

# **Isotherm Estimation and Batch Process Optimization for Preparative Chromatography**

Zur Erlangung des akademischen Grades eines

**Dr.-Ing.**

vom Fachbereich Bio- und Chemieingenieurwesen  
der Universität Dortmund  
genehmigte Dissertation

von

**M. Sc. Weihua Gao**

aus

Shandong, V.R. China

Tag der mündlichen Prüfung: 21. November 2005

1. Gutachter: Prof. Dr.-Ing. Sebastian Engell
2. Gutachter: Prof. Dr.-Ing. Henner Schmidt-Traub

Dortmund 2005



Schriftenreihe des Lehrstuhls für Anlagensteuerungstechnik  
der Universität Dortmund (Prof.-Dr. Sebastian Engell)

Band 4/2005

**Weihua Gao**

**Isotherm Estimation and Batch Process Optimization  
for Preparative Chromatography**

D 290 (Diss. Universität Dortmund)

Shaker Verlag  
Aachen 2005

**Bibliographic information published by Die Deutsche Bibliothek**

Die Deutsche Bibliothek lists this publication in the Deutsche Nationalbibliografie; detailed bibliographic data is available in the internet at <http://dnb.ddb.de>.

Zugl.: Dortmund, Univ., Diss., 2005

Copyright Shaker Verlag 2005

All rights reserved. No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, recording or otherwise, without the prior permission of the publishers.

Printed in Germany.

ISBN 3-8322-4726-2

ISSN 0948-7018

Shaker Verlag GmbH • P.O. BOX 101818 • D-52018 Aachen

Phone: 0049/2407/9596-0 • Telefax: 0049/2407/9596-9

Internet: [www.shaker.de](http://www.shaker.de) • eMail: [info@shaker.de](mailto:info@shaker.de)

# Acknowledgments

The work here described was carried out between July 2002 and May 2005, in the Process Control Laboratory (Lehrstuhl für Anlagensteuerungstechnik) of the Department of Biochemical and Chemical Engineering, Universität Dortmund, in partial fulfillment of the requirements for the **Dr.-Ing.** degree.

First of all I would like to acknowledge the scholarship of the NRW Graduate School of Production Engineering and Logistics at Universität Dortmund for the financial support in the course of this work.

I wish to express my deep gratitude to my supervisor Prof. Dr.-Ing. Sebastian Engell for letting me join his research group at the department of Biochemical and Chemical Engineering, Universität Dortmund and giving me this challenging theme, and also for his valuable advices in my research and support during the entire course of my doctoral program at Universität Dortmund.

During my stay in Dortmund I have received many kinds of supports from the colleagues and ex-colleagues of the research group. I wish to take this opportunity to express my gratitude to them, especially to Dr.-Ing. Chaoyong Wang, Dr.-Ing. Abdelaziz Toumi, Dr.-Ing. Olaf Stursberg, Dr.-Ing. Guido Sand, Dipl.-Ing. Sebastian Panek, Dipl.-Ing. Jochen Till, Dipl.-Ing. Achim Küpper, Dipl.-Ing. Manuel Remelhe, Dipl.-Ing. Ziqiang Wang for their helps. Last but not least, a special thanks to Mrs. Meni Syrou and Mrs. Gundula Pläp from the NRW Graduate School of Production Engineering and Logistics at Universität Dortmund for their attention, friendship and unstinting helps during the whole doctoral program.

Finally, I would also like to express my special thank to my parents, my wife M.Eng. Lijing Dong for their encouragement, patience and support during this process.

# Abstract

Since chromatographic separation processes usually cause a significant share of the production cost, model-based methods are currently applied to optimize the design and the operation of these processes. In this thesis two issues of chromatography are considered: one is the numerical estimation of adsorption isotherms from chromatograms, the other one is the set-point optimization of batch chromatography in presence of plant-model mismatch.

Adsorption isotherms are the most important parameters in rigorous models of chromatographic processes. In this thesis, a numerical method to estimate them from chromatograms is proposed. In contrast to existing numerical methods, the isotherms are represented by a neural network. The weights and the biases of the neural network are optimized by a nonlinear least squares algorithm. Due to the universal approximating capability of the neural network, this method could theoretically retrieve any form of isotherm from the chromatograms. Several issues of the method are studied, which include the chosen type of the neural network, the choice of the mapping relationship, the initialization of the neural network, the importance of the experimental design used to generate the chromatograms, and the consideration of the physical role of the isotherms. The potential of the new method is illustrated by both simulation and experimental studies.

For the set-point optimization of batch chromatography in presence of plant-model mismatch, an iterative gradient-modification optimization strategy is proposed. This strategy transforms the model-based optimization problem into a series of modified optimization problems, which generate set-points converging to the true optimum of the plant. As process-dependent constraints have to be met, the model-based constraint functions are modified using measured plant information in order to satisfy the unknown real constraints. The gradients of the plant mapping which are required by the iterative optimization strategy are computed by a technique which considers the influence of measurement errors and the number of additional set-point perturbations. Simulation studies illustrate the potential of the strategy in the set-point optimization of batch chromatography when large structural mismatch is present.

# Contents

<b>1</b>	<b>Introduction</b>	<b>1</b>
<b>2</b>	<b>Modelling and simulation of chromatography</b>	<b>5</b>
<b>3</b>	<b>Estimation of isotherms</b>	<b>11</b>
3.1	Introduction . . . . .	11
3.2	Model-based estimation of isotherms . . . . .	17
3.3	General isotherm model . . . . .	20
3.3.1	Functional form of the general isotherm model . . . . .	20
3.3.2	Choice of the neural network output . . . . .	25
3.3.3	Initialization of the neural network isotherm model . . . . .	28
3.4	Simulation studies . . . . .	31
3.4.1	Estimation of single-component isotherms . . . . .	31
3.4.2	Estimation of competitive isotherms . . . . .	40
3.4.3	Influence of the mass transfer coefficients . . . . .	60
3.5	Identification based on measured data . . . . .	64
3.6	Summary . . . . .	69
<b>4</b>	<b>Set-point optimization of batch chromatography</b>	<b>70</b>
4.1	Introduction . . . . .	70
4.2	Batch chromatographic separations . . . . .	71
4.3	Iterative optimization strategy . . . . .	74
4.3.1	The ISOPE method . . . . .	75
4.3.2	Redesigned ISOPE . . . . .	76
4.3.3	Handling of process-dependent constraints . . . . .	77
4.3.4	Estimation of the gradients . . . . .	78
4.4	Simulation studies . . . . .	84
4.4.1	Investigation of the constraint handling and the gradient estimation methods . . . . .	84
4.4.2	Comparison of different iterative optimization strategies . . . . .	89
4.4.3	Optimization of the cycle period . . . . .	96
4.5	Summary . . . . .	98

<b>5</b>	<b>Conclusions</b>	<b>99</b>
<b>A</b>	<b>Nomenclature</b>	<b>101</b>
<b>B</b>	<b>Parameters of the SMB process</b>	<b>103</b>
	<b>Bibliography</b>	<b>104</b>