EUROPEAN ROADMAP OF PROCESS INTENSIFICATION

- TECHNOLOGY REPORT -

TECHNOLOGY:
SIMULATED MOVING BED REACTORS

TECHNOLOGY CODE: 2.2.3.1

AUTHOR: Henner Schmidt-Traub, Dortmund University

Table of contents

1. Technology

1.1 Description of technology / working principle

(Feel free to modify/extend the short technology description below)

The Batch Chromatographic Reactor (BCR) is the simplest design for integration of reaction and chromatographic separation. Here the educts are fed into a single column and because of different retention time the products leave the reactor separately at the outlet. The annular chromatographic reactor operates continuously but its efficiency is equivalent to the BCR. Higher efficiencies i. e. increased productivity as well as reduced eluent consumption are achieved by countercurrent flow of solid and liquid phase. The ideal process for countercurrent flow is the True Moving Bed Reactor (TMBR) while in practice the Simulated Moving Bed Reactor (SMBR) is realized (Fricke et al. 2003/2008, Stroehlein et al. (2006), Borren et al. 2006).

In chromatographic separation systems, a fluid mobile phase is in constant contact with the stationary phase during its passage along the column. The mobile phase may be a gas or a liquid, and therefore a distinction between gas chromatographic reactors (GCR) and liquid chromatographic reactors (LCR) can be made. The most common stationary phase in chromatographic reactors is a solid adsorbent, in the form of porous particles or monoliths with large internal and external specific surface areas. The stationary phase may also be a liquid coating on a solid support, or chemical substances of varying chain length and molecular mass bonded to the surface of a support.

The reaction takes place in the stationary phase and/or in the mobile phase. Heterogeneous reactions can be catalyzed by the adsorbent itself or by an additional catalyst that is mixed with the adsorbent.

The basic idea of chromatographic moving bed reactors is the countercurrent flow of a solid and a fluid phase. The stationary flow of both phases is realized as True Moving Bed Reactor (TMBR), but the efficiency of this process is reduced because of unavoidable backmixing of the solid and abrasion of the particles.

The Simulated Moving Bed Reactor (SMBR) overcomes the difficulties related to the movement of the solid phase. The particles are packed in a certain number of columns which are switched periodically countercurrent to the fluid flow. In practice this is achieved by valves which switch the position of the feed and product ports in the direction of the fluid flow after a certain switching time. The time span when the inlet and outlet ports reach their former position again is called cycle time and corresponds to the switching time and the number of columns. Because of this periodic operation the concentration within the columns as well as the extract and raffinate are unsteady during a switching period.

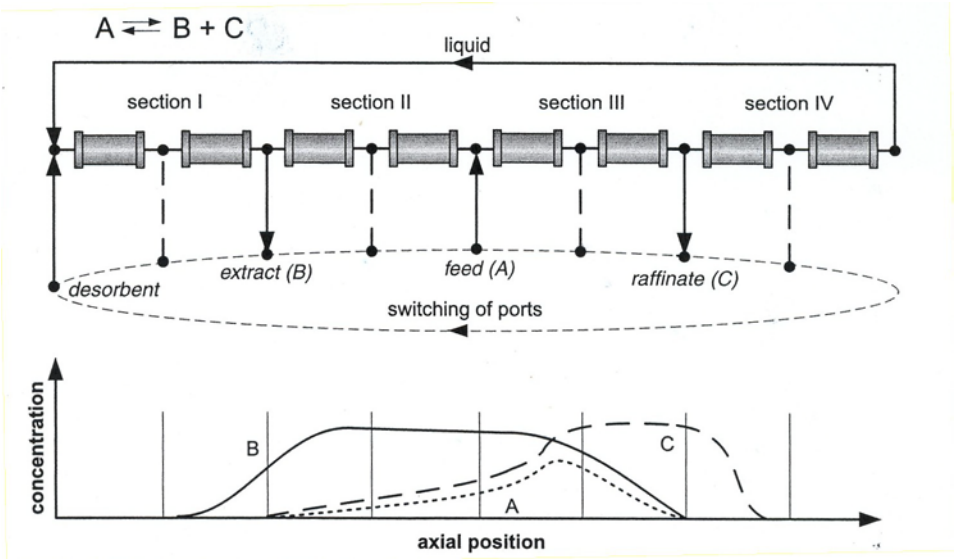

Fig. 1A: Process scheme of a four section SMBR and
1B: Concentration profile at the end of a switching period
for a reaction A ↔ B + C

