EUROPEAN ROADMAP OF PROCESS INTENSIFICATION

- TECHNOLOGY REPORT -

TECHNOLOGY: MICRO-CHANNEL REACTORS
(WITH SPECIAL COMMENTS TO MICROMIXERS)

TECHNOLOGY CODE:

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1. Technology

1.1 Description of technology / working principle

(Feel free to modify/extend the short technology description below)

Definitions

Micro reaction technology is the conduction of reactions in continuous fashion in microengineered reactors (‘*microreactors*’), most prominent among these are microfabricated reactors. In a widely accepted, broader definition, foams, mini fixed beds, capillary / tube reactors, grouped filaments, and other small-sized structured media are also subsumed. It is, however, more and more distinguished between microreactors, typically being no larger than fist size, and microstructured reactors extending to shoebox or even larger dimensions.

Micro process technology embraces micro reaction technology and the extension to other (unit) operations, most prominently separations and the combination of these with the reaction to a whole process. *Micro plant technology* is the transfer of such processes into a new plant architecture provided that indeed a new set-up is used and not only a retro-fit of an existing plant by substitution of one key element has been made.

Past and current state

Microreaction technology emerged at the end of the 80s with the simultaneous growth in microfabrication and microelectronics as well as being motivated by the beginning interest in microfluidic applications. From about 1995 by initiation of the IMRET conferences, an own scientific community was formed and the number of scientific reports increased steadily from then. From about 2002, the reports on industrial applications became more frequently, e.g. several reports on pilot plants and a few on production plants. Since about 2005, microreaction technology is seen as a key technology within the field of process intensification. Benefits of its merging with other enabling technologies are explored, e.g. by combined microwave-microreactor operation. Since 2006, the focus of developments was also targeted to developing tailored processes (‘New Process Windows’) apart from improving only the hardware.

Micro reaction technology is a growing field with tendency to saturation (see Figure 1), as e.g. the number of patents in the field demonstrates which is taken as a measure for the willingness to invest capital. It is a bigger field than some of the other microtechnical fields such as microactuators, but has yet not reached the importance of megatrends such as nanotechnology or lab-on-a-chip (for non-chemical applications such as biochemical, diagnostics or analytical).

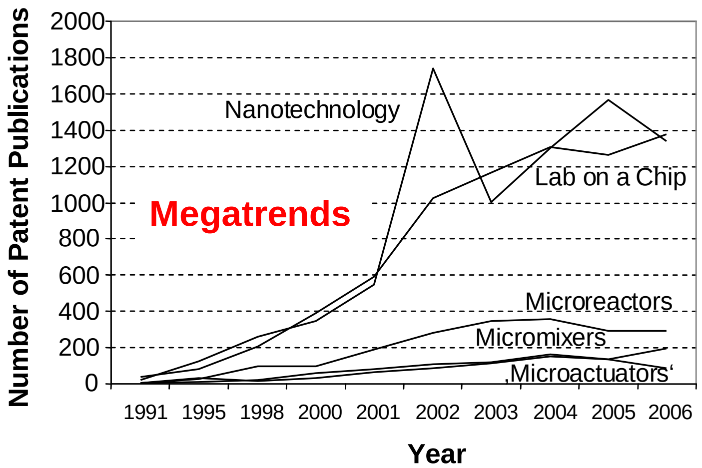

Fig. 1 Number of patent publications for diverse fields over time.

Major applications in industry
Major applications have been done in the field of fine-chemicals in the last ten year or so leading to first reports about production plants within the last five years or so. Investigations about bulk and petrochemicals have been started recently. A strong field of use is energy technology based on catalytic hydrogen making for fuel cells (fuel processing) with implications on transport, storage devices, leisure products, and household supply. Future fields are personal care and food.

Special comments to 'Micromixers'
Micromixers are probably the most frequently used 'microreactor' tool (see Figure 1). While often micromixers do not provide sufficient residence time to act as micromixer-reactor, this can be easily achieved by adding a capillary or tube reactor. This combination is the most frequently found microreactor concept in fine-chemical applications.
'Micromixers' comprise chip-type micromixers (often in silicon, polymer or glass) and laboratory micromixers made in another format (often in steel). As another class, microstructured mixers with throughputs up to 30,000 l/h were reported.
Micromixers can be based on active or passive principles. In the first case, energy is supplied for mixing, e.g. by ultrasound, magnetic fields, bubble motion, etc. In the second case the pumping action is the only energy source and mixing is achieved by virtue of controlling the flow, e.g. splitting into multi-lamellae or inducing recirculation flow by guidance over structured surfaces. Active micromixers were so far only developed for chip devices where electronic or magnetic functions can be easily integrated. There is a very large choice of designs and mixing principles reported and some of them are used in the portfolio of micromixer providers.

1.2 Types and "versions"
(Describe the most important forms/versions of technology under consideration, including their characteristic features, differences and similarities)

As indicated above, the term 'microreactor' comprises several classes of reactors which have in common to exploit the same phenomena in the same manner, however at different level of performance, different throughput, or different ways of scale-out.

