Roadmap Chemical Reaction Engineering

an initiative of the ProcessNet Subject Division
Chemical Reaction Engineering

2nd edition May 2017

EINE INITIATIVE VON DECHEMA UND VDI-GVC

Table of contents

Preface

This 2nd edition of the Roadmap on Chemical Reaction Engineering is a completely updated edition. Furthermore, it is written in English to gain more international visibility and impact. Especially for the European Community of Chemical Reaction Engineers organized under the auspices of European Federation of Chemical Engineering (EFCE) it can be a contribution to help to establish a Roadmap on a European level.

With the 2nd edition of the Roadmap we address the general trend that Chemical Reaction Engineering is directly defining product quality and product properties and, thus, is getting directly involved in the development of innovative application characteristics of products. As an example certain microstructures of polymers or functionalities of nanoparticles can only be achieved if the chemical reaction is controlled in the right way and defined by the tools of Chemical Reaction Engineering. To an increasing extent Chemical Reaction Engineering is also a key for the process and product development of industrial sectors outside the chemical industry such as energy technology or automotive engineering.

Chemical reactors will become tailor-made devices with the design optimized for fluid and particle flow, heat and mass transport, reaction and structural properties with the help of additive manufacturing. This will lead to a reactor design which is optimized for the reaction performed in the reactor, including the optimization of the reaction trajectories which can be followed within the reactor.

However, Chemical Reaction Engineering is not only driven by the need for new products (market pull), but also by a rational approach to technologies (technology push). The combination of digital approaches such as multiscale modeling and simulation in combination with experimentation and space and time-resolved *in situ* measurements opens up the path to a rational approach, starting at the molecular level and ending with the product properties.

To put it concisely, Chemical Reaction Engineering is not anymore only devoted to understand, design and optimize chemical reactors in terms of yield, energy and efficiency. In addition, it is a key enabler for product innovations and new business concepts through e.g. product by process approaches or modular plant concepts.

All the aspects mentioned before are considered now in the 2nd edition of the roadmap including case studies, technical chapters and an outlook updated accordingly.

Finally we wish a stimulating and enjoyable reading of the 2nd edition. We would highly appreciate to get your feedback with suggestions and comments for the next edition. Do not hesitate to contact us.

The Board of the ProcessNet Subject Division Chemical Reaction Engineering

1 What is Chemical Reaction Engineering?

The end products of the chemical industry, such as the polymers, drugs, colorants and other materials found in many of today's consumer goods, have become an indispensable part of everyday life and make a substantial contribution to our high standard of living. Industrial chemistry covers an extensively ramified value supply chain starting from a few raw materials, such as crude oil, natural gas or renewable resources, generating several hundred basic and intermediate products, that are then further processed to thousands of end products. This structure is best illustrated by a tree, with the roots representing the raw materials, the trunk corresponding to the basic chemicals, the branches symbolising the intermediates and the leaves portraying the final products (see Fig. 1). Extending the tree analogy, chemical reaction engineering cultivates the existing tree (by improving existing chemical processes), propagates the growth of new branches and foliage (by developing novel chemical processes for new products) or even seeds the growth of new trees (by facilitating the transition to alternative feedstocks).

Chemical reaction engineering lies at the interface between chemistry and process engineering, spanning the development of new synthesis routes in the laboratory and the industrial-scale manufacture of chemicals.

The evolution of chemical reaction technology is closely linked to the development of the ammonia synthesis by the Haber-Bosch process at the beginning of the 20th century. From around the middle of the 20th century, chemical reaction engineering became recognized as a distinct scientific field and, as such, became firmly established in the curricula for chemical technology education. DECHEMA and VDI (Verein Deutscher Ingenieure) should be mentioned as key organizations that played a major role in the development of chemical reaction engineering as a vigorous and independent discipline in Germany. In 1956, the DECHEMA Expert Committee "Chemical Reaction Engineering" was founded and in 1961 the DECHEMA Working Group "Technical Reactions (Technische Reaktionen)" was established under its patronage. Also in 1956, the Expert Committee "Technical Reaction Engineering" (Technische Reaktionsführung) was set up under the auspices of the former VDI division "Process Engineering". In 2007, ProcessNet was launched as a joint initiative of DECHEMA and VDI-GVC bundling all previous activities

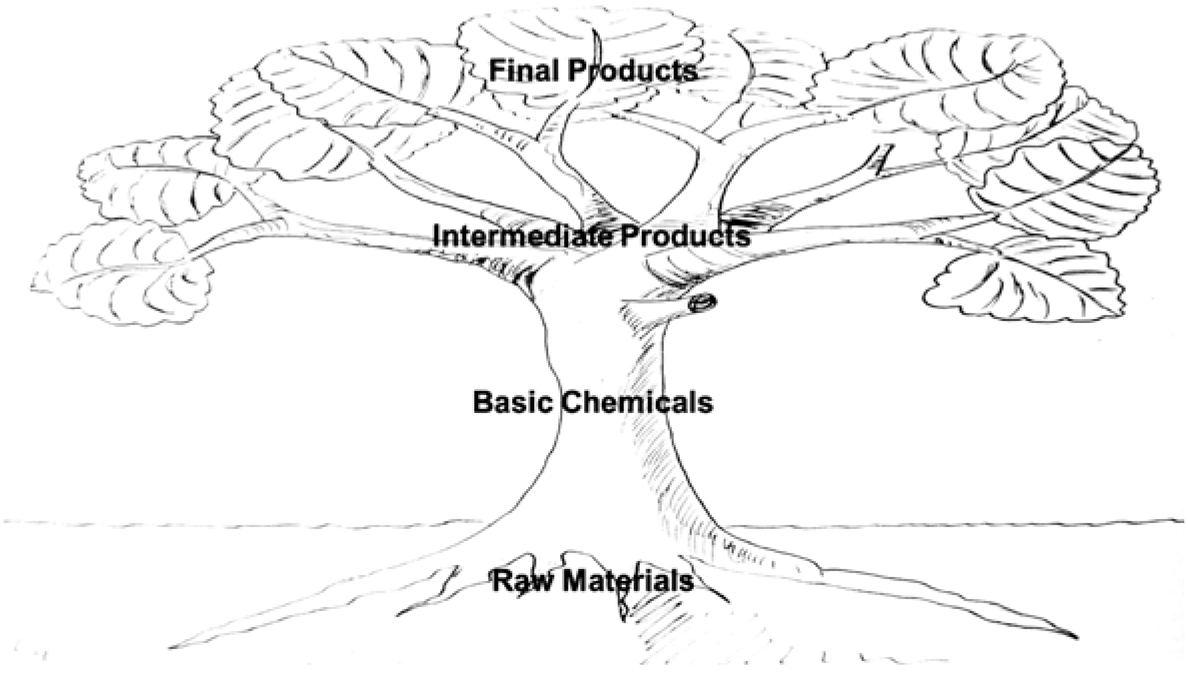


Figure 1: "Chemis-tree" an illustration of the value-added supply chain from raw materials to end products.

in process engineering, chemical engineering and technical chemistry. The working parties in chemical reaction engineering were consequently merged into the ProcessNet Working Group "Technical Reactions". In 2015, as part of a reorganization and consolidation of ProcessNet, the Working Group "Technical Reactions" ceased operations and its activities were integrated into the ProcessNet Subject Division "Chemical Reaction Engineering".

Chemical reaction engineering as a science is based on two pillars: "reaction analysis" and "reactor design".

In reaction analysis the stoichiometry, thermodynamics and kinetics of chemical reactions are scrutinized. Stoichiometry provides the framework to account for the interaction between the various chemical species in a reaction network; thermodynamics indicate the limits imposed on conversions, while kinetics describe how fast individual reactions proceed and thus provide the reaction engineer with the basis for modeling and reactor design. Today, mechanistic kinetics derived from detailed knowledge of the molecular processes are generally preferred over formal kinetic descriptions based fitting empirical rate of reaction expressions to experimental data from kinetic measurements. Establishing mechanistic kinetics also makes use of several chemical disciplines such as physical chemistry, solid-state chemistry and theoretical chemistry, and even physics may be involved in the relevant surface science.

Reactor design can be carried out empirically by scaling-down the technical reactor envisaged to a representative laboratory reactor system and then using this to identify optimal reaction conditions (temperature, pressure, concentrations and catalyst), and even a comparison of alternative reactor types (fluidised-beds, plug-flow reactors, batch reactors,..) is thus possible. Distributed parameter measurements are playing an increasingly important role in this process, since they provide revealing insights into the locally prevailing conditions. Rational reactor design, based on reliable kinetics, taking into account both chemical reactions and the transport processes for mass, heat and momentum involved in the system under consideration, is becoming the norm, with reactor modeling and simulation making an indispensible contribution. New reactor concepts and variations in the reactor operating conditions can be predicted reliably by this means. The conceptual basis for the reactor modeling is the balancing of energy, matter and momentum. Solving these balance equations leads to temperature and concentration fields and reaction rate profiles in the chemical reactor. In addition to reaction kinetics, heat and mass transport as well as fluid dynamics can have a decisive influence on reactor performance.

Figure 2 provides a pictorial summary of the components of chemical reaction engineering.

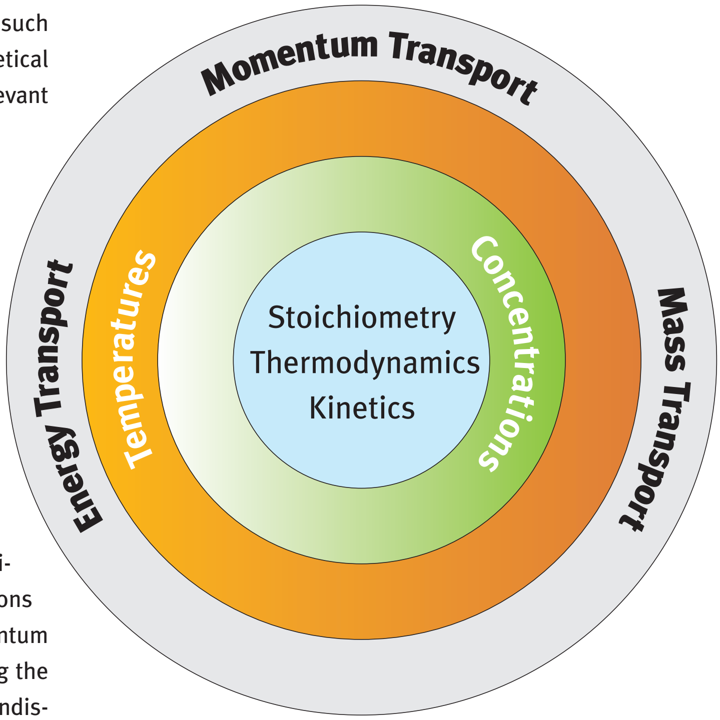


Figure 2: Components of Chemical Reaction Engineering

2 Relevance of Chemical Reaction Engineering

The example of the Haber-Bosch ammonia synthesis process can help to appreciate the significance of chemical reaction engineering in successfully transferring technology from the laboratory to industry.

Fritz Haber, who held the chair of physical chemistry and electrochemistry at the University of Karlsruhe in the beginning of the 20th century, developed the thermodynamic and kinetic fundamentals for the ammonia synthesis. He determined the equilibrium constants and, crucially, proposed an industrial reactor concept with only partial conversion, unreacted feed being recycled following ammonia separation.

Alwin Mittasch, who worked at BASF AG with Carl Bosch in cooperation with Fritz Haber and contributed extensively to the industrial implementation of the ammonia synthesis, wrote in his book “History of ammonia synthesis”:

“When working with a recycle loop, where only a fraction of nitrogen and hydrogen react, it is vital that the gases react even at low contact times. These high space time yields could only be achieved with catalysts that improved upon the performance of those from 1905 by an order of magnitude.”


© DECHEMA

Prior to 1905, Osmium and Uranium were used as catalyst materials. With the development of iron oxide catalysts it was possible to reach sufficient space time yields. To do so, Alwin Mittasch used more than 20 pressurized reactors operated parallel and conducted more than of 10,000 experiments, a technique that served as the forerunner for modern high throughput experimentation methods.

From this time onward, a thorough knowledge of chemical reaction technology has been essential to develop and realize chemical reactions economically. The economic feasibility of a chemical production route is decisively affected by:

- Investment costs
- Operation costs
- Process safety
- Environmental impact

Investments costs can be calculated based on the process flowsheet from major items such as reactors, separation equipment, compressors or pumps. The type, number and size of the major units are influenced significantly by the temperature and pressure operating conditions required for the chemical reaction, by the selectivity-conversion behavior and by the potential space-time-yield of the reactor. While selectivity dictates the complexity of downstream separation complexity, conversion determines the recycle flow rate and the space time yield defines the size of the reactor. Therefore both the selectivity-conversion diagram and the space-time-yield are critical criteria for process development and optimization.

Operational costs are also strongly dependent on the selectivity-conversion behavior, since selectivity decides the raw material efficiency and a combination of selectivity and conversion stipulates the energy required for separation.

Chemical reaction engineering principles, mainly focusing on reactor operation, are used also to enhance process safety. A runaway reaction or the ignition of a reaction on a solid catalyst can be described by a heat balance (Semenov diagram), in which diffusion phenomena and fluid dynamics can play a key role. In such cases, microreaction engineering, for example, can provide an inherently safe production process.

Furthermore, chemical reaction engineering renders essential contributions to reducing the environmental impact of chemical processes, for instance by enabling compliance with emission limits or reducing the CO_2 footprint. This can be achieved by reducing the energy required, further processing of gaseous effluents or wastewater, or even by adapting the process to renewable feedstocks and energy.

Chemical reaction engineering thus is a vital skill for "intensifying" existing and projected chemical processes. It is possible to identify new process windows by investigating the potential modifying temperatures and pressures, dispensing with solvents or replacing them by greener ones, such as supercritical CO_2, on a purely theoretical basis with, or even without, extensive experimental validation.

Chemical reaction engineering therefore continues to be a key discipline for development and implementation of future production concepts for the chemical industry. Furthermore, it supplies a solid foundation for novel innovative products, for the recycling economy and general for the sustainability of the chemical and other industries. As examples of this, one can mention contributions to:

» Nanotechnology, e.g. by controlled synthesis of nanoparticles of defined morphology, composition and functionalities.

» Energy transformation, e.g. by providing kinetically and thermodynamically feasible solutions for chemical energy storage.

» Pharmaceutical industry, e.g. by efficient production of drugs such as artemisinin.

» Automotive sector, e.g. by increasingly sophisticated solutions for exhaust gas catalysis.

3 Experimental Reaction Engineering

Despite the advances in the fields of mathematical modeling and simulation, experimental research is still essential for the validation and optimization of new technical process and simulation tools. The link between experiments and reaction modeling provides a reliable basis for designing more efficient reactors and production plants.

A LABORATORY REACTORS

Nowadays, researchers in the field of reaction engineering have a large number of laboratory-scale reactors at their disposal to perform experimental studies under a variety of conditions. Basic experimental data, such as conversion, yield, selectivity, and catalyst lifetime can be measured to a large extent without difficulty using the standard reactors described in the pertinent literature[1,2]. With advances in instrumentation, it is possible to exercise precise control over the reaction conditions (I.e., temperature, pressure, concentration and reaction duration). Laboratory- and pilot-plants can now be regulated via easily configurable process control systems, so that automated operation is possible over long periods of time. The use of laboratory information acquisition systems also enables the computerized archiving and analysis of laboratory data, which further enhance the output of experimental work. However, the construction and operation of fully automated laboratory reactors remains cost-intensive.

Over the last few years, flow chemistry has emerged as an important new trend in chemical research, with studies focused on the design and development of novel catalytic reactors and manufacturing techniques. Micro-flow reactors are increasingly employed for the synthesis of advanced materials, e.g., nanoparticles with narrow size distributions or particular morphologies.

Larger microstructured reactor systems are currently being developed for energy-related applications, such as gas-to-liquids conversion, and converting excess renewable electrical energy into both gaseous and liquid fuels or chemicals (see Fig. 3). Such applications benefit from the excellent heat transfer performance of microstructured reactors and from the resulting higher space-time-yields and selectivities and longer catalyst lifetimes. In addition, their modularity and superior dynamic operation, including more rapid start-up and shut-down, makes them particularly attractive for decentralized energy generation and utilisation, in the context of a future energy system largely based on renewables.

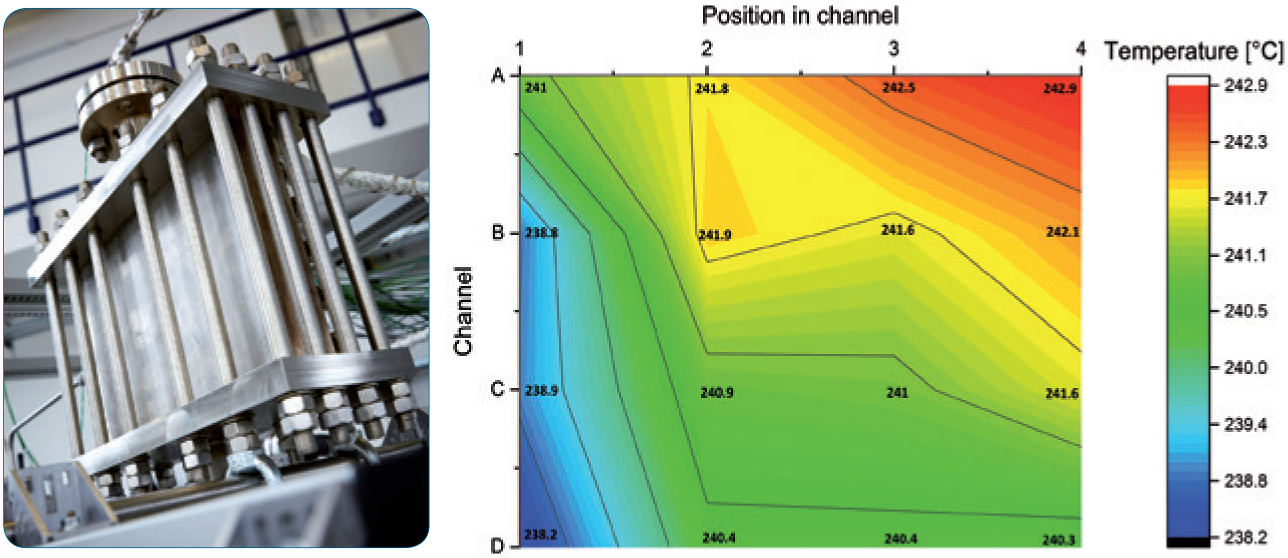


Figure 3: Compact modular Fischer-Tropsch reactor of the KIT spin-off INERATEC GmbH. Almost isothermal conditions were achieved with the innovative evaporation cooling utilized. (source: INERATEC GmbH)

---

[1] M. Baerns, A. Behr, A. Brehm, J. Gmehling, H. Hofmann, U. Onken, A. Renken, K.-O. Hinrichsen, R. Palkovits, Technische Chemie, Wiley-VCH, Weinheim 2013. G. Emig, E. Klemm, Chemische Reaktionstechnik, Springer, Berlin 2017.

[2] A. Jess, P. Wasserscheid, Chemical Technology, Wiley-VCH, Weinheim 2013. H.S. Fogler, Elements of Chemical Reaction Engineering, Prentice Hall PTR, 2006.

Additive manufacturing (AM), also known as 3D printing, permits the fabrication of sophisticated three-dimensional structures of an almost unlimited geometrical complexity and with full integration of additional functionalities (e.g. dosing, phase contacting, cooling/heating, catalytic activity, in-line analysis/reaction monitoring). This can be exploited in the design of specially tailored reactor and process equipment with greatly enhanced performance characteristics.

So far, industrial applications of AM are mainly to be found in the field of medical technologies as well as in the automotive and aerospace sectors In the chemical and pharmaceutical industries, on the other hand, AM is still mainly in the research phase. Nevertheless, a sharp rise in activities has been registered over the last few years involving single phase[3] as well as multiphase reaction systems[4]. A broad range of industrial applications of AM in chemical reaction engineering still requires extensive research in both theory (e.g. correlations and design rules) and practice. An important goal is the additive manufacturing of the catalyst support itself (see Fig. 4), catalytic surface functionalization (e.g. optimized procedures for coating/crystallization) as well as large-scale implementation and utilization of such materials.

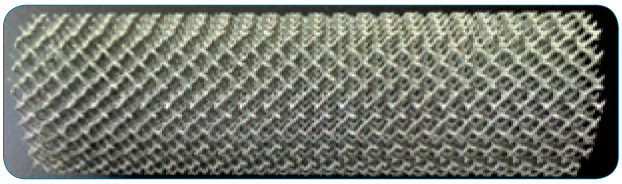


Figure 4: Periodic open cellular structure as catalyst support, additively manufactured by Selective Electron Beam Melting.
(source: INERATEC GmbH)

B HIGH THROUGHPUT TECHNOLOGY

High throughput experimentation (HTE) has become the standard technology for intensified catalyst and process development over the past two decades (see Fig. 5). The two core elements of HTE are parallel or rapid sequential execution of complex sequences of operations, as well as the efficient integration of hard- and software components into the overall high throughput development cycle (design-make-test-model-evaluate)[5,6]. In particular, knowledge of the translational functions in scaling-down operations, has in many cases led to ingenious experimental procedures and a range of new experimental possibilities. Today, nearly all technically relevant reactor configurations and modes of reactor operation can be investigated by a highly parallelized approach in HTE. Improved reactor designs and more precise analytics are critical for obtaining high precision experimental results. Greater precision and the increasingly predictive character of the results acquired with regard to scale-up, has led directly to three new fields of application for HTE I) determination of micro- and macro-kinetics in parallel reactors, II) evaluation of ramp-up and shut-down procedures, III) quality control in catalyst production and benchmarking studies.