Fig. 1A shows the principles of an SMB chromatographic reactor illustrated by a reversible reaction of type A ↔ B + C. The SMB apparatus consists of four sections which are separated by the in- and outlets streams. Each section accomplishes a special task that is realized by an appropriate choice of flow rates:

1. *Section I* is located between the desorbent and the extract nodes. The flow rate is higher than in all the other sections. This high flow rate is necessary to remove the more strongly adsorbed product (component B) from the adsorbent.
2. In *section II*, between the extract and the feed nodes, components B and C are formed. The less strongly adsorbed product (component C) is desorbed, whereas B is still held on the adsorbent. The extract stream therefore contains the more strongly adsorbed product.
3. *Section III* is also needed for the decomposition of component A. Here component B is adsorbed. Thus the fluid collected at the raffinate port has a high concentration of component C.
4. Before the fluid is recycled to section I, it is cleaned in *section IV*. Component C is adsorbed and recycled to section III with the adsorbent.

If proper flow rates in each section are chosen the educt A is trapped in section II and III while pure products B and C are drawn off at the extract and raffinate ports (Fig. 1B)

1.2 Types and "versions"

(Describe the most important forms/versions of technology under consideration, including their characteristic features, differences and similarities)

Besides the concept described above, the SMBR can be varied in different ways. For example, it can be run as open SMBR, i.e., without a recycle stream between section IV and I. In this case, sometimes section IV is omitted, and the raffinate is collected at the outlet of section III.

Another variant has been developed for gas – solid reactions. For the hydrogenation of 1,3,5-trimethylbenzene Bjorklund.et al. (1995) developed a process scheme as shown in Fig. 2. A reactor consisting of three sections is employed. A mixture of adsorbent and catalyst is packed in each column. The feed is injected in the feed section (middle) and reacts to form the product 1,3,5-trimethylcyclohexane, which is less strongly adsorbed than the starting material. After the product stream is totally removed at the outlet of the feed section and the before the starting material 1,3,5-trimethylbenzene reaches the outlet all columns are switched in clockwise direction. The former feed column, which now belongs to the carrier section, contains the starting material and the product. In the carrier section both components are desorbed and fed into the feed section. But it is not possible to totally remove the less strongly adsorbed starting material in this section. This is why a third section (right), known as the extra carrier section, is needed to obtain high product purity. After a second switching the more strongly adsorbed starting material, that remained in the column, is removed by an extra carrier stream. At the end of this cycle this column should no longer contain either component. After a third of switching the valves,-this section becomes the feed section, and again 1,3,5-trimethylcyclohexane can be collected at high purity (Fig. 2:).

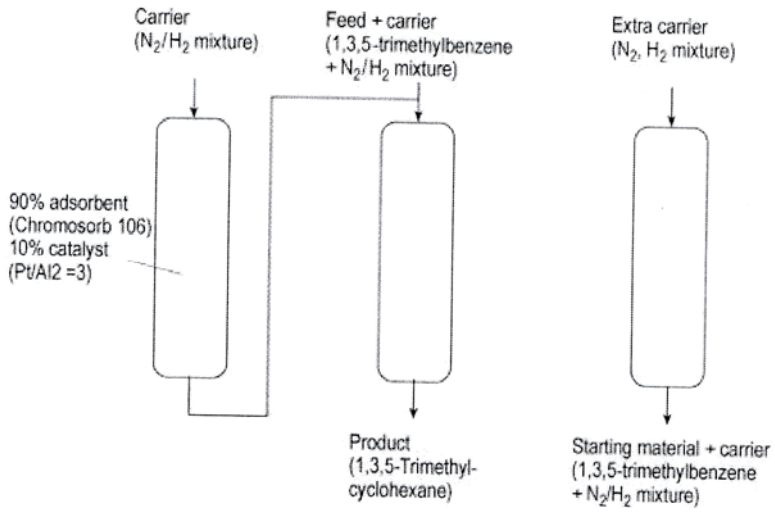

Fig. 2: SMBR for hydrogenation of 1,3,5-trimethylbenzene

Another SMBR concept was developed by Hashimoto et al. (1983) to achieve high conversion in the case of reactions of type A ↔ B, e.g., the isomerization of glucose to fructose. This process consists of different columns containing the adsorbent or the catalyst. The Hashimoto process is also operated according to the concept of simulated moving bed chromatography but consists of three sections (Fig. 3) only. In section III, reaction and adsorption columns alternate, whereas sections I and II consist of adsorption columns only. The switching of the in- and outlets of the adsorption columns is similar to the SMBR, but the position of the reaction columns in section III does not change i. e. they do not move into another section. In section II the starting material is separated from the product and carried back to the reactors in section III.

