the development of mixture designs and retention mapping and their general application to optimisation problems. It is interesting to compare a later paper (Coenegracht et al.) which explores the use of multicriteria decision-making methods with various retention mapping procedures based on different approaches varying mobile phase composition.

The next four papers describe the theory and utilisation of the DryLab simulation software for both gradient and isocratic separations (Snyder), a more theoretical approach to gradient optimisation (Jandera) and the computer simulation of isocratic and gradient ion-exchange separations. The DryLab simulation software appears in many other articles in this book; for example in the optimisation of a separation of pharmaceuticals (Lankmayr et al.), in a comparison with LCSIM (Schmidt) for the optimisation of a gradient separation of OPA-amino acids, in the optimisation of a herbicide mix (Lehman et al.), and for separating intermediates of a leukotriene inhibitor. There are other papers discussing computer simulation such as the Pro-Digest-LC (Massart et al.) for peptide separations, and the MYCASYST system (Jinno et al.) which perhaps bridges simulation approaches and expert systems.

Expert systems are now becoming available as genuinely useful tools for chromatographers and a dozen or so papers attest to their value. The European Community ESPERIT programme supported an extensive system development, the modules for system optimisation (Schoenmakers et al.) and the elegant module to aid in method validation (Mulholland et al.) are well described in the respective papers. Other highlights from this section are descriptions of the LABEL system (Massart et al.) for the selection of the optimum method for determining the label claim of pharmaceutical products, the major development effort devoted to ECAT (Expert Chromatographic Assistance Team), the troubleshooting system of Tsuji et al., Cathie, a gas chromatographic system (Milne), and HPLC–METABOLEXPERT (Valko et al.) which predicts metabolite retention time in HPLC.

Successful utilisation of computer methods requires an ability to determine specific information about separations such as what constitutes an optimum separation or how peaks move relative to each other during optimisation process (peak tracking). Two approaches to peak tracking are described, one based on 'fuzzy' theory (Lankmayr et al.) and a simpler, area-based method (Molnar). Objective, or optimisation, functions continue to be hotly debated and the paper by Cela et al. presents a well-balanced assessment of the main approaches.

Finally there are, interspersed throughout the book, a small number of application papers. It would appear that only a small number of laboratories outside those actually developing computer-based approaches are using such systems 'in anger', so it is still difficult to make a true assessment of their value.

As a 'snapshot in time', this book is undoubtedly of value in that it will give the reader a broad perspective of what the state of the art was in 1990. It is not destined to be a text that will be studied in depth, rather the opposite: a text recommended for those who want to quickly gain a perspective of the many computer-based approaches now available.

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On-line Estimation and Adaptive Control of Bioreactors, by G. Bastin and D. Dochain

Elsevier, Amsterdam, 1990, xiv + 379 pages, price Dfl. 285.00, ISBN 0-444-88430-0

The book gives a very attractive presentation of the various aspects involved in process control in the field of biotechnology. Specific features of biotechnological processes, such as the strong non-linearity and non-stationarity of the processes as well as the lack of analytical information required to implement control strategies, are extensively discussed. The book aims to present a theoretical framework based on *minimal modelling*. It is intended for graduate-level students but it can also be used as a reference text for all those working on design and optimisation of bioprocesses. The authors have based the text on a long experience obtained in the framework of the Biotechnology Action Programme of the European Communities; many experts have been asked for advice.

The first chapter gives a short introduction to classical models followed by a more rigorous theoretical treatment. The dynamical models used aim at the solution of engineering problems and do not intend to give an exhaustive description of the biological processes. The concept of a general state space model is introduced, which forms the backbone for all estimation and control algorithms. In a short second chapter an overview is presented of kinetic modelling, estimation and control in bioreactors. One of the problems encountered is the difficulty of identifying kinetic parameters because of lack of experimental reproducibility. This leads to the conclusion that it would be desirable to design monitoring and control algorithms for bioprocesses in which the need for *a priori* knowledge of the kinetic parameters is minimal. Also the lack of suitable sensors capable of providing direct real-time measurements of the state variables is emphasized. Therefore, in the subsequent chapters algorithms (called 'software sensors') for the on-line estimation of state variables and parameters get much attention. Chapters 3 and 4 deal with extended observers of the Luenberger and Kalman type; their use is illustrated by various well-chosen examples from real-life biotechnological processes. Firstly, the use of observers is treated for the state estimation when the reaction rates are unknown; secondly, attention is paid to methods for state estimation of reaction rates. In Chapter 4 the state and parameter estimation is described when the yield coefficients are unknown.

The last chapter deals with the adaptive control of bioreactors. The adaptive character of the control algorithm implies that a parameter estimator is incorporated in the control algorithm which accounts for the possible variations of the kinetics. In two appendices a nice summary is given of (a) the models reported in the literature for the specific growth rate and (b) an elementary and intuitive presentation of the stability theory of time-varying systems.

The book is stimulating reading and gives a very attractive introduction to the field of modelling and control in biotechnology. For those who are not familiar with basic aspects of process control and/or bioprocesses it is not a simple task to fully appreciate the material but the very clear step-by-step presentation makes it suitable for self-study. The large number of examples gives a good impression of the applicability of the methods. The extensive lists of up-to-date references are very valuable. Altogether a book that can be strongly recommended.

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News

Use of computational methods in drug design

A major area of computational chemistry is the design of new molecules. Work in this area is reported throughout the literature. In addition to this journal, the *Journal of Computer Aided Molecular Design* and *Quantitative Structure Activity Relationships* contain information of interest. An objective of these studies, often referred to as QSAR (quantitative structure activity relationships) is to predict the activity of a molecule prior to synthesis. This can save drug companies huge amounts of money. A brief review of the chemometric aspects is published by Dunn [1] in this journal. There are two main approaches to predicting drug activities. The first is modelling of small molecules — the active drugs. The second is to model the active site of proteins or enzymes. Ideally the drug should fit into the active site in the enzyme to be an effective reagent.

The area of predicting properties of small molecules is of most interest to the chemometrician. *Molecular mechanics* calculations are used to determine the lowest energy and so optimum conformation of molecules using classical mechanical calculations. This approach is closest to the organic