A further new field in reaction engineering that is attracting increasing attention is the evaluation of catalyst performance in complex fluid flow fields. Down-scaled parallel operation of bubble columns, fluidized beds and riser reactors is currently being used for catalyst appraisal. In petrochemical applications, the testing of technically relevant feedstocks and trials with full-sized shaped catalysts have become important technological mainstays.

Two aspects can be highlighted here: a fully modular concept for the construction of test units leading to a fully scalable adaptation from bench- to sub-pilot- and pilot-scale and the use of software environments allowing complete data integration coupled with predictive modeling. High throughput experimentation is certainly a pacesetter within the field of reaction engineering for defining and implementing industry 4.0 standards in catalyst and process development[7].

---

[3] M. Klumpp, A. Inayat, J. Schwerdtfeger, C. Körner, R.F. Singer, H. Freund, W. Schwieger, Chem. Eng. J., 242 (2014) 364-378.

[4] M. Lämmermann, W. Schwieger, H. Freund, Catal. Today, 273 (2016) 161-171.

[5] A. Gordillo, S. Titlbach, C. Futter, M.L. Lejkowski, E. Prasetyo, L.T.A. Rupflin, T. Emmert, S.A. Schunk, Ullmann's Encyclopedia of Industrial Chemistry, Wiley-VCH Verlag GmbH & Co. KGaA, 2000.

[6] C. Futter, L. T. Alvarado Rupflin, N. Brem, R. Födisch, A. Haas, A. Lange de Oliveira, M.L. Lejkowski, A. Müller, A. Sundermann, S. Titlbach, S. K. Weber, S. A. Schunk, Modern Applications of High Throughput R&D in Heterogeneous Catalysis, Bentham Science Publishers, Oak Park, 2014, 3-88.

[7] S.A. Schunk, N. Böhmer, C. Futter, A. Kuschel, E. Prasetyo, T. Roussière, Catalysis: Volume 25 (Specialist Periodical Reports), RSC, 2013, DOI:10.1039/9781849737203-FP001.

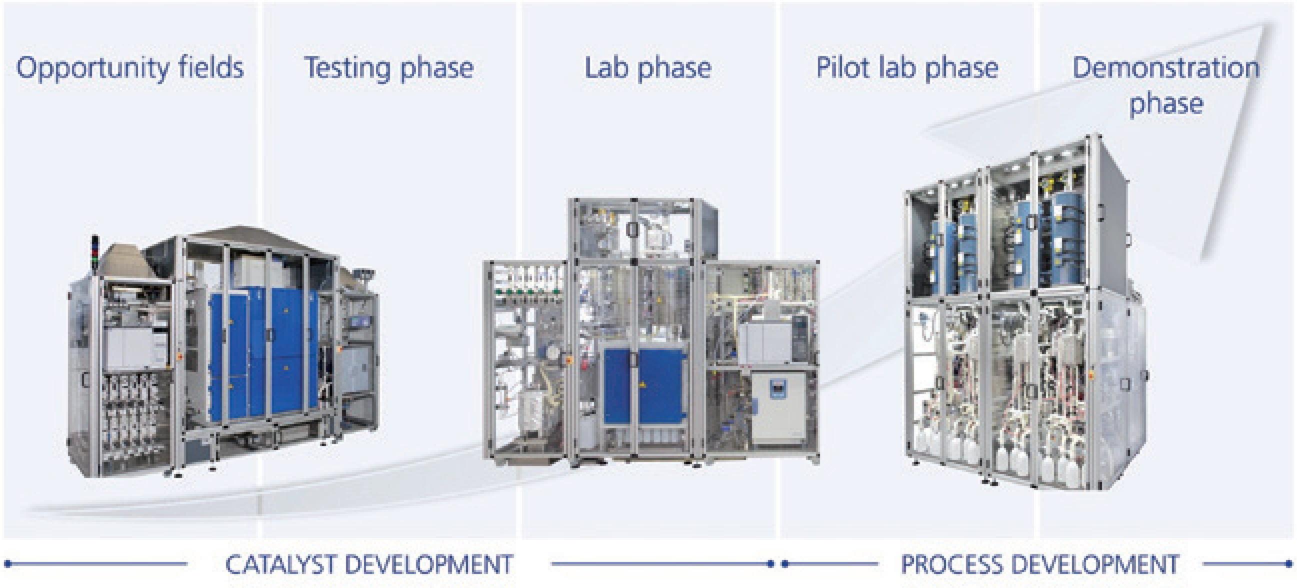


Figure 5: High Throughput Technology (Source: hte GmbH).

C DYNAMIC METHODS

Traditionally, most reactors have been operated in steady-state, e.g. at their optimal operating point. Reactors may, however, also be operated in a forced unsteady-state mode, i.e. with dynamic changes of inlet variables, such as concentrations and temperature[8]. Additionally, for electrochemical reactors, variables such as current and voltage may be modulated with time[9]. The motivation for dynamic operation may lie in external exigencies, as in automotive catalytic converters[10] or for power-to-chemicals concepts[11], where the operating point may shift according to the availability of renewable energy. Alternatively, it may be exploited to improve reactor performance parameters, such as yield, or just for kinetic analysis. Some reactors or the reactions themselves may give rise to either desirable or unwanted autonomous dynamic behavior, such as catalyst degradation or periodic oscillations, which need to be controlled carefully. As has been shown in several studies, the catalyst structure may change as a consequence of the reaction conditions[12]. Thus the steady-state kinetics are often inadequate to describe catalytic processes under constantly fluctuating conditions. Reactor design, scale-up as well as the optimization of operating conditions also necessitates an understanding of the chemical reaction kinetics and their coupling with mass and heat transport. For this purpose, dynamic analysis techniques monitoring and interpreting a reactor's response to various input signals, such as sinusoidal, or step changes in flow or inlet concentrations may be used to identify the time constants of the individual processes, their interactions and optimal operating points. Multiple detection methods may be employed to determine the simultaneous response of several variables, yielding illuminating insights into a variety of phenomena[13].

More accurate kinetic models can be obtained from intrinsic reaction kinetics determined via transient techniques[9,14]. Recently, complex nonlinear analysis methods, such as nonlinear frequency response analysis[8,9] have been employed, which, combined with supporting models, provide an in-depth understanding of process behavior.

---

[8] D. Nikolić, A. Seidel-Morgenstern, M. Petkovska, Chem Eng SCI, 137 (2015) 40-58.
[9] U. Krewer, T. Vidakovic-Koch, L. Rihko-Struckmann, ChemPhysChem, 12 (2011) 2518-2544.
[10] O. Deutschmann, J.-D. Grunwaldt, Chem Ing Tech, 85 (2013) 595-617.
[11] Power to ammonia, http://www.ispt.eu/media/PERSBERICHT-Power-to-ammonia_Eng.pdf
[12] K.F. Kalz, R. Kraehnert, M. Dvoyashkin, R. Dittmeyer, R. Gläser, U. Krewer, K. Reuter, J.-D. Grunwaldt, ChemCatChem, 9 (2017) 17-29.
[13] F. Kubannek, U. Krewer, Electrochimica Acta, 210, 862-873, 2016.
[14] R.J. Berger, F. Kapteijn, J.A. Moulijn, G.B. Marin, J. De Wilde, M. Olea, D. Chen, A. Holmen, L. Lietti, E. Tronconi, Y. Schuurman, Appl. Catal., A: General, 342 (2008) 3-28.

Various experimental methods have been developed to analyze the state of the catalyst, together with concentration and temperature profiles within the reactor, both *in situ* and spatially resolved. A number of these methods (TPD, TPO, TPR, TPSR, SSITKA or TAP) are now firmly established in the field of reaction technology[15]. Such techniques are often combined with spectroscopic methods, such as X-ray spectroscopy[16,23], nuclear magnetic resonance imaging[17] and laser spectroscopy methods[18], to non-invasively visualize the catalyst, porous media and the fluid phase, respectively (see Fig. 6).

Inexpensive capillary techniques[19] have extended the portfolio of experimental techniques to ascertain species concentrations and temperatures inside reactors. Furthermore, multi-scale modeling has led to computational tools for the transient three-dimensional simulation of the flow field, the species and temperature profiles and the state of the catalyst[20]. The fusion of both surface and gas phase experimental methods with multi-scale modeling techniques is expected to afford new insights into understanding of the interactions of kinetics and transport in catalytic reactors, leading to an improved, knowledge-based design and optimization in reaction engineering[21].

D OPERANDO AND *IN SITU* SPECTROSCOPIC METHODS INCLUDING SPATIAL INFORMATION

Rational bottom-up development of catalytic processes requires an understanding of both the reactor and the catalyst itself[12,22,23]. It thus embraces spectroscopic monitoring of (a) the fluid phase (gas/liquid) including reactant/product concentrations and the gradients at the solid/fluid interface and (b) the catalyst itself. These studies should preferentially be conducted on ‘working’ catalysts (“operando”) operating under conditions corresponding to their real-life application[12,23]. Correlating structural changes with the catalytic performance is essential for appreciating complex mechanistic features and providing the basis for knowledge-based catalyst development. A good example is given by operando hard X-ray based methods, which yield information on the local structure and have been further developed for monitoring the interaction of the active sites with reaction intermediates. The high penetration power of X-rays allows the catalyst and its performance to be studied under various temperatures and gas atmospheres in specially engineered microreactor cells. In addition, the highly dynamic structural gradients along the catalyst bed can be monitored by 2D or 3D X-ray tomography,

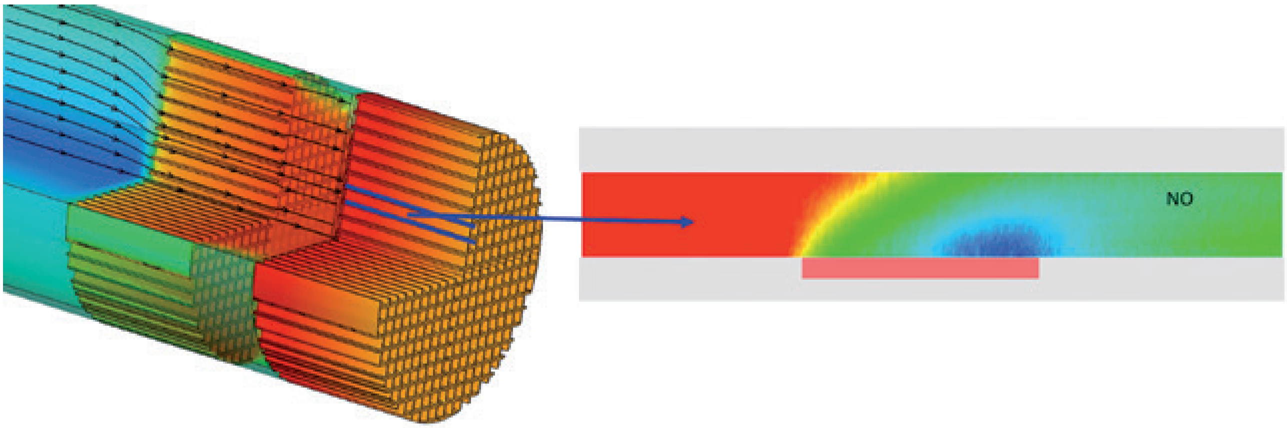


Figure 6: Computed velocity and temperature distribution in a monolithic honeycomb for syngas production (left; adapted from reference 20) and NO concentration in a single (half) channel of a diesel oxidation catalyst measured by Laser Induced Fluorescence (right; adapted from reference 18).

---

[15] TPD: temperature programmed desorption, TPO: temperature programmed oxidation, TPR: temperature programmed reduction, TPSR: temperature programmed surface reaction, SSITKA: steady state isotopic transient kinetic analysis, TAP: temporal analysis of products.

[16] B. Kimmerle, J.-D. Grunwaldt, A. Baiker, P. Glatzel, P. Boye, S. Stephan, C.G. Schroer, J. Phys. Chem. C, 113 (2009) 3037-3040.

[17] A. Brächer, R. Behrens, E. von Harbou, H. Hasse, Chemical Engineering Journal, 306 (2016) 413-421.

[18] A. Zellner, R. Suntz, O. Deutschmann, Angewandte Chemie International Edition, 54 (2015) 2653-2655.

[19] C. Karakaya, R. Otterstätter, L. Maier, O. Deutschmann, , Applied Catalysis A: General, 470 (2014) 31-44.

[20] M. Hettel, C. Diehm, H. Bonart, O. Deutschmann, Catalysis Today, 258, Part 2 (2015) 230-240.

[21] O. Deutschmann, Catal Lett, 145 (2015) 272-289.

[22] O. Deutschmann (Ed.), Wiley-VCH, Weinheim, 2012.

[23] J.-D. Grunwaldt, J.B. Wagner, R.E. Dunin-Borkowski, ChemCatChem, 5 (2013) 62-80.

by exploiting the high time and spatial resolution of these techniques.

As illustrated in Figure 7 for a model Pt/Al_2O_3 diesel exhaust oxidation catalyst, the necessity for temporally and spatially resolved spectroscopic investigations is crucial for an unambiguous interpretation of catalytic behavior during temperature and gas composition transients, which induce intense dynamics in the reaction zone along the catalyst bed. Such dynamic studies will be of increasing importance in future[12,24].

A further example of a powerful non-invasive analytical method is nuclear magnetic resonance (NMR) spectroscopy, which enables both qualitative (structure elucidation) and quantitative characterization. It is thus a valuable tool for *in situ* monitoring of reactions and other processes (see Fig. 8). It can even resolve chemically similar compounds and, in contrast to optical spectroscopy, the composition of mixtures can be directly determined from the spectra measured without prior calibration. This feature is especially useful when analyzing reacting mixtures containing intermediates or products that cannot be otherwise isolated.

Major advances in experimental reaction technology are to be expected in the not too distant future due to the synergy between high-resolution experimental data and numerical simulations.

The further improvement of existing tools, as well as the development of new imaging sensors and measuring methods will enable the multi-dimensional measurement of process and flow parameters (local phase velocities, phase components and concentration and temperature fields).

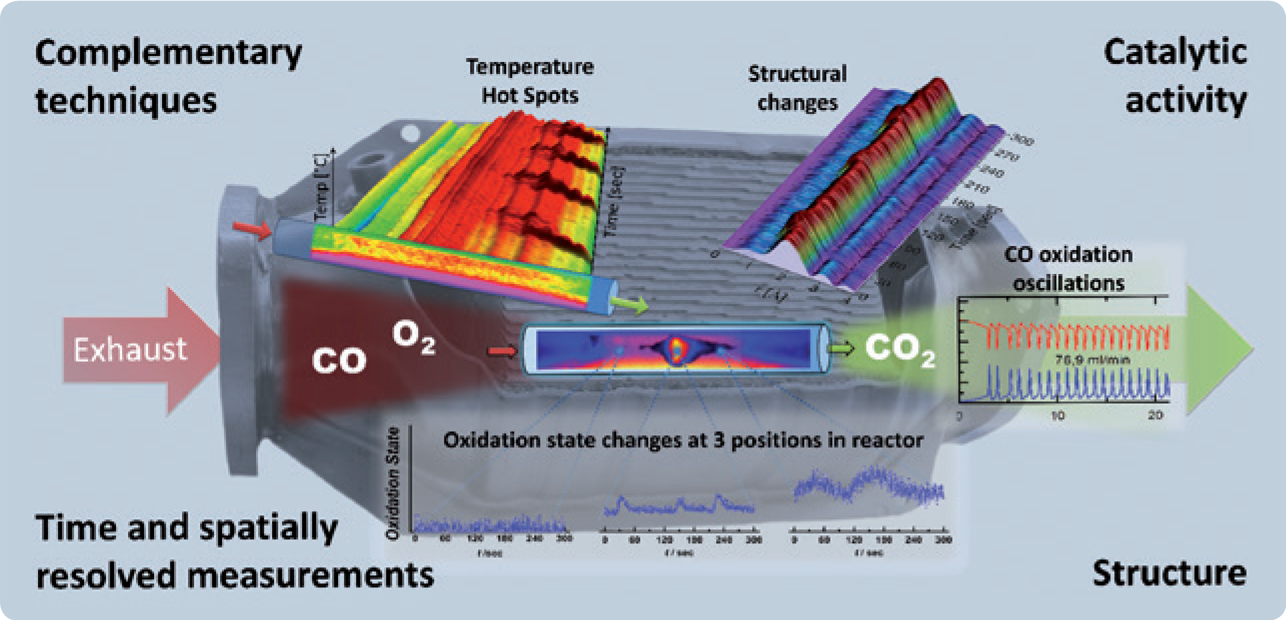


Figure 7: Operando spatially and time-resolved X-ray absorption spectroscopy and infrared thermography study of Pt/Al_2O_3 diesel oxidation catalyst during oscillatory CO oxidation activity (1000 ppm CO, 10 % O_2 in He) at 125°C[24].

---

[24] Reprinted from Journal of Catalysis, 328, Andreas M. Gänzler, Maria Casapu, Alexey Boubnov, Oliver Müller, Sabrina Conrad, Henning Lichtenberg, Ronald Frahm, Jan-Dierk Grunwaldt, Operando spatially and time-resolved X-ray absorption spectroscopy and infrared thermography during oscillatory CO oxidation, 216-244, 2015, with permission from Elsevier.

Research Needs

1. Further development and broader application of kinetic models determined via transient and spatially resolved techniques

2. More extensive utilization of the potential of additive manufacturing for laboratory reactors, especially in developing new material concepts for design and construction

3. Full implementation of Industry 4.0 standards in catalyst and process development

4. Development of new methods and set-up (e.g. microreactor set) that enable the application of operando and *in situ* spectroscopy (such as X-ray based techniques and NMR)

5. Application of more flexible, cost-efficient and compact “low cost spectroscopic devices”, like bench-top NMR spectrometers, for reaction and process monitoring

6. Robust data analysis (comprehensive data sets, small analyte concentrations , complex multicomponent mixtures, etc.) – “Big Data”

7. Functionalization of surfaces in contact with the process media to facilitate corrosion protection, wetting behavior, to introduce a desired catalytic activity and selectivity, to improve surface contact for enhanced local heat and mass transport, or other features

8. Multiscale modeling: generation of models able to simulate product properties and applications from reaction pathways and reaction engineering.

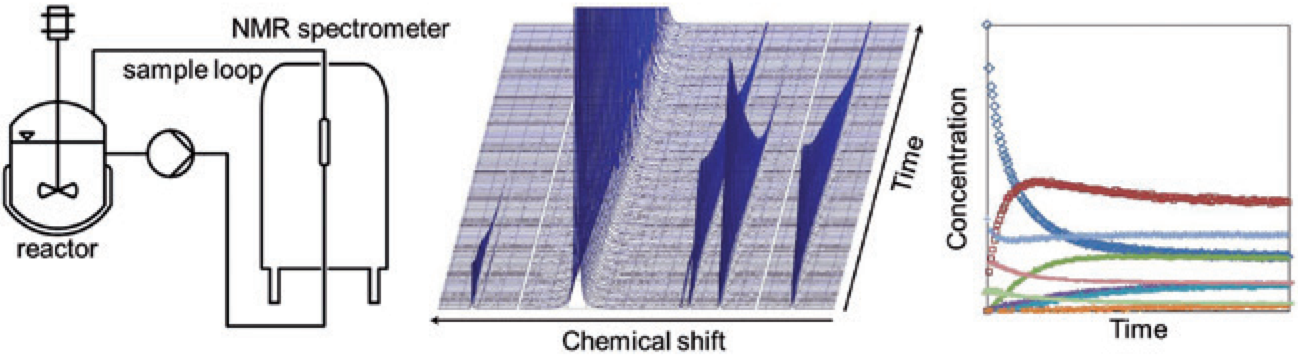


Figure 8: Workflow *in situ* NMR

4 Mathematical Modeling and Simulation

Detailed modeling of a chemical reactor lays the foundation for an efficient and rational design based on insights into the relevant phenomena and processes within the equipment. Additionally, modeling unlocks potential for process intensification and optimization deduced from these insights and, as such, is seen as the key to reliably predicting economic and ecological process parameters for industrial-scale production systems. While the descriptive quality, i.e. the physical and numerical fidelity of models and simulation methods respectively, has been greatly improved over the last decade, there is still a strong need for (i) establishing a suitable modeling platform, as well as (ii) including more rigorous physical models and powerful simulation tools. Given the extreme complexity of reaction engineering problems nowadays, a priority should be assigned to interdisciplinary research efforts, such as strategically focused programs and collaborative research centers.

A CHALLENGES

Mathematical modeling is of central importance in the field of chemical engineering, and is predicted to play a decisive role in the future development of a sustainable and resource-efficient process industry[25,26]. Modeling is especially challenging in the context of chemical reactor engineering. In particular, the following phenomena and processes need to be taken into account:

» **Reactivity**
of complex (i.e. multicomponent) chemical systems, especially networks of chemical reactions, that need to be described on a molecular level (i.e. with intrinsic kinetics).

»

» **Multiphysics**
i.e. the intense interplay and mutual dependence (i.e. close coupling) of the diverse relevant processes.

» **Multiscale**
i.e. the consideration of a wide range of relevant spatial and temporal scales.

» **Multiphase**
i.e. the mutual interaction of multiple phases, including the influence of phase dispersion interfacial effects.