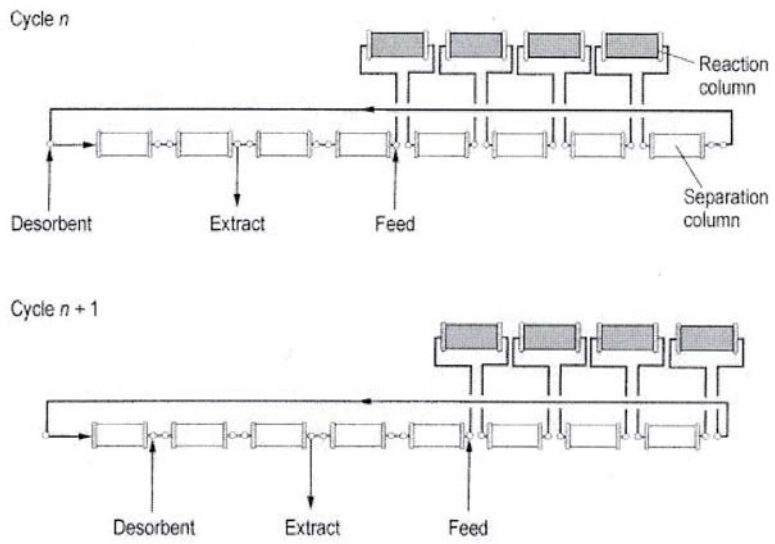

Fig. 3: Hashimoto process for isomerisation A ↔ B

An alternative to the original HCR is the four section process where raffinate is also extracted. This design offers higher productivity (Borren, 2007).

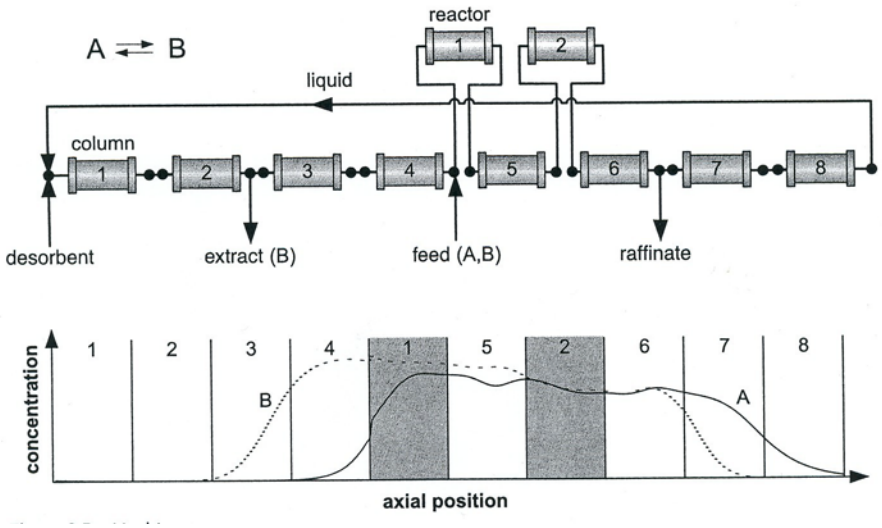

Fig. 4: 4-section Hashimoto process

The VARICOL process is a variation of the SMB separation process which has also been adapted to a new type of SMBR. The basic idea is not to switch all columns at the same time. This results in a non-integer number of columns in each section of the SMBR as average over the cycle time. Theoretical studies show that the individual switching of columns leads to remarkable increase of productivity and reduced eluent consumption. To realize these benefits rigorous optimization tools are essentially (Yu et al. 2005, Tuomi et al. 2004, Küpper 2006).

