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Dynamic simulation of simulated moving bed chromatographic reactors

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Abstract

The combination of a chemical reaction and a chromatographic separation process in a single unit-operation may improve the course of reaction as well as the separation efficiency. Higher conversions and better yields can be achieved by separating educts and products of an equilibrium reaction from each other. Other fields of application exist for the removal of inhibitors, poisons, or acceptor products to enhance reaction yields. Especially for a continuous process, based on a chromatographic simulated-moving-bed (SMB) unit, reactor design and layout is complicated by the integrated process. Dynamic simulation, however, is a powerful tool to assist reactor layout and optimization. This paper presents different types of chromatographic reactors and a simulation based strategy for the design and optimization of SMB chromatographic reactors. Also, dynamic simulation studies using a rigorous model of the SMB process illustrate the advantages of chromatographic reactors in comparison to conventional processes.

Keywords: Simulated-moving-bed chromatography; Preparative chromatography; Dynamic simulation; Reaction kinetics

1. Introduction

Most common processes consist of a reactor section, followed by several separation steps. This sequence is repeated until the final product specification is obtained. In general, this approach offers enough degrees of freedom for process operation to achieve sufficient production rates. In some cases however, this design may limit the conversion rate in the reactor to too great an extent and may cause unacceptable product impurities within the reactor, which have to be eliminated by additional separation steps.

Such disadvantages can be avoided under certain conditions by integrating the separation procedure into the reaction process itself. Reactive distillation

processes for example have been of growing interest to the chemical industry for several years. One example is the production of methyl *tert.*-butyl ether [1].

However, such process integration complicates the process design and subsequently plant operation. Therefore, more precise design calculations and advanced process control systems are required. Rigorous dynamic process simulation is one necessary tool that is used to meet these demands and also provides an improved understanding of process operation.

The integration of chemical or biochemical reactions in chromatographic separation processes has been patented in the early 1960s [2,3]. Meanwhile, an increasing number of theoretical and experimental investigations have been published, e.g., by Barker and co-workers [4,5], Carr et al. [6] and Hashimoto

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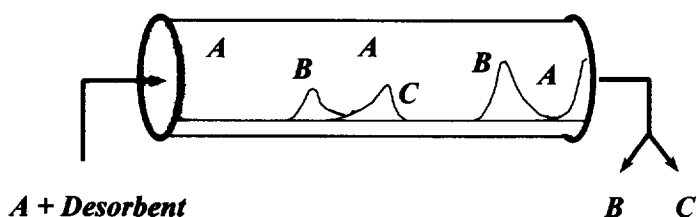


Fig. 1. Batch chromatographic reactor operating principle.

and co-workers [7,8]. In the case of reversible reactions higher conversion rates can be achieved by separating the educts and products, which in turn shifts the reaction equilibrium towards the products. Other possible applications include the removal of inhibitors, catalyst poisons or acceptor products to improve reaction yields.

Fig. 1 illustrates the principal advantage of chromatographic reactors. If the reactor and the chromatographic separation unit are arranged in sequence, the maximum conversion rate for the reversible reaction



is given by the thermodynamic equilibrium. When the pulse of component A is fed into a chromatographic reactor, the educt A and the products B and C are separated continuously because of their different adsorbability. The different retention of the reaction components suppresses the reverse reaction so that the educt can be completely converted. Fig. 1 shows the concentration profile within the reactor and the product pulses leaving the reactor.

The purpose of this paper is to discuss the integration of chromatographic reactors into continuously operating SMB-separation processes.

Fig. 2 illustrates the general flow diagram of such a SMB-CR (simulated-moving-bed chromatographic

reactor) process. As in the case of a SMB-separation process, the feed and the desorbent streams enter the process while the products are withdrawn by the raffinate and extract streams. Ideally, the liquid and the solid-phase pass each other in a counter-current flow. In practice, however, a steady state counter-current flow cannot be realized. Instead, it is approximated by a periodically operating SMB-CR process. Usually, eight separate fixed bed reactors are connected in series to form a closed loop. To simulate counter-current flow of the solid and the liquid phases, the feed and withdrawal points are periodically shifted in the direction of the fluid flow by switching all external fluid streams from one column to the next (note the numbering of the four different zones between the inlet and outlet ports).