» **Turbulence**
in particular the influence of turbulence on chemical reactions – especially regarding their inherent non-linearity and intimate interaction with various transport processes – as

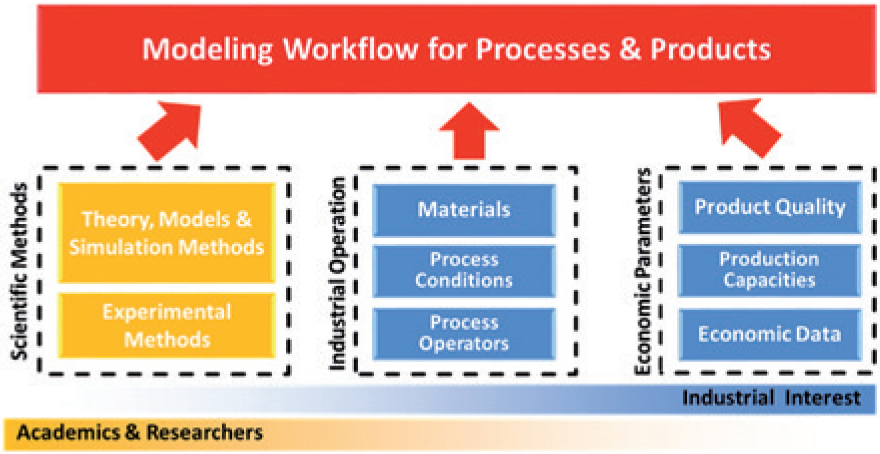


Figure 9: Factors that feed into the modeling workflow to describe chemical conversion processes and its products.

---

[25] F. Agterberg, J. Butler, D. Carrez, M. Gomez, R. Iden, E. Kessenich, et al., The vision for 2025 and beyond - A European Technology Platform for Sustainable Chemistry, 2009.

[26] SPIRE Roadmap, Brussels, Belgium, 2014.

well as the influence of further phases on turbulence in multiphase systems (e.g., turbulence modulation, or cluster induced turbulence).

The characterization of these phenomena and processes can be accomplished experimentally or by means of simulations. However, these two strategies are often closely linked, since only experiments enable mathematical models to be scaled and numerical simulations to be validated.

Thus, in what follows, we accept that every relevant phenomenon can be captured using appropriate mathematical models supplemented with appropriate boundary conditions. We shall focus on three objectives here: (i) establishing a common nomenclature for modeling and simulation, (ii) identifying recent pivotal achievements and trends, but also gaps in current models, simulation & post-processing tools, as well as (iii) defining milestones that help us to sketch out future progress in the field.

B WORKFLOW OF MODELING AND SIMULATION

A number of factors feed into the overall modeling workflow that is used to describe the pertinent processes and to reveal their influence on product quality (see Fig. 9).

Scientific methods comprise the basis of such a workflow and are supplemented by relevant insights from experiments and/or industrial experience. When establishing a rigorous model of an industrial process or product, economic targets also need to be considered, since parameters such as the available production capacity or market volume impose boundary conditions, or are necessary to interpret the final implications of the model.

Each modeling workflow consists of a number of steps, which are illustrated in Figure 10, and described in detail below.

B1 Processes and Phenomena

Reactivity
For chemical reactors a key quantity to be modeled is the reaction rate, which is typically of interest for more than one chemical reaction in the system. A large number of reactions often occur and the individual reaction rates depend on local species concentrations, temperature and pressure. These rates are often predicted based only on postulated rate expressions (formal kinetics) that are fitted to experimental data. More recently, however, simulations of so-called "electronic models" (e.g., quantum Density Functional Theory, DFT[27]), together with atomistic models, have become popular to provide mechanistic insights into reaction pathways. Research that aims to determine the kinetics of a reaction network can be based on a distinct hierarchy of models, from quantum mechanical approaches to Monte Carlo-based methods[28]. The plurality of such formal and intrinsic kinetic models precludes a more detailed discussion here.

Multiphysics Problems
Multiple chemical and physical processes within a chemical reactor are very often found to be strongly coupled, give rise to a so-called a multiphysics problem. When addressing reaction engineering questions using mathematical modeling and

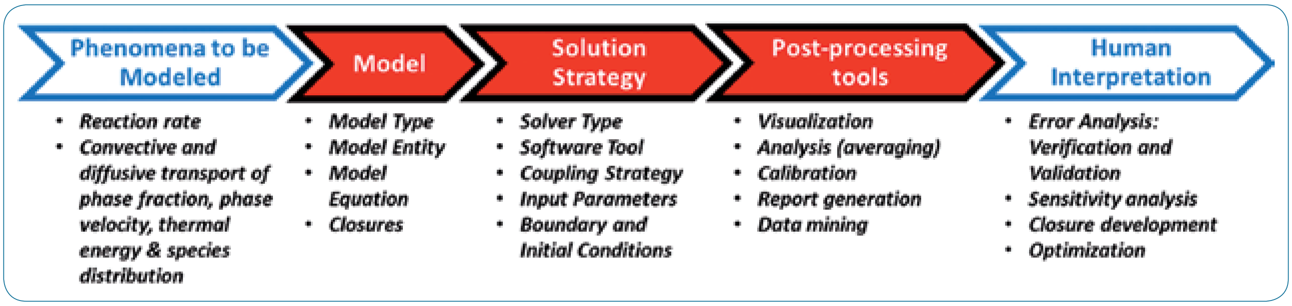


Figure 10: Details of the modeling workflow for a chemical reactor and its products (red panels indicate the most critical components of the workflow).

---

[27] A.F. de Baas, L. Rosso, Modeling in FP7 NMP Programme Materials projects, Brussels, Belgium, 2015.

[28] M. Karplus, M. Levitt, A. Warshel, Development of Multiscale Models for Complex Chemical Systems, in: Nobel Laureate, The Royal Swedish Academy of Sciences, Stockholm, Sweden, 2013

numerical simulation techniques, it is imperative to account for the coupled nature of processes within the system in a consistent manner – both in terms of the mathematical and the numerical model.

Appropriate software tools have to be selected (cf. paragraph on "Solution Strategy"). When dealing with multiphysics problems, software offering the simultaneous solution of coupled equations and implicit discretization techniques are to be preferred whenever coupling of transport processes is expected to be intense and/or to take place at very different scales (i.e. for strong coupling and/or stiffness characterizing the system). Additional care should be taken when choosing a tool with an underlying flexible and extensible software design based on a mature (higher) programming language. Suitable multiphysics platforms, such as COMSOL, ANSYS Multiphysics (proprietary software) and OpenFOAM (open source software) are readily available and form a substantial basis for further developments. Only such platforms will enable and efficiently foster the combination of conventional reaction engineering models and modern approaches of computational continuum mechanics (CCM), in particular, Computational Fluid Dynamics (CFD) for multiphase flows and/or multicomponent systems. Moreover, the integration with established techniques of other disciplines, such as combustion engineering or atmospheric chemistry, has to be further enforced. For example, radiative heat transport has attracted recent research, fueled by the increasing interest in photocatalysis, artificial photosynthesis, and solar thermochemical conversions[29].

Multiscale Problems

If multiple models characterizing distinct processes at different scales are to be combined, one typically defines a "chain of models" to fomulate a so-called hierarchical (or horizontal) multiscale modeling approach. These models are executed simultaneously or sequentially in a side-by-side mode. For the modeling chain to work reliably over the several scales of interest, the consistency and interoperability within such a hierarchical multiscale approach plays a central role.

Apart from hierarchical concepts, integrated (or vertical) multiscale modeling strategies have emerged and made significant progress. These models aim to incorporate processes at multiple scales within a unified, typically more generic, modeling framework. Recent research has addressed the utilization of detailed (physico-)chemical knowledge on a molecular scale: e.g. in order to bridge the gap in scales when describing the viscoelastic flows of polymer solutions or polymer melts, for which so-called micro-macro models have been thoroughly investigated[30]. Such models attempt to couple conservation laws for macroscopic quantities (such as the velocity or the stress) in a consistent manner with other models to evolve a microstructure. Additionally, the spatial filtering (or volume averaging, VA) technique[31] and sub-grid-scale (SGS) models have recently been demonstrated to be a suitable means of addressing multiscale reaction engineering problems, for instance by alleviating the excessive spatial resolution demands of certain two-phase flow features (e.g. local transitions between a dispersed and a segregated flow regime[32,33], or the extreme concentration gradients surrounding rising bubbles[34]).

Generally speaking, there is a widespread need for sound and reliable multiscale modeling concepts based on mechanistic considerations, which can successively supersede traditional empirical approaches. Future research should be devoted to tapping into advances and existing knowledge from the molecular level. To this end, specially integrated multiscale approaches would seem to offer ernormous potential.

Multiphase Flows

The Modeling and simulation of multiphase flows presently involves a variety of different techniques and methodologies, which can best be classified according to the scale at which they are typically applied (i.e. the domain size) and their ability to capture a specific level of detail (i.e. distinct features) directly.

---

[29] J.R. Scheffe, A. Steinfeld, Oxygen exchange materials for solar thermochemical splitting of H_2O and CO_2 : a review, Mater. Today. 17 (2014) 341–348. doi:10.1016/j.mattod.2014.04.025.

[30] R. Keunings, Micro-Macro Methods for the Multi-Scale Simulation of Viscoelastic Flow using Molecular Models of Kinetic Theory, Rheol. Rev. (2004) 67–98.

[31] H. A. Jakobsen, Chemical Reactor Modeling, 2nd Edition, Springer, Cham, Switzerland, 2014.

[32] K.E. Wardle, H.G. Weller, Hybrid Multiphase CFD Solver for Coupled Dispersed / Segregated Flows in Liquid-Liquid Extraction, Int. J. Chem. Eng. (2013) 128936.

[33] H. Marschall, O. Hinrichsen, Numerical Simulation of Multi-Scale Two-Phase Flows Using a Hybrid Interface-Resolving Two-Fluid Model (HIRES-TFM), J. Chem. Eng. Japan. 46 (2013) 517–523. doi:http://doi.org/10.1252/jcej.12we074.

[34] D. Bothe, S. Fleckenstein, A Volume-of-Fluid-based method for mass transfer processes at fluid particles, Chem. Eng. Sci. 101 (2013) 283–302. doi:10.1016/j.ces.2013.05.029.

Direct Numerical Simulation (DNS) methods attempt to resolve all relevant temporal and spatial scales. DNS for multiphase flows can be broken down into (i) interface capturing, (ii) interface tracking and (iii) front tracking methods, depending on how the interface is represented. It is important to stress that the various multiphase DNS methods exhibit different numerical advantages and disadvantage). Also, DNS methods differ in their physical trustworthiness when it comes to the question of whether specific processes and phenomena can be readily incorporated. Discrete Element Methods (DEM) and Eulerian-Lagrangian (EL) methods resolve the dispersed (fluid or solid) phases individually, each up to a certain simplified level of detail. In contrast, the Eulerian-Eulerian (EE) methods only take into account the mutual interaction of the bulk and dispersed phase(s) by means of closure models. Generally speaking, with a decreasing level of detail, the methods' capacity to describe multiphase flow systems at larger scales increases, as does the complexity and challenges of closure modeling.

The finite computational resources available restrict the level of detail that can be dealt with by a particular simulation method for a given domain size (e.g. a representative volume, a section of the reactor, etc.). There is therefore a great demand for modern HPC techniques and specialized numerical methods to alleviate this bottleneck. For instance, the local dynamic adaption of the computational grid and dynamic load balancing significantly cuts computational costs. Flexible approaches for grid refinement and readily accessible load balancing is important for the effective exploitation of these HPC techniques in reaction engineering applications. Figure 11 illustrates an adaptively refined mesh around a single rising air bubble in an aqueous bulk phase, where the mesh has been locally modified according to multiple criteria, such as the location of the gas-liquid interface, the vorticity in the bubble wake, the liquid concentration gradient, etc. Figure 11 also depicts the concentration field of dissolved gas-phase species predicted in the wake of the bubble.

Turbulence

Some significant advances have been made in the field of multiphase turbulence in particulate flows (more precisely, small-scale fluctuations of phase fraction and velocity due to spontaneous clustering and/or turbulent flow phenomena). Appropriate closures for a "cluster scale effectiveness factor" have also been proposed[35]. Recently, transport equations and

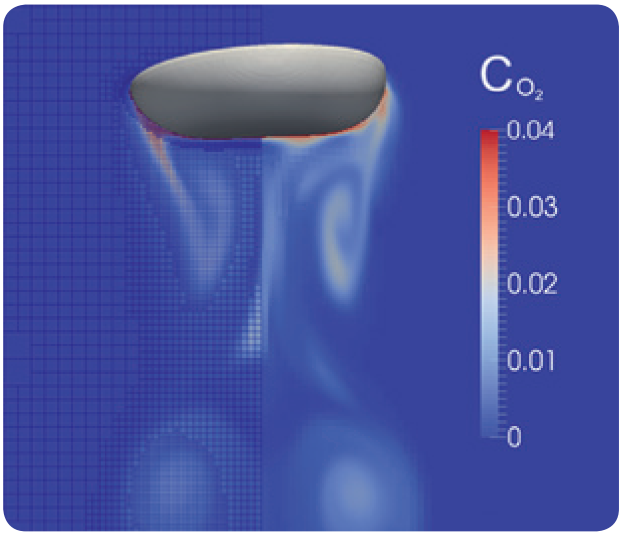


Figure 11: DNS result of oxygen mass transfer from a single rising air bubble using local dynamic adaptive mesh refinement with multiple refinement criteria and dynamic load balancing. Courtesy by Dipl.-Ing. Daniel Deising and Dr.-Ing. Holger Marschall (TU Darmstadt, Mathematical Modeling and Analysis, Prof. Dr. rer. nat. Dieter Bothe).

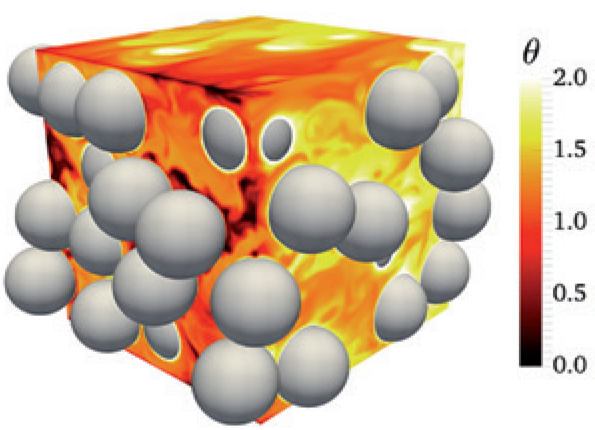


Figure 12: Direct Numerical Simulation of momentum, heat and mass transport in a gas-particle suspension between two infinite parallel adiabatic walls with isothermal particles at Reynolds = 400 and Prandtl = 1. The volume fraction of the particle phase in the computational domain is 0.4. Colors represent the dimensionless fluid temperature field. The simulated domain is discretised using a Cartesian grid of 200 ^{3} cells (reproduced with permission from F. Municchi, TU Graz).

---

[35] W.S. Holloway, Continuum modeling of gas-particle flows across multiple scales, PhD Thesis, Princeton University, 2012.

closures for key fluctuating variables in these flows have been derived[36]. While most of these developments focus on flow predictions for gas-particle systems at high Stokes numbers, they nourish the hope that the corresponding closures for species and thermal transport models will be forthcoming in the not too distant future (see Fig. 12 for a DNS of such systems). This would open the door to more reliable predictions of reaction rates in models devised for large-scale applications, e.g. fluidized bed reactors.

B2 Model Definition

A useful nomenclature for modeling and simulation has been promoted by the European Commission for material modeling[27], which is equally applicable to processes in the chemical industry. Such a nomenclature greatly facilitates the dialogue and mutual understanding between industrial chemical engineers, software developers and academia. Furthermore, this nomenclature can be brought to bear at all modeling levels irrespective of the scale being studied. It defines a model according to:

- its type (deterministic or stochastic, continuum or discrete, etc.),
- the entity to be modeled (a finite volume, a particle, a cloud of bubbles, a compartment, etc.),
- the model equation(s) to be solved (e.g., Newton's equation of motion, a species transport equation, or the radiative transfer equation to predict thermal fluxes), and
- the constitutive equations (i.e. the respective closure models and physical principles formulated as correlations) that are used in the model (e.g., Fickian diffusion approach, or a kinetic expression for the reaction rate). This encompasses classical "static" correlations, the tabulation of closure relations (e.g., via pre-computed, or *in situ* adaptive tabulation[37]), as well as procedures that perform dynamic parameter adjustment (e.g. via re-filtering of the solution[14]).

B3 Solution Strategy

Model-based design of chemical reactors involves different fields of modeling, simulation and optimization. It includes forward simulations with models of different detail and complexity, model analysis such as sensitivity and stability analysis, and rigorous optimization such as parameter estimation and optimal design. These fields together provide fundamental understanding of the occurring physical and chemical phenomena. The model analysis and rigorous optimization allow for designing robust, intensified and efficient chemical reactors and processes. This is especially advantageous when dealing with complex reaction systems since here the optimal reactor design can be quite non-intuitive due to the occurrence of multiple phenomena in these systems. In different simulation fields, the solution strategy differs. Yet one can generally distinguish between the

- numerics and type of solver (e.g., a finite difference method, or a (semi-)analytical solution of a model),
- software tool used (open-source or closed source), including the parallelization strategy (i.e., MPI and/or SMP parallelization) and hardware requirements (CPU- and/or GPU-based),
- coupling strategy between multiple model equations (e.g., explicit or implicit coupling, coupling interval), as well as
- representation of the solution domain (0D/1D/2D/3D), including the initial and boundary conditions

Software quality is decisive for its viability and special attention should therefore be paid to its support, upgrade and compatibility features. A higher programming language and proven software design to bolster these aspects of software quality are seen as the key to guarantee computational performance for future hardware architectures used in high performance computing (HPC) clusters (for a typical result of an Euler-Lagrange simulation using HPC resources see Fig. 13).

---

[36] S. Schneiderbauer, Cluster induced turbulence (CIT) – A spatially averaged two-fluid model (SA-TFM) for dense gas-solid flows, in: 24th ERCOFTAC ADA Pilot Cent. Meet., 2016.

[37] S.B. Pope, Computationally efficient implementation of combustion chemistry using in situ adaptive tabulation, Combust. Theory Model. 1 (1997) 41–63.

[38] A. Ozel, G. Rubinstein, S. Sundaresan, A Dynamic Drag Model Using Sub-grid Scalar Variance of Solid Volume Fraction for Gas-Solid Suspensions Effect of Meso-scale Structures, in: AIChE Annu. Meet. 2016, AIChE, San Francisco, 2016.

Thus some of the most important points when it comes to the software tool used for the solution of model equations are:

- a hierarchical software design (i.e. reusability of individual software components),
- a modular design that permits the extension and exchange of individual modules, as well as
- a rich set of links (software interfaces) to enable online- and offline-hookups (e.g. with other software tools for co-simulation, or on-the-fly post-processing), as well as integration into modeling platforms (i.e. a workflow software that allows the connection of further software tools).

B4 Post-processing

With the increasing amount of raw data to be processed, efficient and effective post-processing has become a must. While post-processing is often packaged within the simulation tool, it is also useful to have both dedicated visualization tools (e.g., ParaView, TecPlot, EnSight, etc.), and modules that can be linked to the solver for on-the-fly post-processing (e.g., CPPPO[39]). The most basic features of such tools are data analysis (e.g. spatial and/or temporal filtering, calculation of statistics), or the automated generation of reports. More sophisticated tools address the automated evaluation of outcomes, e.g. by comparing simulation and experimental data. Calibration workflows that dynamically adjust parameter values during a simulation run are becoming increasingly important, as a consequence of the increasing availability of data and computation resources.

B5 Human Factor

Finally, human interpretation is still a critical factor when it comes to model verification and validation. For instance, it is essential to have access to workflows for automated testing (e.g., as realized using Jenkins, https://jenkins.io) so that staff can devote themselves more to the interpretation of results.

One important component in a modeling workflow is the human brain itself. Recent work has therefore focused on assisting the end-user of the workflow by providing links to a data base for data comparison and final development work (e.g., using the KNIME software[40]).

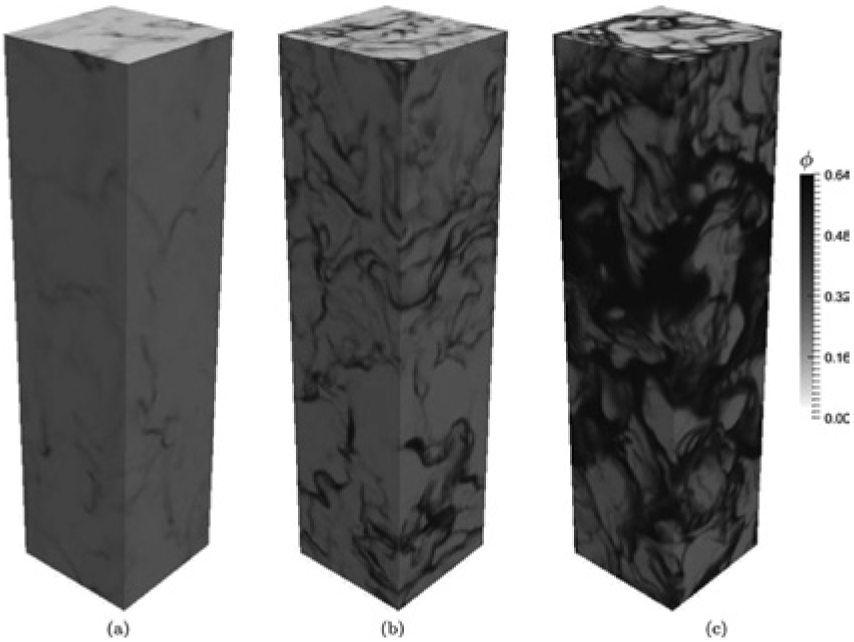


Figure 13: Snapshots of the local particle volume fraction concentration in a fluidized bed involving up to 31.5 million particles (panels illustrate results from different particle volume fractions of (a) 0.02, (b) 0.1 and (c) 0.3; from Ozel et al., Chemical Engineering Science 155(2016):258–267). Reprinted with permission from Elsevier.

