12
Microstructures as a Tool for Production in the Tons per Hour Scale

Dirk Kirschneck and Günter Tekautz

12.1
Introduction

12.1.1
Driving Forces for Using Microstructures

Fine chemical-producing companies have increased market pressure caused by new competitors. This pressure generates a need to increase the performance development and production processes and to reduce costs. As shown in Figure 12.1, process intensification by means of microprocess technology can contribute significant improvements in four segments:

- yield improvement and energy savings
- continuous design of processes
- shorten the time to market
- novel types of products.

Discussions of how microstructures improve the yield and how microprocess engineering can generate savings are topics in several other chapters and will not be repeated here. Continuously working plants have led to a completely different manufacturing structure. Labor costs are the main advantage of the new competitors in the Far East. Automation is easy for continuous working processes using microstructures. Labor costs can be saved and the performance can be increased based on microchemical engineering principles. Scale-out becomes easier, since there is no need for a large number of scale-up experiments. New windows of operation have a significant impact on saving processing costs. As shown later, these tools are well suited to high-speed development. New process regimes offer a wide range of new products, which cannot be produced under conventional conditions.

Micro Process Engineering, Vol. 3: System, Process and Plant Engineering
Edited by V. Hessel, A. Renken, J.C. Schouten, and J.-I. Yoshida

ISBN: 978-3-527-31550-5

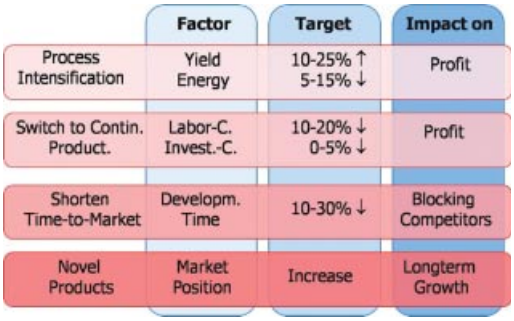

Figure 12.1 Driving forces for process intensification.

12.1.2
Important Impacts on the Development Process

Microprocess technology causes a fundamental change in the development approach. Chemical development is done by chemists in the laboratory. After the chemists have finished their work, the process development is done by the chemical engineers. These two steps are carried out in two different departments one after the other and separated from each other. In microprocess engineering, it is necessary to connect these two. They grow together and permanent interaction leads to a much better production process, since chemists and chemical engineers think in different parameters. The laboratory-scale plant will be the development tool for the chemist and for the chemical engineer. The chemist defines the needs for the reaction and the chemical engineer fulfils these needs by adjusting the laboratory-scale plant. The necessity for and importance of pilot-scale experiments will decrease, since a lot of process development can be done on a laboratory scale. Expensive pilot-scale experiments are reduced to a minimum, since the same dimensions of microstructures are used on every scale. Therefore, microchemical engineering permits a fast and cost-efficient chemical and process development and provides an easy scale-out [1]. Three main factors increase the development speed using laboratory-scale plants based on microprocess engineering. The first is generated by the method. As described above, there is interaction between the chemist and the chemical engineer. Their work packages in a development project will be delivered nearly simultaneously. As second point for development speed-up is that the laboratory-scale plants can easily be automated to run without an operator on a 24 hours, 7 days per week basis. This usually leads to problems in the analytical department, since these plants produce a large number of samples in a very short time. Online analytics can solve this problem. This means that online analytics is the third important factor to speed up the development. Online analytics is a rapidly developing field, and Koch *et al.* give a good overview of the applicability, possibilities and limitations of different methods [2].

The most important paradigm change is caused by a fundamental change in the philosophy of process development. Microstructured devices offer the possibility of designing the plant according to the needs of the process and not the other way round.

Figure 12.2 Example of a small-scale production unit.

The technology offers the possibility of using the advantages of a high-performance process instead of batch technology in completely automated small-scale production plants. This means that all newly developed processes are "intensified" processes. The advantages of large-volume processes can now be reached also for low-volume processes, as is done for most large-volume chemicals and in the petroleum industry.

