

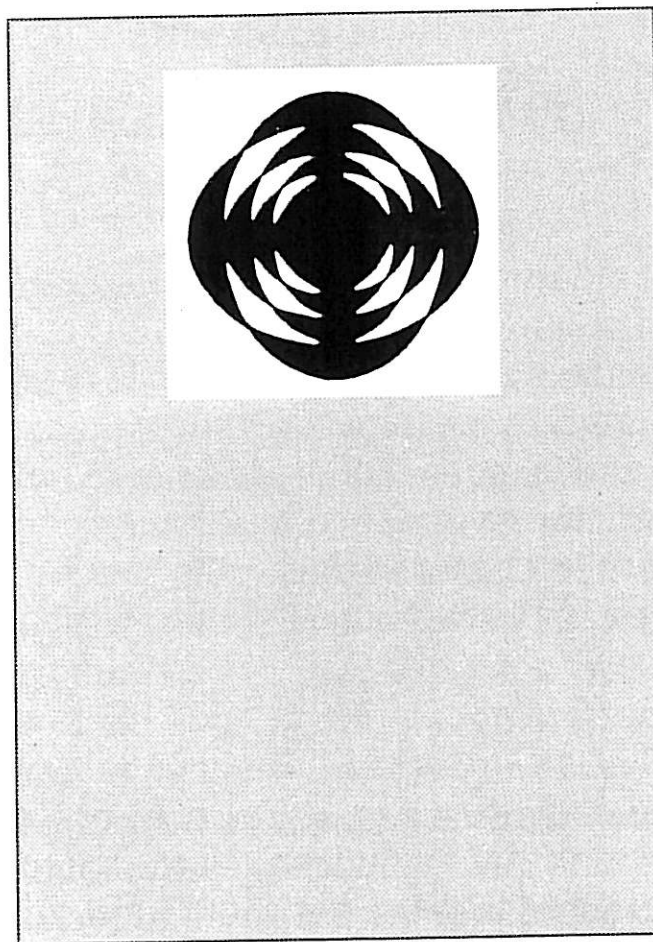
Rodrigues, A.E., and **Pais**, L.S.

The Design of Simulated Moving Bed Chiral Separation Using the Concept of Separation Volume

in *EUROTECH 2000 Chiral Technologies and Enantioseparation*, Cambridge, UK, April 5-7, 2000. (*comunicação oral*)

EUROTECH 2000
Chiral Technologies and
Enantioseparation
April 5 - 7, 2000

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AT QUEENS' COLLEGE
UNIVERSITY OF CAMBRIDGE, UK

ORGANISER Dr. G. SUBRAMANIAN

CHIRAL TECHNOLOGIES AND ENANTIOSEPARATION.

PROGRAMME.

Wednesday 5th

- | | |
|---------------|--|
| 12.00 - 01.00 | Registration |
| 01.30 - 02.30 | Plenary Lecture:
The evolution of Chiral Stationary Phases.
<i>Professor. Daniel W. Armstrong,</i>
<i>University of Missouri-Rolla, USA.</i> |
| 02.30 - 03.00 | Optimisation Strategies for Enantioseparation based upon Laser-based Polarimetric Detection.
<i>Gary W. Yanik, President PDR Chiral Inc., USA.</i> |
| 03.00 - 03.30 | Applications of a Novel Dedicated Detector for Liquid Chromatography of Chiral Compounds.
<i>Professor. Albrecht Mannschreck,</i>
<i>University of Regensburg, Germany.</i> |
| 03.30 - 04.00 | Refreshments. |
| 04.00 - 04.30 | Preparative Electrophoretically-driven Chiral Separation using Sulfated Cyclodextrins.
<i>Apyll M. Stalcup, University of Cincinnati, USA.</i> |
| 04.30 - 05.00 | Chiral Separation by Electro-migration.
<i>Professor. Volker Schurig,</i>
<i>University of Tübingen, Germany.</i> |

- 05.00 - 05.30 **Enantiomeric Separation of Drugs and
Drug Metabolites by Capillary Electrophoresis.**
*Professor. Gottfried Blaschke,
University of Munster, Germany.*
- 05.30 - 06.00 **Enantioseparation in capillary Electrochromatography:
Influence of mobile and stationary phase,
EOF- generation and pH - dependence.**
Kartin. Krause, University of Munster, Germany.
- 06.00 - 06.30 **Separation of Enantiomers in Capillary
Electrochromatography using polysaccharide type
Chiral Stationary Phases.**
Marco Girod. University of Munster, Germany.
- 07.30 **Sherry Reception: Sponsored by
Chiral Technologies Inc, USA.**
- 08.00 **Gala Dinner: Old Hall.**

PROGRAMME.