1.3 Potency for Process Intensification: possible benefits

(In Table 1 describe the most important documented and expected benefits offered by the technology under consideration, focusing primarily on energy; CO_2 emission and costs, providing quantitative data, wherever possible. Add other benefits, if needed).

Table 1: Documented and expected benefits resulting from technology application

Benefit	Magnitude	Remarks
Conversion beyond chemical equilibrium	100%	If only two products are formed it's possible to extract both at 100% purity and to convert all educts. But in this cases productivity might be reduced. Therefore it can be more economic to extract only one product at 100% purity.
Energy savings	negligible	SMB separation is an isothermal high pressure process mainly applied for liquid phases. Its energy consumption depends on pressure drop. In general SMBR processes operate at constant operating conditions.
Less CO_2 emission	negligible	SMBR are potential processes for fine chemicals and pharmaceutical agents as well as large scale liquid phase processes like sugar isomerization.
Increased process efficiency and cost saving	No commercial data available	Savings arise from increased yield as well as reduced eluent consumption and higher productivity (better use of expensive adsorbent).

1.4 Stage of development

The SMBR process and its variations are well understood because of intensive research at different Universities. For the design of SMBR processes short cut methods as well as rigorous simulation tools are available which have been verified by lab experiments.
SMBR are experimentally proven. Process scale up is not a problem as SBM plants for chromatographic separation are used at all scales for industrial production. For fine chemicals and pharmaceuticals the size of lab plants at universities correspond to pilot plants for commercial processes.
An empirical development of SMBR processes is not advisable. In order to realize the benefits of process integration rigorous simulation and optimization tools are necessary.
Adsorbents for chromatographic separation are often very expensive and are utilized at constant separation factors for many years. In contrast to this the activity of catalysts especially enzymes decrease with time. Therefore advanced control methods are necessary to guaranty optimal process operation. Furthermore the design of commercial SMBR should allow a simple exchange of catalyst. Hence mixtures of adsorbent and catalyst in one column should be avoided.

2. Applications

2.1 Existing technology (currently used)

(Describe technology (-ies) that are conventionally used to perform the same or similar operations as the PI-technology under consideration)

In principle the use of SMBR should be taken into account if chromatography is a necessary separation step within a chemical process. Chromatography is applied for components which are difficult to separate like isomers especially stereoisomers. Therefore SMBR applications focus fine chemicals and pharmaceuticals as well as large scale processes like isomerisation of sugar or xylene.
Existing processes are sequential; i. e. a reactor is followed by a chromatographic separation step and may include a recycle stream. Depending on the product

quantity the reactor effluent is separated by batch or annular chromatography or SMB-type processes. It should be kept in mind that annular chromatography is also a continuous process but its efficiency is equivalent to the chromatographic batch process and therefore less compared to a SMB separation.

2.2 Known commercial applications

(Is the technology broadly applied on commercial scale? In which process industry sectors is the technology most often applied: large volume chemicals – specialty chemicals & pharma – consumer products – ingredients based on agro feedstocks? What is the estimated number of existing applications? In Table 2 provide the most prominent examples of realized applications and provide their short characteristics)

Industrial applications are not known from open literature. Unpublished SMBR applications might exist in pharma industries.

Table 2. Industrial-scale applications of the Technology (existing and under realization)

Sector	Company - Process/Product name/type	Short characteristic of application	Production capacity /Plant size	Year of application	Reported effects
					•

2.3 Known demonstration projects

(Are there any demonstration projects known related to the technology under consideration? In which process industry sectors are those projects carried out: large volume chemicals – specialty chemicals & pharma – consumer products – ingredients based on agro feedstocks? In Table 3 provide the short characteristics of those projects.)

A few demonstration projects for fine chemical or pharmaceuticals are carried out in cooperation between universities and industries but are not yet published.

Table 3. Demonstration projects related to the technology (existing and under realization)

Sector	Who is carrying out the project	Short characteristic of application investigated, including product name/type	Aimed year of application	Reported effects
				•

2.4 Potential applications discussed in literature

(Provide a short review, including, wherever possible, the types/examples of products that can be manufactured with this technology)

Potential applications are large as well as small scale processes.
SMB separation has been developed in sugar industries for the first time. It is a well proven technology for large scale separation of isomers like sugar and xylene.
Potential applications of SMBR are all processes where isomerization is used to convert the unwanted isomer, e.g. production of higher fructose corn syrup by isomerization of glucose to fructose (Zhang (2006), da Silva (2006), Bauer (2005), Borren (2005), Tuomi (2004), Borren (2004)).