---

[39] F. Municchi, C. Goniva, S. Radl, Highly efficient spatial data filtering in parallel using the opensource library CPPPO, Comput. Phys. Commun. 207 (2016) 400–414. doi:10.1016/j.cpc.2016.05.026.

[40] A. Tiwari, A.K.T. Sekhar, Workflow based framework for life science informatics, Comput. Biol. Chem. 31 (2007) 305–319. doi:10.1016/j.compbiolchem.2007.08.009.

Finally, following state-of-the-art software engineering principles, such as agile development, is vital when developing or extending reaction engineering software. The typically complex model interaction necessitates test-driven development techniques to counter complexity when developing, or substantially extending software. Software development must also ensure its future compatibility and relevance, even if this sometimes entails re-writing of code, or even creating a new software tool.

C ACHIEVEMENTS & TRENDS

The following achievements and trends can be identified in the field of modeling and simulation of chemical reactors:

» Modeling in certain sub-genres (e.g. microreactors) has made significant progress, and simple (analytical) solutions are readily available (e.g. even for strongly exothermic reactions[41]). Future activities may also incorporate such analytical solutions into simulation platforms.

» A large set of open- and closed-source software tools for describing chemical reactors have been established, which now serve as data generators. Consequently, focus has shifted from data generation to advanced data processing.

» The integration of models and simulation tools into information processing and modeling platforms is currently attracting attention to further optimize and control existing and future processes, as well as to enable knowledge-based decision making taking economic and eco-efficiency into account[26]. This has fueled (even more) rigorous model validation schemes considering realistic process environments, research toward a more complete process understanding (i.e., more rigorous models) and very large-scale models that are able to treat the interaction of full process chains on the plant level.

» Numerous cloud computing solutions are offered nowadays: end users do not have to worry about hardware or software purchasing anymore, with applications instead being offered on a pay-per-use basis. This has significantly lowered the barrier for embarking upon modeling and simulation work. However, challenges with model selection and interpretation of simulation results still remain, requiring highly-trained staff in the field of modeling and simulation.

» While there has been a lot of hype about GPU-based desktop computing, so far there was comparatively little impact on the tools developed. There are a number of reasons for this, e.g. memory limitations, or the restricted scalability of previous attempts to harness multiple GPUs for a single simulation.

» Supercomputing facilities, e-infrastructure, and even “exascale” computing projects have been launched internationally (e.g., http://www.max-centre.eu/mission; http://www.eesi-project.eu). These initiatives focus on exaFLOP computing, i.e. a computing speed of one thousand petaFLOPs (or one quintillion, i.e., 1018 floating point operations per second). This is about 100 times faster than the currently largest computing cluster in Europe and 10 times faster than the leading computing cluster world-wide. Exascale initiatives encourage the hope that ever larger benchmark simulations can be performed in the future and that significantly more detailed simulations (e.g. based on direct numerical simulations) can be carried out that will help in the verification of outcomes. This is important for the discipline as a whole, since gaps in the modeling workflow can be eliminated and greater confidence elicited in models and their results.

Research Needs

In the following, we identify three directions in which research and development activities might potentially have the greatest impact.

Towards unified and formalized modeling and simulation platforms

1. Extending existing toolboxes and making them compatible (e.g. via platforms such as KNIME) is promising, since it can harness the strengths of all the tools on a platform. This is the prerequsite for connecting models with different levels of complexity.

---

[41] T. Westermann, L. Mleczko, Heat Management in Microreactors for Fast Exothermic Organic Syntheses - First Design Principles, Org. Process Res. Dev. 20 (2016) 487–494. doi:10.1021/acs.oprd.5b00205.

2. Formalizing the whole workflow (including problem specification, model selection and solution strategy, as well as post-processing) helps to avoid faults and allows a close integration of the relevant scientific disciplines (i.e. computer and computational science, physics and mathematics, chemistry, chemical engineering). Such an interdisciplinary research perspective, complying with open data and open source doctrines, will significantly accelerate scientific progress in reaction engineering.

3. Modularizing simulation tools (physical & chemical models, closures, as well as numerical methods and algorithms) will be decisive for the success of individual software solutions, since integration into different simulation platforms becomes the limiting factor.

4. Software tools based on an open philosophy (open source, open data, open science), ideally relying on an LGPL license (which allows open- and closed-source modules to be linked into a software product) may have a competitive edge compared to closed-source solutions.

Closing key gaps in the modeling workflow

1. Faster and more robust process models are needed for process optimization and intensification. Also, the (more complex) control of intensified processes, which are often highly integrated and operated in a continuous rather than a batch mode[42], will become an issue that needs to be addressed.

2. A key gap in the holistic optimization of chemical reactors is the modeling of material synthesis and material response: questions like “Which materials are feasible for these operating conditions?”, or “Can we synthesize this catalyst?” still need to be answered with comparatively costly experimentation. Closing this gap would greatly speed up reactor design, as well as the optimization of existing and future reactor technologies.

3. Mechanistic models and closures which describe meso-scale phenomena, e.g., fluctuations of voidage and velocity in two- and multi-phase reactors need to be drawn up, improved, and validated with pilot- and full-scale experimental data.

Adapting to future computing infrastructure

1. It will be decisive to make high performance computing (HPC) available to engineers (e.g., by dedicated training), since desktop solutions may not be able to compete with future (cloud) computing resources that harness HPC resources.

2. It will become important to introduce HPC-ready solution strategies for the model equations, e.g., Lattice-Boltzmann solvers that scale well on more than 1000 CPU cores. Also, in some niche applications GPU-based solutions will be introduced, most likely also necessitating alternative solution strategies to the ones currently employed.

3. Over the next ten years, researchers will have to think about shifting to exascale-ready modeling and software approaches that rely on particle and/or lattice-based solution strategies. Currently, it appears that only these strategies are able to run efficiently on › 1 million CPU cores, i.e. the future HPC resources.

---

[42] European Roadmap for Process Intensification, Ministry of Economic Affairs, Netherlands, 2008

5 Reactor Design and Process Development

The basis for process development and associated reactor design is an exact knowledge of stoichiometry, thermodynamics, kinetics, transport phenomena and relevant safety data. This can be used to determine the characteristic reaction time scale and the heat being released or supplied.

These quantities must be matched to the transport processes in the reactor, so that the reaction can be carried out safely and with high yields. Miniplant studies are often imperative because the process can only be realized and investigated in the detail necessary with recycle streams, partial loading, start-up and shut-down. With the help of a good model, the process can be transferred directly to production plant scale, but a pilot-plant is often built as a further insurance. The current state of chemical reactor development indicates that modern techniques for process intensification have in some cases already entered industrial practice.

A OPTIMIZATION OF TRANSPORT PROCESSES IN THE REACTOR

Transport phenomena can be categorized into momentum, heat and mass transfer processes[43]. Furthermore, the phases involved (solid, liquid, gaseous, supercritical) and phase boundaries as well as interfaces can be identified, on or at which a transfer process with or without a chemical reaction takes place. With transport process one needs to distinguish between diffusion, laminar dispersion and turbulent, chaotic exchange. This brief survey illustrates the complexity of the transport processes between the molecular and the plant equipment scale. In addition to the length scale at which the

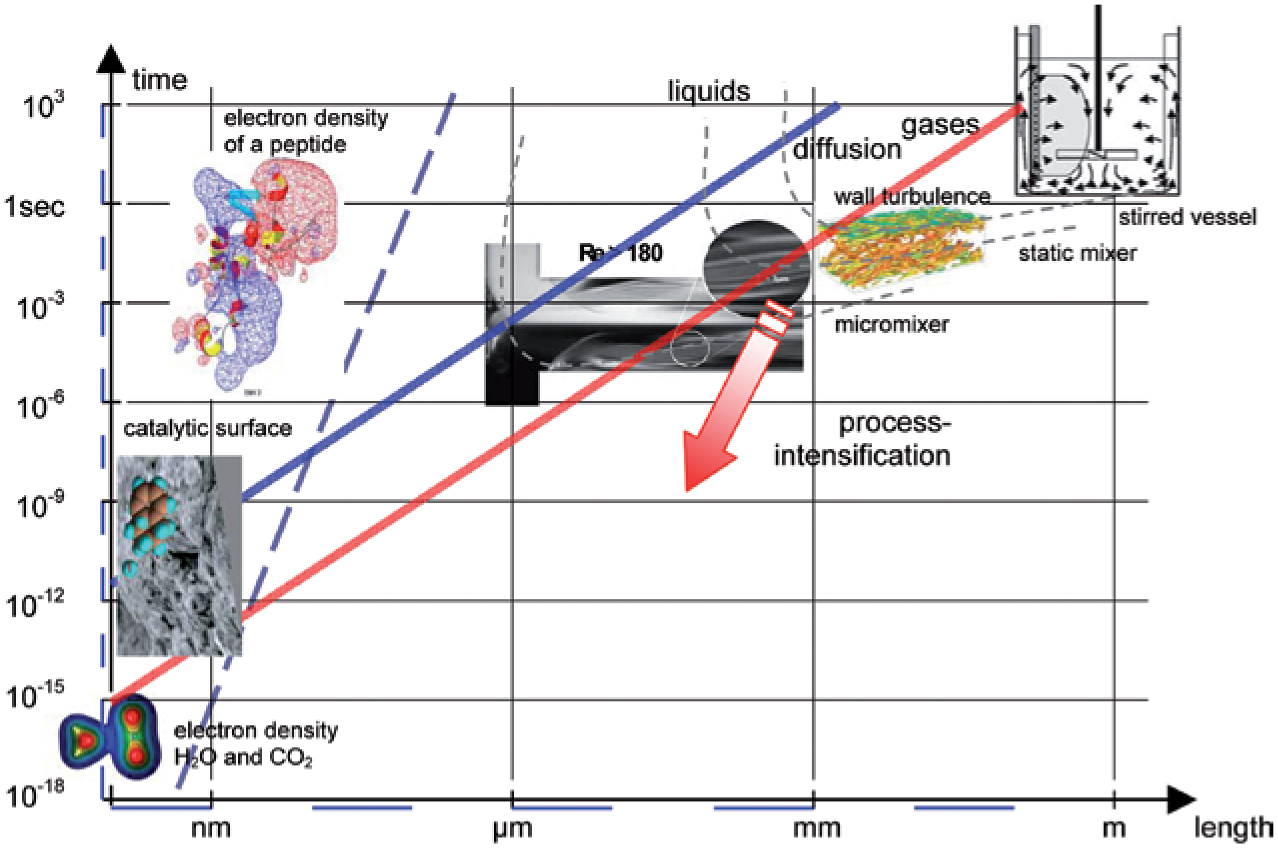


Figure 14: Typical length and time scales of transport processes and chemical transformations relevant for reaction technology

---

[43] Bird, R.B., Stewart, W.E., Lightfoot, E.N., Transport Phenomena, 2. Auflage, Wiley, New York, 2007.

transport processes occur, the time scale is also relevant, because of the relative rates of transport and chemical reaction. For this reason, the transport phenomena for chemical species and energy form a bridge spanning molecular processes up to equipment implementation. Understanding them is thus essential for the successful future development of reaction technology.

Figure 14 depicts the typical time scale of transport processes, depending on the length scale of the process or apparatus. The fastest molecular processes for small molecules proceed within 10-18 s, and catalytic reactions are only slightly slower. The transport rate of macromolecules or diffusion across interfaces is significantly slower and can thus come to dominate the overall process. On the upper right, the typical length and time scales in a stirred tank are given as the standard item for reaction technology. In addition, the numerical simulation of wall turbulence is illustrated. The two sloped lines indicate the average displacement of molecules in gases or liquids in a given time period. In microchannels, for example, fluid structures of a few micrometers with mixing times of less than one millisecond are achieved. The figure shows the large distance between the apparatus-based length and time scales and those of chemical transformations. A major goal of further improvements must be to close this gap.

Transport processes can, in some cases, be described analytically, for instance laminar flow, boundary layer equations, heat conduction and diffusion. Other models are based on dimensionless numbers and their correlations. The description of turbulence is based on concepts that are more than 50 years old. In the meantime, however, numerical methods have become established to the point where they can make a significant contribution in determining turbulent exchange variables. The modeling of the turbulence and the experimental validation on a fine scale nevertheless remain major challenges. Measurement methods have thus been developed and refined, which can measure velocities, temperature and concentration fields at the micrometer scale in simple geometries. The modeling of the residence time distribution is based on standard models, which, however, are only of limited use for real equipment. Local and integral measurements are therefore still essential.

In chemical reactors the participating phases are seldom homogeneously distributed. The majority of reaction systems is heterogeneous and must be described by multiphase flow concepts. The transport processes at phase boundaries have up to now been described by analytical correlations and molecular dynamics simulations, but with a large gap between the continuum and the molecular levels. The same is true for catalysis on solid surfaces and in porous materials.

A promising path to intensify transport processes in reactors as well as to acquire an improved understanding of the fundamentals is the transition from random configurations to well-defined structures in the micro- and millimeter range. Substantial progress has already been made in the description of the transport processes with chemical reactions in small channels, in particular in the case of laminar, single-phase flows and clear-cut two-phase systems, such as the Taylor flow in capillaries. Further current research directions are the use of mini- and micro-emulsions as microreactors, processes in micelles and vesicles in colloid chemistry, as well as the use of sponges and other novel porous media for various reaction-related applications.

Another topical trend is alternative activation and energy supply for chemical reactions. These techniques include energy input by cavitation, ultrasound, micro- or radio waves and light. Novel fluids such as ionic liquids and supercritical media also have a great potential for applications in reaction technology and are still largely a closed book in terms of their influence on the transport properties.

The overall aim is to adapt the mass and heat transport processes to the chemical reactions taking place, so that a maximum degree of conversion is achieved with the highest possible selectivity. The heat transfer must always be carried out as efficiently as possible, in order that the optimum temperature for the chemical reactions is guaranteed at every location in the reactor. In the majority of cases, the most intensive possible transfer of substances possible is sought. However, there are interesting special cases, in which it is an advantage to hinder mass transport processes. This includes, for example, phase transfer catalysis or regio-selective catalysis, in which the access of reactants to and/or the release of products from microporous systems are deliberately restricted. In other multiphase systems, such deliberate impediments to mass transfer processes with advantages in terms of product distribution are conceivable and await development.

The interaction of reaction kinetics and thermodynamics with the associated transport processes in the reactor is a highly coupled system, which is not yet fully understood, particularly in the case of multiphase reactors. Further experimental and theoretical advances are required in this field.

Research Needs

1. Use of micro- and millistructured reactors with well-defined channel dimensions as model systems, especially for multiphase reactions,
2. Experimental and theoretical treatment of turbulent flows in extended multiphase systems,
3. Optimization of mass transfer processes, for example, by tailor-made porous systems in catalysts, micellar systems and microemulsions.

B MINIPLANT TECHNOLOGY AND EXPERIMENTAL SCALE-UP

After finding a promising new chemical route and devising the catalysts needed, the process development process begins. Starting from laboratory synthesis, process concepts are developed and the individual steps of the process are tested in the laboratory and by simulation. The interaction between the individual steps can also be carried out very efficiently in joint simulation and development environments (for example, Aspen Engineering Suite). The influence of initially unknown by-products, which accumulate in recycle streams and possibly lead to fouling, i.e. plugging of pipelines, machines and equipment, but which cannot be entirely captured by simulations, can be investigated and understood with the aid of a minplant comprised of laboratory apparatus items (separation columns, reactors, etc.) . A miniplant is a small-scale, complete plant with production rates of 100 g h^{-1} consisting of raw material preparation, synthesis, downstream processing and all recycles and is thus one of the most powerful experimental tools of modern process development (see Fig. 15).

After validation of the process concept in the miniplant, the next conventional step is the planning and construction of a pilot-plant with a significantly higher capacity. The scale of the pilot plant is between that of the miniplant and that of the subsequent industrial installation. Production capacities of several kg h^{-1} to t h^{-1} permit, for example, application tests or customer deliveries on a larger scale as well as the study of the plant behavior under semi-production conditions. The operation of the pilot-plant is used to complete and verify existing data and documentation. It is one of the main cost drivers in the commercialization of technical processes and often leads to a considerable extension of development times. Hence these days, the construction of a pilot-plant should be the exception rather than the rule.

With the improvement of the simulation programs for the modeling of processes, the so-called holistic “integrated miniplant technology” as a combination of experimental miniplant technology with process simulation has become increasingly important in the last few years, since the synergy between miniplant technology and mathematical simulation results in just as good scale-up reliability as the use of a pilot-plant.

The basis for reactor scale-up is setting up and solving the mass, energy and momentum balances, represented by a system of coupled partial differential equations, which must be solved numerically. In early phases of process development, however, this rigorous method often lacks the necessary material data, kinetic data and clear boundary conditions. Therefore, one still needs to rely on dimensional analysis and

Figure 15: Modular dosing unit for miniplant for various liquids
(source: HNP Mikrotechnik, MoDoS)

dimensionless parameters, reflecting the ratio of system-relevant terms in the above-mentioned balance equations.

The experimental scale-up is particularly easy in the case of multitubular or plate reactors, since the scale-up can be carried out from pilot experiments in the single-tube or one-channel reactor via a “numbering-up”. This strategy is also adopted in the case of microstructured reactors with multiple parallel flow channels, whereby an appropriate design of the distributor is absolutely crucial to ensure an even distribution of flow to the individual channels.

In chemical processes involving large reactor volumes with complex fluid dynamics, a scale-up is at present still only possible via restrictive scale-up factors in order to be able to master the risk of scale transfer.

Research Needs

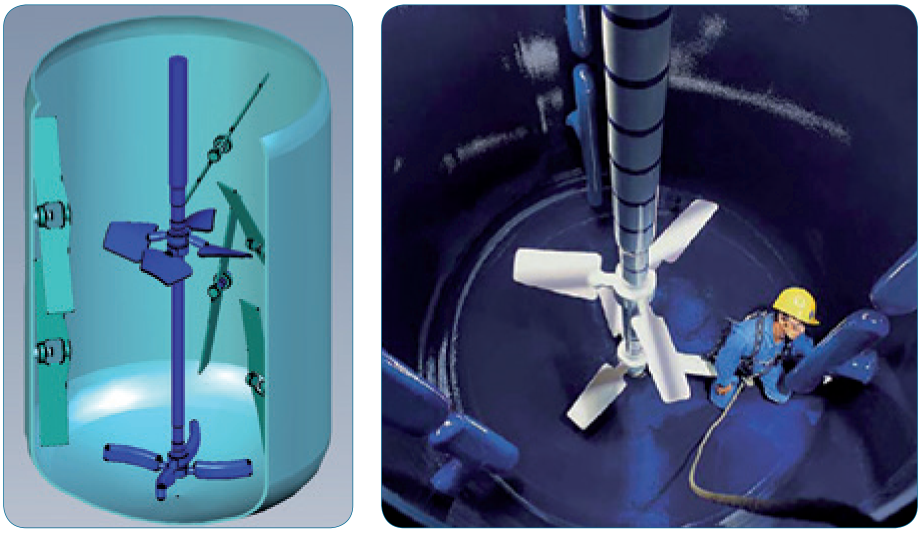
1. Increase the efficiency of the miniplant operation by:
   - cost-effective automation,
   - Employing reusable modules in laboratory systems, the models of which are already accessible in the model library of the simulation environment,
   - Improvement of the scalability of apparatus (for example for the processing of solids) from the laboratory to the technical scale,
   - Enable and exploit additive manufacturing (3D printing) to accelerate toolset development and implementation in labs.
2. Avoidance or reduction of pilot tests by means of validated models for reactor scale-up and development of tools for the assessment and limitation of risks of scale transfer to the production scale,
3. Development of process and plant concepts and reactor technologies, including accelerated and simplified scale-up, e.g. through numbering-up.

C EQUIPMENT DEVELOPMENT

Initial situation / state of the art

The development of the equipment technology for the construction of chemical reactors goes hand in hand with the development of new processes. A historical example of this is the development of high-pressure reactors for ammonia synthesis more than hundred years ago.

At the same time, the range of equipment technology and the reactor design is now as broad as the product range manufactured in chemical plants. Due to its flexibility, the stirred tank is the most commonly used reactor vessel. However, the equipment spectrum extends from classical fixed-bed reactors with salt melt or evaporative cooling, heat exchanger reactors over bubble columns, jet reactors, nozzle reactors, fluidized-bed reactors to high-temperature reactors and more complex reactors, such as microstructured reactors, photochemical reactors, electrochemical reactors, kneader reactors and hybrid systems, such as reactive distillation, extractions or gas scrubbers.



Multibaffling® Pfaudler

OptiMix® DeDietrich

Figure 16: Stirred vessels of Pfaudler und deDietrich

Although the stirred tank is one of the oldest designs of a chemi-

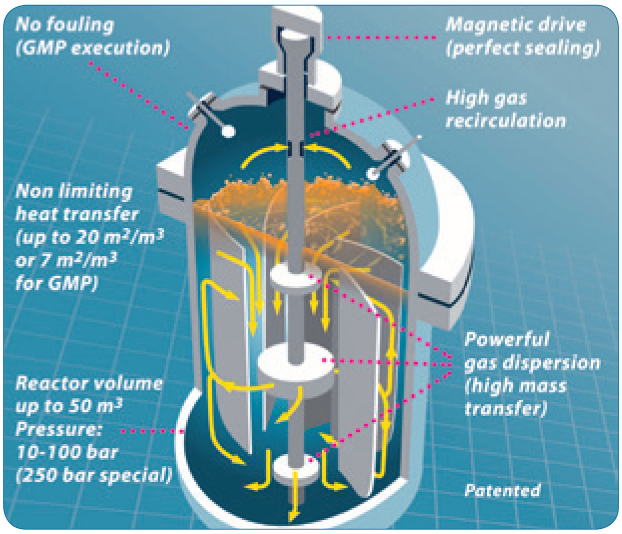


Figure 17: Gas/Liquid-Reactor with heat exchanger plates
(source: Biazzi SA)

Figure 18: Salt bath reactor DWE® Reactors (source: MAN DWE GmbH).