Thursday, 6th

- 08.30 - 09.00** **Intellectual Property and Chiral Drugs**
Professor. Israel Agranat.
The Hebrew University of Jerusalem, Israel.
- 09.00 - 09.30** **Combinatorial Approaches to Recognition of Chirality:
Design of Chromatographic Separation Media with High
Selectivity.**
Frantisek Svec, University of California, USA.
- 09.30 - 10.00** **CHIRABASE: Database current status and derived
research applications using molecular similarity.**
Professor. Christian Roussel,
University Aix-Marseille III, France.
- 10.00 - 10.30** **Standard Reference materials for the evaluation of chiral
stationary phase performance in liquid and supercritical
fluid chromatography.**
*Karen W. Phinney, National Institute of Standards
and Technology, USA.*
- 10.30 - 11.00** **Refreshments**
- 11.00 - 11.30** **Supercritical Fluid Chromatography for Preparative
Chiral Separation:
Easy and Fast Way to Produce Enantiomers.**
Mohamed Shaimi, Chiral Technologies Inc, USA.
- 11.30 - 12.00** **New Technique for Obtaining Chiral Selectivity by HPLC.**
Thomas E. Beesley,
Advanced Separation Technologies Inc, USA.
- 12.00 - 12.30** **Antibodies as Tailor-Made Chiral Selectors.**
Oliver Hofstetter,
The Weizmann Institute of Science, Israel.

- 12.30 - 02.00 **Lunch.**
- 02.00 - 02.30 **Chiral and Chiral Additives to the
mobile phase - separation of Enantiomers
in RP-HPLC systems.**
*Anna Bielejewska,
Insitute of Physical Chemistry, Poland.*
- 02.30 - 03.00 **Automatic Determination of Fluid Phase Equilibrium
Data**
with Minimum Substance Comsumption.
Achim Epping, University of Dortmund, Germany.
- 03.00 - 03.30 **Monolithic Silica:
A novel Support for Chiral Stationary Phase.**
Michael Schulte, MERCK KGaA, Germany.
- 03.30 - 04.00 **Refreshments.**
- 04.00 - 04.30 **The design of SMB, Chiral separation using
the Concept of Separation Volume.**
*Professor. Alirio E. Rodrigues,
University of Porto, Portugal.*
- 04.30 - 05.00 **Improving the productivity of enantioseparations
by coupling SMB and fractional crystallisation.**
Patrick Sheehan, University of Magdeburg, Germany
- 05.00 - 05.30 **Simulation and online Monitoring of
Single Concentrations for Chromatographic
Enantioseparation.**
Andreas Jupke, University of Dortmund, Germany.
- 07.30 **Dinner**

PROGRAMME.

Friday, 7th

- 08.30 - 09.00 **Enantiomer separation using low affinity counter membrane process.**
E.M. Vander Ent, Wageningen University, The Netherlands.
- 09.00 - 09.30 **Opportunities for membrane technology in Chiral Separation.**
M.F.Kemmere, Eindhoven University of Technology, The Netherlands..
- 09.30 - 10.00 **The use of Chromatography for the Manufacture of Enantiopure Drugs.**
Roger-Marc Nicoud, Novasep, France.
- 10.00 - 10.30 **Large Scale enantiomer separation: New developments and systems.**
Professor. Joachim Kinkel, Georg-simon-ohm Fachhochschule, Germany.
- 10.30 - 11.00 **Refreshments**
- 11.00 - 11.30 **Some New Approaches in Enantioseparation.**
Christopher J. Welch Merck Inc, USA.
- 11.30 - 12.00 **New Developments in Chiral Technologies within DSM.**
Rinus Brosterman, DSM Research, The Netherlands.
- 12.00 - 12.30 **Chiral Drugs and their Regulation**
Sarah K. Branch, Medicines Control Agency, UK..

The Design of Simulated Moving Bed Chiral Separation Using the Concept of Separation Volume

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Abstract

The paper deals with chiral separation by Simulated Moving Bed chromatography. When mass transfer resistances are negligible, Equilibrium Theory provides explicit criteria for the choice of the SMB operating conditions. However, in the presence of mass transfer resistances, the SMB operating conditions should be evaluated through simulation. Using a package based on the analogy with the true moving bed operation, this work shows how mass transfer resistance can affect the conditions for enantiomers separation, as well as the critical values stated by Equilibrium Theory. The concept of separation volume is applied to show how the flow-rate constraints, in presence of mass transfer resistances, have to be modified.

1. Introduction

Chiral separation is an important issue in various areas and particularly in the health-related field. It is well known that the two enantiomers can have different therapeutical value and there is pressure of regulatory agencies to the separation of chiral drugs.

A Simulated Moving Bed adsorber is essentially a binary separator, so particularly appropriated for chiral separations. Briefly, SMB chromatography allows the continuous injection and separation of binary mixtures. The simulated countercurrent contact between the solid and liquid phases maximizes the mass-transfer driving force, leading to a significant reduction in mobile and stationary phases consumption when compared with elution chromatography. Hence, with SMB technology, large-scale separations can now be carried out under cost-effective conditions.

The selection of the SMB operating conditions is not straightforward. The main problem of the SMB operation consists in choosing the right solid (switch time interval) and liquid flow-rates. Designed for high productivity separations, SMB units usually operate at high feed concentrations leading to nonlinear competitive adsorption behaviors. Therefore, modeling and simulation tools are of crucial importance before running the system.

The objective of this work is to study the influence of mass transfer resistance on the selection of the SMB operating conditions and on the flow-rate constraints for nonlinear chromatographic separations. In particular, the concept of separation volume will be used to illustrate how the flow-rate constraints have to be modified in presence of mass transfer resistances.

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