Other applications are sucrose inversion (Kurup (2005), Azevedo (2001)) or production of lactosucrose (Pilgrim (2005), Murakami (2003)).
Several esterification reactions have successfully been realized in SBM-reactors at lab scale but their commercial impact is not clear (Stroehlein et al. (2006), Yu (2005), Lode (2003), Yu (2003)).
Production of pharmaceutical agents especially pure enantiomers is very promissing. The separation of stereoisomeres like racemates and mixtures of diastereomres are industrially proven technologies. In case of integrated processes the unwanted enantiomere can be racemized within a simple thermal reactor by just increasing temperature e.g. Troegers Base, thalidomides, amino acids (Borren (2007)).
Gas phase SMB reactors of different design have been investigated by Fissore et al. (2005), Krishna et al. 2005, Meissner et al. (2002), Fissore et al. (2002), Huang et al. (2001), Bjorklund et al. (1995).
Besides aforementioned authors optimal process operation and short cut methods for process design are investigated by Stroehlein et al. (2005), Subramani et al. (2004), Lode et al. (2003), Fricke et al. (2003).
Sophisticated control strategies for VARICOL-SMBR have been developed as well (Küpper 2006).

3. What are the development and application issues?

3.1 Technology development issues

(In Table 4 list and characterize the essential development issues, both technical and non-technical, of the technology under consideration. Pay also attention to "boundary" issues, such as instrumentation and control equipment, models, etc.) Also, provide your opinion on how and by whom these issues should be addressed)

Table 4. Technology development issues

Issue	Description	How and by whom should be addressed?
Commercial products and large scale operation	SMB reactors have been developed and operated at lab scale and proven this technology. But most of the products are test systems and of minor interest for commercial application.	R&D projects carried out in joint projects of universities and pharma-/chemical industries
Modeling simulation, optimization, short cut methods	Short cut methods for feasibility studies as well as simulation tools for rigorous process design and optimization are available at universities. But easy to handle tools are necessary for industrial use.	Cooperation of universities and industry
Process control	Process control is necessary especially to compensated the change of catalyst activity. Sophisticated control methods have been developed by university research. Online detectors are necessary to improve process control.	Cooperation of universities and industry

3.2 Challenges in developing processes based on the technology

(In Table 5 list and characterize the essential challenges, both technical and non-technical, in developing commercial processes based on the technology under consideration. Also, provide your opinion on how and by whom these challenges should be addressed)

Table 5. Challenges in developing processes based on the technology

Challenge	Description	How and by whom should the challenge be addressed?
Catalyst development	The activity as well as life time of catalyst especially enzymes for chromatographic reactors has to be improved. Decreasing activity of catalyst require adaptation of operating conditions which is a big disadvantage for long time continuous operation of SMBR. In general process conditions for reaction and chromatographic separation are the same. Therefore it is still a challenge to find adsorbents and catalysts which guaranty optimal selectivity as well as high yield and reaction rates at the same temperature.	R&D projects at universities
Design tools	Powerful methods for design and optimization of SMBR have been developed by universities. They should transferred into tools which are applicable for industries.	Industries in cooperation with universities
Investment cost	Research paid very little attention to economics of SMBR in comparison to a conventional sequential arrangement of a reactor followed by a chromatographic separation.	Cooperation of universities and manufacturer

4. Where can information be found?

4.1 Key publications

(Provide the list of key publications in Table 6)

Table 6. Key publications on the technology

Publication	Publication type (research paper/review/book/ report)	Remarks
Zhang y., Hidajat,K. Ray,A. 2007, Modified reactive SMB for production of high concentrated fructose syrup by isomerization of glucose to fructose, Biochemical Eng. J. 35(3) 341-351	research paper	
Borges da Silva, E, Ulson de Souza A., De Souza, S. Rodrigues, A., 2006, Analysis of the high-fructose syrup production using reactive SMB technology, Chem. Eng. J. 118(3), 167-181	research paper	
Fissore, D., Tejedor, D., Baressi, A., (2006), Experimental Investigation of the SCR of NO_x in a simulated moving bed reactor, AICHE J. 52(9), 3146-3154	research paper	
Stroehlein, G., Assuncao, Y., Dube, N., Bardow, A., Mazotti, M., Morbidelli, M., (2006), Esterification of acrylic acid with methanol by reactive chromatography: Experiments and simulation, Chem. Eng. Sci. 61(16), 5296-5306	research paper	
Borren, T., Fricke, J., Schmidt-Traub, H., 2006, Reactive liquid chromatography, In: Schmidt-Traub, H., Gorak, A.,	book report	

