Optimization of simulated moving bed chromatography with fractionation and feedback incorporating an enrichment step

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Abstract
An enrichment step is proposed to simulated moving bed chromatography with fractionation and feedback (FF-SMB), a new variation of SMB, to concentrate recyclates before they are fed back into the unit. Effectiveness of this operation is evaluated by systematic optimization studies. Case studies reveal that enriching recyclates is advantageous to FF-SMB and provides further improvement in separation performance over the non-enriched case.

Keywords: simulated moving bed, fractionation, feedback, enrichment, optimization.

1. Introduction
Simulated moving bed (SMB) chromatography is a continuous and efficient separation technology and extensively applied in sugar, petrochemical, and fine chemical industries. Extending SMB to the pharmaceutical industry has also gained increasing interest. Recently, a novel process modification, referred to as fractionation and feedback SMB (FF-SMB), has been suggested [1]. A schematic representation of an SMB unit realizing fractionation and feedback is shown in Fig. 1. During the operation of FF-SMB, the outlet streams are fractionized into the product and recycle fractions, thus splitting each cycle (here defined as the time between two successive port switches) into a production period of length $\tau^k_{\text{Production}}$ and a recycle period of length $\tau^k_{\text{Recycle}}$, $k = E, R$ (see Fig. 2a and b). Over $\tau^k_{\text{Production}}$, the outlet stream fulfills a given purity requirement and is withdrawn as a product. Within the recycle period, the stream is directed to the buffer vessel and collected as an “off-spec” product which is then fed...
back into the unit alternatingly with the fresh feed. Alternating use of different feed sources results in a distinct feeding regime shown in Fig. 2c, where a specific feeding sequence of using the raffinate buffer vessel first, followed by the original feed, and finally the extract buffer vessel (abbreviated as “RFE”), is chosen for illustration purposes. Such feeding regime divides one complete cycle into three sub-periods, i.e., the raffinate feedback period $\tau_{\text{Feedback}}^R$, feeding period $\tau_{\text{Feeding}}$ and extract feedback period $\tau_{\text{Feedback}}^E$.

![Fig. 2. Illustration of outlet fractionation and feeding regime of FF-SMB. (a) Extract outlet fractionation; (b) Raffinate outlet fractionation; (c) Feeding sequence “RFE” and feeding scheme. Solid lines: concentration profiles for A; dotted lines: concentration profiles for B. The concentration of each component is normalized with respect to that in the feed tank.](image)

A systematic model-based optimization approach has been employed to evaluate the potential of FF-SMB [2, 3]. In our previous studies, it is found that the “off-spec” fractions (i.e., recyclates) collected in the buffer vessels are partially separated and of favorable compositions. However, compared to the original feed, they are significantly diluted. In this work, a continuous enrichment step is introduced to the recyclates, allowing them to achieve higher feedback concentrations. The resulting more concentrated versions are then fed back into the inlet in a certain feeding sequence. A similar idea was also adopted in Enriched Extract SMB (EE-SMB) [5], where a portion of the extract stream is concentrated and re-injected at the same point of the SMB unit. Using solvent evaporation as an illustrative example, the effectiveness of this operation will be evaluated with the help of the optimization method developed previously for FF-SMB. The effect of evaporating rate on the performance achievable by the evaporative FF-SMB is also studied.

2. Mathematic modeling of FF-SMB with enrichment step

The equilibrium dispersive model was used to describe the chromatographic columns

$$\frac{\partial C_i}{\partial t} + \frac{1 - \varepsilon}{\varepsilon} \frac{\partial q_i}{\partial t} + u \frac{\partial C_i}{\partial z} - D_{\text{ap},i} \frac{\partial^2 C_i}{\partial z^2} = 0, \quad i = A, B$$

(1)

with the initial and boundary conditions:

$$C_i(t, z) \big|_{t=0} = 0, \quad D_{\text{ap},i} \frac{\partial C_i}{\partial z} \bigg|_{z=0} - u(C_i \big|_{z=0} - C_i^{\text{in}}) = 0, \quad D_{\text{ap},i} \frac{\partial C_i}{\partial z} \bigg|_{z=L} = 0$$

(2)

The apparent axial dispersion coefficient $D_{\text{ap},i}$ was assumed to be the same for both components and calculated by using

$$D_{\text{ap},i} = \frac{uL}{2N}$$

(3)

