Production and Characteristics of Microreactors Made from Glass*

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For centuries, glass has been a very well-known material. Even today new interesting applications are discovered. As described in the paper below, micro process engineering enables new approaches in the development and production of chemical compounds. Since there are many examples of aggressive chemicals which have to be handled, an inert material such as glass is of great interest.

There are many advantages of microreactors, for example, good control of chemical reactions by individual channel design and efficient heat exchange due to large surface to volume ratios. In addition, for glass microreactors further properties due to the glass can be added, i.e.:

- Optical transparency for analytics or applications in photochemistry;
- Chemical stability to handle aggressive chemicals;
- Good heat resistivity for applications at higher temperatures.

In the following article the advantages of micromixers made out of glass are described. In addition, the structurization technology as well as available modules are presented. The background of a whole microreaction system is described which supports the special characteristics of glass micromixers.

1 Microstructuring of Glass

Various glass types have been used for different applications in micro technology. Among those are glasses bondable with silicon (e.g., Borofloat from Schott or Pyrex from Corning) or quartz glass, which is used if a high optical (UV) transparency is necessary. A special material for microfluidic components is the photo-structurable glass FOTURAN, of which the components described in this work were made. The microstructuring of these glass types is carried out under special clean room conditions, which enable clean and particle-free processing. Under these conditions, fine structures in the range of 10 μm to a few hundred micrometers can be manufactured cleanly and free of defects.

1.1 Isotropic Etching of Glass

Usually glass is microstructured with methods derived from semiconductor technology, shown in Fig. 1. A well polished glass surface is coated with an adhesion layer (approx. 100 nm Ti or Cr) and then a photoresist is spin-coated. This resist is exposed through a mask which contains the required structures. The protection resist is then removed from the exposed areas and this opens the glass surface to attack by the etchant.

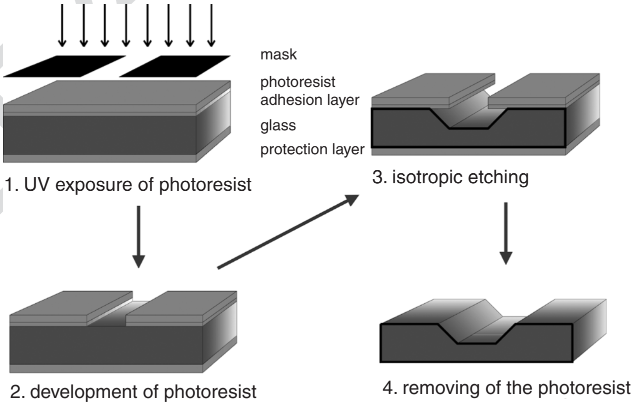

Figure 1. Microstructuring of glass.

In most cases, hydrofluoric acid (HF) is used as an etchant. With a 10 % hydrofluoric acid concentration, etching rates of 0.5–3.0 μm/min can be achieved with possible etching depths between 10–300 μm. This limit of a maximum etching depth is due to the fact that the hydrofluoric acid also attacks the adhesion layers. After a while the photoresist is under-etched and removed by the HF. If very flat channels of a few micrometers depth are required (e.g., for biochips), a very slow, but very precise etching rate is necessary. This can be achieved by using a buffered hydrofluoric acid (HF/NH_4F). Under these conditions, etching rates are within the range of 100–1000 nm/min with possible etching depths of 1–20 μm.

Plasma etching processes are also suitable for the production of structures in glass. Here, a photoresist protection layer is used to protect the areas which should not be etched by a SF_6/O_2-plasma. The etching rates are up to 1 μm/min with possible etching depths on a 1–20 μm scale.

Glass is an amorphous material. That means that it is etched in all directions with the same speed. Therefore, the etchant etches not only into the depth, but also attacks the

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side walls. This leads to an under-etching of the protection layer. The resulting structure is therefore always at least twice as wide as deep. In other words, the aspect ratio is always small.

1.2 Production of Microstructures from FOTURAN [1]

To achieve a high aspect ratio (deep but narrow holes) in glass, FOTURAN glass should be used. This glass is itself photosensitive and can be exposed directly through a mask. A photoresist is not necessary. The principle process steps are illustrated in Fig. 2.