12.1.3
Small-scale Production Solutions

The small-scale demand has been increasing ever since the products became more and more customer specific and time-to-market is of increasing importance [3]. Microchemical engineering offers the possibility of running a continuous plant in a laboratory environment, for example in a walk-in fume cupboard as shown in Figure 12.2. Compared with conventional production methods, benefits can be generated in two fields. First, the laboratory-scale method can be used directly as a production method. Scaling factors up to 50 cause minor changes in the plant. Adjustments can easily be carried out within a few hours. Especially for usual process conditions such as high pressure and low temperature, the transfer to production can be extremely shortened [4].

The second important point is the new chance to perform small-scale production tasks in a dedicated plant and not in a multi-purpose plant. The continuous process becomes a serious competitor to multi-purpose processes. It is a known problem of multi-purpose-plants that only part of the installed equipment is in use. Manpower is needed to run the plant and to rebuild the plant for the next product. Plants containing microstructured devices can be designed for multi-purpose applications, but the range of difference in use is usually smaller, since a typical microreactor is less flexible than a batch vessel. The decrease in flexibility is usually small compared with

the benefits caused by the shift from batch to MRT processes. MRT plants can be equipped with a high level of automation. Three points need to be considered if a dedicated plant is to produce in a laboratory environment:

- storage of educts and products
- separation steps, which are necessary to clean the product
- energy supply (heat, cooling).

These three points are not very different from conventional production. The separation in microtechnology is still under development and it depends on the application, if it is already available. If they are not available on the micro-scale, the plant size increases and one reaches the next level. The next level will be a dedicated plant in a pilot-scale environment or a plant in a container. For the first and third points, the storage and the energy supply are just a question of infrastructure. These things are not that common in a laboratory environment at present, but there is no problem in principle in installing it there. Figure 12.2 shows a plant in a fume cupboard. For infrastructure reasons, it may be useful to install it in a pilot-plant environment, since the described infrastructure is usually present. If possible, it can be interesting to install the plant in a fume cupboard, since this could be a possible way to cope with the ATEX regulations. The technology has the potential to reach areas far beyond the development laboratory inside large companies. The technology offers the possibility of preparing customized products at the point of sale. Pharmacies can prepare creams according to the skin type of a specific person. Drug delivery systems can be adjusted to diagnostic results.

12.1.4
Multi-purpose or Dedicated for Small Volumes

At present 60% of traded chemicals have production volumes of less than 10 t p.a. This shows a clear need for an effective way to produce these small quantities. Up to now, small quantities in chemical synthesis can only be produced in batch on a multi-purpose basis. The first question to answer is which production mode is the more economic: batch or continuous? This question is new, since there was hardly any adequate equipment to carry out small applications in a continuous mode. Microchemical engineering offers several new possibilities to improve this situation. There are some strong arguments to produce these small quantities in a continuous mode:

- 40–60% of the installed equipment will usually not be used.
- Most of the top 300 chemicals are produced continuously for economic reasons.
- Automation is easier for continuous processes (saves manpower).
- Processes can be adjusted to the process needs by means of microreaction technology.
- High costs due to transfer to production, product change and cleaning.
- Possibility of carrying out processes up to 30 kg h^{-1} in a laboratory environment.
- Possibility of designing dedicated processes for small volumes.

There are also some arguments for batch production:

- Existing plants need to be used (more plants than products).
- Existing methods for production.
- High experience level with plants and methods.

The decision for a plant concept must be taken separately for each individual case and no general suggestion can be given here. However, there are some possible factors that give hints for continuous production. Important factors, among others, are:

- large yield improvement for high-price products
- high saving potential in labor costs
- insufficient process performance in batch (e.g. due to exothermic character).

In general the concept opens up many possibilities for strengthening the competitiveness of chemical companies.

12.1.5
Microstructures as a Production-scale Solution

Microreaction technology is no longer solely of academic interest. It should also become an effective tool for process intensification for the chemical industry. That is why numerous companies have taken the opportunity to carry out some research work in this field [5]. Some of them are even subsidized by research projects such as DEMIS (Demonstration Project to Evaluate Microreaction Technology for Industrial Systems) [6] and IMPULSE (Integrated Multiscale Process Units with Locally Structured Elements) [7].