The nonlinear competitive Langmuir isotherms were used to characterize the adsorption behavior of the two components:
To enrich the “off-spec” fractions, many strategies, such as solvent evaporation and membrane filtration, can be applied. Throughout this paper, the solvent removal by evaporation was used for evaluation purposes. A model with perfectly mixed conditions was assumed to predict the behavior of each buffer vessel. $Q^k_{\text{Exp}}$ was introduced to represent the flow rate of solvent evaporated from the buffer vessel $k$ (see Fig. 3), for which the following mass balance equations can be easily derived:

$$
\frac{d(V^k_{\text{Buffer}} C^k_{\text{Buffer}})}{dt} = Q^k_{\text{in}}(t) C^k_{\text{in}}(t) - Q^k_{\text{out}}(t) C^k_{\text{out}}(t) + \frac{dV^k_{\text{Buffer}}}{dt} = Q^k_{\text{in}}(t) - Q^k_{\text{out}}(t) - Q^k_{\text{Exp}}
$$

with the initial conditions $V^k_{\text{Buffer}}|_{t=0} = V^k_{\text{Buffer}0}$, $C^k_{\text{Buffer}}|_{t=0} = C^k_{\text{Buffer}0}, i = A, B, k = E, R$.

Within each cycle, the liquid volume recycled from the corresponding outlet to the buffer vessel $V^k_{\text{Recycle}} = (1 - \tau^k_{\text{Production}}) V^k_{S E_k}$, the volume evaporated $V^k_{\text{Exp}} = Q^k_{\text{Exp}} t_S$ and the volume fed back to the unit $V^k_{\text{Feedback}} = \tau^k_{\text{Feedback}} V^k_{S F}$. For the other modeling details which are the same as those of FF-SMB, the reader is referred to [3].

3. Optimization problem formulation

As shown in Section 1, the fractionation and feedback regime offers additional degrees of freedom, i.e., $\tau^k_{\text{Production}}$ and $\tau^k_{\text{Feedback}}$, $k = E, R$, and the feeding sequence. Here we restrict our attention to one case where $V^k_{\text{Recycle}} = V^k_{\text{Feedback}} + V^k_{\text{Exp}}$, thus ensuring that each buffer vessel neither “runs dry” nor overflows. The two feedback periods can then be excluded from the independent variables. The feeding sequence, as done in [3], is also fixed at “RFE” in this paper (see Fig. 2c). The feed throughput maximization problem can be formulated as below:

$$
\max_{m_1, m_2, \ldots, m_{IV}, Q_F, Q_F, \tau^E_{\text{Production}}, \tau^E_{\text{Production}}} Q^F_F = Q_F (1 - \tau^E_{\text{Feedback}} - \tau^E_{\text{Feedback}})
$$

s. t.

Product purity specifications:

$$
Pur_E \geq Pur_{E,\text{min}}, \quad Pur_R = \int_{0}^{\tau^E_{\text{Production}}} C^R(t) \, d\tau \geq Pur_{R,\text{min}}
$$

Maximum flow-rate limitation:

$$
Q_F \leq Q_{\text{max}}
$$

Feasibility constraints on feedback periods:

$$
0 \leq \tau^E_{\text{Feedback}} \leq 1, \quad 0 \leq \tau^R_{\text{Feedback}} \leq 1, \quad 0 \leq \tau^E_{\text{Feedback}} + \tau^R_{\text{Feedback}} \leq 1
$$

Feasibility requirements on $m$-values:

$$
m_1 - m_{IV} > 0, \quad m_2 - m_{IV} > 0, \quad m_{III} - m_{IV} > 0, \quad m_{III} - m_{IV} > 0
$$
In the optimization variables, the four dimensionless \( m \)-values are defined as the net flow-rate ratios [4]: \( m_j = \frac{Q_I^{t_S} - V_{\text{col}}^{E}}{(1 - \varepsilon)V_{\text{col}}} \), \( j = I, II, III, IV \). The objective function \( Q_F^* \) denotes the average rate of processing fresh feed of the FF-SMB unit. The sequential approach [2, 3] was used to solve the nonlinear programming (NLP) problem. The partial differential equations in Section 2 were discretized in space by orthogonal collocation on finite elements method, and the resulting system of differential algebraic equations (DAEs) was integrated using DASPK solver. A sequential quadratic programming optimizer E04UCF from the NAG Fortran Library, was chosen for optimization. When the deviation between the concentration profiles at the end of two successive cycles fulfills a pre-specified tolerance, the cyclic steady state was considered to be attained. The gradients of the purity constraints were numerically approximated by finite difference scheme, while the others were determined analytically.