Chip reactors
These handheld reactors have a layered and bonded design, typically of no more than two or three layers, and are made by standard micromachining techniques such as photoresist-etching technology. Silicon and glass are the most prominent materials here, polymeric materials being also used.
Due to the way of fabrication, there is a chance to integrate other functionalities which can be made by modern microfabrication, e.g. heating and sensing elements. Also, electronics can be incorporated in a smart way. The throughput is usually rather low, sometimes even less than 1 ml/h, but this is to a certain extent variable, as the dimensions may be enlarged above most current settings. Nonetheless, reaction and substrate screening is major application of chip devices. Process development is also possible.

Microstructured reactors
The change of the preposition 'micro' to 'microstructured' implies that, albeit the reactor interior contains micro dimensions, the outer dimensions can be quite large. Thus, the reactor body itself is not micro, but its internal fluidic ducts, and even these may be so only in one dimension.

Microstructured reactors are made in steel or metals preferably, but the materials mentioned above as well as ceramics are suitable as well. Since the fluidic ducts are tentatively larger than for the microreactors, often precision engineering methods such as milling can be used to complement the real microfabrication methods such as chemical etching in the case of the steels. In near future, mass manufacture methods will have to be developed, as this class of reactors can be used also for applications requiring large numbers of reactors.

Special comments to 'Micromixers'
Micromixers comprise the same classes as given above for micro-channel reactors. Almost all of reported high-throughput devices for chemical production are microstructured mixers which demonstrates that scale-out can be done here most beneficially. On the other side, a wide choice of micromixers has been developed for lab-on-a-chip applications.
Concerning the unit operation itself, mixing is probably the most deeply and frequently studied microfluidic operation. Mechanism and details are largely known, providing an engineering basis for specific solutions.

1.3 Potency for Process Intensification: possible benefits

(In Table 1 describe the most important documented and expected benefits offered by the technology under consideration, focusing primarily on energy; CO_2 emission and costs, providing quantitative data, wherever possible. Add other benefits, if needed).

Table 1: Documented and expected benefits resulting from technology application

Benefit	Magnitude	Remarks
Process simplification / Reduction of capital and energy costs	Omitting a distillation step in purification	Phenyl boronic acid process (Clariant, Frankfurt)
Increase in production speed	Unknown, probably order of magnitude	Production of polymer intermediate (DSM, Linz)
Increase in production speed	Unknown, probably order of magnitude	Microinnova production example
Better material quality	Average particle size from about 30 to 8 µm	Azo pigments by Trustchem, China
More facile process conditions; energy saving	Change from cryogenic to ambient conditions	Enolate process, Merck, Germany
More facile process conditions; energy saving	Change from cryogenic to ambient conditions	Phenyl boronic acid process (Clariant, Frankfurt)
Increase in yield	~20%	Enolate process, Merck, Darmstadt
Increase in yield	~15%	Vitamin precursor process, BASF, Ludwigshafen
Reduction in reaction time	Reduction of process time from 18h to 14 min	2-(Trimethylsilyl)ethyl 4-nitrophenyl carbonate synthesis, Sigma-Aldrich, Büchi
Increase in selectivity	Microreactor selectivity to overalkylated sideproduct: 0.18%, 1.56% for batch	(S)-2-Acetyl tetrahydrofuran synthesis, SK Corporation, Daejeon / Korea
Change of reaction temperature to ambient at same selectivity	Microreactor: 15°C; Static mixers: -20 – 0°C	Synthesis of intermediate for quinolone antibiotic drug, SK Corporation, Daejeon / Korea

Control over reaction heat to prevent thermal runaway	Enabling pilot of safety relevant reaction; conven-tionally not possible	Methyl carbamate synthesis Johnson & Johnson Pharmaceutical Research & Development, Raritan / USA
Decrease in reaction time by higher temperature	Microreactor: 14 min; conventional: not given	Newman-Kuart rearrange-ment, Johnson & Johnson Pharmaceutical Research & Development, Raritan / USA
Control over reaction heat to prevent thermal runaway	Enabling pilot of safety relevant reaction; conven-tionally not possible	Ring-expansion reaction of N-Boc-4-piperidone, Johnson & Johnson Pharmaceutical Research & Development, Raritan / USA
Increase in yield and reaction temperature (energy saving)	Batch: 80%, -65°C Microreactor: 87%, -40°C	Tertiary alcohol formation from 3-methoxyphenyllithium and cyclohexanone, Lonza, Visp / Switzerland
Step-change decrease in reaction time or Step-change decrease in reactor size at fixed throughput	Several 100 to a few 1000 From hours to minutes; from minutes to seconds	Kolbe-Schmitt Synthesis, IMM, Mainz / Germany Many other examples known

1.4 Stage of development

Hardware & process control
Several SME-type companies provide components. The choice is increasingly large, comprising micromixers and micro heat exchangers as main components, but also evaporators, gas-liquid contactors, and more. Separation components are still largely missing. Isolated approaches exist for extraction and chromatography tools. Some of these providers offer system solutions, i.e. complete micro chemical plants. In a few cases, on-line analytics are integrated, but the choice here is limited. Big companies such as Corning and Siemens complement since recently the SME offers. Siemens also introduced process automation tools to the system approach. For large-throughput applications, pilot microstructured reactors are meanwhile also available from suppliers. This opened the door to bulk-chemical and petrochemical applications where investigations just have started.

