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Experimental assessment of simulated moving bed and varicol processes using a single-column setup

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Abstract

A novel single-column setup for experimentally reproducing the steady periodic behavior of simulated countercurrent multicolumn chromatography is presented. The system relies on accurate online monitoring of the outlet effluent composition, processing the measured data through a node balance, and feeding it back into the column with an appropriate time delay using a multi-pump configuration to reproduce the desired inlet stream. The feasibility of the proposed system is demonstrated on the linear separation of two nucleosides using three different column configurations, which include both synchronous and asynchronous port switchings. By judiciously selecting the switching interval for process startup and applying a model-based startup procedure, the periodic state can be attained in just one or two cycles. Therefore, mobile phase and solute consumptions required to experimentally reproduce the periodic state of the equivalent multicolumn process are reduced to a minimum. This may be an economic, optimal manner of experimentally testing a set of operating conditions or cycle policy to achieve a given separation performance for a new multicolumn chromatographic separation.

Keywords: Simulated moving bed; Varicol; One-column analog; Reversed phase; Nucleoside separation

1. Introduction

Simulated moving bed (SMB) chromatography is a multicolumn continuous separation process that increases throughput, purity and yield relative to batch chromatography [1–3]. SMB utilizes a series of columns that are interconnected circularly with moving inlet and outlet ports. By periodically moving the input and withdrawal ports in the direction of fluid flow, the countercurrent contact between the stationary and mobile phases is simulated [4]. Contrary to a true countercurrent process, the SMB reaches a cyclic steady state (CSS) where the internal concentration profiles move in the direction of fluid flow and the outlet compositions are time periodic [5]. The SMB has been increasingly applied for the separation of pure substances, at all production scales, in the pharmaceutical, fine chemistry, and biotechnology industries [6].

The recent rapid development of SMB applications has led to the introduction of novel SMB schemes that are substantially different from the conventional SMB process. The new schemes provide further gains, but usually at the expense of additional complexity. This additional complexity requires highly versatile SMB equipment [7], advanced optimization tools [9,10,8,11–14], and robust control procedures [16,15,17–19].

A number of variables can be manipulated in SMB operation to improve its performance. These include, among others, the asynchronous shift of the inlet/outlet ports [20,21] and the cyclic modulation of feed flow [22–26] or feed concentration [27,28]. The potential of modulating solvent strength during the switching interval has not yet been realized, though the benefits of applying solvent-gradient operation to the SMB have already been demonstrated [29–32]. These newly emerged cyclic operation schemes are pushing the trend towards the use of units with a small number of columns, since less stationary phase is used, the setup is more economic, and the overall pressure drop can be reduced.

Uncertainties in isotherm parameters, band broadening, pump stability and calibration, temperature stability, dead volumes, and packing reproducibility, are inevitable in every SMB process. Many of these uncertainties can be properly accounted for if analytical data is complemented with small-scale SMB runs when scaling up to production scale. Furthermore, it is advisable that newly developed operating schemes be exten-

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sively validated by experiment at small scale, to identify possible operational bottlenecks and robustness issues, before porting them to larger scale.

In this paper a novel single-column setup to experimentally reproduce the steady periodic behavior of simulated countercurrent multicolumn chromatography is presented. The system was not devised to be a practical separation device, as the one proposed in [33], but instead to be an economic and fast method of experimentally exploring different column configurations and cyclic operation policies. As such, it is ideally suited for applied research studies but may also be useful in the early stages of development, optimization, and validation of a new chromatographic separation.

We start by briefly reviewing the fundamentals of single-column chromatography with recycle analogous to processes using multicolumn schemes based on the SMB concept. In particular, we focus on the single-column chromatograph with recycle lag which is the basis for the proposed setup. Its practical implementation and operation are then described in detail. The feasibility of the proposed setup is demonstrated on the linear separation by reversed phase of two nucleosides. Three different multicolumn configurations, including both synchronous and asynchronous port switchings, are optimized and experimentally reproduced by the single-column setup. In most cases of practical interest the initial transient is of no interest, but only the fully established periodic state. For those cases, it is shown that the duration of the experiment can be significantly reduced by applying a fast model-based startup procedure. The merits and constraints of the proposed system are discussed before summarizing the work and drawing final conclusions.

2. Theory

Fig. 1 shows the schematic representation of a generic node connecting two consecutive columns, say $j-1$ and j, of an SMB unit. The notation employed is as follows: Q is the liquid flow rate, $c^{\text{out}}_{i,j-1}$ is the concentration of solute i at the outlet of column $j-1$ and $c^{\text{in}}_{i,j}$ is the corresponding solute concentration at the inlet of column j. The solute concentration and flow rate of the external inlet/outlet lines are identified by scripts E (eluent), X (extract), F (feed), and R (raffinate).