4. Results and discussion

A binary separation characterized by nonlinear Langmuir isotherms and performed in a 4-zone laboratory-scale SMB unit was used as a model process. The operating conditions and model parameters are summarized in Table 1.

The maximum feed throughput delivered by the conventional SMB (i.e., \( Q_F \)) and FF-SMB (i.e., \( Q_F^* \)) with and without evaporation with respect to different purity requirements is shown in Fig. 4. Note that in this case study, the evaporating rate for both buffer vessels was fixed at 0.06 mL/min. Selection of such a relatively low value is due to the small dimension of the unit under consideration. For the 5-column SMB, the configuration of 1/1/2/1 representing two columns in section III and one each in other sections was considered. It is observed that the 4-column SMB is feasible only for the purity of 90%. The evaporation allows the 4-column FF-SMB to achieve a feed throughput comparable to that of the 5-column SMB, and to clearly outperform the non-evaporative scenario. The improvement over the normal FF-SMB becomes more significant as the higher purity is required. For the purity of 95%, the ability of processing fresh feed can be enhanced by 150%, while such an improvement is only 14% for the purity of 90%. The optimal performance of the 4-column FF-SMB with different solvent evaporating rates is shown in Fig. 5, where the minimum purity requirement was specified as 95% for both products. As can be seen in this figure, the improvement of the feed throughput increases linearly with increasing the evaporating rate. At a rate of 0.09 mL/min or

| Column parameters and operating conditions |
|-----------------|-----------------|
| \( D \, [\text{cm}] \) | 1 |
| \( L \, [\text{cm}] \) | 10 |
| \( \varepsilon \, [-] \) | 0.667 |
| \( N \, [-] \) | 40 |
| \( V_{\text{Buffer}} \, [\text{mL}] \) | 4 |
| \( Q_{\text{max}} \, [\text{mL/min}] \) | 10 |
| \( C_{\text{Buffer}} \, [\text{g/L}] \) | 0 |

| Adsorption isotherm coefficients in Eq. (4) |
|-----------------|-----------------|
| \( A \, [\text{L/g}] \) | 5.078 |
| \( B \, [\text{L/g}] \) | 5.718 |

Fig. 4. Comparison of optimum feed throughput for different operating regimes.

![Fig. 4. Comparison of optimum feed throughput for different operating regimes.](image_url)
higher, the optimal value exceeds that of the 5-column SMB. It should be pointed out that typically the two components in the fresh feed reach their solubility limits. Care should be taken to avoid excessive solvent evaporation. We have checked that for both case studies, each component after evaporation is more concentrated, but remains lower than its feed concentration.

5. Conclusions

Considering solvent evaporation as an example, effectiveness of an enrichment step has been evaluated by systematic optimization studies. The optimal performance of FF-SMB including an enrichment step is compared to that of SMB and FF-SMB. Quantitative results show that significant improvement over the non-enriched case and conventional concept can be achieved. The benefit attainable becomes more pronounced as the evaporating rate increases. It can be expected that the idea is particularly attractive for cases where the process is not operated close to solubility limits of the components. Experimental validation of this operation on FF-SMB is our future work.

Nomenclature

$C$: liquid phase concentration [g/L]; $D$: column diameter [cm]; $H$: Henry coefficient [-]; $K$: adsorption parameter [L/g]; $L$: column length [cm]; $N$: number of theoretical plates per column [-]; $Pur$: product purity [%]; $Q$: liquid phase flow-rate [mL/min]; $q$: solid phase concentration [g/L]; $t$: time [min]; $t_s$: cycle time [min]; $u$: interstitial liquid velocity [cm/s]; $V$: liquid volume [mL]; $V_{Col}$: column volume [mL]; $z$: axial coordinate [cm]; $\varepsilon$: column porosity [-]; $\tau$: dimensionless time defined as $\tau = t/t_s$ [-]; $I, II, III, IV$: SMB zone index; $Buffer$: buffer vessel; $E$: extract; $Evp$: evaporation; $F$: feed; $Feed$: original feed tank; $Feedback$: outlet stream is recycled to buffer vessel; $Feeding$: feed from original feed; $i$: component index, $i = A, B$; $in$: inlet of buffer vessel; $k$: SMB outlet or buffer vessel index, $k = E, R$; $out$: outlet of buffer vessel; $Production$: outlet stream is collected as product; $R$: raffinate; $Recycle$: outlet stream is recycled to buffer vessel.

References