In the case of a solid-phase catalyst, the fixed bed reactor will contain a mixture of adsorbent and catalyst. If a soluble catalyst is used, the fixed bed is only formed by the adsorbent, and the catalyst is fed into the reactor as a component of the desorbent stream.

2. Reactor modelling

Modelling and simulation of chromatographic reactors lead to deeper insight into reactor behaviour

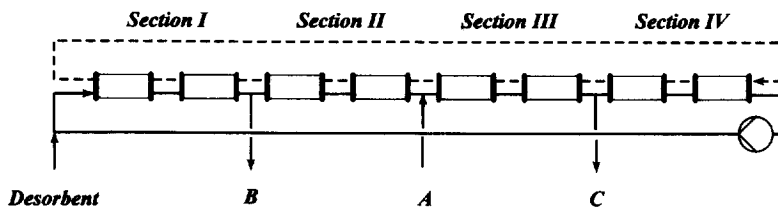


Fig. 2. Schematic representation of the SMB chromatographic reactor.

and reactor performance. Additionally, using a detailed model of the integrated reactor–separator, simulation studies allow to reduce the experimental effort for reactor design and process optimization.

The aim of this paper is to introduce a new modelling approach for SMB chromatographic reactors to improve the description of the reactor behaviour. Therefore, all process calculations presented here are based upon a rigorous dynamic model of the SMB chromatographic reactor, where axial back mixing, a mass transfer resistance within the fluid and solid-phases, as well as the periodic fluid port switching of the SMB process are all accounted for. Furthermore, it is possible to adapt this model to any adsorption isotherm and suitable chemical kinetics.

The stationary phase of the reactor is supposed to be a homogeneous mixture of catalyst and adsorbent. In contrary to other publications, separate mass balances for the catalyst and the adsorbent phase are assumed to describe better the different solid loads on both phases. Taking into account the detailed description of the adsorption process and of the external fluid port switching together with the additional mass balance, a good agreement between real reactor behaviour and simulation results is expected.

Liquid phase:

$$\begin{aligned} \frac{\partial c_i}{\partial t} = & -v_{\text{fluid}} \frac{\partial c_i}{\partial x} + D_{\text{axial}} \frac{\partial^2 c_i}{\partial x^2} \\ & - (1 - X_{\text{Cat}}) k_{\text{eff,Ads}} \frac{6}{d_{\text{p,Ads}}} \frac{1 - \epsilon}{\epsilon} (c_i - c_{\text{pAds},i}) \\ & - X_{\text{Cat}} k_{\text{eff,Cat}} \frac{6}{d_{\text{p,Cat}}} \frac{1 - \epsilon}{\epsilon} (c_i - c_{\text{pCat},i}) - r_f \end{aligned} \quad (2)$$

Adsorbent phase:

$$\frac{\partial q_{\text{Ads},i}}{\partial t} = k_{\text{eff,Ads}} \frac{6}{d_{\text{p,Ads}}} (c_i - c_{\text{pAds},i}) \quad (3)$$

Catalyst phase:

$$\frac{\partial q_{\text{Cat},i}}{\partial t} = k_{\text{eff,Cat}} \frac{6}{d_{\text{p,Cat}}} (c_i - c_{\text{pCat},i}) - r_s \quad (4)$$

Isotherm:

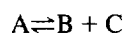
$$\begin{aligned} q_i = & q_{\text{Cat},i} + q_{\text{Ads},i} \\ = & f(c_{\text{pAds},i}, c_{\text{pCat},i}, c_{\text{pAds},j \neq i}, c_{\text{pCat},j \neq i}, T) \end{aligned} \quad (5)$$

The catalytic reaction rates r_s and r_f apply for an immobilized and a dissolved catalyst, respectively. If the process is operated with a liquid phase catalyst, the equation set is reduced to the liquid phase balance with $X_{\text{Cat}} = 0$ and the adsorbent phase balance.

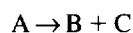
To solve this set of equations numerically, the partial differential equations are transferred into ordinary differential equations using the method of lines. For the finite difference scheme in the axial direction, a formula proposed by Leonard [9] has been shown to be the best approximation. The simulation package SPEEDUP was used to solve the algebraic and ordinary differential equations.