The efforts of industry and academia have led to the successful installation of microreactors in existing production plants. In the following, a few examples of the industrial application of microstructured devices are given.

One of these striking examples is a high-performance microreactor used in a main production step at DSM Fine Chemicals. About 300 t of a high-quality product were produced during a 10-week campaign. The reactor is able to handle throughputs of about 1.7 t h^{-1} of liquid educt.

A micro heat exchanger developed by the Forschungszentrum Karlsruhe (FZK) was installed in a coffee powder-producing plant in 2002. It is responsible for the cooling of carbon dioxide [8].

In 2005, Xi'an Huian Chemical Industry Co. started the production of nitroglycerine using a microreactor plant, which allows a throughput of about 15 kg h^{-1} of product. It is worth mentioning that the nitroglycerine produced is used for medical purposes and therefore has to be of high quality. These demands were met fully with the help of microreaction technology [9].

However, these plants are not the only ones that are running successfully using microreaction technology. Hessel *et al.* [10] state that there are 30–40 plants installed worldwide, of which about 20 are mentioned in the literature.

Due to the excellent applicability of microreactors for industrial purposes, many well-known companies are testing this technology at the laboratory or pilot-plant level. Degussa and Uhde have investigated microreaction technology for the catalytic gas-phase epoxidation of propene with hydrogen peroxide [11]. A plant consisting of a microreactor, micromixer and microevaporator was constructed on the pilot scale and successfully tested [6, 12]. Clariant was able to intensify the processes of synthesizing phenylboronic acid [13] and azo pigments [14] by building up microreactor pilot plants. UOP performed pilot-plant processing and economic evaluation for the direct synthesis of hydrogen peroxide. During the test phase, 90% conversion and 85% selectivity could be achieved [15]. Lonza [16] and Sigma-Aldrich [17] have also carried out some serious research work concerning the applicability of microreaction technology for industrial purposes.

This list could be continued; – for details, see the literature [18–20].

12.2 Production-scale Case Study

12.2.1 The Batch Process

This case study report deals with the production of fine chemicals. This summary of the application is based on a previous publication by Kirschneck and Tekautz [21]. The basic aim of the project was to enhance the capacity of an existing plant by process intensification and by switching to a continuous plant operation. An additional benefit should be gained by less reaction volume in continuous operation mode, as one of the educts is strongly toxic. Microreaction technology was a most promising technology to fulfill these aims.

Prior to the need for enhancing the plant capacity, the process was carried out discontinuously in a 10-m^3 batch vessel. The process itself is separated into two steps. The first is a strongly exothermic chemical reaction. As one of the educts therein is a highly toxic and volatile chemical, the vessel had to be strongly cooled to avoid evaporation and high pressure. On the other hand, the second reaction step is endothermic, and it needs to be heated for hours to finish the reaction. The end of reaction one is defined as the time when all of the volatile and toxic educt has reacted. This is the point when heating of the reaction mixture can be started.

The process of the two steps took several hours and an overall throughput of about 1800 kg h^{-1} resulted. A throughput of about 3500 kg h^{-1} should be achieved by the new processing method. No further details of the process or the chemical reaction can be given here due to a non-disclosure agreement with the customer.

12.2.2 Basic Feasibility

The first step in this project was a basic feasibility study. The aim of such a study is to gain information about the process in microstructured devices to help the customer

to make further decisions. Additionally, a basic R&D flow sheet is created for a laboratory-scale plant to do further process optimization. Both cannot be achieved by literature study alone.

The process information is obtained by performing the reaction in a customizable laboratory-scale plant. This plant is modified during the study to find the best-fitting equipment. The conveying system, microstructured reactor and peripheral devices are varied and the plant design is optimized to create a laboratory-scale plant that is able to carry out the reaction successfully. The most important step in this procedure is the reactor selection, as this has a direct impact on the step of scaling out. There are already numerous microreactors available off the shelf and many more are available on request in collaboration with the manufacturer. A detailed description of reactor selection can be found in Chapter 3 of this volume. At this point, only the importance of the impact of the further processing of the results of such a feasibility study on the selection process should be noted. A successful feasibility study with a reactor operating in the microliters per minute range may be of no or small relevance if the customer needs a tons per hour scale plant to be realized on a relative short time scale. Even if there are numbering-up methods available they may be expensive and time consuming.

