{dc_i(\theta)}{d\theta} = \sum_{j=1}^{n} [c_j(\theta) - A(\theta)]a_{ij} - G[c_i(\theta), q_i(\theta)] \qquad (A25)$$

$$\frac{dq_i(\theta)}{d\theta} = J[c_i(\theta), q_i(\theta)] \qquad (A26)$$

$$c_i(0) = q_i(0) = 0, \qquad i = 1, \dots, n \qquad (A27)$$

where

$$\alpha = (a_{ij}) = -\left[P_n P_n^T + \frac{1}{nPe} EE^T\right]^{-1}\left[P_n^T + \frac{I_{(n \times n)}}{Pe}\right]$$ (A28)

$$J(C,Q) = k_A C[1 - Q] - k_B Q$$ (A29)

$$G(C,Q) = F(C,Q)B$$ (A30)

$$c_i(\theta) = \frac{n}{Z} \int_{(i-1)Z/n}^{iZ/n} C(z,\theta)\,dz$$ (A31)

$$q_i(\theta) = \frac{n}{Z} \int_{(i-1)Z/n}^{iZ/n} Q(z,\theta)\,dz$$ (A32)

If we are noting

$$c_{ij} = \frac{m}{\theta_{tot}} \int_{(j-1)\theta_{tot}/m}^{j\theta_{tot}/m} c_i(\theta)\,d\theta$$ (A33)

$$q_{i,j} = \frac{m}{\theta_{tot}} \int_{(j-1)\theta_{tot}/m}^{j\theta_{tot}/m} q_i(\theta)\,d\theta$$ (A34)

$$\vec{C}_j = \begin{bmatrix} c_{1j} \\ \ldots \\ c_{nj} \end{bmatrix}, \qquad \vec{Q}_j = \begin{bmatrix} q_{1j} \\ \ldots \\ q_{nj} \end{bmatrix}$$ (A35), (A36)

Applying the forward recursive formula [15] to eqns. A25–A27, we eventually find algebraic recursive relations

$$\vec{C}_{j+1} = \left(I - \frac{\theta_{tot}}{2m}\alpha\right)^{-1}\left\{\left(I + \frac{\theta_{tot}}{2m}\alpha\right)\vec{C}_j - \right.$$
$$\left. \frac{\theta_{tot}}{2m}\left[\Gamma(j)A(\theta)\alpha E + G(\vec{C}_j,\vec{Q}_j) + G(\vec{C}_{j+1},\vec{Q}_{j+1})\right]\right\}$$ (A37)

$$\vec{Q}_{j+1} = \vec{Q}_j + \frac{\theta_{tot}}{2m}\left[J(\vec{C}_j,Q_j) + J(\vec{C}_{j+1},\vec{Q}_{j+1})\right]$$ (A38)

for $j = 0, 1, \ldots, m - 1$

$$\vec{C}_0 = \vec{Q}_0 = 0 \tag{A39}$$

$$\Gamma(j) = \left\{ \begin{array}{l} 1, j = 0 \\ 2, j > 0 \end{array} \right\} \tag{A40}$$

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