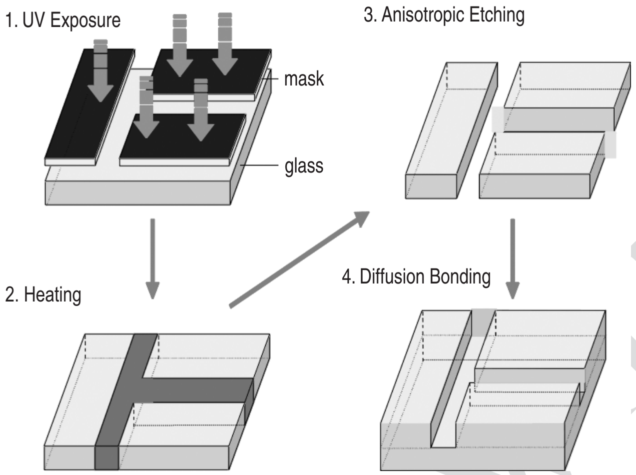

Figure 2. Structuring of FOTURAN.

FOTURAN is a lithium aluminum silicate glass, which is melted together with different additives, among others about 0.1 % Ag_2O and about 0.015 % CeO_2. In the glass a thermodynamically unstable mixture of Ce^{3+} and Ag^+ ions is present. If the glass is exposed to UV light at approx. 310 nm, the Ce-ions are oxidized and reduce the Ag-ions to form silver atoms.

During an annealing process the silver atoms agglomerate at approx. 500 °C to larger crystallization seeds, around which (at approx. 600 °C) the glass crystallizes. This annealing is a very critical process and strongly influences the characteristics of the later structures. Therefore, very precise furnaces with homogeneous temperature profiles are necessary.

The crystallized areas can be etched in 10 % hydrofluoric acid. The etching ratio between the exposed and the unexposed areas can increase up to 30:1. Since the surrounding glass is also slightly etched, a small etching angle of 1°–2° develops.

The size of the developed crystals (3–5 μm) defines both the roughness of the etched walls ($r_a \approx 1$ μm) and the smallest possible hole diameters of approx. 25 μm. With this technology, any 2D structure can be etched into the glass because there is no preferred etching direction in contrast to, e.g., the crystal structure of silicon.

1.3 Connecting Technologies

Micro-fluidic components are usually built out of several layers, each of them containing different functions. These layers are connected by bonding processes to 3D channel structures. The following processes are most frequently used to bond glass layers:

- **Diffusion bonding**: Two or more glass layers with well polished surfaces are adjusted on top of each other and bonded under pressure and at temperatures around the glass transition temperature. For this process it is necessary that the different layers have the same coefficient of thermal expansion (cte). The large advantage of such a connection is that it works without intermediate layers (e.g., glue) and therefore leads to a chemically very stable structure.
- **Glass soldering**: In some cases a direct bonding without intermediate layers can be used. For example, it can be necessary to manufacture a window from a different material than the micro-structured channel plate. Different materials with different ctes cannot be diffusion bonded directly. A glass solder as an intermediate layer helps to overcome the cte mismatch by having a cte in between the those of the glass plates and by using lower processing temperatures. Glass solder is a mixture of small particles of a low melting glass and an organic solvent. It is printed in the form of a paste onto the surface of one of the plates.
- **Gluing**: If chemical needs are not too critical, standard glues can be a less expensive alternative to connect different structured layers.
- **Other processes**: To connect silicon or metals, other connecting techniques like anodic bonding, sputtering, evaporation, or electroforming can be used.

2 Available Microreactors Made from Glass

Today there are different mixers, heat exchangers, reactors, dwell devices etc. all made from glass and commercially available. Some examples of these components with their corresponding applications will be mentioned in the following paragraphs:

2.1 Nitration of Aromatic Compounds [2]

Conventional nitration of aromatic compounds exhibits some significant problems:

- The reactions are strongly exothermic and can even lead to explosive mixtures.
- In order to control the reactions and suppress by-products, very expensive cooling of the reaction mixture is necessary.
- The reaction kinetics are so fast that the mixing of the components is the rate-determining step.

- Due to the extremely high exothermicity and the fast reactions, different secondary, side, and competitive reactions occur.

The nitration of naphthaline with nitrogen pentoxide in glass microreactors has been examined by the Fraunhofer Institute of Chemical Technology (ICT). It could be shown that all these issues can be controlled. Using conventional technology, the reaction has to be performed at –50 °C in order to handle the reaction safely and it is difficult to select the meta-, ortho-, or para-position of the nitro-group or to stop the reaction after the mononitration.

In microreactors the reaction temperature can be increased to + 30 °C, which leads to substantial energy savings. The reaction parameters can be controlled to achieve mainly the mono-nitro-naphthaline.