(Eds.), Integrated reaction and separation operations, Springer, Berlin, Heidelberg, New York		
Küpper, A., Tuomi, A., Engell, S., 2006, Optimization and control of reactive chromatographic processes, , In: Schmidt-Traub, H., Gorak, A., (Eds.), Integrated reaction and separation operations, Springer, Berlin, Heidelberg, New York	book report	
Pilgrim, A., Kawase, M., Matsuda, F., Miura, K., 2005, Modelling of the simulated moving-bed reactor for enzyme-catalysed production of lactosucrose, Chem. Eng. Sci. 61(2), 353-362	research paper	
Stroehlein, G., Mazotti, M., Morbidelli, M., (2005), Simulated moving bed reactors, In: Sundmacher, K., Seidel-morgenstern, A.,(Eds.) Integrated chemical processes, Wiley-VCH, Weinheim	book report	
Yu, W., Hidajat, K, Ray, A. 2005, Optimization of reactive simulated moving bed and Varicol systems for hydrolysis of methyl acetate, Chem. Eng. J. 112(1-3), 57-72	research paper	
Baur, R., Krishna, R., 2005, A moving bed reactor concept for alkane isomerozation, Chem. Eng. J. 109(1-3), 107 113	research paper	
Kurup, A., Subbramani, H., Hidajat, K., Ray, A., 2005, Optimal design and operation of SMB bioreactor for sucrose inversion, Chem. Eng. J., 108(1-2), 19-33	research paper	
Borren, T., Fricke, J., 2005, Chromatographic reactors, In: Schmidt-Traub, H., (Ed.), Preparative Chromatography, Wiley-VCH, Weinheim	book report	
Stroelein, G., Mazotti, M., Morbidelli, M., 2005, Optimal operation of simulated-moving-bed-reactors for non-linear adsorption isotherms and equilibrium reaction, Chem. Eng. Sci., 60(6), 1525-1533	research paper	
Krishna, R. Baur, R., 2005, On the Langmuir-Hinshelwood formulation for zeolite catalysed reaction, Chem. Eng. Sci., 60(4), 1155-1166	research paper	
Borren, T., Schmidt-Traub, H. 2004, Comparison of chromatographic reactor design, Chem. Ing. Techn. 76(6), 805-814	review	
Toumi, A., Engelll, S., 2004, Optimization-based control of a reactive simulated moving bed process for glucose isomerization, Chem. Eng. Sci., 59(18), 3777-3792	research paper	
Subramani, H., Zhang, Z., Hidajat, K., Ray, A., (2004), Multiobjective optimization of simulated moving bed reactor and its modification Varicol process. Can. J. Chem. Eng. 82(3), 590-598	research paper	
Fricke, J., Kawase, M., Schmidt-Traub, H., (2003/2008), Chromatographic reactors, In: Ullmann Enzyclopedia of Industrial Chemisry, 7(8)th edition Wiley-VCH, Weinheim.	review	
Murakami, K., Fujita, K., Hara, K., Pilgrim, A., Kawase, M., 2003, Production of lactosucrose using simulated moving bed, Sieto Gijutsu Kenkyu Kaishi 51, 13-18	research paper	
Lode, F. Francesconi, G., Mazzotti, M., Morbidelli, M., 2003, Synthesis of methyl acetate in a simulated moving bed reactor: experiments and modelling, AICHE J. 49(6), 1516-1524	research paper	
Fricke, J., Schmidt-Traub, H., 2003, A new method supporting the design of simulated moving bed chromatographic reactors, Chem. Eng. and Prog. 42(3), 237-248	research paper	
Lode, F., Mazzotti, M., Morbidelli, M., 2003, Comparing true moving bed and simulated moving-bed chromatographic reactors, AICHE J. 49(4), 977-990	research paper	
Yu, W., Hidajat, K., Ray, A., 2003, Modelling, simulation and experimental study of a simulated moving bed reactor for the synthesis of methyl acetate ester, 6743-6754	research paper	
Meissner, J., Carta, G., 2002, Continuous regioselective enzymatic esterification in a simulated moving bed reactor, Ind. & Eng. Chem. Res. 41(19), 4722-4732	research paper	
Fisssore, D., Barresi, A., 2002, Comparison between reverse flow reactor and a network of reactors for the oxidation of lean VOC mixtures, Chem. Eng. & Tech. 25(4), 421-426	research paper	
Azevedo, D., Rodrigues, A. 2001, Design methodology and operation of a simulated moving bed reactor for the inversion of sucrose and glucose-fructose separation, Chem. Eng. J. 82(1-2), 95-107	research paper	
Huang, S., Carr, R., 2001, A simple adsorber dynamics approach to simulated countercurrent moving bed reactor performance, Chem. Eng. J., 82(1-3), 87-94	research paper	
Bjorklund, M., Carr, R., (1995), Catal. Today 25, 159-168	research paper	