When a stable operating plant is designed, the influence of some key process parameters, such as temperature, pressure or concentrations, is estimated by experiments at two extreme values. This gives a first guess at a parameter window and/or an idea of how to modify the parameters for process optimization.

The basic R&D flow sheet is a direct result of the optimization process during the feasibility study. This and the first experiments with process parameters are the basis for a laboratory-scale plant for a possible further process optimization.

12.2.3 StarLam Concept

For the development of production applications in the range 1–5 t h^{-1}, which is the target range for the throughput of this project, the StarLam reactor concept can be a good solution, as four different StarLam reactors are commercially available in a throughput range from 6 to 30 000 L h^{-1}. This "scaling out" has been carried out through a smart increase in characteristic size [22]. The pros and cons of this method have been discussed elsewhere. Especially reactors up to 5 t h^{-1} have been characterized very well. Another argument for the Starlaminator is the option of internal numbering-up [23]. This gives the possibility of varying the microstructure to fit it to a given process in a certain range. In this way, channel diameters can easily be varied and the correlation of throughput, pressure drop and mixing quality can be adjusted to some extent. Also, differences in the phase ratio or in viscosities can be considered in the micromixer set-up.

One drawback of the StarLam reactor concept is the lack of a real "laboratory-scale" sized reactor. The smallest Starlaminator (StarLam 30) is designed for 30 L h^{-1}. By adapting the internal mixing stack of platelets, good mixing qualities can be achieved at throughputs above 6 L h^{-1}. This is a fairly high throughput for extensive parameter

screening and process development and therefore leads to a high consumption of chemicals. Other issues are mixing quality and heat dissipation capability. Both can sometimes be achieved in other microreactors to a greater extent. However, the Starlaminator combines a still very good mixing quality with a wide range of applicability. The Starlaminator has no integrated cooling circuit but for almost all, even highly exothermic, reactions, it is sufficient to cool the reaction mixture right after the reactor exit. This is due to very short residence times in the reactor.

12.2.4
Laboratory-scale Plant

This project was started by carrying out a basic feasibility study. It is known that reactions in continuous microreactor plants can be made under severe conditions that are not achievable in common equipment, for example higher pressure to obtain higher reaction temperatures [24]. Reaction times can be reduced from hours to seconds due to the raised temperature and the microstructure often without suffering in selectivity [13, 25, 26]. The aim was to execute the first reaction step under pressure to avoid the evaporation of the volatile, toxic educt. The feasibility study should show if the good mixing quality in the microreactor and the higher temperature accelerate the reaction sufficiently to finish it on a reasonable time scale for continuous processing.

A continuous laboratory-scale plant was adapted to fit the needs of the process. In the first step, a high-pressure version of IMM's SIMM was used. This was due to the known good mixing quality and the high reachable temperature. After first successful experiments with this reactor, proving the feasibility of the reaction on a microreactor plant, it was decided to change to the StarLam reactor concept. This reactor change was motivated by the advantages discussed in Section 12.2.3.

Due to short residence times inside the micromixer almost no heat was released there. In the residence time tube, temperatures up to 150 °C have been observed. In these experiments, we were able to show that it is possible to finish the first reaction step on the continuous microreactor laboratory-scale plant in less than 60 s. The same reaction step in the cooled batch vessel of the production plant took about 4 h. With these results, we came to the conclusion that it should be possible to realize the first exothermic step of the process in a microreactor. After finishing this step continuously in a closed system, the reaction solution could be transferred into the existing batch vessel and be heated there to finish the second reaction step. As the time for the first step is reduced from several hours to a few minutes for the same amount of product, it should be possible nearly to double the capacity just by installing a microreactor right before the existing batch vessel to mix the first two educts.

12.2.5
Optimization and Integration

The further optimization of the process was done by the customer. Microinnova delivered a laboratory-scale microreactor plant and gave support for the optimization.

Figure 12.3 StarLam 3000 in production surroundings [21].

