Chimia 54 (2000) 6–8

ISSN 0009–4293

Focal Point: Industrial Chemistry

ILMAC Congress: October 14, 1999

Process Simulation in Industrial Chemistry, Biotechnology, and Chemical Technology*

The chemical and biotechnological process industry is confronted with a time and capital consuming industrial reality in a more competitive environment. The need for leaner development and design of processes is increasing. Today and in the future, computer simulation is and will become an even more important tool for the development of new chemical or biotechnological processes and for the design of new plants. The objective of this one-day meeting was to review significant applications and technologies in this field. With the presentation of selected cases, we aimed to give a deeper insight in the working methods which should be used to get faster results and reduce development time and costs. The session should encourage a better understanding of the application of special software in industrial practice. Abstracts by the authors are given.

Keywords: Biotechnology · Chemical technology · ILMAC · Industrial chemistry · Process simulation

Simulation of a Fixed-Bed Reactor for Scale-up from Miniplant to Production
Simulation eines Festbettreaktors für den Scale-up vom Miniplant in die Produktion

Volkmar Bösch[a], Juan Ramon Herguijuela[a], Thomas Kircher[a], Joerg Frauhammer[b], and Ute Friedel[b]
[a]F. Hoffmann–La Roche AG, Division Vitamins and Fine Chemicals, CH–4070 Basel, Switzerland
[b]Universität Stuttgart, Institut für Chemische Verfahrenstechnik, Böblinger Strasse 72, D–70199 Stuttgart, Germany

In einen Herstellprozess für ein wichtiges Vitamin-Zwischenprodukt wurde ein neues Verfahren mit einem Festbettkatalysator eingeführt, welches sich im Miniplant als sehr vielversprechend erwiesen hatte. Eine Simulation des Festbettreaktors ermöglichte einen direkten Scale-up auf den Produktionsmassstab.
Für die Modellbildung wurde ein quasihomogener, zweidimensionaler und stationärer Ansatz gewählt und mit der im Roche-Labor gemessenen Formalkinetik kombiniert. Die Beziehungen für den Wärme- und Stofftransport wurden dem VDI-Wärmeatlas entnommen. Die Lösung der Modellgleichungen erfolgte mit dem Simulator 'Pdexpack' der Universität Stuttgart, welcher auf einem 'Method of Lines'-Algorithmus basiert.

Die Verifizierung des Modells erfolgte durch einen Vergleich mit den Labormesswerten und durch eine Sensitivitätsanalyse wichtiger Modellparameter. So konnte beispielsweise gezeigt werden, dass die Geschwindigkeitsverteilung über die Schüttung nur einen geringen Einfluss hat.
Zur Dimensionierung des Reaktors wurden wichtige Grössen wie Rohrgeometrie, Eintrittstemperatur und Durchsatz variiert und daraus die optimalen Bedingungen abgeleitet. Die so ausgelegten Reaktoren wurden in die Neuanlage integriert, erste Betriebserfahrungen sind nach der Inbetriebnahme zu erwarten.

Economic Optimization of an Industrial Semibatch Reactor
Optimierung der Wirtschaftlichkeit eines industriellen Semibatch-Prozesses

Andreas Keller
F. Hoffmann-La Roche Ltd., Vitamins and Fine Chemicals, CH–4070 Basel, Switzerland

Eine Methodik für die Optimierung von Semibatch-Prozessen wird vorgeschlagen. Diese Methodik beinhaltet die Schritte Aufstellen eines mathematischen Modells, Analyse des Prozesses im aktuellen Zustand, Definition von Entscheidungskriterien, Optimierung der Betriebsweise und Vereinfachung dieses Optimums, so dass eine Einführung im Betrieb möglich wird. Diese Methodik wurde für die Optimierung einer Stufe einer Monoanlage für die Herstellung eines Vitamins eingesetzt. Die Zielgrösse war dabei minimale Produktionskosten. Als Randbedingung musste eine vorgegebene jährliche Produktionsmenge eingehalten werden. Für die Optimierung wurde die dynamische Programmierung eingesetzt. Mit dieser Optimierungsmethode wurde ein mehrstufiges Dosierprofil erhalten. Dieses wurde zu einem zweistufigen Dosierprofil vereinfacht, welches in der bestehenden Anlage ohne zusätzliche Investition eingeführt werden konnte. Beide Dosierprofile führten zu einer Verlängerung der Batchdauer, doch wurde diese Reduktion der Produktivität durch die bessere Ausbeute kompensiert.