In this paper, the following types of chemical reactions are taken into consideration:

Equilibrium decomposition reactions:



Irreversible decomposition reactions:



3. Batch chromatographic reactors

First, to illustrate the fundamental behaviour of chromatographic reactors, the batch operation of a single reactor–separator unit will be discussed. For a reversible reaction occurring on a solid catalyst phase the following characteristic parameters of an enzymatic hydrolysis are assumed (Table 1):

Adsorption isotherm:

$$q_{\text{Ads},i} = H_{\text{Ads},i} \frac{c_{\text{pAds},i}}{(1 + b_i c_{\text{pAds},i})} \quad (6)$$

Reaction kinetics:

$$r_s = k \left(c_A - \frac{c_B c_C}{k_{\text{eq}}} \right) \quad (7)$$

Fig. 3 shows the concentration profiles within a column of 500 mm length after 100, 500 and 1000 s. The educt A is continuously converted into the products B and C. At the same time, the products B and C are chromatographically separated while they pass along the reactor. Depending on the length of

Table 1
Characteristic parameters of an enzymatic hydrolysis

Geometry			
Column length, L	[cm]	Variable	
Column diameter, D	[cm]	1.5	
Catalyst fraction, X_{cat}	[-]	0.5	
Material properties			
Interparticle void fraction, ϵ	[-]	0.4	
Particle diameter, d_p	[cm]	5.0E-4	
Average fluid density, ρ	[g cm ⁻³]	1.02	
Viscosity	[g cm ⁻¹ s ⁻¹]	1.18E-2	
Mass transfer coefficient	$k_{eff,A}$	[cm s ⁻¹]	3.0E-4
	$k_{eff,B}$	[cm s ⁻¹]	1.3E-4
	$k_{eff,C}$	[cm s ⁻¹]	1.3E-4
Adsorption			
$H_{Ads,A}$	[-]	1.5	
$H_{Ads,B}$	[-]	1.86	
$H_{Ads,C}$	[-]	1.1	
b_A	[cm ³ g ⁻¹]	0.023	
b_B	[cm ³ g ⁻¹]	0.025	
b_C	[cm ³ g ⁻¹]	0.02	
$q_{Cat,i}$	[g cm ⁻³]	0	
Reaction kinetics			
Reaction rate, k	[s ⁻¹]	0.2	
Equilibrium constant, k_{eq}	[g cm ⁻³]	0.01	

the chromatographic reactor, a conversion rate of up to 100% can be achieved. In a conventional reactor, thermodynamic equilibrium would be established, thereby limiting the conversion. In this example, the equilibrium conversion varies between 20 and 70%,

based on educt concentration of about 0.01 and 0.2 g/cm³, respectively.

3.1. Slope of the isotherms

The maximum production rate in a chromatographic reactor depends on the adsorption isotherms of all components. An optimum is reached if the slope of the isotherms

$$K_i = \frac{dq_{Ads,i}}{dc_{pAds,i}} = f(c_{pAds,i}) \quad (8)$$

for the educt lies in between the slopes of the products. In this case, the reverse reaction cannot take place because the product components are continuously transported out of the reaction zone while the rest of the educt remains there. Fig. 4a represents the optimum outlet concentrations of a batch reactor. This occurs when $K_B > K_A > K_C$. When the ratio of the slopes of the isotherms is unfavourable, for example $K_B > K_C > K_A$, less than optimum outlet concentrations result as shown in Fig. 4b.

The high separation factors between A, B and C in the example depicted in Fig. 4a, allow total conversion of A, even with high desorbent flows or short reactors. If the educt A is either the best or the worst adsorbable component (Fig. 4b) however, good separation does not enhance reactor performance; both products move in the same direction relative to A, and the reverse reaction is not significantly suppressed.