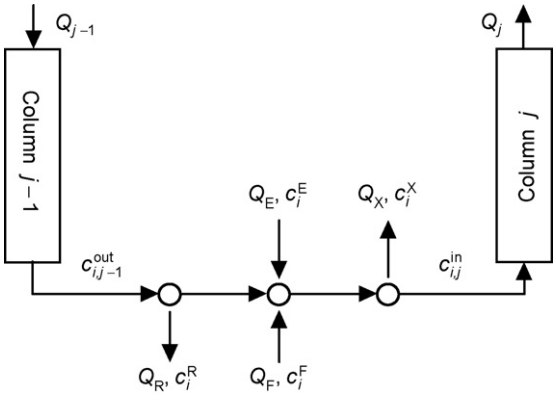

Fig. 1. Schematic representation of the node connecting columns $j-1$ and j of an SMB unit. The concentration of solute i in liquid phase is c_i and Q is the volumetric flow rate. E, X, F, and R denote eluent, extract, feed and raffinate lines, respectively.

Note that in the schematic diagram of Fig. 1 the sequence in which the inlet/outlet lines are connected to the node is such that it allows certain zones to cease to exist temporarily, while avoiding mixing issues and occurrence of short-cut streams. For example, an optimized asynchronous port switching typically suppresses zone I and zone IV over certain periods of the switching interval [11,12,14]. In the former case eluent is added and extract is withdrawn simultaneously on the same node, whereas in the latter case raffinate is withdrawn from the node into which eluent is being simultaneously introduced. The equations given below are of general applicability provided that lines do not cross each other and that adjacent zones do not cease to exist simultaneously.

Under the assumptions discussed above, the solute node balance can be written as

$$\begin{cases} Q_{\text{III}}\, c^{\text{in}}_{i,j} = Q_{\text{II}}\, c^{\text{out}}_{i,j-1} + (Q_{\text{III}} - Q_{\text{II}})\, c^{\text{F}}_i & \text{(feed node)} \\ Q_{\text{I}}\, c^{\text{in}}_{i,j} = Q_{\text{IV}}\, c^{\text{out}}_{i,j-1} + (Q_{\text{I}} - Q_{\text{IV}})\, c^{\text{E}}_i & \text{(eluent node)} \\ c^{\text{in}}_{i,j} = c^{\text{out}}_{i,j-1} & \text{(otherwise)} \end{cases}, \quad (1)$$

where $Q_{\text{I}}, \ldots, Q_{\text{IV}}$ are the flow rates in the four sections of the SMB, and are determined by the global node balances

$$Q_{\text{I}} = Q_{\text{IV}} + Q_{\text{E}}, \quad (2)$$

$$Q_{\text{II}} = Q_{\text{I}} - Q_{\text{X}}, \quad (3)$$

$$Q_{\text{III}} = Q_{\text{II}} + Q_{\text{F}}, \quad (4)$$

$$Q_{\text{IV}} = Q_{\text{III}} - Q_{\text{R}}. \quad (5)$$

The cyclic operation of the SMB process is achieved by moving the inlet and outlet ports one column downstream (i.e. in the direction of fluid flow) every τ time units, where τ is the switching interval. Mathematically, this can be expressed as

$$\Omega_j(t) = \Omega(t_j), \quad t_j = [t - (j-1)\tau] \bmod N\tau, \quad (6)$$

where Ω_j denotes the set of input variables for column j, which includes Q_j and the state (opened or closed) of the four inlet/outlet lines connected to its inlet node; 'mod' defines the usual modulo operator: $a \bmod b \equiv a - b\,\text{int}(a/b)$. Note that Eq. (6) imposes a $N\tau$ periodicity on $\Omega_j(t)$ and that

$$\Omega_{j-1}(t) = \Omega_j(t + \tau). \quad (7)$$

As in previous work from our group [33,34], we do not track the internal composition profile circulating around the multicolumn loop, but instead follow its steady periodic behavior in one of the columns step by step over the cycle. To detach the selected column from the system, making it autonomous, while still maintaining the same CSS dynamics, its outlet stream is used as a replacement for that of the neighboring upstream column with a time lag of $(N-1)\tau$ [33]. This is equivalent to replacing Eq. (1) by

$$\begin{cases} Q_{\text{III}}\, c^{\text{in}}_i(t) = Q_{\text{II}}\, c^{\text{out}}_i(t') + (Q_{\text{III}} - Q_{\text{II}})\, c^{\text{F}}_i & \text{(feed mode)} \\ Q_{\text{I}}\, c^{\text{in}}_i(t) = Q_{\text{IV}}\, c^{\text{out}}_i(t') + (Q_{\text{I}} - Q_{\text{IV}})\, c^{\text{E}}_i & \text{(eluent mode)} \\ c^{\text{in}}_i(t) = c^{\text{out}}_i(t') & \text{(otherwise)} \end{cases}, \quad (8)$$