Organized by:
Dr. Hans-Rudolf Dettwiler
Lonza AG
PAFE
CH–3930 Visp
Tel.: +41 27 948 56 39
Fax: +41 27 948 61 80
E-Mail: hans-rudolf.dettwiler@lonza.ch

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Process Simulation as an Integral Working Tool for Chemists, Engineers, and Managers: Discussion of an Actual LONZA Project

Brigitta Frank and *David Ruppen*
Lonzagroup, Walliser Werke, CH–3930 Visp, Switzerland

The discussed process consists of one continuous and two batchwise operated stages; characteristics that are a real challenge for an integrated process simulation application.
Part one: Reaction and thermal separation operations describe the continuous stage of the process. A well-known and established process simulator is used for process development and design of new plant facilities. The presentation focused on process simulation as an enabler for a simultaneous approach not only for R&D but also specifically for plant design. This was a key issue for success under the given tight timeframe.
Part two: Simple neutralization reactions, sophisticated crystallization and solid–liquid separation operations in the batch part of the process. Here, one is confronted with limitations in rigorous process simulation and experimental work is of more importance. However, existing production facilities have to be used and evaluation of plant alternatives is a task that can be supported by simulation. For this purpose a new batch process simulator was evaluated.
Finally, the challenge was to combine both parts of the process. Experience made on route to a fully integrated process simulation was summarized.

The Complementary Role of Mathematical Methods and Numerical Simulations in Process Design and Development

Marco Mazzotti and Giuseppe Storti, ETH Zürich, CH–8092 Zürich, Switzerland

The non-empirical design of processes requires process modeling, which is an iterative activity calling for a tight interaction between experimental investigation and theoretical analysis. This allows the formulation of a correct and meaningful mathematical model, which must then be solved properly. Mathematical methods leading to an explicit or semi-analytical solution of the model equations enable a synthetic understanding of the process, which is of the greatest value despite the simplifications required. Numerical simulations of the detailed non-simplified model provide information only about process performance at given operating conditions and are better suited for final process optimization. Examples of the interaction between mathematical methods and numerical simulations in process design and development were discussed; these are taken from azeotropic distillation, continuous preparative chromatography, and chemical reaction engineering.

Propargyl Chloride Synthesis: Integrated and Computer-Aided Process Development

Martin Roth and Bernhard Urwyler
Process Development, Novartis Crop Protection Münchwilen AG, CH–4333 Münchwilen, Switzerland

Chemical process development, whose goal is to bring chemical transformations from the laboratory to industrial production scale, encompasses activities that include process screening, engineering, process safety, waste treatment, quality challenge, and scale-up. But also change in the process or know-how demand a chemical re-examination and re-design of the processes. In the example provided, various computer-aided tools were used to obtain the safest, most technically feasible and economic process which satisfied our quality needs.
Following a successful introduction of a first generation process, it became necessary, for various market, chemical and technical reasons, to re-examine and re-design the process.
An interdisciplinary re-design team was composed of staff from chemical process development and analytics together with production and process safety to reduce product costs by improving chemical yield and capacity. A new process was found but the chemical process development had to put great efforts into the safe synthesis of the quality-determining key intermediate propargyl chloride. The use of commercially available propargyl chloride involved transport, storage, and quality issues.

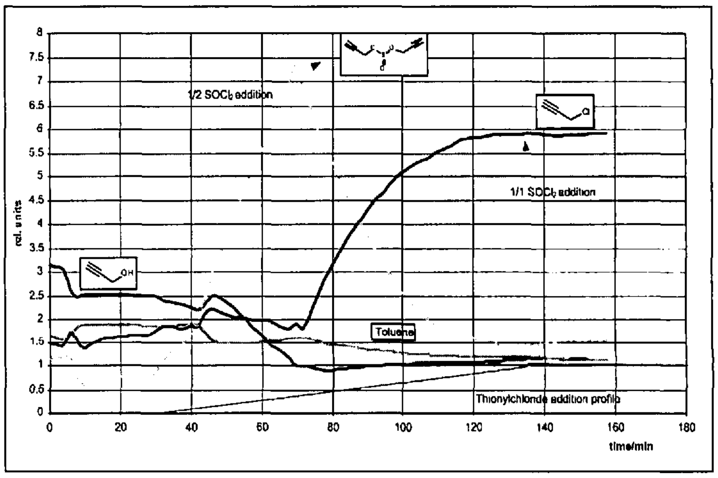

Figure. Reaction profile of the chlorination of propargylic alcohol with thionylchloride

A manufacturing process to produce propargyl chloride has been developed by using computer-aided tools such as online heat flow, React-IR and NIR measurements. Also scale-up experiments were used to challenge the feasibility and identify the best reaction conditions for safe propargyl chloride synthesis of a very high quality. Here the heat flow measurements and online React-IR are excellent and powerful tools to evaluate the most important parameters of a process such as kinetic or dynamic behavior and safety data under nearly industrial conditions. In a first step, we measured the thermochemical reaction and decomposition parameters by means of a RC1 and a DSC. In a second step, online React-IR measurements monitored the profiles of the reaction intermediates and products, identified by multicomponent analysis calculated from the 3D-IR surface area (Figure). These readings, together with the findings from heatflow measurements, helped staff understand the synthesis mechanisms and kinetics. NIR was introduced as an easy tool to handle deviations from the normal course of reaction. A safety-relevant charging failure can be detected before accumulated heat is liberated spontaneously which could lead to a runaway. The robustness of the process was tested further on a bench scale and successfully demonstrated on a pilot scale. Here staff gathered important experience on stirring, heat exchange and overall cycle time.
The whole investment in the process development re-design will be paid back by about four months' production.