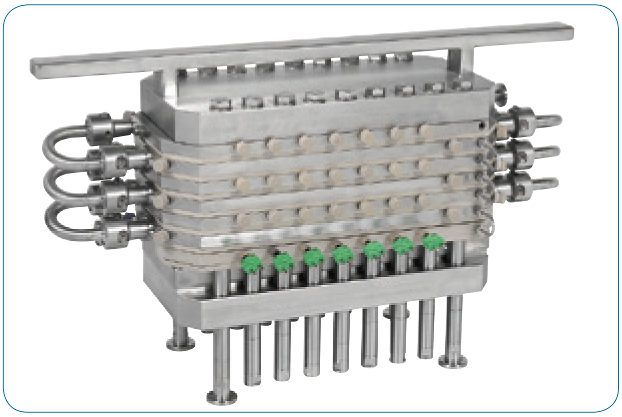


Figure 19: Alfa Laval ART® Plate Reactor

cal reactor, it is undergoing continuous refinement. In the glass-lined stirred tank (see Fig. 16), e.g. new solutions (in this case, flexible current interrupter arrangements) have been developed, which have significantly increased the flexibility and energy efficiency in gas-liquid systems, despite the otherwise limited production potential of glass-lined devices.

To improve the heat removal in stirred vessels, so-called heat exchanger plates (see Fig. 17) are used, which offer more extensive heat exchange surfaces than internally installed heat exchanger coils. Thus exothermic reactions in multiphase systems, e.g. suspension hydrogenation may be better controlled.

Salt bath reactors are conventional fixed-bed reactors for exothermic, heterogeneously catalyzed gas-phase reactions (see Fig. 18). They are used for example with partial oxidation reactions, such as the synthesis of acrylic acid.

When the requirements for heat removal or temperature control become more stringent, so-called heat exchange reactors are used. Based on plate heat exchangers (see Fig. 19), very high heat exchange performance can be achieved for single-phase systems.

In recent years the development of microstructured reactors[44] has shown that the intensification of heat transfer in manufacturing technologies was mainly confined to and driven by single-phase systems. Microstructured reactors (see Fig. 20) are characterized by internal structures of ten to several thousand micrometers. With such structures, liquid heating rates in the range of milliseconds become feasible.

The reactor is constructed of Hastelloy C-22, diffusion-welded and consists of a mixing module and four reaction modules. On the reaction side, it achieves a throughput of approx. 1.5 t h^{-1} and has been used successfully for several production campaigns at DSM Fine Chemicals Austria in Linz over many weeks.

In principle, microstructured reactors can also be used for multiphase systems. However, effects such as surface tension or wetting lead to alternative equipment solutions for large

---

[44] V. Hessel, A. Renken, J.C. Schouten, J.I. Yoshida, Micro Process Engineering, Wiley-VCH, Weinheim, 2009.

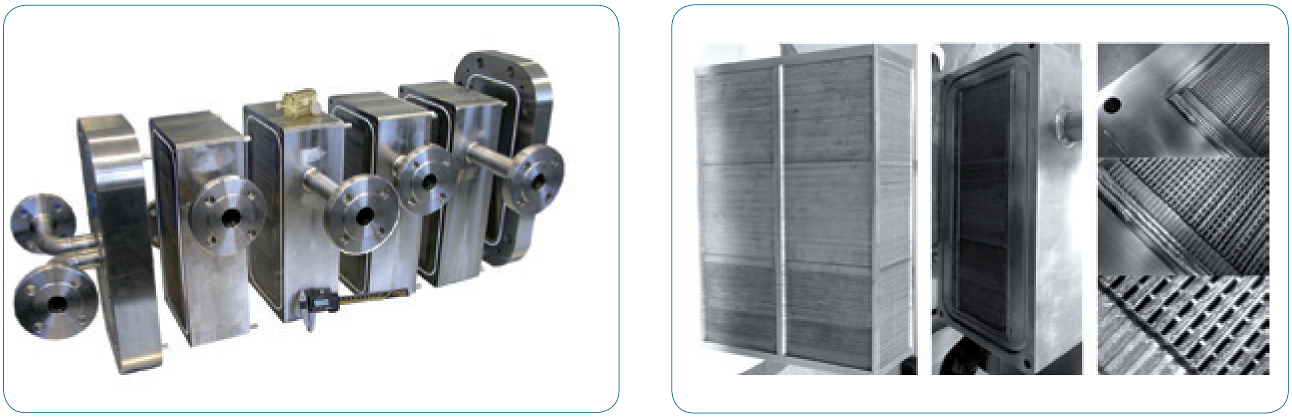


Figure 20: Microstructured production reactor of IMVT for the synthesis of diace-tonacrylamide from diacetone alcohol and acrylonitrile. The plates with channels of 0.5 mm depth and 2 mm width are diffusion-welded. (source: Institute for Microprocess Technology (IMVT), Karlsruher Institute of Technology (KIT))

reactors. Currently such multiphase reactors are therefore limited to the laboratory scale.

In process intensification, the heterogeneously catalyzed reactive distillation instigated equipment development in order to optimize the interaction of catalysis, reaction and separation. The fixation of the solid catalyst in the reactive distillation column, for example, is realized by incorporating the catalyst into the separating column internals (see Fig.21).

For the development and design of equipment, manufacturers employ, in addition to mechanical strength calculations, complex CFD calculations to quantitatively describe the fluid dynamics as well as mass and heat transfer. Especially for single-phase reaction systems, these CFD calculations now achieve design quality.

Safety requirements normally lead either to a pressure-resistant design or to the use of pressure relief devices. Modern reactors can, however, also be operated in a safe mode with the help of measurement and control technologies using reaction-technical model calculations, as a result of which the above-mentioned safety measures are no longer required, resulting in economically more attractive concepts.

Technical scientific challenges

Better process control by *in situ* analytical methods and improved measurement techniques, e.g. heat flow sensors or in-line viscosity measurements is desirable, as quality control is significantly improved, particularly in batch syntheses. In addition, batch processing times can be shortened as part of the process optimization is shifted to the production

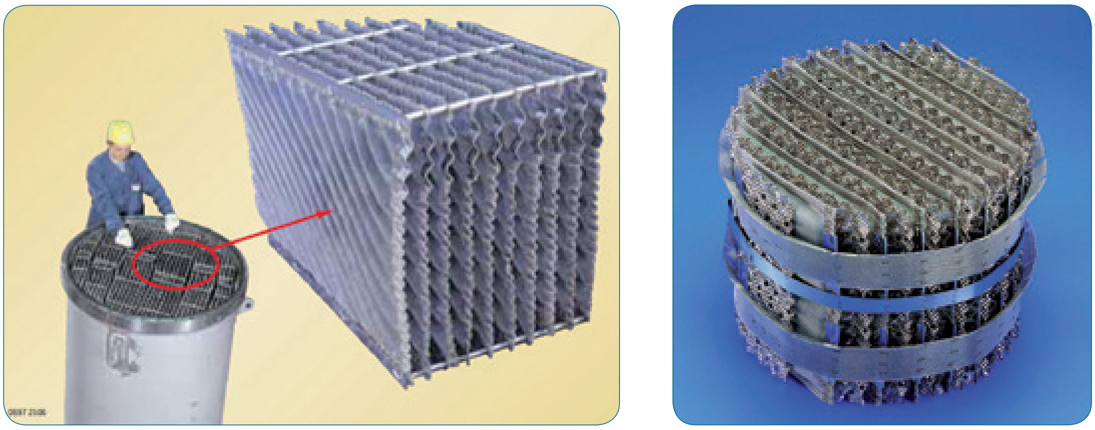


Figure 21: Wire mesh Katapak™ of Sulzer ChemTech (L. Götze, O. Bailer, Sulzer technical review 1999)

phase through improved process control. This is particularly interesting in the case of agrochemicals and pharmaceutical products, since the demands imposed on the development times are particularly tight. Analytical techniques, e.g. online NMR or spectroscopic methods such as UV-VIS, IR and Raman spectroscopy, have already demonstrated huge potential for process optimization.

Some biotechnological processes require large reactor volumes of the order of more than 1000 m^3 as well as high specific mass transfer rates, which lead to motor power requirements in excess of 10 MW for conventional aeration systems, which are mechanically difficult to implement. It would be desirable to avoid such high drive torques by hybrid gassing devices and thus to increase the overall energy efficiency for such intense mass transfer.

Directly coating heat exchanger elements in microreactors with a solid catalyst (see Fig. 22) can open up new possibilities for the control of strongly exothermic reactions. For this purpose, coating techniques providing reliable and reproducible coatings at the microreactor scale, must be developed. In addition, suitable characterization procedures for the quality control of such coatings must be devised.

The development of novel equipment concepts is a complex process. Ideally, the reactor provides the optimal transport characteristics for heat, mass, and momentum needed for the best reaction yield or selectivity. This presupposes knowledge of the optimal operating profile for the reaction, which should be determined as an ideal benchmark without imposing any equipment restrictions. Subsequently, the optimum temperature and concentration profiles ascertained in this way have to be approximated as far as possible within the constraints of a technical reactor. In order to attain a generally valid solution from a particular procedure, new optimization methods are necessary. In addition, further development of simulation tools for heat, mass and momentum transfer is required, especially in complex geometries and/or multi-phase systems (see Chapter 4).

Research Needs

1. New *in situ* analytical methods and new process measurement techniques to improve process control in production and to help shorten development times for batch processes

2. New coating methods of heat exchanger reactors with catalysts to create a new class of high performance reactors.

3. New methods for design and construction to allow model-based development of new reactor concepts realizing an optimal reaction management.

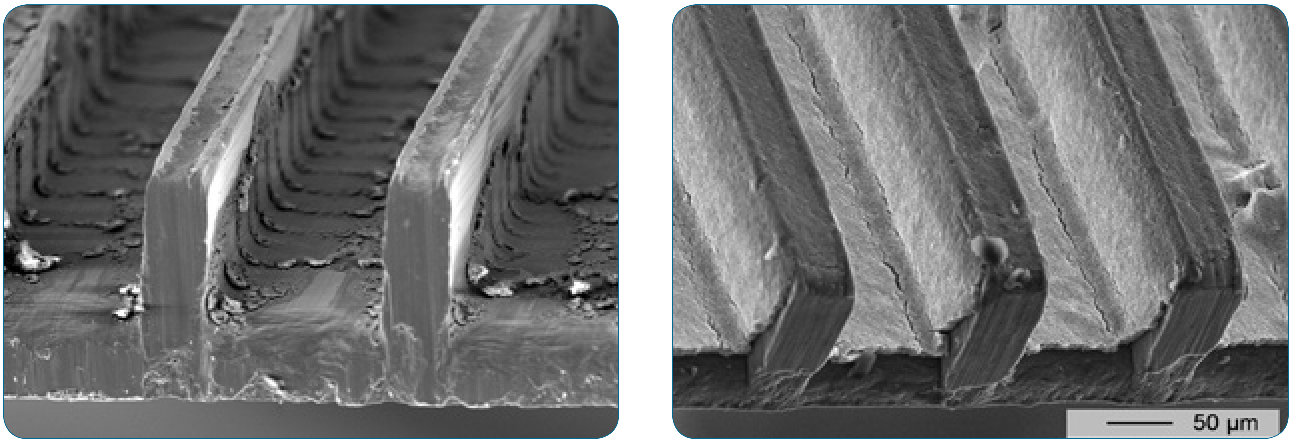


Figure 22: Left: Sol-gel coating of a microstructured stainless steel foil with 5 % Pt / CeO_2 for the water gas shift reaction. Right: Washcoat layer of a microstructured stainless steel foil with Cu/ZnO nanoparticles for methanol reforming.
(source: Institute for Microprocess Technology (IMVT), Karlsruher Institute of Technology (KIT))

D PROCESS INTENSIFICATION

Process intensification aims at a clear economic and ecological increase in the efficiency of chemical and biotechnological processes and the generation of new products or product qualities. It makes use of an interdisciplinary, holistic approach, as well as a multi-scale process analysis from the molecular level to the global site network. It deals with targeted measures for process structuring and integration and promotes the effective exploitation of innovative equipment and technologies[45,46].

In connection with reaction technology, the following principal process intensification measures are used, which favor the spatial, temporal, thermodynamic and functional design of the reaction system:

» Miniaturization

» Hybridization

» Structuring

» Dynamization

» Novel reaction media and energy supply

» Integration and rationalization

The miniaturization, i.e. the operation of 'microreactors' with characteristic dimensions in the millimeter or micrometer range, pursues the goal of eliminating mass and heat transfer limitations, which often interfere with the pure, chemical 'reactivity'. High specific heat exchange surfaces as well as increased mass transfer due to intensive mixing ensure excellent well-defined operating conditions. The stochastic processes in conventional reactors are largely eliminated and replaced by the uniform processing profile of the microscale operating mode. The low internal volume of microstructured devices is highly advantageous for both safety reasons and the processing of expensive materials.

The successful exploitation of the potential performance increase due to microreactors in technical production requires the existence of reliable parallelization strategies, which ensure an even distribution of the flow across numerous microchannels. The production of microstructured reactors also entails high costs, which must be justified by the improved reactor performance. In order to minimize the manufacturing expense, the structures used should be designed to be as fine as necessary but as coarse as possible.

Hybridization of the chemical reaction with separation units can enable synergies for both processes, as in the case of reactive distillation. Removal of a (by-) product from the reaction mixture allows one to overcome conversion restrictions due to chemical equilibrium, while a reaction can prevent formation of an azeotropic mixture. In principle, each separation operation can be integrated with a reaction in a multifunctional device. The reactive absorption is, for example, a mature technology for numerous gas purification processes and synthesis reactions. The reactive distillation is also commercially well-established for certain applications. Chromatographic and membrane reactors have been researched extensively for decades and are already used technically in niche applications. From the perspective of the reaction engineer, the integration of additional unit operations offers a very useful tool for manipulating the concentration and temperature profiles in the reactor. However, the harmonization between the reaction and the separation process usually requires compromises, which can lead to suboptimal operation of the individual processes, sacrificing degrees of freedom, or completely preventing a meaningful integration (see Fig. 23).

In the case of reactive distillation, special packings are required in order to meet the conflicting requirements of both processes with respect to residence time and interfacial area. The macro- and micro-structuring of the various functionalities in the reactor have proved to be particularly effective means for resolving possible contradictions, rather than a simple unstructured combination. Catalytic packings can usually be expediently used in certain sections of reactive distillation columns, whereas in the other sections only distillation without reaction takes place. The identification of

---

[45] A. Stankiewicz, J.A. Moulijn (eds.), Re-engineering the chemical process plant – process intensification, Marcel Dekker Inc. NY, 2004.

[46] F.J. Keil (ed.), Modeling of process intensification, Wiley-VCH, Weinheim, 2007.

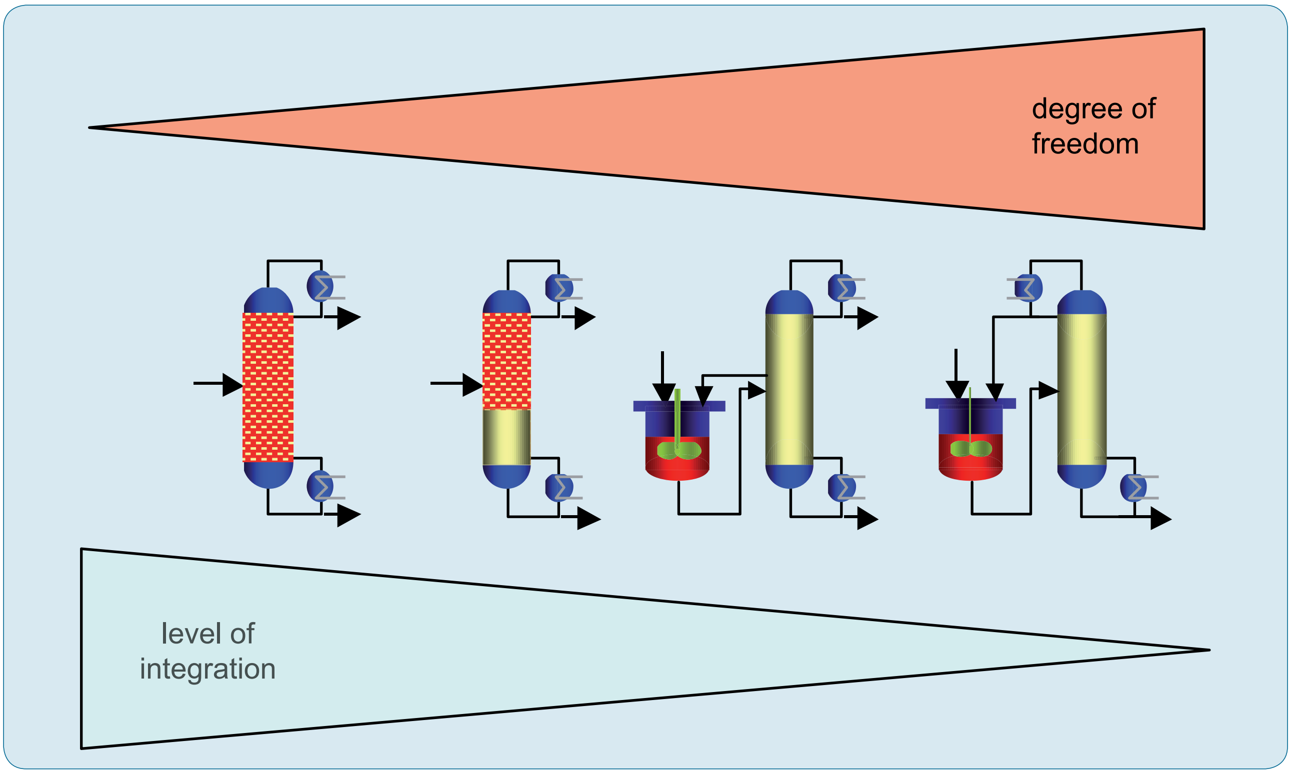


Figure 23: Degree of freedom vs. integration level of multifunctional reactors

the optimum degree of integration and the possibilities for implementing it are major challenges in the design of multifunctional reactors.

Local structuring of the reaction space or of a heterogeneous catalyst often offers extensive potential for improving reactor operation. Thus, by diluting the catalyst in the region of the hot spot, a better harmonization between the reactive heat generation and heat removal by reactor cooling can be achieved. Owing to a non-uniform distribution of the catalytic activity in the catalyst core, deactivation phenomena can be retarded. Novel catalyst structures, such as catalytic sponges (see Fig. 24), permit a deliberate adjustment of mass and heat transfer characteristics with low pressure loss. Although the optimization task appears to be very complex in structuring measures, it often leads to simple asymptotic solutions.

The dynamization of the reactor operation can be interpreted as a temporal structuring of the reaction regime and is by no means an unknown approach in conventional reactor technology, for example in the semi-batch reactor process. However, dynamic reactor operation must not interfere with the steady-state operation of the remaining plant items. By periodically modulating the liquid

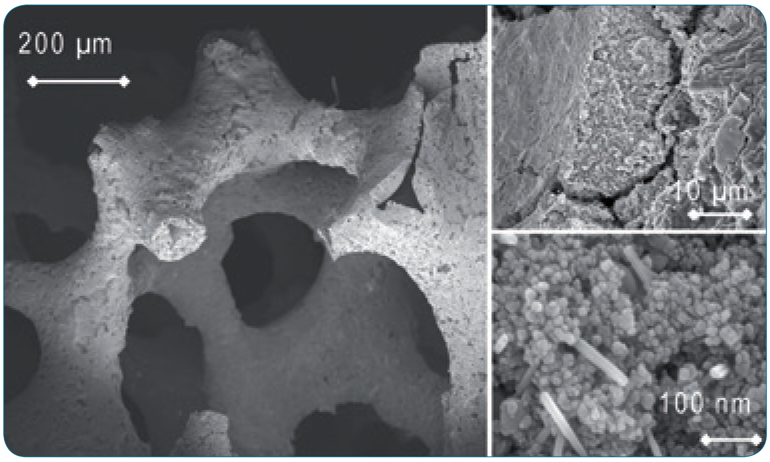


Figure 24: Ceramic sponge impregnated with SCR catalyst (left: sponge structure, top right: catalyst layer, bottom right: TiO_2 (spherical particles) and V_2O_5 (needles). (source: Engler-Bunte Institute, Division Gas, Oil, and Coal, Karlsruher Institute of Technology (KIT))

feed into a trickle bed reactor, the accessibility of the catalyst surface for the gas phase, and thus the conversion rate, can be significantly enhanced. Similar advantages can be gained by using a rotating liquid distributor. By pressure pulsation, diffusive transport processes can be considerably accelerated by convective contributions. Furthermore, a cyclic reactor procedure utilizes storage effects and can thus realise temperature and concentration conditions, which cannot be achieved in steady-state operation, as in the case of the reverse-flow reactor for oxidative waste gas treatment. The exact manipulation of the concentration and temperature profiles in microreactors should facilitate the technical implementation of dynamic operation.

Novel reaction media, such as supercritical fluids, perfluorinated solvents and ionic liquids, enable a made-to-measure design of the reaction environment, a targeted influence on the activities of individual reaction partners and improved transport properties compared to conventional reaction systems. In addition, they often offer environmental benefits over conventional organic solvents. On the other hand, they are usually more expensive and can involve costly equipment, e.g. due to high pressure operation. So-called “rich” operation methods without inert diluents or solvents are regarded as promising, albeit ambitious reaction technology targets, which could significantly reduce the extent of downstream processing. However, issues of safety engineering or product quality have to be clarified in advance.

