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# Three column intermittent simulated moving bed chromatography: 1. Process description and comparative assessment

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ABSTRACT

The three column intermittent simulated moving bed (3C-ISMB) process is a new type of multi-column chromatographic process for binary separations and can be regarded as a modification of the I-SMB process commercialized by Nippon Rensui Corporation. In contrast to conventional I-SMB, this enables the use of only three instead of four columns without compromising product purity and throughput. The novel mode of operation is characterized by intermittent feeding and product withdrawal as well as by partial recycling of the weakly retained component from section III to section I.

Due to the smaller number of columns with respect to conventional I-SMB, higher internal flow rates can be applied without violating pressure drop constraints. Therefore, the application of 3C-ISMB allows for a higher throughput whilst using a smaller number of columns. As a result, we expect that the productivity given in terms of throughput per unit time and unit volume of stationary phase can be significantly increased.

In this contribution, we describe the new process concept in detail and analyze its cyclic steady state behavior through an extensive simulation study. The latter shows that 3C-ISMB can be easily designed by Triangle Theory even under highly non-linear conditions. The simple process design is an important advantage to other advanced SMB-like processes. Moreover, the simulation study demonstrates the superior performance of 3C-ISMB, namely productivity increases by roughly 60% with respect to conventional I-SMB without significantly sacrificing solvent consumption.



## 1. Introduction

Simulated moving bed (SMB) chromatography [1,2] is a well established multi-column continuous binary separation process. Owing to its excellent performance as compared to batch chromatography, namely high purity levels at high productivity and low solvent consumption, SMB has become an important unit operation for the separation of enantiomers [3]. Since the need for expensive chiral stationary phases (CSP) is a major cost factor, there is a continuous effort into finding modified SMB schemes yielding higher productivities, i.e. higher throughput per unit time and unit volume of CSP [3].

The most successful modifications to conventional SMB are process schemes with non-constant operating conditions, i.e. processes wherein the switch time is divided into two or more sub steps, which allows variation of the operating parameters in a stepwise manner and thus increases the number of degrees of freedom. In general the additional complexity hampers the design since simple short-cut design methods such as Triangle Theory [4] are no longer applicable. The increased complexity is, however, compensated by an increase in productivity. The most prominent examples of this class of operating modes are among others VariCol (variation of the column configuration) [5], PowerFeed (variation of the internal and external flow rates) [6,7], partial feed/partial withdrawal (variation of feed and raffinate flow rates so as to keep $Q_I$, $Q_{II}$ and $Q_{IV}$ constant) [8], ModiCon (variation of the feed concentration to influence the migration velocities) [9], and intermittent SMB (I-SMB) which can be regarded as a special case of PowerFeed and is discussed in more detail in Section 2.1.

Another straightforward method to reduce the number of columns is the adoption of a three-section concept, i.e. the removal of the fourth section [10]. This modification results, however, in a highly diluted raffinate product and an increased solvent consumption due to the lack of a solvent recycle. Attempts to overcome these drawbacks were proposed by both Zang et al. and Lee et al. [11–13]; the former exploited the fact that the raffinate outlet consists essentially of pure solvent at the beginning of the switch period by recycling the corresponding part of the raffinate stream to section I

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[11], whereas the latter proposed a so-called raffinate rear-portion recycle [12,13]. The rear-portion recycle concept is fundamentally different from all other concepts discussed so far, since the raffinate is only recovered at the beginning of the switching period and completely recycled to section I towards the end of the switching period. Thus, instead of recycling pure solvent, a stream that is rich in the weakly retained component is fed to section I. This concept works if the recycling period is initiated only when section I is already regenerated to a large extent and when it lasts for a relatively short fraction of the switching period. In other words, it has to be designed so as the front of the weakly retained component neither catches up the tail of the strongly retained component nor reaches the extract port. To the best of our knowledge such an uncommon recycling regime is quite unique and we are not aware of any other processes making use of the same principle.

Despite the partial withdrawal of the raffinate, the process scheme proposed by Lee et al. is operated fully continuously and is thus likely to suffer from the influence of the port shift discontinuity in the same manner as conventional SMB in 1-1-1-1 configuration [14,15]. However, incorporating the principle of raffinate rear-portion recycle into I-SMB allows for exploiting the benefits of both concepts, namely a reduced number of sections and the possibility of achieving high purity levels with only one column per section. Therefore, we herein propose for the first time a three column intermittent SMB process, termed 3C-ISMB, that is characterized by intermittent feed and withdrawal as well as by recycling of the weakly retained component from section III to section I.