The plant was the outcome of the feasibility study. Therefore, the plant configuration was fitted well to the needs of the process. After the optimization of the process on the laboratory scale, the integration of the StarLam reactor into the existing plant followed directly. Calculations based on dimensionless numbers carried out by the engineering team of Microinnova were the basis for the definition of the inside set-up. A photograph of the installed StarLam 3000 in the production surroundings can be seen in Figure 12.3. The inlet pipes of the two starting educts to the batch vessel were simply connected to the StarLam reactor. The only change to the previous feed lines was the installation of appropriate instrumentation and of filter cartridges right before the entries to the microstructured reactor. Of course this was necessary to avoid blocking of the reactor. The pressure drop in the line was lower than 3 bar, which made it possible to keep the hitherto used pumps in the plant. This decision has kept the costs as low as useful to reach the aim of the project. At the outlet of the reactor, a retention tube was installed to give the necessary time to finish the first reaction step. It showed during the optimization that it was sufficient to insulate the reaction tube to achieve a high enough temperature to finish the reaction. The pipe ends directly in the batch vessel where the second endothermic reaction step is realized as previously.

The first start-up of the plant took place in June 2005. Process parameters of this start-up are shown in Figure 12.4. The graphs in the bottom diagram show that the final throughput of 3600 kg h^{-1} was reached in three steps. The diagram at the top

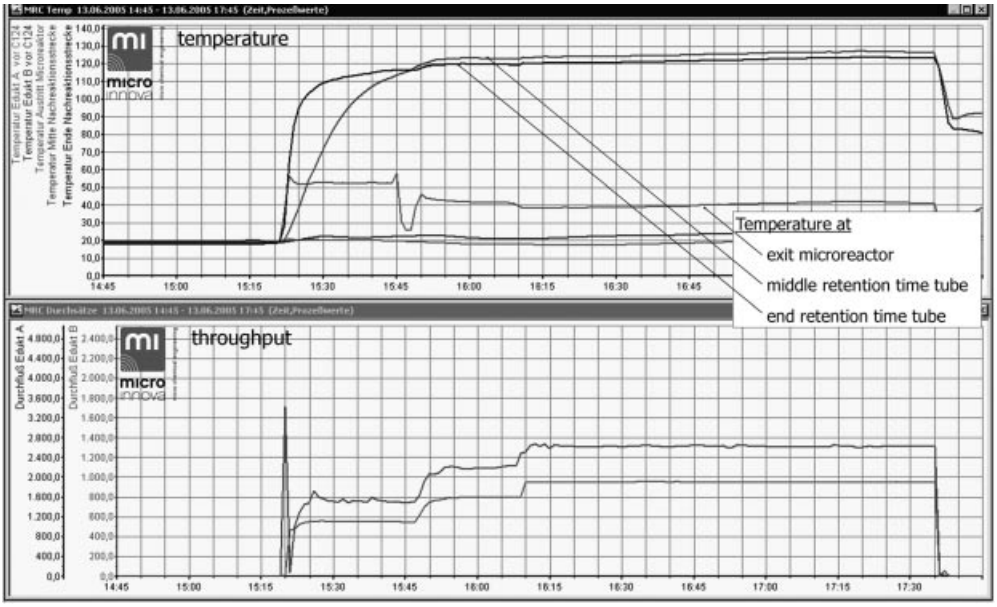

Figure 12.4 Process parameter diagram for the first test run.

shows three temperature graphs. The first was installed directly after the micromixer. This graph shows a maximum temperature of about 40 °C. This value proves that almost no heat release can be observed inside the micromixer. The second graph in the temperature diagram shows that all reaction enthalpy is released by the second measuring point in the middle of the retention tube. The temperature graph at the outlet of the retention tube shows a sliding decrease in temperature compared with the measuring point in the middle. This can be explained by a loss caused by insufficient insulation.

Already in this first test run good product was achieved and no further major adjustments had to be made to meet the specifications of the product. The temperature of the solution leaving the retention time tube was about 130 °C, which means that the heating process for the second endothermic reaction step needs less energy.