For alternative energy supply, plasma reactors, e.g. for acetylene production, are already state- of-the-art. The volumetric energy input by means of microwaves or shear forces does not require temperature gradients and is therefore particularly suitable for temperature-sensitive liquids and solids. The use of ultrasound is especially appropriate for mass-transfer limited reactions or for heterogeneous catalysis, because the reactive surface can be kept fresh by cavitation. Such unconventional energy forms are, of course, complex, and the uniform energy input on a larger scale is regarded as problematic. By means of centrifugal fields, a countercurrent flow of two fluids can be achieved, even in very finely structured packings, which may help overcome a substantial shortcoming of microreactor technology.

It can be seen that process intensification measures often complement one another, but this considerably increases the complexity of the reaction management or the reactor design. The use of continuous instead of batch operation at relatively low production capacities, as well as fast and flexible reaction management according to the market demand by process intensification measures, can effectively achieve a rationalization of the entire production process. Furthermore, process intensification opens up new horizons for direct synthesis and local process monitoring and control.

While many of the aforementioned process intensification measures have been successfully demonstrated in research projects, the task now is to exploit these findings and results on a broad basis in industrial processes. For this purpose, it is necessary to be able to evaluate the various options for process intensification even in an early phase of process development. In order to get from the current approach based on specific examples to such a generalizable model-based methodology, however, further specialised fundamentals are required. The goal is to put the process intensification on a theoretically sound foundation and to evaluate the suitability of process intensification measures by means of systems-analytical methods in the integrated plant environment.

Research Needs

1. Universal methodology for integrating process intensification measures in process synthesis and process development
2. Development of reliable parallelization strategies for microreactor technology
3. Development of a suitable microprocess technology to supplement microreactor technology
4. Development of systematic approaches for the spatial and temporal structuring of different functionalities in the reaction zone
5. Development of low-noise dynamic reactor systems
6. Improved scale-up capability for novel energy sources
7. Robust catalyst: development of catalysts which are stable against biobased, water containing feedstocks and against high fluctuations in throughput.

E SYSTEMS ENGINEERING APPROACHES FOR REACTOR ANALYSIS, SYNTHESIS, OPERATION AND CONTROL

Reactor analysis in a process-wide context

Each chemical reactor is embedded in a complex chemical production process consisting of many other process units, such as separators, mixers, heat exchangers and compressors (see Fig. 25). Thus, the reactor cannot be designed, analyzed and optimized as an isolated component, but should be considered as a unit which is linked by many functional connections to the overall production system. The reactor communicates with the other process units via the mass and energy fluxes. In particular, the reactor output defines the inlet conditions of the sub-sequent downstream processes. Non-converted reactants must be separated in the downstream process section and recycled back to the reactor. Recycle loops may enrich the levels of undesired by-products in the process, which can lead to severe operational problems both in the reactor itself and other parts of the plant. It is thus imperative to analyze the reactor-separator-recycle systems rather than just the stand-alone reactors. In some cases, recycling of intermediates formed during the reaction can have a positive effect on the productivity and selectivity. Moreover, analyzing the reactor-separator-recycle (RSR) is very important, because the effort for separating the reactor outlet mixture depends on its composition. In particular, the existence of azeotropic mixtures makes vapor-liquid separations difficult and thus must be considered carefully before stipulating the reactor performance. Furthermore, the thermal management of the reactor and its thermal integration with the downstream separation processes require a systems perspective, particularly with respect to the optimal design of the heat exchange network (HEN). The temperature and pressure levels of all units, including the reactor, must be set optimally in order to

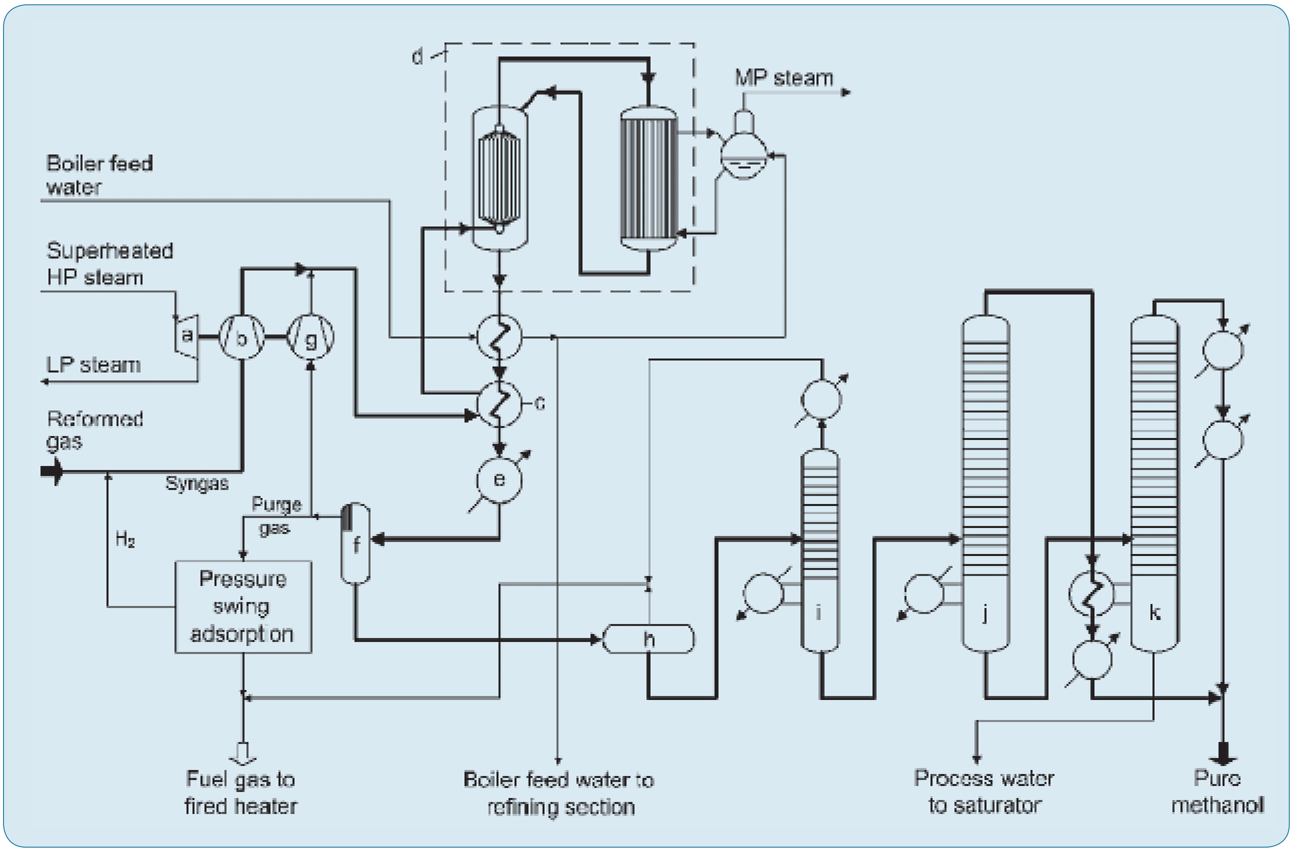
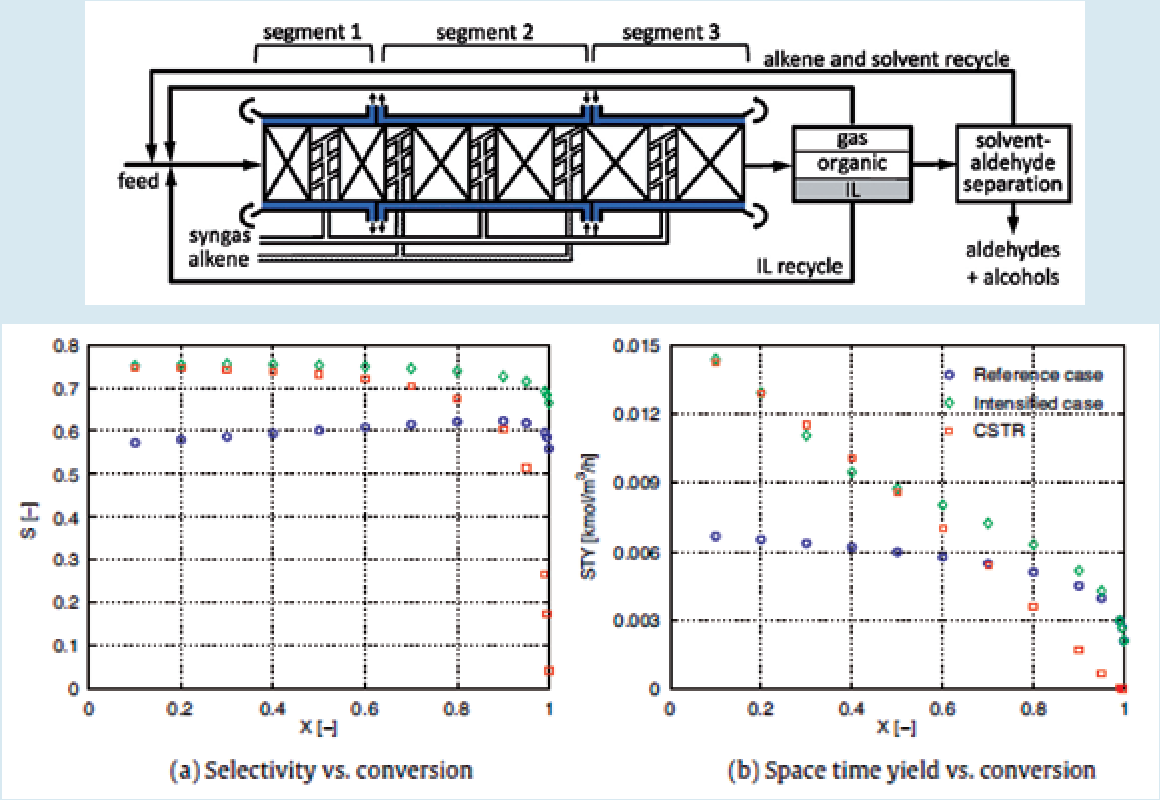


Figure 25: Flowsheet of the Lurgi MegaMethanol production process system. The two-stage reactor section has multiple interactions via the mass and energy fluxes to and from the feed pretreatment section and the downstream separation section. a) Turbine for synthesis gas and recycle compressor; b) synthesis gas compressor; c) trim heater; d) combined converter system; e) final cooler; f) methanol separator; g) recycle gas compressor; h) expansion vessel; i) light ends column; j) pure methanol pressurized column; k) atmospheric methanol column.
(Reprint from Ullmann's Encyclopedia of Industrial Chemistry, 2012, with permission by Wiley-VCH, Weinheim)

maximize the energetic efficiency of the process as a whole. In doing so, not only performance indices, but also process-wide safety aspects must be taken into account.

Reactor synthesis

While the above-mentioned aspects are classical questions of Process Systems Engineering (PSE), the translation of a detailed microkinetic reaction network into the optimal reactor configuration belongs to PSE research at the interface to Chemical Reaction Engineering. Classical reactor synthesis methods, such as the Attainable Regions (AR) approach, are usually based on simplified reaction kinetic expressions. With the advent and extensive use of computational chemistry tools, much more detailed kinetic information becomes available at the level of elementary reaction steps. Using this information for optimal reactor design is a must for identifying ground-breaking reaction engineering solutions for challenging problems, particularly in the context of chemical energy conversion and sustainable production processes. Detailed microkinetics enables the rational design of reactors featuring sophisticated feed dosing and product extraction strategies for the species involved in the underlying reaction networks. The best design solutions can be determined by solving dynamic optimization problems for material elements moving through the reactor, where the mass and energy fluxes are used as controls for guiding such elements along the optimal trajectory in the state-space (see Fig. 26). The ideal pathway can be approximated by means of a continuous process unit network. This can be achieved by means of (Mixed Integer) Nonlinear Programming techniques (MINLP/NLP) whereby the best reactor system configuration is identified from a superstructure of process units (reactor stages, mixers, separators, heat exchangers, compressors/expanders). In the context of sustainable reaction engineering, multi-objective optimization (MOO) is becoming an increasingly important



(a) Selectivity vs. conversion

(b) Space time yield vs. conversion

Figure 26: Results obtained from dynamic optimization of the trajectory of material elements passing through a hydroformylation process of 1-octene. The optimal trajectory can be approximated via a segmented tubular reactor equipped with staged dosing of syngas and octane. This design leads to (a) higher selectivity and (b) higher space-time-yield (green symbols) compared to a CSTR (orange symbols) operated at optimal conditions. The optimization accounted for the recycling conditions of the solvent, catalyst and unconverted reactants.
(Reprint from Peschel et al., 2012, Chemical Engineering Journal; with permission by Elsevier)

tool for generating Pareto-optimal sets of reactor configurations in order to find the best compromise between economic and ecological performance criteria. In other words, the evaluation of innovative reactor design solutions should always be done as part of the Sustainability Analysis and Life Cycle Assessment (LCA) of the overall chemical production process.

Integrated molecular and process synthesis

Another important future direction is the integrated design of reactor systems and reaction auxiliary agents (solvents, catalysts) in a process-wide context. The ultimate goal is to combine computer models for molecules and process units, in order to formulate optimization problems in terms of i) binary variables for molecular and process structures, and ii) continuous variables for all other decision variables (pressure, temperatures, fluxes). This approach is denoted as integrated Computer-Aided Molecular and Process Design (CAMPD). One of the challenges here is to find global solutions for large-scale MINLPs resulting from CAMPD. Another big task is the formulation of validated molecular models for describing the thermodynamic and kinetic properties of pure substances and mixtures in terms of molecular group contributions (GC). GC-based methods are also required for modeling the EHS-relevant (EHS: environmental, health & safety) properties of molecules in a reaction process. For mathematical optimization purposes, first-principle molecular models are often not the best suited. Thus, surrogate models should be derived to cut the computational effort and time. Artificial neural networks (ANN) and Kriging models represent the most popular classes of reduced model formulations.

Reactor operation and control

In the first step, the evaluation of the reactor performance within a chemical production process is often primarily based on the conversion-selectivity characteristics and the catalyst aging profile. However, for the fast modification of production targets to market dynamics, load changes occur more frequently than in classical continuous reactor operation. Hence, the operational flexibility becomes an additional performance criterion in reactor optimization. In this context the stability of temporally attained steady-state operational points, trajectory planning for load changes and real-time optimization (RTO) are also aspects of increasing importance. Advanced control strategies must thus to be developed and implemented for industrially important reactors. To contribute effectively to enhanced process performance, such control strategies should be fed with a large amount of *in situ* operational data with reasonably high resolutions in time and space. Such data can be harvested via modern sensor networks installed in chemical reactors and other process units. This is part of the Process Industry 4.0 scenario, in which data-driven process control and operation is of paramount importance for smart chemical production. With this development, it is foreseeable that networks of decentralized processes and different production sites of enterprises will communicate with each other via the Internet of Things. This will lead to a qualitatively higher complexity of chemical production systems that can only be handled with the help of new data-driven computer models. Such models must be rapidly calibrated in real-time and used in a very flexible manner for optimal process operation and control.

Research Needs

1. Advanced methods for model-based reactor analysis and optimization within process systems, accounting for performance, flexibility, parametric sensitivity and uncertainties.

2. Rational design of chemical reactors based on detailed microkinetics of the underlying elementary reaction mechanisms.

3. Advanced superstructure approaches for synthesis of optimal multistage reactor networks and reactor-separator networks.

4. Integrated design of reactors with reaction solvents and catalysts by use of advanced molecular models and computational chemistry tools.

5. Methods and tools for the operation and control of continuous reactors for frequent load changes and under dynamic conditions for use of fluctuating renewable energies and biomass as feedstocks with variable composition.

6. Data-driven approaches and tools for optimal operation and control using advanced sensor technologies.

6 Case Studies

CASE STUDY 1: THE ENVINOX® PROCESS

Background

The EnviNOx® process developed by ThyssenKrupp Industrial Solutions (formerly Uhde) removes the environmentally harmful nitrogen oxides NO_x and N_2O from the tail gases of chemical plants, in particular from nitric acid production plants[47]. During the manufacture of nitric acid based on the combustion of ammonia according to the Ostwald process, 5 to 10 kg N_2O per tonne of nitric acid are typically formed, which would then be emitted to the atmosphere without exhaust gas cleaning. In light of a global yearly nitric acid production of about 60 million tonnes and the fact that nitrous oxide has a global warming potential 265 times higher than that of carbon dioxide, measures for emissions reduction are inevitable. In the EnviNOx® process, N_2O and NO_x are almost completely removed in a reactor containing special iron zeolite catalysts[48], which are marketed by Clariant under the brand names EnviCat® N_2O and EnviCat® NO_x. Depending on temperature and tail gas composition, the removal of N_2O is either accomplished by catalytic decomposition to N_2 and O_2 (process variant 1) or by catalytic reduction with hydrocarbons (process variant 2, see Fig. 27). NO_x removal is effected by selective catalytic reduction with ammonia and can run in parallel to the N_2O abatement. The EnviNOx® plants built by ThyssenKrupp so far have already cut CO_2-equivalent emissions by more than 12 million tonnes per year.

Contribution through reaction engineering

The EnviNOx® reactor involves several different reactions with complex kinetics, some of which are extremely fast. As a consequence, significant concentration gradients occur in the porous structure even if small catalyst particles or thin layers are employed. Therefore, measured data from laboratory reactors

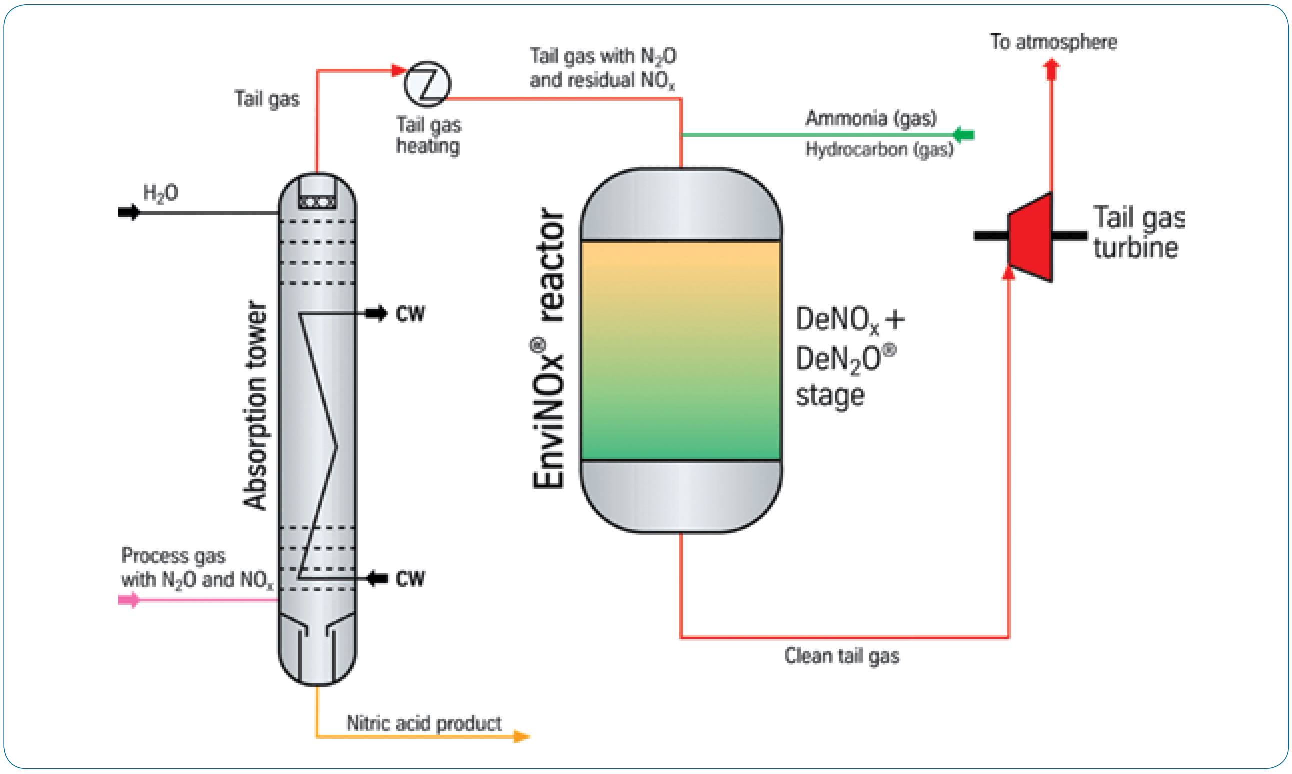


Figure 27: EnviNOx® process variant

---

[47] M.C.E. Groves, A. Sasonov, Uhde EnviNOx® technology for NOx and N2O abatement: a contribution to reducing emissions from nitric acid plants, J. Integr. Environ. Sci. 7 (2010) 211–222, dx.doi.org/10.1080/19438151003621334

[48] S. Brandenberger, O. Kröcher, A. Tissler, R. Althoff, The State of the Art in Selective Catalytic Reduction of NOx by Ammonia Using Metal-Exchanged Zeolite Catalysts, Catal. Rev. 50 (2008) 492–531, dx.doi.org/10.1080/01614940802480122

can only successfully be evaluated with the aid of appropriate reactor models[49]. These models may be formulated dynamically in order to describe time-dependent phenomena such as start-up and shut-down of a reactor[50].