Hashimoto, K., Adachi, S., Noujima, H., Ueda, Y., (1983), A new process combining adsorption and enzyme reaction for producing higher-fructose syrup, Biotech. Bioeng. 25(10), 2371-2393	research paper	

4.2 Relevant patents and patent holders

(Provide the list of relevant patents in Table 7. Under "remarks" provide, where applicable, the names/types of products targeted by the given patent.)

Table 7. Relevant patents

Patent	Patent holder	Remarks, including names/types of products targeted by the patent
WO 2005113476: Industrial process for acetals production (2005)	Universidade Do Porto, Port.	
US 6518454: Production of carboxylic acid esters in moving bed reactors in the presence of catalysts (2003)	Eastman Chemical Company, USA	
US 6476239: Process for the preparation of ascorbic acid from 2-keto-L-gulonic acid or its derivatives using a simulated moving bed reactor (2002)	Eastman Chemical Company, USA	

4.3 Institutes/companies working on the technology

(Provide the list of most important research centers and companies in Table 8)

Table 8. Institutes and companies working on the technology

Institute/Company	Country	Remarks
National University of Singapore (Prof. A. K. Ray)	Singapore	Theoretical optimization
University of Porto (Prof. A. Rodrigues)	Portugal	Broad range of theor. and exp. research
ETH (Prof. M. Mazotti, Prof. M. Morbidelli)	Switzerland	Broad range of theoretical and experimental research
University of Dortmund (Prof. S.Engell)	Germany	Process control and optimization, theoretical and experimental research
Kyoto University (Dr. M. Kawase)	Japan	Lactosucrose production
University of Minnesota (Prof. R. Carr)	USA	Gas phase chromatographic reactors
University of Amsterdam (Prof. R. Krishna)	Netherland	Isomerization

5. Stakeholders

5.1 Suppliers and developers

(Provide the list of key suppliers/developers in Table 9)

Main stakeholders are manufacturer and producers

Table 9. Supplier and developers

Institute/Company	Country	Remarks
NOVASEP S.A.S.	Pompey/France	World´s biggest supplier of chromatographic plants
Calgon Carbon	USA	Multifunctional ISEP-technology, Ion exchange
Eurodia Industrie SA	Rungis Cedex/France	ISMB, License Nippon Rensui
Bayer Technology Services GmbH	Leverkusen/Germany	
KNAUER Advanced Scientific Instruments	Berlin/Germany	Well experienced in small scale chromatographic equipment

5.2 End users

(Describe the existing and potential end-users, other than those already listed in Table 2)

Potential end-users are companies producing fine chemicals and pharmaceutical as well as bulk products like sugar.

6. Expert's brief final judgment on the technology

(maximum 5 sentences)

The application of integrated SMB reactors should be taken into account if chromatography is a necessary separation step.

Reduced life time and deceasing activity of catalysts especially of biocatalysts (enzymes) are still restricting industrial applications of SMBR.

The functionality and applicability of SMB reactors is theoretically as well as experimentally proven by a number of university search projects.

SMBR offers increased productivity and reduced eluent consumption.

In any case it should be investigated if additional investment and process control for SMBR are justified in comparison to a traditional sequential process where the reactor is followed by a chromatographic separation.