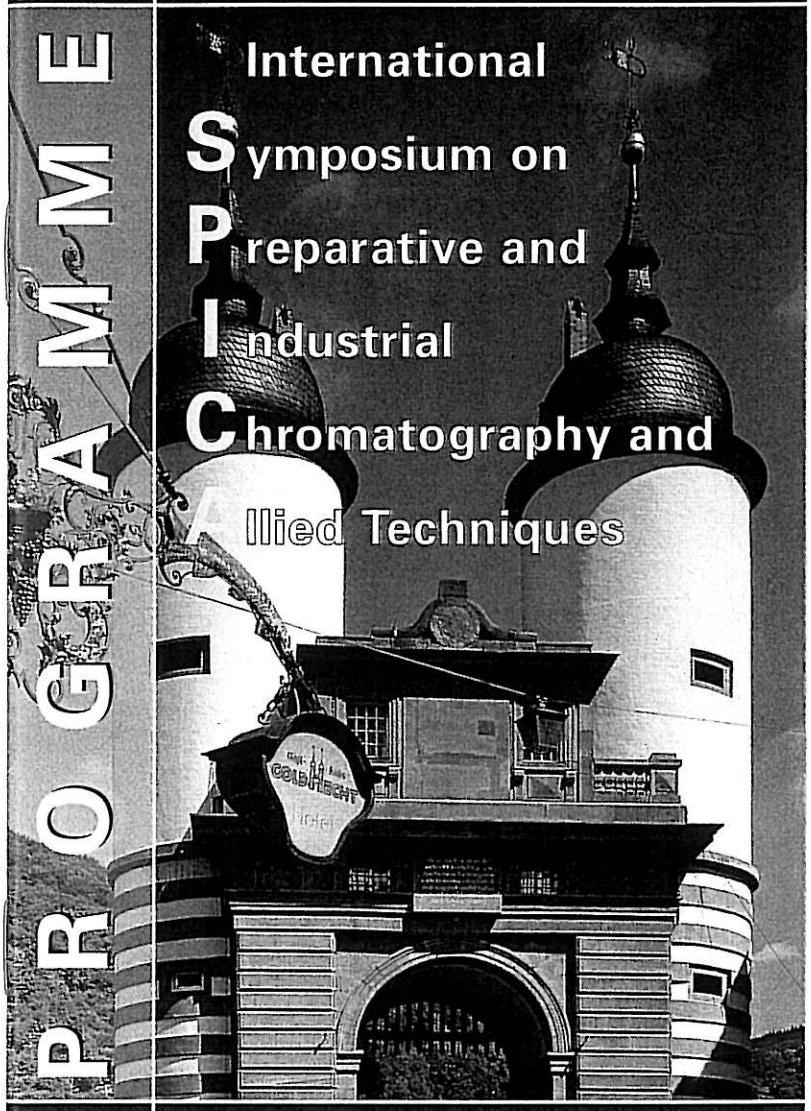
Pais, L.S., and Rodrigues, A.E.

Design of Simulated Moving Bed and Varicol Processes for Preparative Separations

in *SPIC-I 2002 – International Symposium on Preparative and Industrial Chromatography and Allied Techniques*, Heidelberg, Germany, October 6-9, 2002. *(comunicação oral)*

SPICA 2002

PROGRAMME



International Symposium on Preparative and Industrial Chromatography and Allied Techniques

October 6 – 9, 2002
Heidelberg/Germany

DECHEMA e.V.

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. Guiochon

10:25 Coffee Break

11:00 R. Hahn
11:25 U. Tallarek
11:50 M.-E. Avramescu
12:15 K. Unger

12:40 Lunch

High Throughput Separation

14:00 R. Thiericke
14:25 A. Foucault
14:50 A. Podgornik

15:15 Coffee Break

15:45 G. Baron
16:10 Poster I
16:40-
21:30 Poster Mixer

TUE, October 8

8:30 Keynote Lecture
I. Sutherland

Product Isolation

9:05 S. Cartellieri
9:30 F. Cattoli
9:55 R. Freitag
10:20 J. Strube

10:45 Coffee Break

Process Integration

11:15 C. Strawson
11:40 L. Castilho
12:05 R. Schlegl
12:30 J. Fricke

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. Pais
10:20 A. Toumi

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

8:30 **Keynote Lecture:**
Simulated moving bed technology: Applications and challenges
M. Mazzotti, M. Morbidelli, ETH Zürich/CH

Simulated Moving Bed Technology

9:05 **Batch and SMB chromatographic resolution of a pharmaceutical racemate**
L. Miller, C. Grill, T. Yan, Pharmacia, Skokie/USA; M. Juza, CarboGen Laboratories, Aarau/Switzerland; O. Dapremont, Aerojet Fine Chemicals, Rancho Cordova/USA

9:30 **Application of the Varicol process to the separation of the isomers of the SB-553261 racemate**
O. Ludemann-Hombourger, G. Pigorini, R.M. Nicoud, Novasep SAS, Pompey/F; D. Ross, GlaxoSmithKline, Tonbridge/UK; G. Terfloth, GlaxoSmithKline, King of Prussia/USA

9:55 **Design of simulated moving bed and Varicol processes for preparative separations**
L.S. Pais, Escola Superior de Tecnologia e de Gestão, Bragança/P; A.E. Rodrigues, University of Porto/P

10:20 **Optimal operation and control of a reactive SMB process**
A. Toumi, S. Engell, University of Dortmund/D

10:45 **Coffee Break**

11:15 **Development of production processes for optically active pharmaceutical chemicals using chiral simulated moving bed systems**
K. Akita, DAICEL Chemical Industries, Himeji-City/J