Processes & costing
On the process side, a large variety of chemical reactions were investigated meanwhile and the benefits of microreaction technology are very clear. In addition, cost analyses give indications on the commercial benefit. The provision of complete plants with separation and peripheral units, being fully automated, is however still a future issue.

Tailored protocols
The finding of tailored processing and protocols has just started, i.e. the exploration of reaction conditions with increased productivity such as processing at high temperatures, high pressures, solvent-less and –free, in the explosive regime, etc. Here, other emerging technologies such as supercritical fluids, ionic liquids, microwave heating, etc. can assist in optimizing the potential of microreaction technology.

Merging with other continuous techniques

Microreaction technology is a dominant, but not the only technology for continuous chemical processing. There is a overlap with capillary and tube reactor processing as well as processing done with foams, monoliths, and other structured media.

Special comments to 'Micromixers'
A wide choice of micromixers is available from providers, including pilot- and production scale equipment. Mixers for special performance such as droplet or particle making were also developed.

2. Applications

2.1 Existing technology (currently used)

(Describe technology (-ies) that are conventionally used to perform the same or similar operations as the PI-technology under consideration)

1. Batch reactors: stirred vessels applying impeller technology for reaction and mixing.
2. Continuous tube reactors of larger internal dimensions
3. Static mixers
4. Plate-type heat exchangers (compact heat exchangers)
5. Monoliths
6. PI-equipment such as spinning-disk reactor
7. Same reactors, but with larger internal dimensions, e.g. conventional falling film reactors

Special comments to 'Micromixers'
Besides stirred vessels and static mixers, simple T- and Y-junctions are in competition with micromixers. The latter are known to provide efficient mixing at high Re numbers given that the internal dimensions are sufficiently small (e.g. 200 µm).

2.2 Known commercial applications

(Is the technology broadly applied on commercial scale? In which process industry sectors is the technology most often applied: large volume chemicals – specialty chemicals & pharma – consumer products – ingredients based on agro feedstocks? What is the estimated number of existing applications? In Table 2 provide the most prominent examples of realized applications and provide their short characteristics)

Table 2. Industrial-scale applications of the Technology (existing and under realization)

Sector	Company - Process/Product name/type	Short characteristic of application	Production capacity/Plant size	Year of application	Reported effects
Fine Chemistry	Production of polymer inter-mediate (DSM, Linz)	Fast, exothermic reaction	1700 kg/h	2006	• Control over heat release
Fine Chemistry	Production of polymer inter-mediate (Xi'an Company, Xi'an / China)	Fast, exothermic reaction	15 kg/h	2006	• Control over heat release, safety improvement
Materials	Yellow Nano	Particle	70 t/a	2006	Finer and more

	pigment manufacture, Fuji, Tokyo / Japan	precipitation			narrowly sized particles
Polymers	MMA polymerization, Idemitsu-Kosan, Chiba / Japan	Radical polymerisation	14.7 kg/24h (5 t/a)	2006	Continuous, flexible process with small and reliable PDI
Materials	Azopigments, Clariant, Frankfurt / Germany	Particle precipitation	10 t/a initially; later 100 t/a	2002	Colour strength: micro/conventional : 139% Brightness: 6 steps glossier Transparency: 6 steps more trans-parent
Fine Chemistry	Not disclosed; report by Micro-Innova, CET 4 (2007)	Two-step reaction; no further details given	29 kt/a	2006	Making first contacting step simpler and faster and reduces reactant evaporation. 60 s instead of 4 h In operation since June 2005
Fine Chemistry	Merck, Darmstadt / Germany	Enolate synthesis by Grignard	Not known	1999	Increase of yield from 72 to 92% Increase of reaction tempera-ture from -20 to -10°C In operation for about five years
Energy / Leisure	Truma, Ottobrunn / Germany	LPG Reformer-Fuel cell system	500 W	2007	Reduction in noise Clean process Auxiliary and flexible power generation
Energy	Total, Paris / France	Fischer-Tropsch process	World scale (> 100 kt/a) or distribu-ted units (>10 kt/a)	2007	Reduction in capital costs Distributed production Faster process by control over heat release

Special comments to 'Micromixers'
Many of the above reported commercial applications use micromixers as key component.

2.3 Known demonstration projects

(Are there any demonstration projects known related to the technology under consideration? In which process industry sectors are those projects carried out: large volume chemicals – specialty chemicals & pharma – consumer products – ingredients based on agro feedstocks? In Table 3 provide the short characteristics of those projects.)

