Pais, I.S., and Rodrigues, A.E.
Design of Simulated Moving Bed and Varicol Processes for Preparative Separations
SPICA 2002

International Symposium on Preparative and Industrial Chromatography and Allied Techniques

October 6 – 9, 2002
Heidelberg/Germany

DECHEMA e.V.
Programme at a Glance

SUN, October 6

- < 13:30 Snacks
- Workshops
  - 13:30 Workshop 1 (K. Unger)
  - Workshop 3 (J. Strube)
- 15:00 Coffee break
- 15:30 Workshop 2 (A. Jungbauer)
- Workshop 4 (M. Mazzotti)
- 18:00 Welcome Reception

MON, October 7

- 8:30 Opening
- 8:35 Keynote Lecture
  - R. Ditz
- Stationary Phases
  - 9:10 M. Hofmann
  - 9:35 K. Gebauer
  - 10:00 G. Gulochon
- 10:25 Coffee Break
- 11:00 R. Hahn
- 11:25 U. Tallarek
- 11:50 M.-E. Avramescu
- 12:15 K. Unger
- 12:40 Lunch

TUE, October 8

- 8:30 Keynote Lecture
  - I. Sutherland
- Product Isolation
  - 9:05 S. Cartellieri
  - 9:30 F. Cavallari
  - 9:55 R. Freitag
  - 10:20 J. Strube
- 10:45 Coffee Break
- Process Integration
  - 11:15 C. Strawson
  - 11:40 L. Castillo
  - 12:05 R. Schlegel
  - 12:30 J. Frick
- 12:55 Lunch
- 14:15 Poster II
- 16:00 Coffee Break
- Equilibria & Transport
  - 16:30 H. Yoshida
  - 16:55 A. Rajendran
  - 17:20 H. Colin
- 19:00 Conference Dinner

WED, October 9

- 8:30 Keynote Lecture
  - M. Mazzotti
- Simulated Moving Bed Technology
  - 9:05 L. Miller
  - 9:30 O. Ludemann-Hombourger
  - 9:55 L. Pals
  - 10:20 A. Youmi
- 10:45 Coffee Break
- 11:15 K. Akita
- 11:40 M. Juza
- 12:05 S. Peper
- 12:30 S. Abel
- 12:55 Close
### Lecture Programme

**Wednesday, October 9, 2002**

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
<th>Speaker(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>8:30</td>
<td>Keynote Lecture: Simulated moving bed technology: Applications and challenges</td>
<td>M. Mazzotti, M. Morbidelli, ETH Zürich/CH</td>
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<tr>
<td>9:05</td>
<td>Batch and SMB chromatographic resolution of a pharmaceutical racemate</td>
<td>L. Miller, C. Grill, T. Yan, Pharmacia, Skokie/USA; M. Juza, CarboGen Laboratories, Aarau/Switzerland; O. Depremond, Aerojet Fine Chemicals, Rancho Cordova/USA</td>
</tr>
<tr>
<td>9:30</td>
<td>Application of the Varicol process to the separation of the isomers of the SB-553261 racemate</td>
<td>O. Ludemann-Homburger, G. Pigorini, R.M. Nicoud, Novasep SAS, Pompon/f; D. Ross, GlaxoSmithKline, Tonbridge/UK; G. Terflot, GlaxoSmithKline, King of Prussia/USA</td>
</tr>
<tr>
<td>9:55</td>
<td>Design of simulated moving bed and Varicol processes for preparative separations</td>
<td>J.S. Pais, Escola Superior de Tecnologia e de Gestao, Braganca/P; A.E. Rodrigues, University of Porto/P</td>
</tr>
<tr>
<td>10:20</td>
<td>Optimal operation and control of a reactive SMB process</td>
<td>A. Tournil, S. Engell, University of Dortmund/D</td>
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<td>10:45</td>
<td>Coffee Break</td>
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<tr>
<td>11:15</td>
<td>Development of production processes for optically active pharmaceutical chemicals using chiral simulated moving bed systems</td>
<td>K. Akita, DAICEL Chemical Industries, Himeji-City/J</td>
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<tr>
<td>11:40</td>
<td>Less common applications of simulated moving bed chromatography in the pharmaceutical industry</td>
<td>M. Juza, CarboGen Laboratories, Aarau/CH</td>
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<tr>
<td>12:30</td>
<td>Model predictive control of simulated moving bed separations</td>
<td>S. Abel, G. Erdem, M. Mazzotti, M. Morari, M. Morbidelli, ETH Zürich/CH</td>
</tr>
<tr>
<td>12:55</td>
<td>Close</td>
<td></td>
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</tbody>
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### Poster Programme