11:40 **Less common applications of simulated moving bed chromatography in the pharmaceutical industry**
M. Juza, CarboGen Laboratories, Aarau/CH

12:05 **Supercritical fluid simulated moving bed chromatography: Simulation – Operation – Optimisation**
S. Peper, M. Johannsen, G. Brunner, TU Hamburg-Harburg/D

12:30 **Model predictive control of simulated moving bed separations**
S. Abel, G. Erdem, M. Mazzotti, M. Morari, M. Morbidelli, ETH Zürich/CH

12:55 **Close**

Poster Programme

Stationary Phases and Column Characteristics

1 **Smart polymers in bioseparation**
I. Galaev, B. Mattiasson, Lund University, Lund/S

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 monolithic porous media**
F. Leinweber, U. Tallarek, University of Magdeburg/D

5 **Heat effects with a continuous annular chromatographic reactor**
H.-J. Bart, J. Brozio, L. García Diez, University of Kaiserslautern/D

6 **Separation and quantitative analysis of glycols using chromarod**
T. Srivastava, D.C. Saxena, Dheeraj Sud, Sant Longowal Institut of Technology, Longowal, Punjab/IND; S.R. Vidyarthi, Chemical Engg., HBTI, Kampur/IND

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. Jelinek, Zeochem 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. Solodenko, University of Hannover/D

10 **Non-porous mineral-polymer magnetic matrices for chromatography**
H.G. Balayan, S.S. Hayrapetyan, H.G. Khachatyran, "Chemtech" Scientific-Research Institute, Yerevan/ARM

11 **New polymeric tentacle chromatography beads for fast production scale ion exchange**
A. Stein, L. Britsch, A. Heinen-Kreuzig, H. Herbert, Merck KGaA, Darmstadt/D

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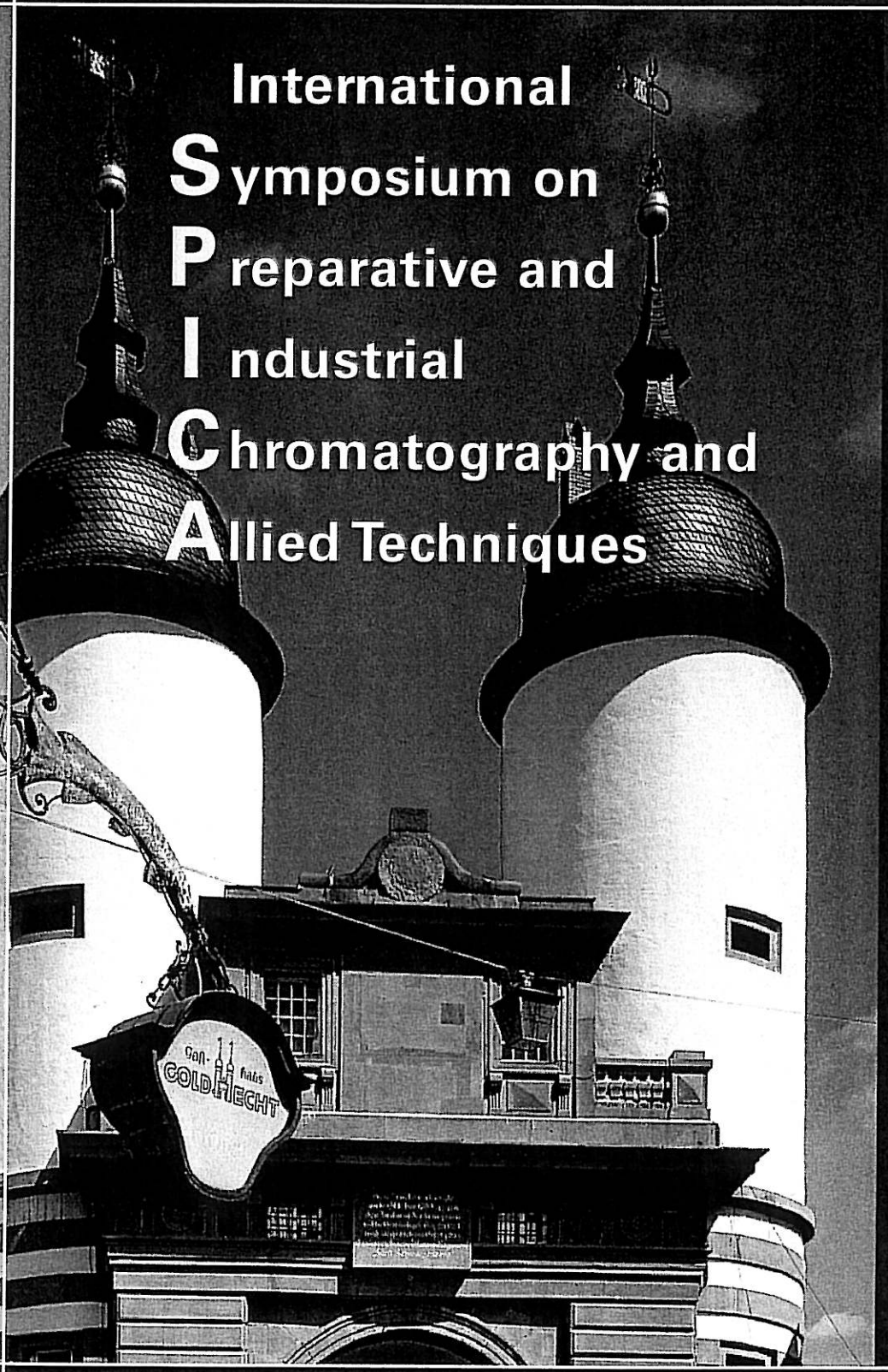
BOOK OF ABSTRACTS



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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.