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Simulation in the Process Industry: Expenditure, Result, and Profit
Simulationsgestützte Anlagenplanung mit Simple++ für die Prozessindustrie

Philippe Michel
Chemgineering GmbH, Hessbrühlstrasse 15,
D–70565 Stuttgart, Germany

Summary
Simulation studies are not only performed during the planning of new plants. Existing plants are increasingly being optimized by simulation. This includes modifications such as renovation, extension, or removal of existing production plants. These modifications are the result of an evolution of technology or market adaptation.
A simulation study must be performed step by step. From the definition of the goals to the presentation of the results in graphical or tabular form, the main steps were presented in the conference.
The procedure of a simulation study was illustrated by an example of a simulation in the pharmaceutical industry

Zusammenfassung
Simulationsstudien werden nicht mehr ausschliesslich bei der Planung von neuen Anlagen durchgeführt. Auch die bestehenden Anlagen werden immer mehr durch die Simulation optimiert. Dabei geht es um Änderungen wie z.B. Umbauten, Erweiterungen oder Verlagerungen von Produktionseinrichtungen. Diese Änderungen sind bedingt durch den Fortschritt der Technik oder die Anpassung an den Absatzmarkt. Um erfolgreich zu sein, muss aber eine Simulationsstudie nach bestimmten einzuhaltenden Schritten durchgeführt werden. Von der Festlegung der Zielsetzung bis zur Darstellung der Ergebnisse in grafischer und tabellarischer Form, wurden die wichtigsten Schritte im Vortrag vorgestellt.
Anhand von einem konkreten Beispiel einer Prozesssimulation in der pharmazeutische Industrie wurde die Vorgehensweise einer Simulationsstudie veranschaulicht.

Advantages of Dynamic Process Simulation for Quality Assurance of Control Software

Beat Buser
BS Consulting & Engineering AG, Schützenweg 63
CH–4123 Allschwil, Switzerland

Contemporary control systems are becoming more complex and cover a broad range of applications. Although hardware is getting cheaper, the total costs of such systems are increasing. The required functionality, which was described in detail, in the functional specification has to be verified during installation and operational qualification. For manufacturing facilities with an extensive amount of control software modules, partial testing must be performed at an early stage of the project. Due to short project execution times, only a small number of errors can be accepted during startup to reach the project target date. The application and the process functionality must be checked before integration in the commissioning phase. Software errors must be corrected immediately and should not require huge rework on already tested or copied software modules. To meet the requirements and expectations of the control software, this has to be tested in a artificial environment that emulates the real physical behavior of the plant.
Modern control systems are equipped with easy to use tools for offline testing. Simple algorithms can be written to simulate process behavior within the control software environment. Therefore it is possible to run the process simulation and the control software in the same controller without interference of the two different programs. With very little hardware, the plant can be run without physical inputs and outputs.
Most people still believe that only a simulation where complex differential equations are performed is adequate to represent the process behavior. In this case, a separate computer with dedicated hardware has to be linked to the control system. The costs and effort of such a system should not be underestimated. The complexity of the computer model for the process simulation does not directly result in better control software. Application software errors can be detected with less equipment and cheaper software tools.
It can be shown that simple process models for the physical properties are sufficient to debug the individual software modules. Typical errors can be eliminated through easy and systematic dynamic testing.
Running the simulation and control application on the same system has several advantages. Only one programming, debugging, visualization and documentation tool is needed. Less introduction time, no dependence on rarely available specialists, and an easier handling of the entire system is guaranteed. A comparison of effort and achievable software quality gives an indication of the practical use of process simulation.

Computer Simulation for the Analysis of Complex Multipurpose Batch Plants
Computersimulation bei der Analyse komplexer Mehrzweck-Batchanlagen

Hugo Franz Betschart
Ciba Spezialitätenchemie, CH–4002 Basel, Switzerland

Der Einsatz der Simulationstechnik erweist sich bei komplexen Mehrzweck-Batchanlagen als ein wichtiges Instrument bei der Analyse von bisherigen als auch bei der Planung neuer Produktionsanlagen. Nach der Erstellung eines Modells der zu untersuchenden Prozesse werden durch Simulation das dynamische Verhalten, die Engpässe und die freien Standzeiten eruiert und die Anlagenkapazität bestimmt. Daraus werden neue Konzepte entwickelt und auf ihre Eignung untersucht; die Simulationsergebnisse erlauben, wichtige Investitionsentscheide mit zusätzlicher Information zu untermauern.
Bei diesen Analysen stehen die ereignisorientierten Simulationen im Vordergrund. Daneben werden auf unterschiedlichen Ebenen auch diverse andere Softwarepakete eingesetzt, z.B. zur Auslegung von Destillationskolonnen, zur Simulation komplexer Reaktionsmechanismen oder zur Berechnung von Stoff- und Energieaustausch.
Anhand von mehreren Beispielen sind der Nutzen und die Ergebnisse aufgezeigt worden.