Table 3. Demonstration projects related to the technology (existing and under realization)

Sector	Who is carrying out the project	Short characteristic of application investigated, including product name/type	Aimed year of applicati on	Reported effects
Bulk chemistry	Uhde, Dortmund / Germany, and Degussa, Hanau / Germany	Propylene oxide process	Since 2005	Safe handling of hazardous substances (DEMIS project)
Fine chemistry	FMC, Princeton / USA	Hydrogen peroxide process	Since 2006	Safe handling of hazardous substances
Fine chemistry	Bayer-Schering Pharma, Berlin / Germany	Steroide ozonolysis	Since 2006	Safe handling of hazardous substances Reduction of reaction time from 6 h to 15 s (ZOHIR project)
Materials	Merck-Covion, Darmstadt / Germany	Polycondensation by Suzuki coupling	Since 2006	Improvement of material properties by increase in product purity (POKOMI project)
Materials	Evonik Degussa GmbH, Hanau / Germany; BASF, Ludwigshafen / Germany	Synthesis of organic peroxides and other oxidation reactions	Since 2006	Improvement of material properties by increase in product purity (µ.PRO.CHEM project)
Materials	IoLiTec GmbH, Denzlingen / Germany	Ionic Liquid synthesis	Since 2006	Improvement of product purity (NEMESIS project)
Materials	Bayer Technology Services, Leverkusen /Germany IGV GmbH, Nuthetal, Bergholz-Rehbrücke /Germany	Photoreaction	Since 2006	Increase in lifetime for radiation source from 1000 to 10,000 or 50,000 operating hours Reduction in capital investment (µPR project)
Energy	Evonik Degussa GmbH, Hanau / Germany	Hybrid transport of cryogenic fuels for decentralised energy conversion	Since 2006	Efficiency increase for renewable energies in the energy mix and reduction of CO_2-emisions by a new energy infrastructure

Special comments to 'Micromixers'
Many of the above reported demonstration projects use micromixers as key component.

2.4 Potential applications discussed in literature

(Provide a short review, including, wherever possible, the types/examples of products that can be manufactured with this technology)

1. Fine-chemical and pharmaceutical products
2. Polymers
3. Basic chemicals
4. Hydrogen and other process gases
5. Emulsions
6. Particles and pigments

7. Personal care and home care products
8. Food

Special comments to 'Micromixers'
Micromixers are especially needed for potential applications 1-3 and 5-8.

3. What are the development and application issues?

3.1 Technology development issues

(In Table 4 list and characterize the essential development issues, both technical and non-technical, of the technology under consideration. Pay also attention to "boundary" issues, such as instrumentation and control equipment, models, etc.) Also, provide your opinion on how and by whom these issues should be addressed)

Table 4. Technology development issues

Issue	**Description**	**How and by whom should be addressed?**
Production technologies for large-sized reactors	Applications in bulk chemistry demand large-sized microstructured reactors, e.g. for reasons of a high parallelisation degree. The present standard of shoebox-sized reactors needs to be enlarged to meter dimensions This is also needed for large pilot microstructured reactors for fine chemistry.	Initiation by leading institutes Mass fabrication pro-ducers at the edge to the field of microstructuring, e.g. with business in rolling or soldering Large companies such as DSM, BASF, Shell, Degussa, Uhde, …
Mass-production technologies for microreactors	Applications in personal care demand for cheaper microreactors, probably also with change in material choice (polymers are preferred).	Initiation by leading institutes Mass fabrication pro-ducers at the edge to the field of microstructuring, e.g. with business in injection moulding Large companies such as Procter & Gamble, Unilever, L'Oreal, …
Completion of plant architecture	Issues of separation, analytics and process control are still not addressed with the same emphasis as reaction engineering. The same goes for the integration of these units together. Thus, existing micro process plants may have a quite different standard on their different units and operations.	System suppliers such as Siemens, Corning, mikroglas together with plant engineers, e.g. from Uhde or Zeton
Scale-out	There is not a generally accepted way of moving from laboratory to pilot and production tools. Numbering-up as well as smart up-scaling are made, sometimes in a mixed fashion. For numbering-up, measures for flow distribution and process control are needed.	Leading institutes and universities for the theoretical background Large-reactor suppliers such as Velocys Process control companies like Yokogawa
Basic	Although a number of fundamental studies have	Leading institutes and

understanding of underlying phenomena	been carried out, basic understanding is still to be further improved. Many decisions are still undertaken in a 'black-box' manner, i.e. which micromixer to be used.	universities
Automation / Process control	Many microreactor plants are still manually operated. The full potential is released if automated operation allows to determine a large parameter space.	Process automation and control companies like Yokogawa / Endress& Hauser or Siemens

Special comments to 'Micromixers'
All statements done above on the component level are also true for micromixers.