Since the nitrating reagents are chemically very aggressive, glass was the material of choice. The microreactor developed by mikroglas in cooperation with the ICT consists of twenty parallel reaction channels. Fig. 3 shows one of these channels. The design has been chosen to have the reaction terminated within the microreactor. A heat exchanger for temperature control has been integrated, whose respective channels are separated from the reaction channels by a glass layer with a thickness of 150 µm.

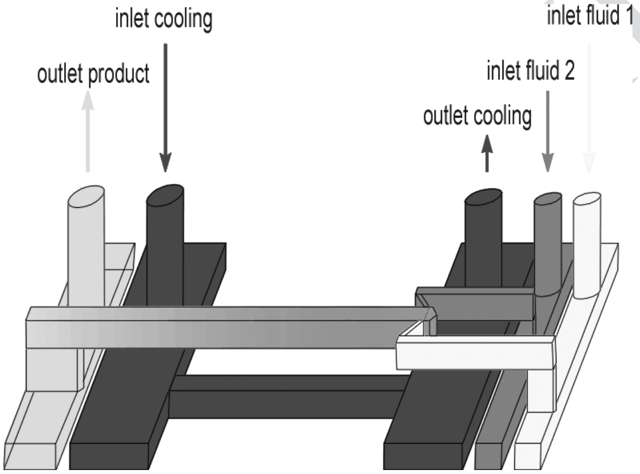

Figure 3. Channel system of a microreactor for the nitration of naphthaline.

2.2 Mixing of Different Liquid Phases [3]

Using the synthesis of Benzaldehyde from benzal chloride and sulfuric acid as an example, it could be shown that even aqueous and organic phases can be mixed easily in a suitable micromixer for an effective reaction. Standard reaction times of several hours can be reduced to minutes by this approach.

For this kind of reaction a multi-lamination mixer was developed and built by mikroglas and the Institute of Microtechnology Mainz (IMM) (see Fig. 4). Within this reactor, two liquid streams are split up into a row of smaller streams, which are brought together again “interdigitally” (= A B A B ...). Due to the low Reynolds numbers, a laminar flow without turbulences is the result. Mixing in such a laminar flow occurs only via diffusion.

Glass was used as the material for the microfluidic device because it permits observation of the mixing behavior directly in a microscope. Different studies could be performed to improve the design of such a micromixer. With the support of these investigations, the “Superfocus Mixer” has been developed: a hundred and twenty four channels (2 groups of 62) lead into a mixing chamber, which is focused into the 500 µm wide reaction channel. The resulting lamellae have a width of only 4 µm. Using typical flow rates of 8 L/h of aqueous solutions, a complete mixing takes place within the channel length of 50 mm.

2.3 Gas-Liquid Mixing [4]

For gas-liquid mixtures the IMM has developed a glass component called the cyclone mixer (see Fig. 5). Within this component, the two reactants are directed by tangential aligned nozzles (50 µm by 150 µm) into a central mixing chamber (diameter 10 mm, height 2.15 mm). This leads to a “cyclone” formation with a very homogeneous gas bubble size (~ 150 µm) in the liquid phase. Thus, e.g., the solubility of oxygen in water/isopropanol could be increased to 35 g/L.

2.4 Heat Exchangers Made from Glass

Heat exchangers made of glass can be important for special applications. As could be shown, the good heat conductivity of metals is not always useful. In metal reactors the heat is conducted mainly within the walls of the channel system instead of traveling perpendicularly through the walls. Glass with a heat conductivity λ of 0.67–1.38 W/m K shows a substantially more effective heat transfer [5] (see Fig. 6).

A mikroglas heat exchanger was tested in a production environment at Roche. Fig. 7 shows the heat exchanger system, which was the size of a tabletop. Eight modules were used in parallel in order to handle and control a throughput of 200 L/h. It was proven that with regular cooling water (no special cleaning) a reliable use of micro heat exchangers under production conditions is possible.

3 Microchemical Plants

Different microfluidic components from different materials have been developed and tested within the past few years. In order to be able to use these components, plants must be developed in which the actual microreactor is only the smallest part. To operate these reactors, plants must be built using physical and chemical sensors, valves, pumps, filters, tubings, and safety units, including the respective connection technology.