In this paper we introduce the new 3C-ISMB process and benchmark its performance in terms of productivity and solvent consumption against conventional I-SMB by means of a thorough simulation study. Furthermore, it is shown that 3C-ISMB can be designed by Triangle Theory, which is an important advantage compared to other modified SMB processes. Moreover, we discuss how the new process scheme yields the same high purity levels as its four columns analogue, but at significantly higher productivity and comparable solvent consumption. Finally, we discuss the potential of the novel 3C-ISMB mode of operation, in light of the theoretical results reported; showing that 3C-ISMB is a powerful alternative to other modified SMB processes, especially for separations requiring expensive stationary phase materials.

## 2. Background

In order to better understand the development of the new 3C-ISMB process described in Section 3 it is worth reviewing briefly the I-SMB process (Section 2.1). Furthermore, we comment on the extension of Triangle Theory to I-SMB design (Section 2.2), which we will later use for designing 3C-ISMB separations as well. We will continue by defining the most common separation performance parameters that later enable the benchmarking of 3C-ISMB against conventional I-SMB (Section 2.3). Finally, we conclude this section with a concise description of the mathematical model and numerical solution adopted in this work (Section 2.4).

### 2.1. The conventional I-SMB process

The I-SMB process is commercially used, as originally patented by Nippon Rensui Corporation [16,17] for sugar separations. Recently, our group studied the process in great detail [14,15,18] which demonstrated its potential for a wider range of applications, particularly for chiral separations under nonlinear chromatographic conditions. Fig. 1 shows a scheme of conventional I-SMB consisting of four sections each comprising one chromatographic column. The switch time is divided into two sub steps; in sub step 1 the unit is operated as a standard SMB, however, without flow

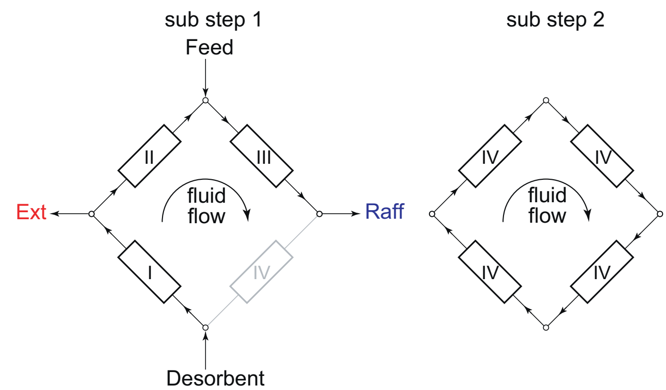


**Fig. 1.** Process scheme of closed loop intermittent simulated moving bed (I-SMB) chromatography. Feed and desorbent supply as well as withdrawal of the product streams raffinate and extract is conducted during in sub step 1, whereas in sub step 2 all inlet and outlet ports are closed. After the end of sub step 2 the ports are switched in direction of the fluid flow and sub step 1 is repeated.

in section IV. In sub step 2 all inlet and outlet ports are closed and the fluid is just circulated through the column train in order to adjust the relative position of the concentration fronts. It has been shown that I-SMB in 1-1-1-1 configuration doubles the productivity of 1-2-2-1 standard SMB whilst fulfilling the same high purity specifications [14,18]. This is a result of the semi-continuous mode of operation which ensures that the leading edge of the more retained component (component A) has a large clearing from the raffinate port at the time of product withdrawal. Similarly the trailing edge of the weakly retained component (component B) is far from the extract port during the withdrawal phase, therefore also a high extract purity can be achieved. The continuously operated standard SMB in contrast, features much narrower gaps between the decisive edges of the compositions fronts, namely the front of A and the tail of B, which are much closer to the product ports, thus making dispersion cause a drop in purity. In order to counter the negative effects caused by dispersion, it is therefore necessary to better approximate the counter-current movement of the solid phase, i.e. to use a higher number of chromatographic columns per section. This is the reason why standard SMB units are usually operated with at least six columns, for example in 1-2-2-1 configuration.

### 2.2. Short-cut design method (Triangle Theory)

Conventional SMB processes are frequently designed by applying a powerful short-cut design method, the so-called "Triangle Theory" [4]. The key idea of that method is the introduction of dimensionless flow rate ratios $m_j$ defined as

$$m_j = \frac{Q_j t^* - V\epsilon^*}{V(1-\epsilon^*)} \tag{1}$$

where $Q_j$ is the volumetric flow rate in section $j$, $t^*$ is the switching time, $V$ the column volume and $\epsilon^*$ the overall void fraction. Under linear conditions, it can be easily shown, that the constraints for complete separation and complete regeneration of the solid and fluid phase, respectively, read as:

$$H_A \le m_I \tag{2a}$$

$$H_B \le m_{II} \le H_A \tag{2b}$$

$$H_B \le m_{III} \le H_A \tag{2c}$$

$$m_{IV} \le H_B \tag{2d}$$

where $H_i$ are the Henry constants of component $i$. Constraints (2b) and (2c) define a triangular region of complete separation in the