#### Stationary Phases and Column Characteristics

| 1 | Smart polymers in bioseparation | I. Galaev, B. Mattiasson, Lund University, Lunds/SE     |
| 2 | Polymerics: A viable alternative to RP-Silica's for prep and process chromatography | M. Millichip, L. Lloyd, F. Warner, Polymer Laboratories, Church Stretton, Shropshire/GB |
| 3 | Polybutadiene coated titanium dioxide as a reverse phase sorbent in LC | J. Winkler, B. Hirthe, G. Benkner, C. Spitzwieser, R. Wittenberg, Sachtleben Chemie GmbH, Duisburg/D |
| 4 | Friction factor – Reynolds number relation and hydrodynamic dispersion in monoelisitic porous media | F. Lainweder, U. Tallaruk, University of Magdeburg/D |
| 5 | Heat effects with a continuous annular chromatographic reactor | H.-J. Bart, J. Brozio, L. Garcia Diez, University of Kaiserslautern/D |
| 7 | Reverse phase titanium dioxide sorbent for LC | J. Winkler, B. Hirthe, G. Benkner, C. Spitzwieser, R. Wittenberg, Sachtleben Chemie GmbH, Duisburg/D |
| 8 | Characterisation of silica based stationary phases | Th. Keller, R. Wellauer, L. Jarina, Zeocel AG, Uetikon/CH |
| 9 | Polymer/carrier composites as materials and reactors for organic synthesis | U. Kunz, H. Schönfeld, TU Clausthal-Zellerfeld/D; A. Kirschning, W. Sohlenkohn, University of Hannover/D |
| 11 | New polymeric tetradeck chromatography beads for fast production scale ion exchange | A. Stein, L. Britsch, A. Heinzen-Krauzig, H. Herbert, Merck KGaA, Darmstadt/D |

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DEHEMA e.V.
Design of Simulated Moving Bed and Varicol Processes for Preparative Separations

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Simulated Moving Bed (SMB) is a continuous chromatographic process that overcomes the usual limitations of standard preparative chromatographic methods, namely the high inventories of solvent and adsorbent needed and the high dilution of products. SMB technology, which has been used for decades in large-scale separations in the petrochemical and carbohydrate industries, has recently found new successful applications in the areas of biotechnology, pharmaceuticals and fine chemistry.

The design of SMB units requires the use of modeling and simulation tools. The problem of modeling a SMB separation process can be analyzed by two different strategies: one, by simulating the system directly, taking into account its intermittent behavior, other by representing its operation in terms of a true countercurrent system. The first model represents the real SMB and considers the periodic switch of the injection and collection points. The second, is developed by assuming the equivalence with the true moving bed (TMB), where solid and fluid phases flow in opposite directions.

Recent applications in the pharmaceutical industry uses SMB systems containing a low total number of columns, usually four to eight. Novasep, a leading supplier of SMB industrial units, has announced the installation of the largest unit for chiral separations with only six columns. In these cases, the evaluation of the SMB operating conditions shall avoid the use of the countercurrent TMB model, and a more realistic SMB model, which takes into account the periodic switch of the injection and collection points, is needed. For an effective comparison between the predictions given by the two strategies of modeling, two-dimension separation regions can be evaluated using the TMB and SMB models. The differences obtained by the two models depend particularly on the number of columns used and its configuration.

Recently, Novasep proposed a new continuous chromatographic process, called Varicol. The principle of the Varicol process is based on a non-synchronous shift of the inlet and outlet valves in a multicolumn system, in contrast to the SMB operation where this shift is synchronous. This new process makes possible the operation with a number of columns per section that is not constant in time, and can show advantages over the classical SMB operation, particularly when using a low number of columns.

The objective of this work is to evaluate and compare the performance of SMB and Varicol systems with a low number of columns. Simulation results will be shown for units with 4, 5, and 6 columns. A special attention will be put on the choice of the better operating conditions for these units, particularly with the objective of solvent consumption minimization. The concept of separation volume, developed by the authors, will be used to analyze this optimization problem.