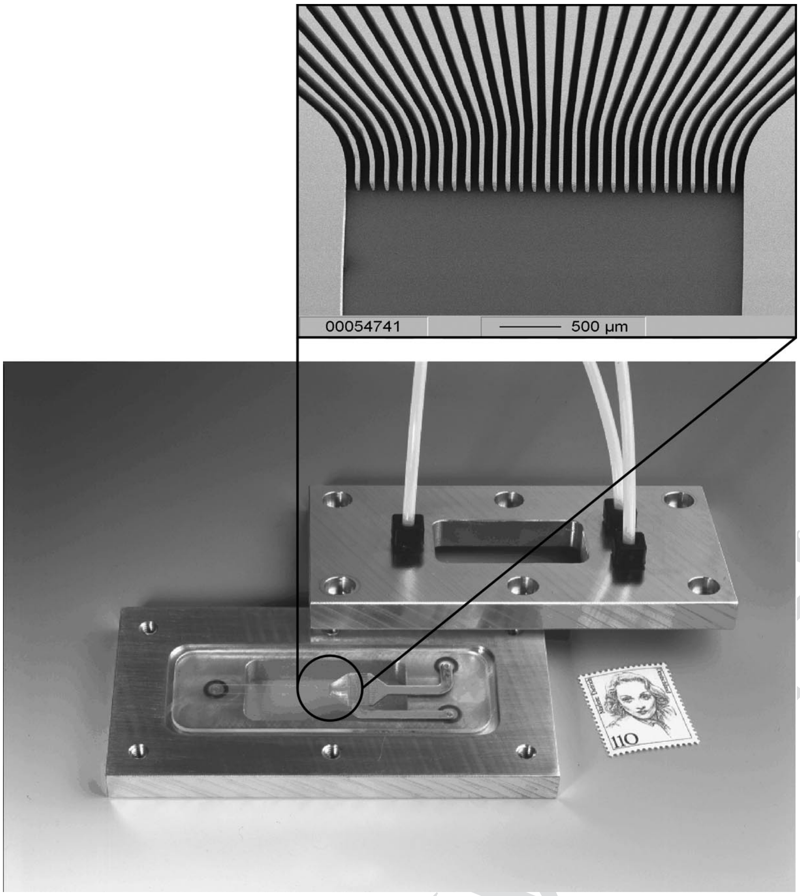

Figure 4. Interdigital mixer.

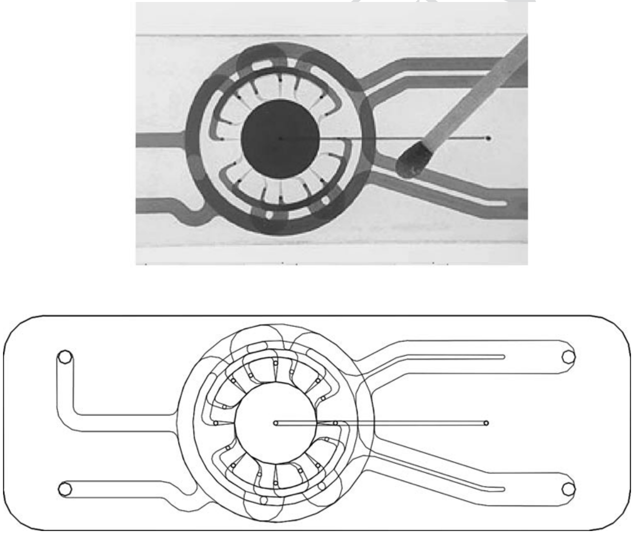

Figure 5. Cyclone mixer for gas-liquid mixing.

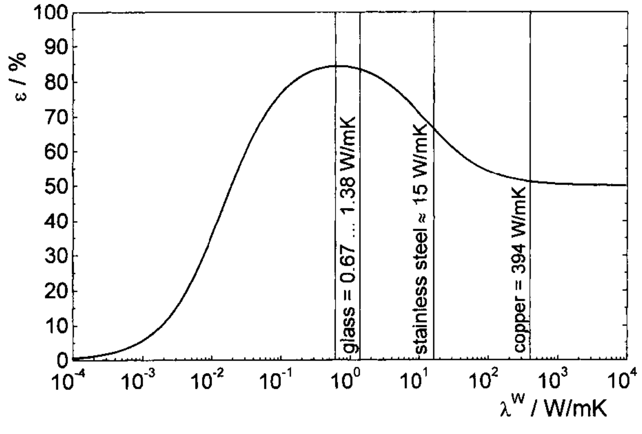

Figure 6. Effective heat transfer for different wall materials with different heat conductivities.