3.2 Challenges in developing processes based on the technology

(In Table 5 list and characterize the essential challenges, both technical and non-technical, in developing commercial processes based on the technology under consideration. Also, provide your opinion on how and by whom these challenges should be addressed)

Table 5. Challenges in developing processes based on the technology

Challenge	Description	How and by whom should the challenge be addressed?
Cost view	First cost analyses were made and are part of running projects. Still, the knowledge needs to be increased.	Leading institutes and companies in the field.
Tailored processing ('New Process Windows')	Process protocols resemble the limitations of existing batch technology. Vice versa, these often are not matched to the innovative capabilities of microreactors. If the latter is done consequently and systematically, new process windows, e.g. with regard to temperature and pressure, will have to be accessed. A generic view on the respective possibilities is needed.	Leading institutes. Launching of specific funding programmes.
Education	Microreaction technology is know-how and skill based. Newcomers often have a hard job to enter into practice, as it is very different from what they learnt. Education at an early stage (at the universities) helps to familiarize with the new technology.	Leading universities. Launching of specific funding programmes.
Awareness / Information	Also, microreaction technology is a term is probably widely known meanwhile, there are still many uncertainties and rumors on the exact potential. Access to expertise opinions is needed here. At the SME level, even basic information may be missing.	Scouting seminars and events to promote the technology. Supply of information in written form. Installation of demonstration units at various sites.
Experiences with at-site operation	Most of the microreactors are still operated in an 'artificial' environment in laboratories. At industrial production site, demands are harsher. There are a few investigations done at such sites. However, there is no reporting accessible and the overall level of information is limited.	Chemical industry users. Flagship projects from funding agencies
Life-time of equipment and long-term processing	Related to the missing at-site information, is uncertainness about life-time of equipment and long-term processing. Some providers have selected products running in long-term tests, but the information is limited (clogged - non	Microreactor providers and chemical industry users

	clogged) and not diffused.	
Explore other application fields	Food, personal and home care, transport, leisure	Companies and Leading universities / institutes active in the field. Launching of specific funding programmes
Legislation / Plant approval	Legislation / plant approval for micro chemical plants is still done in the classical way. No specific consideration of the microreactor itself is usually done. It is unclear if the use of microreaction technology helps to have faster legislation / plant approval.	Legislative authorities Chemical industry users

Special comments to 'Micromixers'
All statements done above on the component level are also true for micromixers.

4. Where can information be found?

4.1 Key publications

(Provide the list of key publications in Table 6)

Table 6. Key publications on the technology

Publication	Publication type (research paper/review/book/report)	Remarks
S. T. Haswell, P. Watts, *Green Chemistry* **2003**, *5*, 240.	Review	Organic synthesis review
K. F. Jensen, *Chem. Eng. Sci*. **2001**, *56*, 293.	Review	Broad engineering review with focus on silicon reactors
A. Gavriilidis, P. Angeli, E. Cao, K. K. Yeong, Y. S. S. Wan, *Trans. IChemE.* **2002**, *80/A*, 3.	Review	Broad review, well balanced between engineering and applications
V. Hessel, H. Löwe, A. Müller, G. Kolb, *Chemical Micro Process Engineering - Processing and Plants*, Wiley-VCH, Weinheim **2005**.	Book	Topical chapters on micromixers, catalyst screening, fuel processing, and micro process plant design
V. Hessel, S. Hardt, H. Löwe, H., *Chemical Micro Process Engineering - Fundamentals, Modelling and Reactions*, Wiley-VCH, Weinheim **2004**.	Book	Topical chapters for general considerations, simulation, liquid, gas-liquid and gas reactions
H. Pennemann, P. Watts, S. Haswell, V. Hessel, H. Löwe, *Org. Proc. Res. Dev.* **2004**, *8*, 422.	Review	Benchmarking with conventional technology for organic synthesis
K. Jähnisch, V. Hessel, H. Löwe, M. Baerns, *Angew. Chem. Int. Ed.* **2004**, *43*, 406.	Review	Organic synthesis review
G. Kolb, V. Hessel, *Chem. Eng. J.* **2004**, *98*, 1.	Review	Review on gas-phase applications
P. Pennemann, V. Hessel, H. Löwe, *Chem. Eng. Sci.* **2005**, *59*, 4789.	Review	General review, with many industrial applications
S. Schwalbe, A. Kursawe, J. Sommer, *Chem. Eng. Tech.* **2005**, *28*, 408.	Review	Organic synthesis review
V. Hessel, P. Löb, H. Löwe, *Curr. Org. Chem.*	Review	Organic synthesis review