12.2.6 Summary

The conventional set-up of the plant was able to manage a throughput of 1.8 t h^{-1}. The double throughput of 3.6 t h^{-1} was already achieved in the first test run. The throughput in the production process was finally reduced to about 3 t h^{-1}, due to overall process necessities. One of the main reasons was the work-up of the product. Hence the main goal set by the customer was achieved by the installation of the microreactor. This installation and the associated speed-up of the first reaction step lead to a doubling of the throughput. In comparison with the installation of a

new batch vessel, which would have been necessary for capacity doubling with conventional methods, the installation of the StarLam 3000 was much more cost saving. A new batch reactor would have been up to 10 times more expensive. No additional problems due to the microstructured reactor occurred during the authorization procedure.

The second great benefit of this project was the realization of savings on energy costs. In the conventional process, the first step of the reaction had to be cooled. The energy needed for the cooling process can be saved. With the new continuous process, it is possible to do the first step without cooling and at higher temperatures. Additionally, the product solution leaving the process tube is hot, so less energy is necessary for heating the solution for the last process step.

The installation of the StarLam 3000 took place in June 2005. Since then, the reactor has been in permanent production use and so far no severe problems with the microreactor have occurred. About 1-months after the first test run the first inspection took place in a plant maintenance period. The reactor was dismantled and the foils of the reactor were inspected. No signs of corrosion were visible after 10 months of production use.

12.3 Conclusion

To the best of our knowledge, the microreactor described is the one with the highest throughput running permanently in a production process. It shows the possibility of intensifying chemical processes on the tons per hour scale. We think that this is just a beginning. There are many reactions that can benefit from intensification in microstructured devices. More complex reactions will need special devices fitted to the problem. However, there are already devices existing that can be integrated in conventional plants as it has been shown in this example. Hence it is possible to do specific steps of the overall process in microreactors and not every single step needs to be fitted to microreaction technology. Microstructured devices should only be used where they are beneficial. Therefore, we think that microreaction technology will become a very important tool for chemical engineering in the near future, especially for fine chemicals and pharmaceuticals production.

There are strong driving forces for a fundamental change in the process industries. Complete plant automation, process intensification, alternative energy input and process on demand or in-transit processing are just a few catch phrases to show the possible direction of these changes [27–30]. Microreaction technology will be one important tool for many of these strategies. These new possibilities will cause changes in the structure of the development process towards being faster, cheaper and less resource wasting. However, first pilot- and production-scale examples, such as that described here, give strong hints that microprocess technology will become an important production-scale technology in the medium-term future also.

References

1 D. Kirschneck, M. Kober, R. Marr, New scopes in process design using microstructured devices, *Chem. Eng. Technol.* **2005**, *28*, 314–317.

2 M. Koch, K. Vanden Bussche, R. Chrisman, *Micro Instrumentation for High Throughput Experimentation and Process Intensification – a Tool for PAT*, Wiley-VCH Verlag GmbH, Weinheim, **2007**.

3 D. Kirschneck, Strategies for labscale development, in *Microchemical Engineering in Practice* (ed. T. Dietrich), Blackwell, Ames, IA, In print, Chapter 3. 2.

4 D. Schmalz, M. Häberl, N. Oldenburg, M. Grund, H. Muntermann, U. Kunz, Potenzialabschätzung der Mikroreaktionstechnik für den Einsatz in der Prozessentwicklung, *Chem. Ing. Tech.* **2005**, *77*, 859–866.

5 O. Machhammer, *Chem. Ing. Tech.* **2005**, *77*, 1635.

6 A. Hüther, A. Geisselmann, H. Hahn, *Chem. Ing. Tech.* **2005**, *77*, 1829–1837.

7 http://www.impulse-project.net.

8 http://www.fzk.de/imvt.

9 A.M. Thayer, Harnessing microreactors, *Chem. Eng. News* **2005**, *83* (22), 43–52.

10 V. Hessel, H. Löwe, P. Löb, Fit für den Produktionseinsatz, *Chem. Tech.* **2006**, *5*, 24–28.

11 G. Markowz, S. Schirmeister, J. Albrecht, F. Becker, R. Schütte, K. Carspary, E. Klemm, Microstructured reactors for heterogeneously catalyzed gas-phase reactions on an industrial scale, *Chem. Eng. Technol.* **2005**, *28*, 459–464.