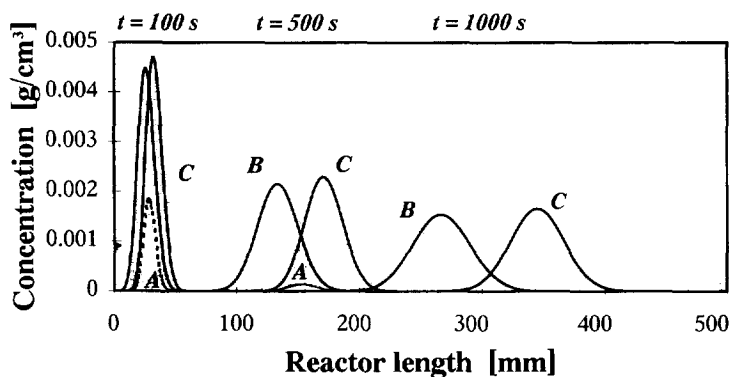


Fig. 3. Concentration profile within a Batch-CR.

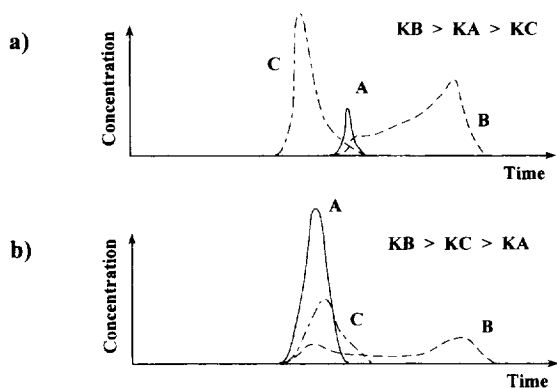


Fig. 4. Effect of relative adsorbabilities on the conversion rate.

3.2. Reactor composition

The chromatographic reactor discussed above consists of a homogeneous mixture of catalytic and adsorbent material. Alternatively, the catalyst and the adsorbent may be packed in alternating sections. For a given total reactor volume, the influence of this partitioning on the overall conversion rate is shown in Fig. 5. A partition of 2, for example, represents a chromatographic reactor separated into two reactor and two separation sections. A heterogeneous reactor with an infinite partition operates very similarly to the homogeneous reactor. A partition of 2 already leads to a considerable increase in the conversion rate compared to a conventional reactor. As illustrated in Fig. 5, the homogeneous mixture of catalyst and adsorbent is favourable, but good results can already be obtained with small partition numbers.

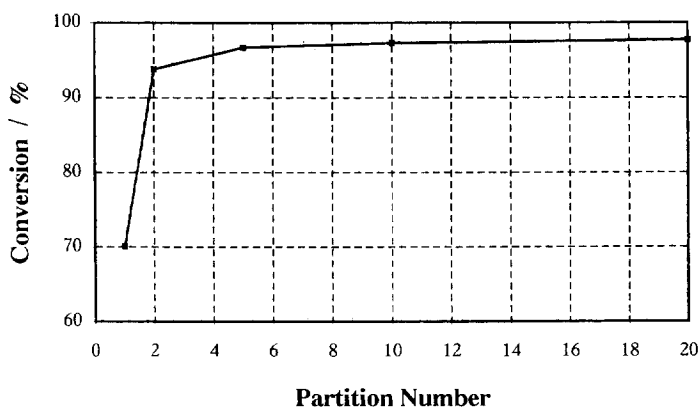


Fig. 5. Effect of partitioning on the conversion rate.

4. SMB chromatographic reactors

To demonstrate the performance of the simulation system introduced in Section 2, a simulation based design strategy for SMB chromatographic reactors is presented in the next sections. Furthermore, it is shown that chromatographic reactors are applicable not only to reversible but also to irreversible reactions.

4.1. Equilibrium reactions

Based on the reaction system for the simulation studies of the batch chromatographic reactor described above (Table 1), a strategy for the design and optimization of a continuous SMB chromatographic reactor is proposed. The procedure is divided into three main steps:

1. general process layout—determination of the size and the number of columns
2. calculation of a first set of operating parameters using an analytical process model
3. process optimization.

As a good starting point for the reactor layout, a SMB process containing eight columns with two columns in each functional zone is assumed. The reactor length is chosen to be 200 mm for each column.