Reaction engineering also permits the design of suitable catalytic reactors for the EnviNOx® process. The catalyst extrudates currently available are preferably employed as a randomly packed bed in radial flow reactors in order to minimize pressure drop in the large nitric acid tail gas streams[51]. It has also been shown that honeycomb monolith catalysts are attractive alternative geometries because they allow both better utilization of active material and the design of more compact reactors.

CASE STUDY 2: REDOX-FLOW BATTERIES

Background

Redox-flow batteries (RFB) are promising systems for the storage of electrical energy. Although their energy density is too low for mobile applications, these batteries are an excellent option for stationary storage given their high efficiency, durability, and flexibility regarding independent adjustment of energy content and power[52,53]. RFB consist of a cell stack which is built up similar to the one of fuel cells (see Fig. 28). While the stack area determines the battery power, the energy content is given by the amount of redox-active species, which are typically dissolved in aqueous solutions in the two stor-

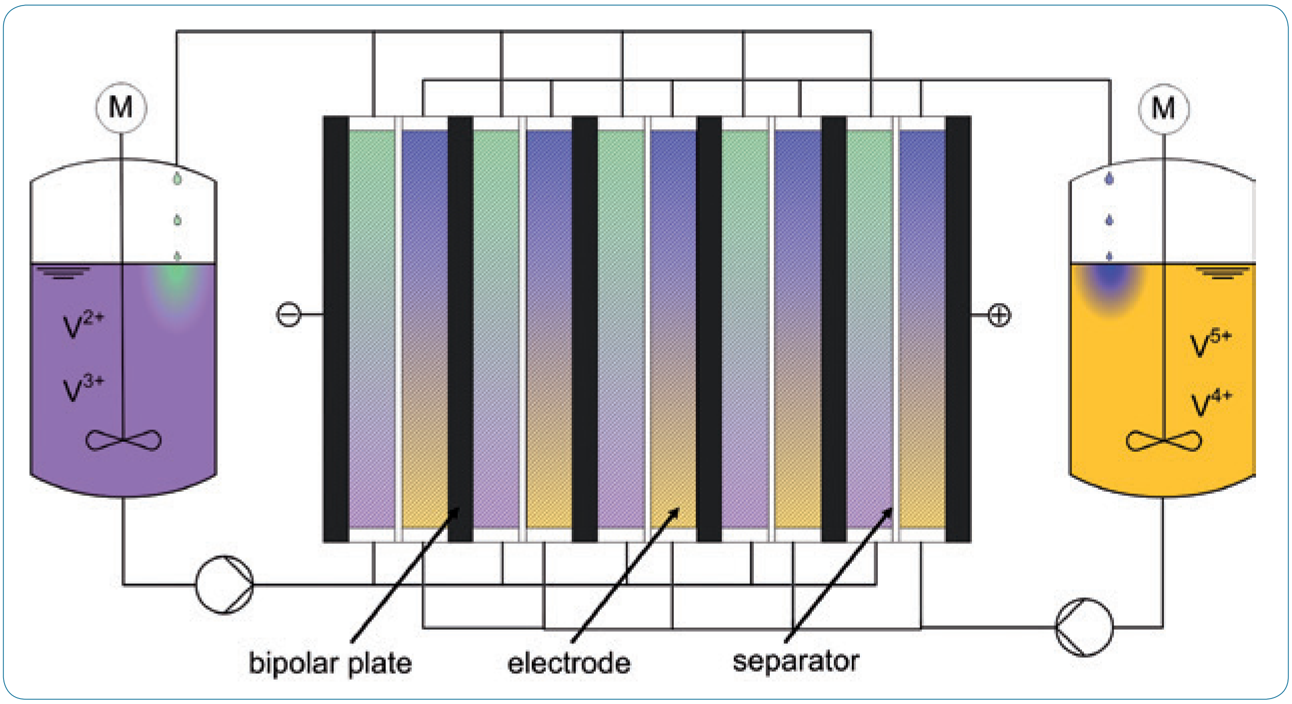


Figure 28: Scheme of a redox-flow battery stack with core components. Core components of the cell are the bipolar plates which are typically made of carbon-filled polymers, the porous electrodes which are also based on carbon as electrochemically active surface, and a membrane or separator that prevents the positive (V^{4+}/V^{5+}) and negative (V^{2+}/V^{3+}) electrolytes from mixing while providing sufficient ionic conductivity.

---

[49] V. Bacher, C. Perbandt, M. Schwefer, R. Siefert, S. Pinnow, T. Turek, Kinetics of ammonia consumption during the selective catalytic reduction of NOx over an iron zeolite catalyst, Appl. Catal. B 162 (2015) 158–166, dx.doi.org/10.1016/j.apcatb.2014.06.039

[50] M. Colombo, I. Nova, C. Ciardelli, E. Tronconi, V. Schmeisser, M. Weibel, Mathematical modeling of cold start effects over zeolite SCR catalysts for exhaust gas aftertreatment, Catal. Today 231 (2014) 99–104, dx.doi.org/10.1016/j.cattod.2013.01.044

[51] C. Perbandt, V. Bacher, M. Groves, M. Schwefer, R. Siefert, T. Turek, Kinetics and Reactor Design for N2O Decomposition in the EnviNOx® Process, Chem. Ing. Tech. 85 (2013) 705–709, dx.doi.org/10.1002/cite.201200163

[52] A.Z. Weber, M.M. Mench, J.P. Meyers, P.N. Ross, J.T. Gostick, Q. Liu, Redox flow batteries: a review, J. Appl. Electrochem. 41 (2011) 1137–1164, dx.doi.org/10.1007/s10800-011-0348-2

[53] M. Skyllas-Kazacos, M.H. Chakrabarti, S.A. Hajimolana, F.S. Mjalli, M. Saleem, Progress in Flow Battery Research and Development, J. Electrochem. Soc. 158 (2011) R55-R79, dx.doi.org/10.1149/1.3599565

age tanks. Many different redox pairs have been suggested and successfully tested in RFB. Among these possibilities, the so-called “all vanadium” system containing vanadium ions in valence states between V^{2+} and V^{5+} is presently the most promising option, although alternative organic redox species are under development[54].

Contribution through Reaction Engineering

Since the RFB system, consisting of a cell stack connected with electrolyte tanks, can be regarded as an electrochemical reactor in recycle mode, reaction engineering obviously plays a decisive role during the further development and optimisation of these batteries. The following research areas can be identified:

- **Electrode and cell configuration:** In contrast to fuel cells with gaseous reactants, diffusion of ions in the liquid electrolytes is slow, which is the main reason why the carbon electrodes in RFB have been until now usually employed in flow-through mode. However, for RFB much larger than the presently available systems with about 0.1 m^2 cell area, this would lead to an unacceptably high pressure drop. Therefore, new flow designs are required for industrial RFB[55,56]. Moreover, at a high current density significant mass transfer resistances occur during RFB operation which lead to higher over-voltages and reduced overall efficiency. For optimisation of the electrode utilisation, appropriate reactor models must be developed[57] and validated through spatially resolved measurement techniques[58].

- **Membrane and system optimisation:** The separator in the RFB is the component with the highest ohmic losses, especially if ion-selective membranes are employed. In addition, a certain cross-over through the separator of vanadium species and also water cannot be prevented. This phenomenon partially discharges the battery and may also lead to quite significant shifts of volume and species concentrations in the two electrolyte tanks over prolonged operation with repeated charge and discharge. Side reactions such as hydrogen evolution also contribute to capacity losses.[59] For these reasons, better membrane materials with reduced cross-over, appropriate membrane transport models[60] and also strategies for electrolyte management[61] are required.

CASE STUDY 3: ON-BOARD DIAGNOSTICS FOR AUTOMOTIVE EMISSION CONTROL

Background

On-board diagnostics (OBD) in automotive vehicles is understood as the vehicle’s self-diagnostic and reporting capability. OBD systems give the driver and the repair technicians access to the status of the various vehicle subsystems. Today, OBD is required in every automobile for controlling the status and the performance of the exhaust-gas after-treatment. On one hand, the status (temperature, the amount of stored oxygen or nitrogen oxides) of the catalysts experiences changes within seconds due to the continuously varying raw emissions (mass flow, temperature, raw exhaust gas composition) caused by the driver’s actions. On the other hand, the catalysts age, i.e. loss of activity, over the years of operation. Both phenomena have to be covered by on-board diagnostics to efficiently control the emission reduction and to signal failure of the exhaust-gas after-treatment, respectively. Technically, OBD is today realized by an interplay of sensors, e.g. for the measurement of concentration of oxygen or nitrogen oxides

---

[54] K. Lin, R. Gómez-Bombarelli, E.S. Beh, L. Tong, Q. Chen, A. Valle, A. Aspuru-Guzik, M.J. Aziz, R.G. Gordon, A redox-flow battery with an alloxazine-based organic electrolyte, Nature Energy 1 (2016) 16102, dx.doi.org/ 10.1038/nenergy.2016.102

[55] D. Reed, E. Thomsen, B. Li, W. Wang, Z.M. Nie, B. Koeppel, V. Sprenkle, Performance of a low cost interdigitated flow design on a 1 kW class all vanadium mixed acid redox flow battery, J. Power Sources 306 (2016) 24-31, dx.doi.org/ 10.1016/j.jpowsour.2015.11.089

[56] G.D. Polcyn, N. Bredemeyer, C. Roosen, D. Donst, P. Toros, P. Woltering, D. Hoormann, P. Hofmann, S. Köberle, F. Funck, W. Stolp, B. Langanke, Flow Type Electrochemical Cell, WO 2014/033238 A1

[57] A.A. Shah, M.J. Watt-Smith, F.C. Walsh, A dynamic performance model for redox-flow batteries involving soluble species, Electrochim. Acta 53 (2008) 8087–8100, dx.doi.org/10.1016/j.electacta.2008.05.067

[58] M. Becker, N. Bredemeyer, N. Tenhumberg, T. Turek, Polarization curve measurements combined with potential probe sensing for determining current density distribution in vanadium redox-flow batteries, J. Power Sources 307 (2016) 826 – 833, dx.doi.org/10.1016/j.jpowsour.2016.01.011

[59] S. Rudolph, U. Schröder, I.M. Bayanov, On-line controlled state of charge rebalancing in vanadium redox flow battery, J. Electroanal. Chem. 703 (2013) 29.37, dx.doi.org/10.1016/j.jelechem.2013.05.011

[60] M. Paidar, V. Fateev, K. Bouzek, Membrane electrolysis - History, current status and perspective, Electrochim. Acta 209 (2016) 737-756, dx.doi.org/ 10.1016/j.electacta.2016.05.209

[61] K. Wang, L. Liu, J. Xi, Z. Wu, X. Qiu, Reduction of capacity decay in vanadium flow batteries by an electrolyte-reflow method, J. Power Sources 338 (2017) 17-25, dx.doi.org/10.1016/j.jpowsour.2016.11.031

in the exhaust, and mathematical models (see Fig. 29). With increasing complexity of the catalyst materials and the entire emission control system with usually several catalysts and even addition of further chemicals such as reducing agents for NOx removal, simple models are not able anymore to predict the complex interactions of chemical kinetics and mass and heat transport in the real system. However, more detailed models are time consuming and therefore inadequate for integration into the control strategies. Therefore, the use of dual-layer catalysts introduced a further challenge for the models.

Dual-layer architectures allow the combination of the functionality of two different washcoats in one single catalyst. One example of such a multifunctional catalyst is the ammonia oxidation catalyst that contains a Pt-layer for NH_3 oxidation and a SCR (Selective Catalytic Reduction) layer for the reduction of NO by NH_3[62,63]. However, the numerical simulation of a dual-layer catalyst is numerically demanding, since at each axial location the reaction- diffusion equations for the two washcoat layers need to be solved. Due to long computation times, model application becomes impractical for many purposes, especially for applications that require vast quantities of simulations such as kinetic parameter fitting or automated optimization of ammonia dosing.

Contribution through reaction engineering

In a joint effort between industry and academia, a model approach was developed to numerically simulate the processes in the catalyst with a dual-layer washcoat within a sufficiently short computing time[64,65]. For the solution of the radial mass balances, each washcoat layer is represented by a single volume element and the diffusive mass fluxes into and within the washcoat are computed based on the concept of the internal mass transfer coefficients. The comparison of the new simulator with a reference simulator that fully resolves the concentration profiles in the washcoat showed only small, acceptable differences. With the new simulator, the 1800 s of

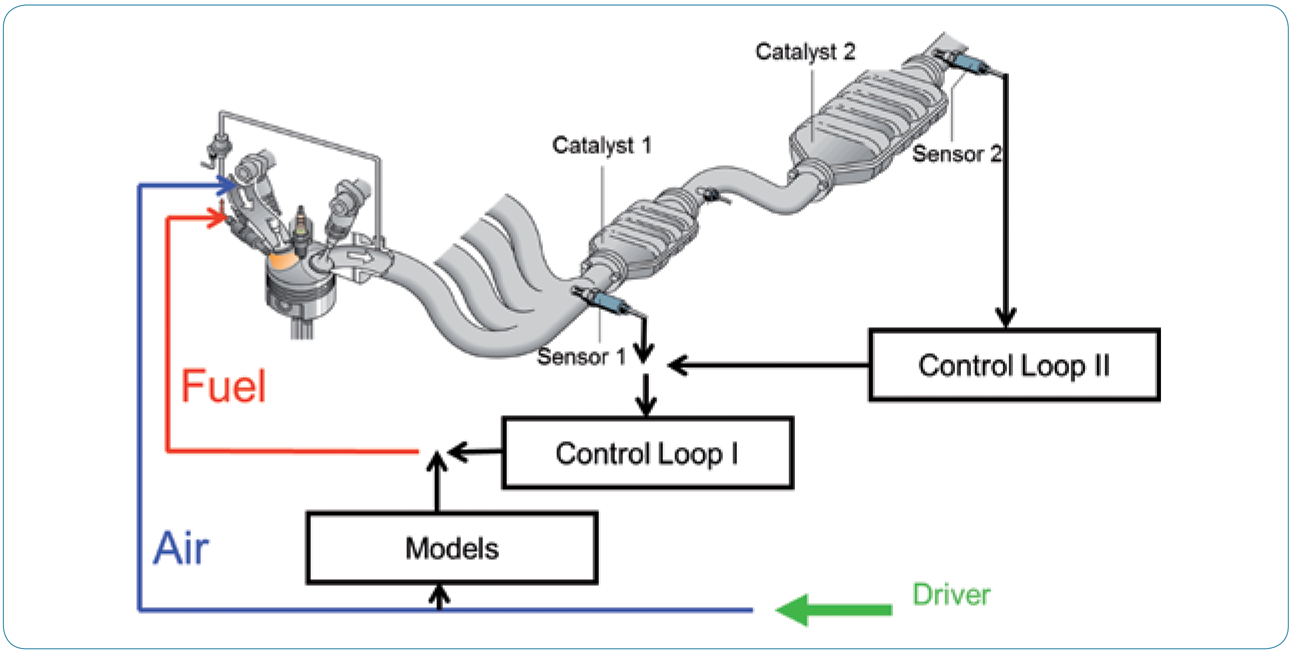


Figure 29: Example for model-based on-board diagnostics in automotive emission control

---

[62] A. Scheuer, W. Hauptmann, A. Drochner, J. Gieshoff, H. Vogel, M. Votsmeier. Dual layer automotive ammonia oxidation catalysts: Experiments and computer simulation. Appl. Catal. B 111–112 (2012) 445–455.

[63] M. Colombo, I. Nova, E. Tronconi, V. Schmeisser, B. Bandl-Konrad, L.R. Zimmermann. Experimental and modeling study of a dual-layer (SCR+PGM) NH3 slip monolith catalyst (ASC) for automotive SCR after treatment systems. Appl. Catal. B 142–143 (2013) 337–343.

[64] B. Mozaffari, S. Tischer, M. Votsmeier, O. Deutschmann. A one-dimensional modeling approach for dual-layer monolithic catalysts. Chem. Eng. Sci. 139 (2016) 196–210.

[65] J. Rink, B. Mozaffari, S. Tischer, O. Deutschmann, M. Votsmeier. Real-time simulation of dual-layer catalytic converters. Topics in Catalysis (2016) 1-5.

a transient driving cycle can be simulated within 53 s on a standard laptop, 30 times faster than real time. The new simulator for dual layer catalysts was implemented and its performance was demonstrated using the example of the dual-layer ammonia oxidation / SCR catalyst[65]. Applying detailed understanding of reaction engineering, here the interaction of chemical kinetics and mass transport, supports the development of improved exhaust-gas after-treatment systems leading to ultra-low emissions of pollutants from automobile vehicles.

CASE STUDY 4: SIMULATION-BASED PRODUCT DESIGN IN HIGH-PRESSURE POLYMERIZATION TECHNOLOGY

Background

The rising importance of plastics and polymers becomes apparent when looking at commodity products in daily life as well as specialty applications. A growing polymer market points out the need for further development and improvement in this sector as well as its future potential. Emulsions and coatings are an important example of large-scale products, which are usually produced via solution or emulsion polymerization. Another interesting but unique polymerization process is the high-pressure ethylene polymerization which yields mainly packaging material such as films and bags. But also specialty needs can be addressed: highly pure LDPE (low-density polyethylene) is utilized in medicinal products and waxes can be used as flow improvers.

Whenever treating polymeric materials, one has to keep in mind, that an ensemble of macromolecules with varying chain-length and topology is present. These characteristics determine processability and application properties of a product. Designing processes to meet desired product properties is thus a main task in the field of polymer reaction engineering. In this context reaction engineering proves a powerful tool, as trial-and-error methods as well as high-throughput experiments are unsuitable for high-pressure processes - mainly because high-pressure experiments in mini-plants are time-consuming and extremely expensive. While in the 1970s and 80s conversion and molecular weights were calculated[66,67] using numerous simplifications and assumptions, the frontiers have been pushed further. Improvements were made due to a growing understanding of the process with its underlying kinetics and improved methods for the determination of rate coefficients such as the PLP-SEC method[68,69], but also thanks to a drastic growth of computational power as well as enhanced mathematical models. A drastic improvement of reactor modeling can be found in the complete field of polymerizations[70].

Contribution through reaction engineering

In order to perform process optimizations as well as product design successfully in the field of high-pressure polymerizations a careful analysis of the underlying kinetics as well as thermodynamics of the system is essential. If these have been determined sufficiently precise, new reaction controls and product designs can be introduced via computer-aided simulations.

Main challenges in the high-pressure polymerization field are dealing with the heat balance, complex reaction networks – especially when looking at copolymerization – and polydispersity of the system simultaneously. Moreover, multi-scale modeling as well as computational fluid dynamics (CFD) gain more and more attention especially when structure-property-relationships and fluid dynamics are investigated.

Simulation-based product design in high-pressure polymerization technology utilizes a toolbox of modeling approaches: mass and heat balance, the detailed microkinetics as well as polymer properties (such as mean values and the molecular weight distribution) are calculated numerically, for example employing a customized software such as *Predici®*[71]. The re-

---

[66] J. Villermaux and L. Blavier, Chemical Engineering Science 1984, 39(1), 87-99.

[67] S. Goto, K. Yamamoto S. Furui and M. Sugimoto, J. Appl. Polym. Sci: Appl. Polym. Symp. 1981, 36, 21-40.

[68] O. F. Olaj, I. Bitai and F. Hinkelmann, Makromol. Chem. 1987, 188, 1689-1702.

[69] M. Buback, R. G. Gilbert, R. A. Hutchinson, B. Klumperman, F.-D. Kuchta, B. G. Mandersd, K. F. O'Driscolle, G. T. Russello and J. Schweer, Macromol. Chem. Phys. 1996, 196, 33267-3280.

[70] C. Kiparissides, Chem. Eng. Sci. 1996, 51(10), 1637-1659.

[71] M. Wulkow, Macromol. React. Eng. 2008, 2, 461-494

action coefficients for the detailed kinetics are derived from independent laboratory experiments and the corresponding polymer samples were characterized thoroughly with respect to molecular weight distribution, branching and functional groups. This makes it possible to use the resulting deterministic model to describe various reactor types ranging from mini-plant to world scale.

The special feature and challenge within the free radical high-pressure (ethylene) polymerization are the resulting (randomly) branched macromolecules, because branching structure (topology) and distribution influence processability and product properties dramatically. Thus, the interest in modeling branching degree and distributions is high[72]. When it comes to distinct branching structures and macromolecular topology, Monte Carlo techniques proved to be a powerful tool. Both, full Monte Carlo simulations[73] as well as hybrid stochastic approaches[74,75] have been developed and applied successfully[76]. (Hybrid) Monte-Carlo simulations yield the topologies of individual macromolecules and thus give a better and deeper understanding of branching structure (see Fig. 30).

In the next step the molecular topologies produced in Monte Carlo simulation can be used to model the rheological behavior of the respective product and thus hint at possible application properties[77]. In that way, the full range of model based design from process conditions, reactor configuration and operation to polymer characteristics and finally to application properties of products is accessible.