12 N. Steinfeldt, D. Linke, K. Jähnisch, M. Baerns, Anwendung eines mikrostrukturierten Mehrkanalreaktors für kinetische Untersuchungen der oxidativen Dehydrierung von Propan, *Chem. Ing. Tech.* **2004**, *76*, 625–630.

13 V. Hessel, C. Hofmann, H. Löwe, A. Meudt, S. Scherer, F. Schönfeld, B. Werner, Selectivity gains and energy savings for the industrial process using micromixer/tubular reactors, *Org. Process Res. Dev.* **2004**, *8*, 511–523.

14 C. Wille, H. Gabski, T. Haller, H. Kim, L. Unverdorben, R. Winter, Synthesis of pigments in a three-stage microreactor pilot plant – an experimental technical report, *Chem. Eng. J.* **2004**, *101*, 179–185.

15 H. Pennemann, V. Hessel, H. Löwe, Chemical microprocess technology – from laboratory-scale to production, *Chem. Eng. Sci.* **2004**, *59*, 4789–4794.

16 D.M. Roberge, L. Ducry, N. Bieler, P. Cretton, B. Zimmermenn, Microreactor technology: a revolution for the fine chemical and pharmaceutical industries? *Chem. Eng. Technol.* **2005**, *28*, 318–323.

17 M.A. Rouhi, Microreactors eyed for industrial use, *Chem. Eng. News* **2004**, *82* (27), 18–19.

18 O. Wörz, K. Jäckel, T. Richter, A. Wolf, Microreactors, a new efficient tool for optimum reactor design, *Chem. Eng. Sci.* **2001**, *56*, 1029–1033.

19 A.J. deMello, R. Wootton, But what is it good for? Applications of microreactor technology for the fine chemical industry, *Lab Chip* **2002**, *2*, 7N–13N.

20 J. Choe, Y. Kwon, Y. Kim, H. Song, K. Song, Micromixer as a continuous flow reactor for the synthesis of a pharmaceutical intermediate, *Korean J. Chem. Eng.* **2003**, *20*, 268–272.

21 D. Kirschneck, G. Tekautz, Integration of a microreactor in an existing production plant, *Chem. Eng. Technol.* **2007**, *30*, 305–308.

22 V. Hessel, P. Löb, H. Löwe, Industrial and real-life uses of microstructured reactors, in *Proceedings of the 17th International Congress of Chemical and Process Engineering; Prague*, **2006**.

23 B. Werner, V. Hessel, P. Löb, Mixers with microstructured foils for chemical production purposes, *Chem. Eng. Technol.* **2005**, *28*, 401–407.

24 K. Yube, M. Kazuhiro, Efficient Oxidation of aromatics with peroxides under severe conditions using a microreaction system, *Chem. Eng. Technol.* **2005**, *28*, 331–336.

25 H. Krummradt, U. Kopp, J. Stoldt, Experiences with the use of microreactors in organic synthesis, in *Microreaction Technology: 3rd International Conference on Microreaction Technology, Proceedings of IMRET 3*, **2000**.

26 V. Hessel, C. Hofmann, P. Löb, J. Löhndorf, H. Löwe, Minimizing reaction times for the Kolbe-Schmitt synthesis with resorcinol using high p.T-processing in a microreactor setup, *Chem. Eng. Trans.* **2005**, *6*, 49–54.

27 J.J. Font Freide, Mini vs. maxi: the miniaturization and intensification of technology, in *Proceedings of the 17th International Congress of Chemical and Process Engineering, Prague*, **2006**.

28 A. Stankiewicz, Energy matters: alternative sources and forms of energy for intensification of chemical and biochemical processes, *Chem. Eng. Res. Des.* **2006**, *84* (A7), 511–521.

29 T. Mason, J. Lorimer, *Applied Sonochemsitry – Uses of Power Ultrasound in Chemistry and Processing*, Wiley-VCH Verlag GmbH, Weinheim, **2002**.

30 R. Schütte, M. Rudek, G. Markowz, H. Hahn, U. Plöcker, *Prozessintensivierung bei Degussa: Bessere Produkte plus neue Produkte, at Infotag Prozessintensivierung – Ansichten der Industrie, DECHEMA, Frankfurt,* **2006**.