To calculate a first set of operating parameters, a method developed by Nicoud [11], which we have modified for chromatographic reactors can be used. This approach is based on a simplified equilibrium model of a countercurrent chromatographic reactor,

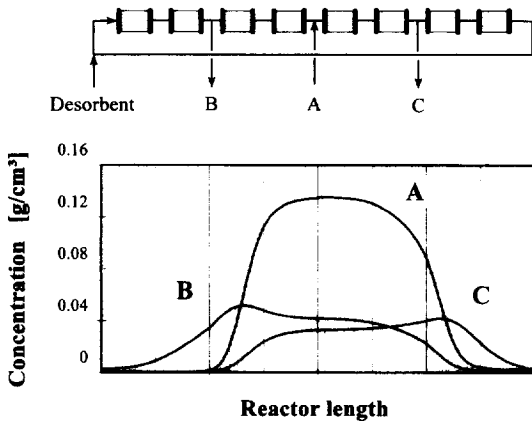


Fig. 6. SMB-CR for the hydrolysis of an ester-concentration profile obtained with the simplified process model.

neglecting axial back mixing and mass transfer resistances. These assumptions allow the model equations to be solved analytically. Using this set of operating parameters and the rigorous process model, one arrives at an axial concentration profile within the reactor for the quasi-stationary state at the end of a switching period, as depicted in Fig. 6. The reactor performance for this set of parameters is summarized in Table 2.

For reasonable process optimization, the rigorous, dynamic model of the SMB chromatographic reactor, described by Eqs. (2–7), has to be used. By modifying the switching time and the external fluid streams, the process operation can be optimized to: (1) maximize the conversion rate, product purity, and the

Table 2
Operating parameters

		Configuration I, analytical model (Fig. 6)	Configuration I, 8 columns (Fig. 8a)	Configuration II, 9 columns (Fig. 8b)
F_{Feed}	[cm ³ /s]	0.0084	0.0022	0.0030
F_{Extract}	[cm ³ /s]	0.0109	0.0074	0.0074
$F_{\text{Raffinate}}$	[cm ³ /s]	0.0099	0.0069	0.0073
$F_{\text{Desorbent}}$	[cm ³ /s]	0.0124	0.0121	0.0117
t_{switch}	[s]	770	720	720
Product purity	[%]	11–48	>99.8	>99.8

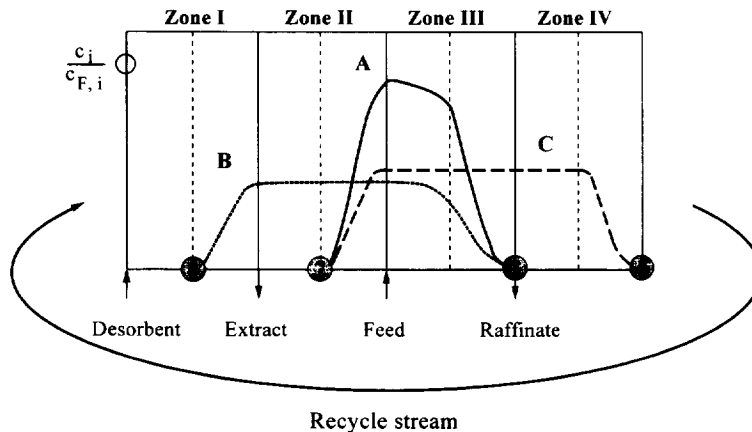


Fig. 7. Idealized axial profile of a SMB chromatographic reactor.

feed throughput, and (2) minimize the consumption of desorbent and the dilution of the products.

Fig. 7 depicts the transformation of these optimization goals into a theoretical concentration profile at the end of a switching period. The conversion rate is maximized if the educt A remains between points (2) and (3). In order to be able to withdraw both products in a pure form, the concentration fronts of component B and C cannot enter zone IV and zone I, respectively. The purity of the desorbent recycle stream is ensured if component C is not allowed to go beyond point (4). Similarly, the purity of the adsorbent is guaranteed if component B cannot reach the area past point (1). If these points are exactly met, product dilution and desorbent consumption are minimized.

As a result of this optimization procedure, a final set of operating parameters is obtained, which are summarized in Table 2. Fig. 8a represents the resulting axial concentration profile. Complete conversion of the educt A and high product purities of over 99% are achieved.