Performing reactive CFD simulations of the system provide temperature distributions and the forces that act on the polymer chains. This can in return help to deepen our understanding of the microkinetics such as the mechanical scission of polymer chains. Another example is the investigation of boundary layer phenomena: in wall-near areas product with high molecular weight is produced, which is responsible for

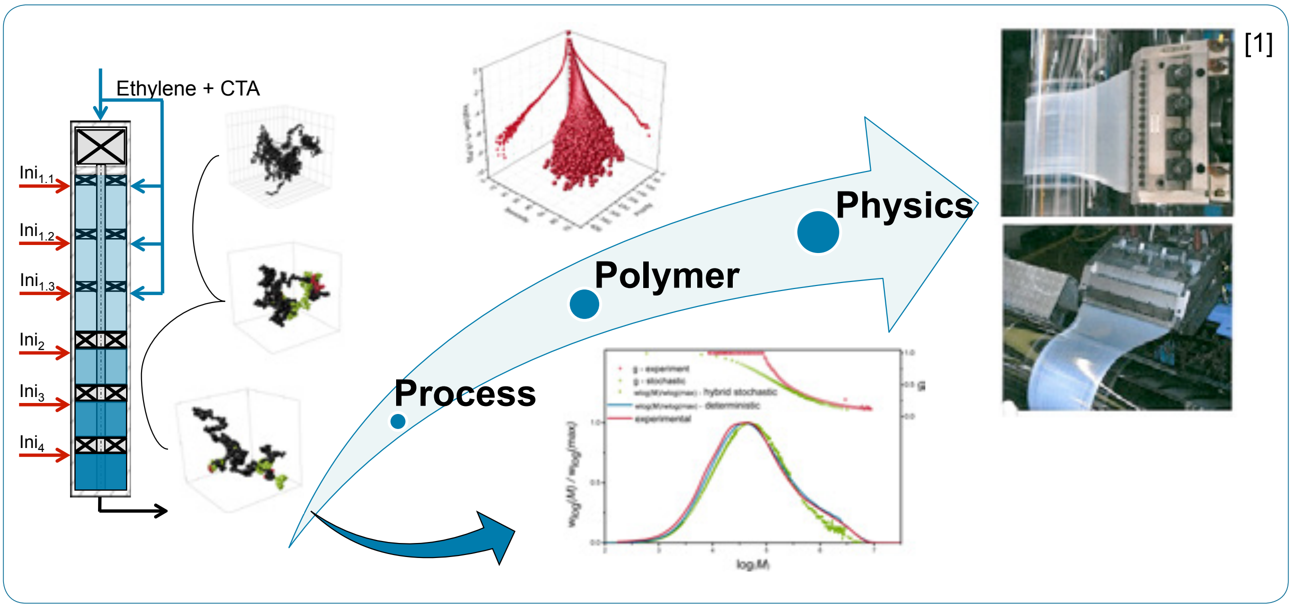


Figure 30: Schematic illustration of high-pressure polymer reaction engineering: with the help of process data deterministic simulations coupled with a hybrid Monte-Carlo approach yield polymer properties and molecular topologies which can be used to predict polymer physics and application properties (1: with kind permission of I. Vittorias, World Congress on Chemical Engineering, Montreal 2009).

---

72 P. D. Iedema, M. Wulkow and H. C. J. Hoefsloot, Macromol. 2000, 33, 7173-7184.
73 H. Tobita, J. Polym. Sci. Part B Polym. Phys. 2001, 39, 391-403.
74 D. Eckes and M. Busch, Macromol. Symp. 2016, 360, 23-31.
75 S. Fries, D. M. Castañeda-Zúñiga, J. Duchateau, P. Neuteboom, C. Toloza Porras and M. Busch, Macromol. Symp. 2016, 360, 78-86.
76 A. L. Brandão, J. B. Soares, J. C. Pinto and A. L. Alberton, Macromol. React. Eng. 2015, 9(3), 141-185.
77 D. J. Read, D. Auhl, C. Das, J. Den Doelder, M. Kapnistos, I. Vittorias and T. C. McLeish, Science 2011, 333(6051), 1871-1874.

the so-called fouling of the reactor. Investigating the underlying kinetic and diffusional effects is important to understand and avoid this unwanted heat-transfer-limiting effect[74,75].

This toolbox gives a consistent picture and thus makes it possible to perform reverse-engineering, so that both product properties and process conditions can be optimized and predicted by performing the corresponding simulations. However, it has to be highlighted that employing rational-predictive methods is crucial for reliable and successful simulation-based process optimizations and product design.

CASE STUDY 5: CONTINUOUS SYNTHESIS OF ARTEMISININ AND ARTEMISININ-DERIVED MEDICINES

Background

Numerous continuous reaction processes have been developed in the last century to produce the large amount of bulk chemicals and commodities required. These processes allow production under steady sate conditions, which offers extensive use of automation and provides improved product quality compared to batch operation. The current technologies to produce ethylene, propylene, methanol and ammonia provide just a few examples for the application of continuously operated reactors. In contrast, batch-wise operation is still prevailing in the area of producing fine chemicals and specialties. However, batch processes are significantly more labor-intensive, they require often solvent removals and purifications of intermediates following each reaction step. Also in chemical synthesis intensive efforts were made in the last decade to develop “Flow Chemistry”[78]. The use of potentially dangerous reagents, such as oxygen or sodium borohydride, becomes possible in flow and allows for new reaction pathways. The ability to combine and interchange different reaction modules allows for the production of a variety of APIs. Continuous and modular concepts possess attractive scientific and conceptual implications for the synthesis of small molecules. To develop and implement continuous manufacturing processes requires beyond the reaction steps the implementation of continuously operated separation and purification processes[79]. Also in this area significant progress has been achieved in the last years exploiting e.g. the potential of Simulated Moving Bed (SMB) chromatography and dedicated crystallization processes[80,81,82].

Contribution through reaction engineering

A demonstration of the power of a fully continuous multi-step synthesis regime combined with a continuous three-stage purification method was recently given for the production of artemisinin based antimalaria drugs.

The Chinese scientist Tu Youyou received in 2015 the Nobel Prize in Physiology or Medicine for the discovery and investigation of the antimalarial activity of artemisinin, a secondary metabolite of sweet wormwood (*Artemisia Annua*).

Since the amount of artemisinin produced from plants is not sufficient to treat the worldwide malaria cases, an effective semisynthetic method was developed that is capable of producing artemisinin from dihydroartemisinic acid (DHAA) obtained as a byproduct during the extraction of artemisinin from plant leaves. The essential step is a photocatalytic reaction to convert continuously DHAA into a precursor of artemisinin exploiting a tubular reactor[83].

A subsequently developed continuous, divergent synthesis system which is coupled to continuous purification and capable of producing four anti-malarial APIs is described in[84]. The

---

[78] Kirschning A. (Ed.), Chemistry in flow systems, Thematic Series in the Open Access Beilstein Journal of Organic Chemistry.

[79] Mascia, Heider, Zhang, Lakerveld R. , Benyahia, Barton P. , Braatz R. , Cooney, Evans, Jamison, Jensen K., Myerson A., Trout B., End-to-end continuous manufacturing of pharmaceuticals, Angew. Chem. Int. Ed., 52, 2013, 12359.

[80] O’Brien A.G., Horváth Z., Lévesque F., Lee J.W., Seidel-Morgenstern A., Seeberger P.H., Continuous synthesis and purification by direct coupling of a flow reactor with simulated moving-bed chromatography, Angew. Chem. Int. Ed., 2012, 51, 7028-7030.

[81] Lee J.W., Horváth Z., O’Brien A.G., Seeberger P.H., Seidel-Morgenstern A., Design and optimization of coupling a continuously operated reactor with simulated moving bed chromatography, Chem. Eng. J., 2014, 251, 355-370.

[82] Kaemmerer H., Horvath Z., Lee J.W., Kaspereit M., Arnell R., Hedberg M., Herschend B., Jones M.J., Larson K., Lorenz H., Seidel-Morgenstern A., Separation of racemic bicalutamide by an optimized combination of continuous chromatography and selective crystallization, Organic Process Research and Development, 2012, 16, 331-342.

[83] Kopetzki D., Lévesque F., Seeberger P.H., A Continuous-flow process for the synthesis of artemisinin, Chem. Eur. J., 2013, 19, 5450-5456.

[84] Gilmore K., Kopetzki D., Lee J.W., Horváth Z., McQuade D.T., Seidel-Morgenstern A., Seeberger P.H., Continuous synthesis of artemisinin-derived medicines, Chem. Comm., 2014,50, 12652-12655.

system is comprised of three linked reaction modules for photooxidation/cyclization, reduction, and derivatization. A fourth module couples the crude reaction stream with continuous purification exploiting dilution/filtration, gradient chromatography and crystallization[84,85] (see Fig. 31).

The possible synthesis of the four anti-malarial APIs described here illustrates the applicability of the general principle. With this example of coupled divergent, multi-step continuous synthesis and purification processes, many efficient routes to provide drugs can be envisioned.

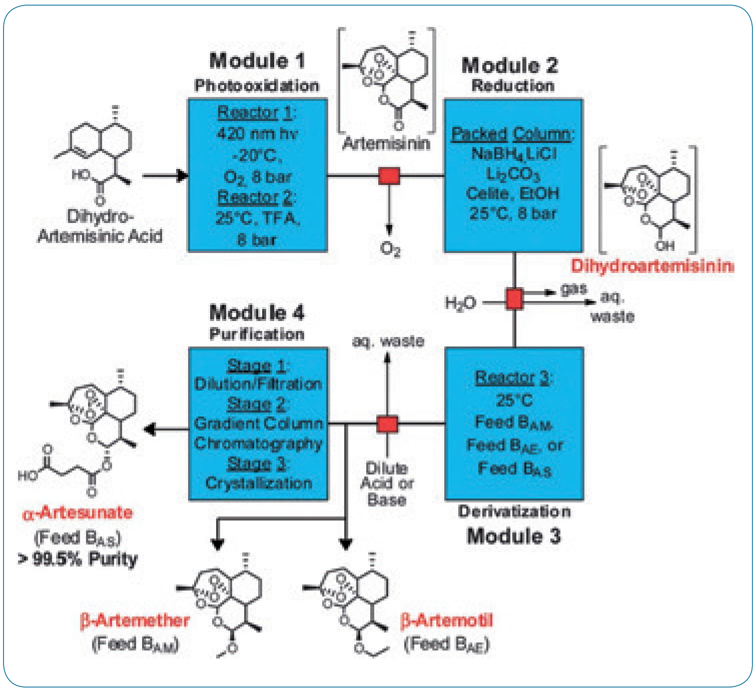


Figure 31: Overall production scheme of anti-malaria APIs from dihydroartemisinin and artemisinin obtained by traditional extraction from Artemisia annua using four module system for the continuous synthesis and purification of four artemisinin based APIs (marked in red): dihydroartemisinin (combined with piperaquine in Eurartesim, Artekin and Duo-Cotecxin), β-artemether (combined with lumefantrine in Coartem), β-arteether (Artemotil), and α-artesunate (combined with amodiaquine in Coarsucam and ASAQ-Winthrop)[84].

---

[85] Horváth Z., Horosanskaia E., Lee J.W., Lorenz H., Gilmore K., Seeberger P.H., Seidel-Morgenstern A., Recovery of artemisinin from a complex reaction mixture using continuous chromatography and crystallization, Organic Process Research and Development, 2015, 19, 624-634.

7 Outlook

In a globally integrated world with a growing world population, the demand for sufficient accessibility of high quality drinking water and food as well as living space and energy is increasing. In addition, local individual customer needs are changing with increasing wealth in developing and emerging countries. This opens up many opportunities for new products, technologies and markets. Consequently, the chemical industry is facing a variety of challenges to deliver to social and economic "market pulls" for novel products whilst meeting environmental standards and new regulatory constraints (see Fig. 32). Alternative process routes will be required. In Europe, the objectives of the German Federal Ministry for the Environment, Nature Conservation, Building and Nuclear Safety regarding renewable energies are a pioneering example for novel technological requirements. Furthermore, the rapid changes in society and industry through digitalization and other enabling technologies foster innovation and will determine the future chemical engineering toolboxes.

The finite nature of fossil resources together with the intended reduction in the emission of greenhouse gases are the main drivers to develop processes for renewable feedstocks, preferably utilizing renewable energy. Research fields currently emerging from this undertaking are the **Power-to-X-technologies (PtX),** the utilization of biomass and of CO_2. PtX-technologies aim to store the increasing amounts of electric energy available from renewable sources in chemical compounds. While **electrochemical and photochemical routes** are, in principle, capable of achieving the energy conversions sought, the challenges of implementating them into industrial processes are still high and call for further research.

The reduction of the CO_2 footprint of the chemical industry can be tackled by developing more energy efficient processes and competitive process technologies for biomass and CO_2 conversion. **Carbon-Capture-and-Utilization concepts** might further contribute to the reduction of the CO_2-footprint and provide a new C1-platform. All these technologies have in common that the appropriate approaches will be locally diverse, depending on the boundary conditions of the region and production site.

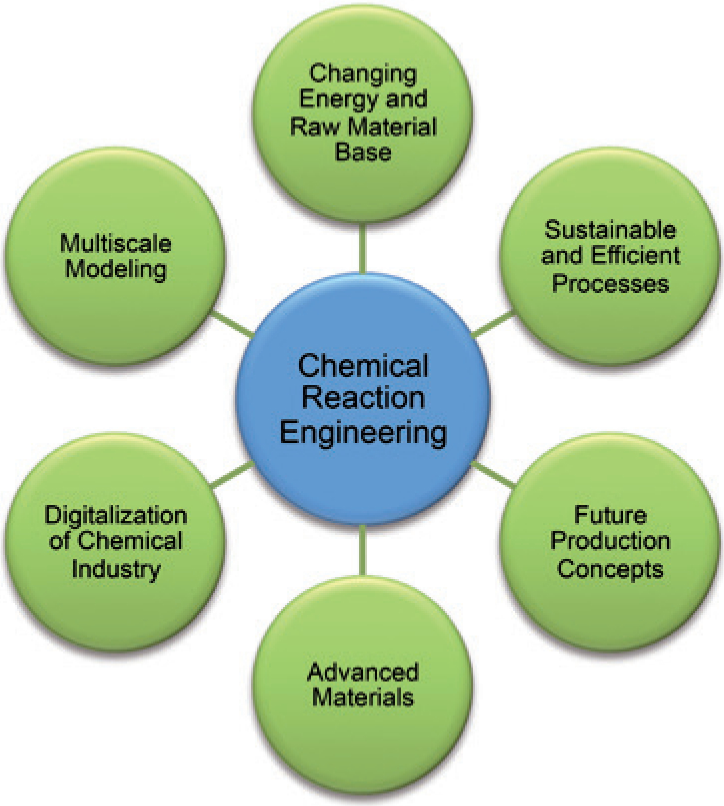


Figure 32: Key trends and future challenges for Chemical Reaction Engineering.

The changing raw material situation and ongoing environmental pollution concerns have been the subject of much attention over the last decades. Growing customer awareness and the demand for sustainable products have motivated calls for novel **bio-derived chemical routes** as well as **waste stream utilization strategies.** Holistic process design along the whole value chain is a key factor in the bid to achieve a **"circular economy". Heat and mass integration** in such more diverse process landscapes, **zero liquid discharge concepts** and **recycling of urban waste streams** into the chemical industry will form the future focuses of academic and industrial research and development.

The above-mentioned transformation in economy and ecology necessitate production concepts, which are able to process new raw materials and can utilize renewable electricity. Both these inputs are of a fluctuating nature, implying an additional need for **unsteady state operations.** The utilization of electricity as alternative energy source (or as ultrasound, microwave, plasma, light, etc.) means a switch from conventional dedicated and optimized processes to robust arrangements suitable for dynamic operation. As a novel design paradigm, such **tolerant processes** both offer and demand high flexibility through original plant designs or operational innovations.

Modular, transportable plants enable one to increase production locally and flexibly and thus shorten project lead-times for the global production footprint. Modular plant design based on **intensified processes** with **hybrid and multi-functional equipment** ensure process efficiency together with process robustness through technological flexibility. Such plant concepts also permit multi-purpose production in a continuous operation mode.

In **heterogeneous catalysis,** fundamental developments of forgiving process technologies or novel robust catalysts are essential. Unsteady state operations, bio-based products, increased demands for higher selectivity and reduced energy consumption as well as REACH regulations are all predicated upon innovative solutions for catalytic materials, supports, reactors and operational strategies.

New advanced materials with specially tailored qualitative characteristics and functionalities are enablers for e.g high performance batteries or lightweight construction materials for cars and airplanes. Technical solutions are not based on chemical compositions alone. They also have to be combined with structural features, e.g. composites including nano-scale particles or tubes. Microreaction technology and large-scale additive manufacturing processes offer new opportunities to manufacture innovative products. The field of advanced materials clearly highlights the importance of interaction between material science and engineering disciplines in the development of industrially scalable processes.

The impact of **digitalization** on manufacturing industries, including the chemical industry, is growing steadily. **Industry 4.0** will drastically affect the interaction of industry with customers, and the availability of data, but will also unlock novel process design and optimization tools. Two main fields of relevance for chemical processing can be identified: the development of advanced process control systems and the management of **"big data"**. Both fields can be applied to the optimization and intensification of chemical processes, but the largest impact can be expected on the development of the next generation of production processes from scratch, making intense use of digital technologies and linking plants along the value chain with one naother. New fields of education, research and development are required, such as "data" engineers or chemists, who will handle and analyze the huge amounts of data involved. A new kind of research is essential to ensure the correct interpretation of the insights and correlations to be gained from Big Data. The benefit will be especially significant if the data for entire production sites is networked and fluctuations, e.g. in energy, can be compensated for by high-level control of all production plants based on real-time data. The link between IT and chemical engineering is becoming a key factor for success.

The development, design, optimization and scale-up of chemical processes are premised upon reliable models. In most cases, a detailed understanding at multiple scales – from the catalyst up to the whole plant – is a prerequisite for the development of these models. Thus, **multi-scale modeling** approaches from different fields, such as quantum mechanics, computational fluid dynamics, reaction engineering and fluid separation technology need to be combined. The shift towards forgiving processes mentioned above, further raises the bar for model development (e.g. dynamic process models) and significantly increases the need for robust models. Model reduction methods therefore need to be developed, which can serve as a basis for conceptual process design, e.g.

with limited property data. In addition, such models can cut the numerical effort for optimizing a process considerably by identifying unfeasible operating conditions and by narrowing down the range of operating parameters prior optimization with more detailed models. Furthermore, the continuous improvement in the reliability of the process models calls for methods that facilitate model adaptations and refinements based on the comparison of the measurement data ("big data") available from plant operation with the model predictions. **Hydrid models** amalgamate deterministic modeling with data-driven approaches, like artificial neuronal networks or nonlinear statistics.

Opportunities from the changes in global markets combined with demands for innovative products, raw materials, technologies, energy supply and legislation entail new research activities based on **highly interdisciplinary approaches for fundamental and applied research.** Industrial and academic research has to become more closely entwined. The development of PtX-technologies, processes for CO_2 capture and utilization as well as biomass conversion offer textbook examples. Close cooperation between material science, biotechnology and chemistry as well as process, reaction and polymer engineers is required. Future chemical engineers require a thorough training in chemical engineering fundamentals complemented by interdisciplinary courses with special focus on the above-mentioned topics. The education should emphasize the synergy between experiment and model as well as the importance of holistic thinking, to enable the next generation of engineers to master the challenges they will encounter. Innovation will take place more and more at the interface between disciplines.

IMPRINT

Authors:

David W. Agar	TU Dortmund
Martin Bertau	TU Bergakademie Freiberg
Markus Busch	TU Darmstadt
Maria Casapu	KIT – Karlsruher Institut für Technologie
Peter Claus	TU Darmstadt
Karla Herrera Delgado	KIT – Karlsruher Institut für Technologie
Dana Demtröder	DECHEMA e.V., Frankfurt
Olaf Deutschmann	KIT – Karlsruher Institut für Technologie
Roland Dittmeyer	KIT – Karlsruher Institut für Technologie
Christian Dreiser	Clariant Produkte (Deutschland) GmbH, Frankfurt
David Eckes	TU Darmstadt
Bastian Etzold	TU Darmstadt
Georg Fieg	TU Hamburg-Harburg
Hannsjörg Freund	Universität Erlangen-Nürnberg
Jan-Dierck Grunwaldt	KIT – Karlsruher Institut für Technologie
Robert Güttel	Universität Ulm
Erik von Harbou	TU Kaiserslautern
Thomas Herrmann	TU Darmstadt
Kai-Olaf Hinrichsen	TU München
Johannes Khinast	TU Graz
Elias Klemm	Universität Stuttgart
Norbert Kockmann	TU Dortmund
Ulrike Krewer	TU Braunschweig
Michael Nilles	BASF SE, Ludwigshafen
Holger Marschall	TU Darmstadt
Martin Muhler	Ruhr-Universität Bochum
Stefan Palkovits	RWTH Aachen
Michael Paul	hte GmbH, Heidelberg
Kristina Pflug	TU Darmstadt
Stefan Radl	TU Graz
Jörg Sauer	KIT – Karlsruher Institut für Technologie
Stephan Schunk	hte GmbH, Heidelberg
Andreas Seidel-Morgenstern	Otto-von-Guericke-Universität Magdeburg
Michael Schlüter	TU Hamburg-Harburg
Markus Schubert	Forschungszentrum Dresden-Rossendorf e.V.
Kai Sundmacher	Otto-von-Guericke-Universität Magdeburg
Thomas Turek	TU Clausthal
Iakovos Vittorias	Lyondell Basell Industries, Frankfurt
Herbert Vogel	TU Darmstadt
Olaf Wachsen	Clariant Produkte (Deutschland) GmbH, Frankfurt
Horst-Werner Zanthoff	Evonik Technology & Infrastructure GmbH, Marl
Dirk Ziegenbalg	Universität Stuttgart

Publisher:
ProcessNet Subject Division
Chemical Reaction Engineering

Responsible for content under the terms of press legislations:
DECHEMA e.V.
Dr. Andreas Förster
Theodor-Heuss-Allee 25
60486 Frankfurt am Main
Germany

Publication date: May 2017

ISBN: 978-3-89746-193-2

DECHEMA
Gesellschaft für Chemische Technik
und Biotechnologie e.V.
Theodor-Heuss Allee 25
60486 Frankfurt am Main
www.dechema.de

ISBN: 978-3-89746-193-2