2005, *9*, 765.		with proposition of tailored processing (New Process Windows)
P. D. I. Fletcher, S. J. Haswell, E. Pombo-Villar, B. H. Warrington, P. Watts, S. Y. F. Wong, X. Zhang, *Tetrahedron* **2002**, *58*, 4735.	Review	Organic synthesis review for chip reactors
J.-I. Yoshida, H. Okamoto, Industrial Production Plants in Japan (Chapter 15), in Micro Process Engineering - Fundamentals, Devices, Fabrication, and Applications, (Ed.: N. Kockmann), **2006**, pp. 439-462.	Book Chapter	Japan's industrial micro process plants
Micro Process Engineering - Fundamentals, Devices, Fabrication, and Applications, (Ed.: N. Kockmann), **2006**, pp. 439-462.	Book	Book with fundamentals, engineering, applications
Nature 442, 7101 (2006) focal topic : lab-on-a-chip; industry use of microreactors in pp. 351-352	Reviews; Report	This Nature issue contains a feature report and several high-ranked reviews on the topic
Dutch PI Roadmap – Arthur D. Little Full Study	Market Study	120-pages report on process intensification including microreaction technology
S. Deibel, CHEManager 2 (2006)	Book	Deibel is Corporate Manager Engineering at BASF
Microreactor technology and process intensification, ACS Symposium Series 914 (eds.: Wang, J. and Holladay, J.D.), ACS Books Department (2005).	Book	Edited Book with mixed conference contributions; man in the field of fuel processing
"Micro-Instrumentation for High Throughput Experimentation and Process Intensification: A Tool for PAT". eds.: Koch, M., Vanden Bussche, K., Holmes, N., Wiley-VCH, Weinheim (2006).	Book	Book with chapters both on micro-instrumentation and organic synthesis applications
Microreactors in Organic Chemistry and Catalysis". ed.: Wirth, T., Wiley-VCH, Weinheim (2008).	Book	Book on organic synthesis and industrial applications

Special comments to 'Micromixers'

The following citations are selected micromixer reviews and micromixer technical papers.

Reviews

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[2] Nguyen, N.-T., Wu, Z.; *"Micromixers - a review"*, Journal of Micromechanics and Microengineering **15,** (2005).

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4.2 Relevant patents and patent holders

(Provide the list of relevant patents in Table 7. Under "remarks" provide, where applicable, the names/types of products targeted by the given patent.)

Table 7. Relevant patents

Patent	**Patent holder**	**Remarks, including names/types of products targeted by the patent**
Loehder, W.; Bergann, L. DD246257A1 (1986); Verfahrenstechnische Mikroapparaturen und Verfahren zu ihrer Herstellung.	Akademie der Wissenschaften in Berlin / Germany	First-hour patent with generic description of stacked-plate assembly
Schubert, K., Bier, W., Linder, G., Schmid, P.,	Forschungszentrum	First-hour patent with

Bichler, P., Brunner, W., Simon, W. US5152060 (1992); Process for manufacturing fine-structured bodies.	Karlsruhe / Germany	generic description of stacked-plate assembly
Breuer, N., Meyer, H.: US2002/0119079A1 (2002).	Atotech in Berlin / Germany	Manufacturing patent using electroforming
Wegeng, R., Drost, M. K., Call, C. J., Birmingham, J. G., McDonald, C. E., Kurath, D. E., Friedrich, M.: US5811062 (1998); Microcomponent chemical process sheet architecture.	Battelle Memorial Institute in Richland / USA	Basic patent on sheet-like process archi-tecture
Yasuda, S., Ezaki, T.: JP2007044619 (2007), Micromixer, microreactor, fluid mixing method and fluid reaction method.	Canon K. K. in Tokyo / Japan	Micromixer and a fluid mixing method with easy cleaning of the inner part
Moreno, M., Woehl, P.: EP1400280A1 (2004), Apparatus and method for operating a microreactor at high pressure.	Corning Incorporated in New York / USA	Basic patent on glass microreactor archi-tecture
Markowz, G., Albrecht, J., Ehrlich, J., Jucys, M., Klemm, E., Lange de Oliveira, A., Machnik, R., Rapp, J., Schuette, R., Schirrmeister, S., Von Morstein, O., Hederer, H., Schmitz-Niederau, M.: WO2004/091771A1 (2004) Microreactor composed of plates and comprising a catalyst.	Uhde GmbH in Dortmund / Germany and Degussa AG in Düsseldorf / Germany	Basic patent on plate-to-plate architecture for large-scale applications
Nagasawa, H., Mae, K.: US2005/0036921A1 (2005), Reaction method using a microreactor.	Fuji Photo Film Co Ltd in Kanagawa / Japan	Microreactor with a plurality of supply routes for co-axial laminationl
Ehrfeld, W., Michel, F., Hessel, V.: DE19927556A1 (2000); Statischer Mikromischer.	Institut für Mikrotechnik Mainz GmbH in Mainz / Germany	Production-type microstructured mixer
Mies, M. J. M., Rebrov, E. V., De Croon, M. H. J., Schouten, J. C.: WO2004/073861A2 (2003); Microreactor for rapid parallel testing of catalysts.	Stichting voor de Technische Wetenschappen in Utrecht / Netherlands	Parallel catalyst screening reactor
Tonkovich, A. L., Wang, Y., Wegeng, R. S., Gao, Y.: US7045114 (2006): Method and apparatus for obtaining enhanced production rate of thermal chemical reactions.	Battelle Memorial Institute in Richlnad / USA	Catalytic conversion reactor
Schwalbe, T., Oberbeck, S., Golbig, K., Hohmann, M., Oberbeck, A.: US7056477B1 (2006); Modular chemical production system incorporating a microreactor.	Cellular Process Systems Inc in Richland / USA	Complete modular chemical production system with a micro-reactor as core unit
Buehler, R., Krohlas, G.: WO2006/100296A1 (2006); Process engineering facility, especially micro-process engineering facility.	Siemens AG in Munich / Germany	Microchemical plant with autarkic operation modules linked to a superordinated automation unit
Loewe, H., Hausner, O., Richter, T.: US7172735B1 (2007); Modular microreaction system.	Institut für Mikro-technik Mainz GmbH in Mainz / Germany	Modular microreaction system comprising a housing and functional base modules therein which arranged in a row
Wegeng, R. S., Tegrotenhuis, W. E., Whyatt, G. A.: US7125540 (2006): Microsystem process networks.	Battelle Memorial Institute in Richland / USA	Micro-channel device for performing unit process operations involving transfer of