Based on the final set of operating parameters, variations upon the original reactor layout have been

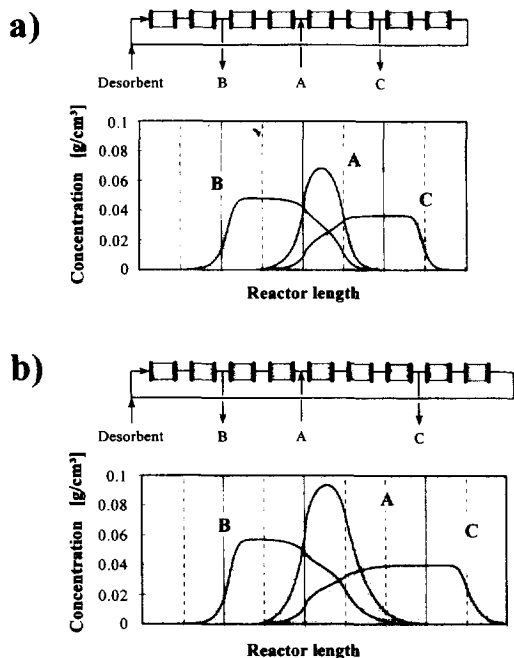


Fig. 8. SMB-CR for the hydrolysis of an ester-optimized concentration profiles.

tested to enhance the feed throughput. Using 400 mm columns instead of 200 mm, does not provide a significant increase in throughput. The insertion of an additional column into zone III however, increases the maximum feed throughput by more than 35% (Fig. 8b).

4.2. Irreversible reactions

The application of SMB-CR processes to irreversible reaction systems is not as profitable as it is in the case of reversible reactions. Since no reverse reaction exists, the conversion rate cannot be increased by integrating a chromatographic separation of educts and products into the reactor. The question is, whether it is advisable to run a conventional reactor with several chromatographic batch separation processes (Process 1) instead of one continuous SMB-CR process (Process 2).

An example of this problem is the enzymatic hydrolysis of sucrose (A) by invertase to fructose (B) and glucose (C). This system has been investigated by Barker and Sarmidi [10]. The reaction can be described by a Michaelis–Menten equation including substrate inhibition.

$$-\frac{dc_A}{dt} = \frac{V_{\max} \cdot c_A}{c_A + K_m + \frac{c_A^2}{K_I}} \quad (9)$$

Fig. 9 shows the concentration profiles within the SMB-CR process (Process 2) for a quasi steady state at the end of the switching period. Sucrose is

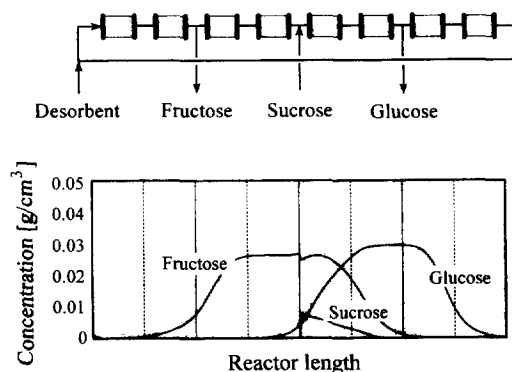


Fig. 9. SMB-CR for the enzymatic inversion of sucrose.

completely converted inside the first column of section III. The chosen process conditions allow a product purity of over 97% to be achieved.

To simplify the calculation for the batch system (Process 1), total conversion is assumed in the conventional inversion reactor. The role of the chromatographic separation units then lies only in the separation of glucose and fructose. For both processes, the batch system and the SMB-CR, Fig. 10a shows the effect of the feed stream on product purity. In the region above 80% product purity, the advantage of the SMB-CR process is apparent. For certain product purities the batch process is limited to much lower feed streams. Fig. 10b depicts a similar effect on the desorbent streams; the amount of desorbent necessary to reach a given purity is significantly lower for the SMB-CR process than in the batch process.

Further comparison of the SMB-CR and a conventional process for the inversion of sucrose, consisting of an inversion reactor and a SMB separation unit, can be found in [12].