		heat or mass in power generation, chemical production and heating and cooling systems
Maeta, H., Shimizu, Y., Sato, T.: US7160380 (2006), Organic pigment fine-particle, and method of producing.	Fuji Photo Film Co., Ltd., Minami-Ashigara / Japan	Production of fine particles of organic pigments for dispersions
Hubel, R., Markowz, G., Recksik, M., Rudek, M., Wewers, D., Zeller-Schuldes, F.: US2005/0245628A1 (2005): Alkoxylations in microstructured capillary reactors.	Degussa AG in Hanau / Germany	Process patent on polyether alcohols with narrow molecular weight distribution
Nickel, U., Jung, R., Saitmacher, K., Unverdorben, L.: EP1257602B1 (2003), Method for production of azo dyes in microreactors.	Clariant Inter-national Ltd In Muttenz / Switzerland	Process patent on the synthesis of azo dyes using microreactors
Bruemmer, H., Eichmann, M., Haverkamp, V., Sojka, B., Laue, J., Sanders, J.: CA2554850AA (2007): Gas-phase phosgenation process.	Bayer Material Science AG in Leverkusen / Germany	Process patent on the phosgenation of amines in the gas phase
Wurziger, H., Pieper, G., Schwesinger, N.: WO01/70649A1 (2001), Method for reducing organic compounds in a microreactor by means of hydrides and/or derivatives thereof.	Merck AG in Darmstadt / Germany	Process patent on the reduction of aliphatic, aromatic and heterocyclic organic compounds using hydrides or their derivatives
Wurziger, H., Stoldt, J., Pieper, G., Schwesinger, N.: WO01/74822A1 (2001), Method for the 1,3 dipolar cycloaddition of organic compounds in a microreactor.	Merck AG in Darmstadt / Germany	Process patent on the synthesis of 1,3 dipolar cycloadditions
Antes, J., Boskovic, D., Haase, J., Loebbecke, S., Ruloff, C., Tuercke, T.: WO2005/077883A1 (2005), Method for the production of liquid nitrate esters.	Dynamit Nobel GmbH Explosivstoff- und Systemtechnik in Leverkusen / Germany	Process patent on the synthesis of liquid nitrate esters, e.g. nitro glycerine
Verfahren zur Herstellung von Aryl- und Alkyl-Bor-Verbindungen in Mikroreaktoren, Koch, M., Wehle, D., Scherer, S., Forstinger, K., Meudt, A., Hessel, V., Werner, B.: EP1285924A1 (2003).	Clariant GmbH in Frankfurt / Germany	Process patent on the synthesis of aryl and alkyl boron compounds from aryl or alkyl magnesium halogenides with boron precursors
Auto-oxidation production of hydrogen peroxide via oxidation in a microreactor, Sethi, D. S., Dada, E. A., Hammack, K., Zhou, X.: US2007/0053829A1 (2007).	FMC Corporation in Philadelphia / USA	Process patent on the synthesis of hydrogen peroxide by an auto-oxidation method
Iwasaki, T., Yoshida, J., Hasebe, S.: JP2006199767 (2006); Method for producing radically polymerised polymer and microreactor.	Idemitsu Kosan Co in Tokyo / Japan	Process patent on radical solution polymerisation
Ataka, K., Miyata, H., Kawaguchi, T., Yoshida, J., Mae, K.: EP1710223A1 (2006); Process for producing aldehyde compound ir ketone compound with use of microreactor.	Ube Industries Ltd in Yamaguchi / Japan	Process patent on the synthesis of an aldehyde or ketone from a primary or secondary alcohol
Roberge, D., Ducry, L.: WO2007/087816A1 (2007); Nitration of activated aromatics in microreactors.	Lonza in Visp / Switzerland	Process patent on the nitration of activated aromatic or heteroaromatic compounds with a

		nitrating agent
Bueker, K., Hausmann, R., Schirrmeister, S., Geisselmann, A., Langanke, B., Markowz, G.: CA2584173 (2006); Reactor and method for synthesising vinyl acetate in the gaseous phase.	Uhde GmbH in Düsseldorf / Germany	Process patent on the production of vinyl acetate from gaseous ethylene, acetic acid and oxygen

Special comments to 'Micromixers'
The list of patents contains inventions based on micromixers and processes with a micromixer as central component.

4.3 Institutes/companies working on the technology

(Provide the list of most important research centers and companies in Table 8)

Table 8. Institutes and companies working on the technology

Institute/Company	Country	Remarks
MERCK PATENT GMBH	Germany	
BATTELLE MEMORIAL INSTITUTE / PACIFIC NATIONAL LABORATORY	USA	
VELOCYS INC.	USA	
FORSCHUNGSZENTRUM KARLSRUHE GMBH	Germany	
UHDE GMBH	Germany	
SIEMENS AKTIENGESELL-SCHAFT, SIEMENS AXIVA GMBH & CO. KG	Germany	
CASIO COMPUTER CO., LTD.	Japan	
EVONIK-DEGUSSA AG	Germany	
BAYER AG	Germany	
INSTITUT FUER MIKROTECHNIK MAINZ GMBH	Germany	
CLARIANT INTERNATIONAL LTD.	Germany / Switzerland	
FRAUNHOFER-GESELLSCHAFT	Germany	
FUJI PHOTO FILM CO., LTD.	Japan	
CORNING INCORPORATED	France / USA	
LONZA	Switzerland	
KYOTO UNIVERSITY	Japan	
TOKYO UNIVERSITY	Japan	
LYON UNIVERSITY / CNRS	France	
STEVENS INSTITUTE	USA	
SIGMA-ALDRICH	Switzerland	
RHODIA	France	
DSM	Austria	
DSM	The Netherlands	
AKZO-NOBEL	The Netherlands	
EINDHOVEN UNIVERSITY	The Netherlands	
TWENTE UNIVERSITY	The Netherlands	
RWTH AACHEN	Germany	
CHEMNITZ UNIVERSITY	Germany	
FRAUNHOFER INSTITUT	Germany	

CHEMICAL TECHNOLOGY ICT		
LEIBNIZ-INSTITUT FÜR KATALYSE (LIKAT), branch Berlin	Germany	
NANCY UNIVERSITY	France	

Special comments to 'Micromixers'
Micromixers are employed by virtually all of these entities.

5. Stakeholders

5.1 Suppliers and developers

(Provide the list of key suppliers/developers in Table 9)

Table 9. Supplier and developers

Institute/Company	Country	Remarks
BATTELLE MEMORIAL INSTITUTE / PACIFIC NATIONAL LABORATORY	USA	Supplier
VELOCYS INC.	USA	Supplier
FORSCHUNGSZENTRUM KARLSRUHE GMBH	Germany	Supplier
SIEMENS AKTIENGESELL-SCHAFT, SIEMENS AXIVA GMBH & CO. KG	Germany	Supplier
EVONIK-DEGUSSA AG	Germany	Developer; Project House Process Intensification
BTS-EHRFELD GmbH	Germany	Supplier
INSTITUT FUER MIKROTECHNIK MAINZ GMBH	Germany	Supplier
CORNING INCORPORATED	France / USA	Supplier
STEVENS INSTITUTE	USA	Supplier
MIKROGLAS CHEMTEC AG	Germany	Supplier
MICRONIT	The Netherlands	Supplier
CPC	Germany	Supplier
LITTLE THINGS FACTORY	Germany	Supplier
SYNTICS	Germany	Supplier
TORAY ENGINEERING CO	Japan	Supplier, Mixers
HITACHI PLANT TECHNOLOGIES CO	Japan	Supplier; Plant technologies
DAI NIPPON SCREEN CO established 'Micro Chemical Initiative' ('MCI') in cooperating with OMRON, OLYMPUS, NIPPON ZEON, HORIBA and YAMATAKE in 2004.	Japan	
FUJI FILM CO	Japan	Developer, for own purpose
YAMATAKE CO	Japan	Developer, for own purpose

Special comments to 'Micromixers'
Micromixers are supplied by virtually all of these entities.

5.2 End users

(Describe the existing and potential end-users, other than those already listed in Table 2)

See companies listed in Table 8. Existing users come mainly from the fields of fine chemistry and pharmacy. Implementation in bulk chemistry (e.g. DSM) has started. Future end-users come from the field of personal care (e.g. P&G, Unilever, L'Oreal), food (e.g. Krafft) or energy technology (e.g. Peugeot, Truma)

6. Expert's brief final judgment on the technology

(maximum 5 sentences)

Microreaction technology has proven step-change improvement for chemical processing, i.e. true process intensification. Micromixers are key elements for this purpose. The use of microreaction technology demands for a holistic approach, where education has a central role – thus, non-experience users still have problems to easily implement the technology. Presently, developments move from laboratory investigations to pilots and production. In future, the developments of chemical industry will be uptaken in the fields of personal care, food, or energy technology