4.3. Open loop and recycle processes

In practice, it may be necessary to remove by-products and other impurities in order to arrive the desired product quality. This could be done in an open loop SMB-CR process, in which the recycle stream from zone IV to zone I is cut. By-products are withdrawn with the effluent at the end of zone IV. This design still offers the advantages concerning conversion rate and product quality discussed above, but it reduces the profitability of the process because of the increased demand for fresh desorbent and the need to refine the effluent. Another argument for open loop processes is the simplified operation of the SMB unit.

In other cases, the desorption zone IV has to be removed totally. This requirement arises, for example, if the product in the raffinate stream is not adsorbable. Such is the case for the enzymatic production of the polymer dextran and fructose from sucrose. Because of its high molecular-mass, dextran is not adsorbable on common stationary phases.

Another interesting application of chromatographic reactors is the field of enantioselective synthesis. Here, the purpose is to recover one special enantio-

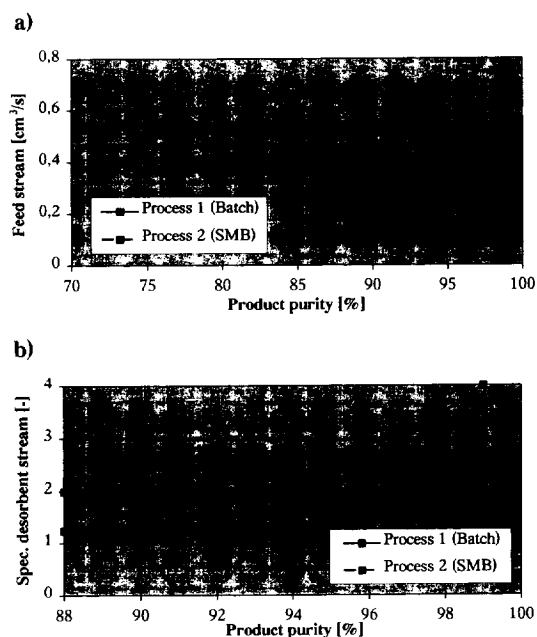


Fig. 10. Comparison of a conventional batch process and the SMB-CR for the inversion of sucrose.

mer from a less or non enantioselective reaction. The educt can be either a racemic mixture or a single prochiral component. In a conventional process, the educt is converted to a racemic mixture of the product, which has to be separated in a chromatographic unit or by crystallisation. To enhance the total reaction yield, the second enantiomer is racemized in a second reactor and fed back into the separation unit.

Using a chromatographic reactor, one of the reaction steps, either the conversion of the educts or the racemization of the second product, is combined with the separation unit. Depending on the reaction kinetics, the integrated reactor–separator may allow increased enantioselectivity, reaction yield and conversion rate. As an additional advantage, the integration of the reaction in a SMB separation unit makes it possible to operate the whole process continuously.

5. Conclusion

The SMB-CR process offers many interesting advantages for reversible reactions. Because of the

integrated chromatographic separation and the countercurrent flow of the liquid and the solid-phase, high conversion rates and good product qualities can be achieved. The recycling of the adsorbent further increases the profitability of this process. Even in the case of irreversible reactions, the chromatographic reactor offers advantages over conventional processes.

On the other hand, SMB-CR processes are difficult to operate such that rigorous dynamic simulation tools are necessary. Design rules, which have been established for SMB separation processes, are also valid for SMB-CR processes.

6. Notation

6.1. Symbols

b	Langmuir parameter
c	fluid phase concentration
c_p	fluid phase concentration in the adsorbent/catalyst pores
D_{axial}	axial dispersion coefficient
H	distribution coefficient
k	reaction rate
k_{eq}	reverse reaction rate
k_{eff}	overall mass transfer coefficient
K	slope of the isotherm = dq/dc_p
K_i	inhibition constant
K_m	Michaelis constant
q	solid load
r_f	reaction rate in the mobile phase

r_s	reaction rate on the solid-phase
t_{switch}	switching time
v_{fluid}	interstitial mobile phase velocity
V_{max}	maximum reaction rate
X_{Cat}	catalyst fraction

6.2. Subscripts

A	component A
B	component B
C	component C
Ads	adsorbent phase
Cat	catalyst phase
i	component i

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