These components have to have certain properties:

- The materials used must be chemically stable. In particular, when using glass as an inert reactor material, the remaining components should also have this advantage.
- A high accuracy of active (e.g., pumps) and passive components (e.g., sensors) is necessary, since very small amount of reactants, sometimes within the µL-range, must be handled.
- Depending on the application, pressures can occur up to a few times 10 bar.
- Temperatures from –40 °C to a few hundred degrees can be necessary.
- Modularity is very important. It must be possible to exchange different modules for others to modify the plant as required by the next application.

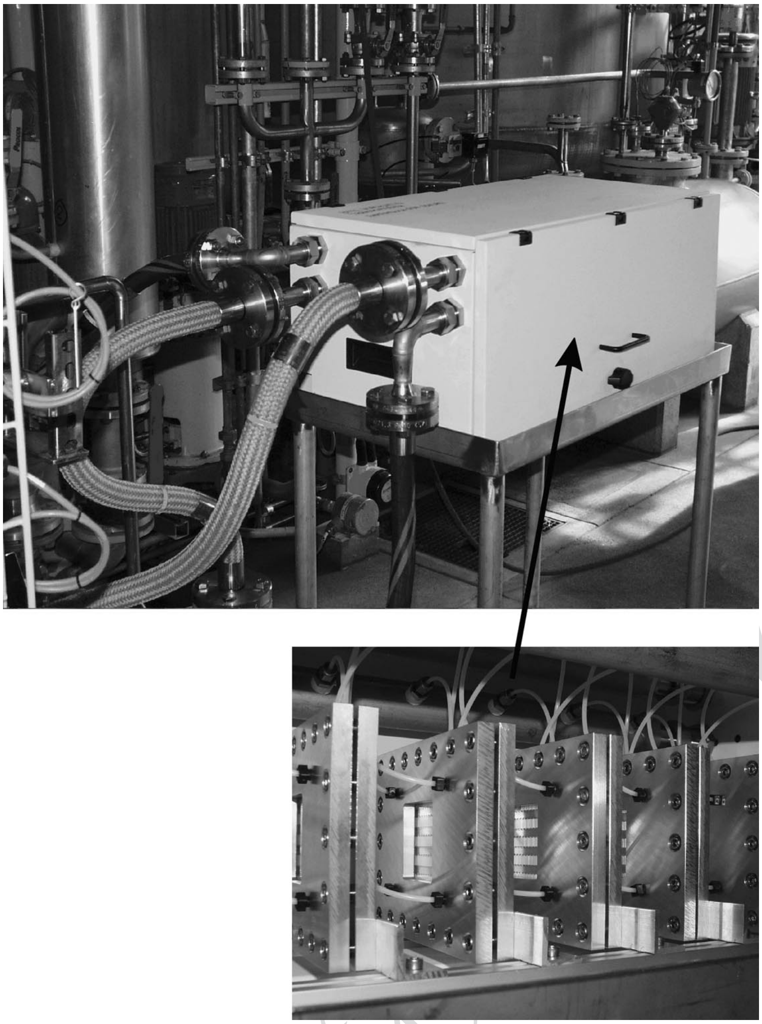

Figure 7. Micro heat exchangers made from glass in an industrial cooling system.

3.1 Connection Technology

Usually the glass reactors are connected with teflon tubes. Fig. 8 shows a metal frame, which mechanically protects the glass reactors and also presses the teflon tubes with standard HPLC fittings onto the glass surface. This connection has the main advantage that only chemically stable materials (glass and teflon) come into contact with the media. In addition, the tubing can be disconnected at any time, e.g., to change or to clean the microfluidic modules. These connectors can be used up to a pressure of 20 bar.

3.2 Process Control

To work with a microreaction plant an automatic process control unit is necessary. This control system makes it possible to display and regulate all process parameters, including a controlled starting process, an investigation and optimization of reaction parameters, production control, and safety supervision.

With the appropriate software it is possible to install a system which is self-optimizing: the plant changes pressures, flows and temperatures of the different components using a given program. With suitable additional equipment, i.e., autosampler or fraction collector, different chemicals can be used. The result of each reaction is evaluated and then the next experiment follows. With such a procedure, this plant is able to optimize the reaction conditions itself.

Mikroglas has adapted a modified version of the Simatic S7 control unit (SIEMENS) for microreactors. This control unit allows the administration of approximately a thousand parameters. This is necessary in order to supervise a plant for a two-step-reaction accurately. Software and hardware are modular, so it is possible to change the set up for new reactions or reaction conditions easily ("Multi-Purpose-Plant").

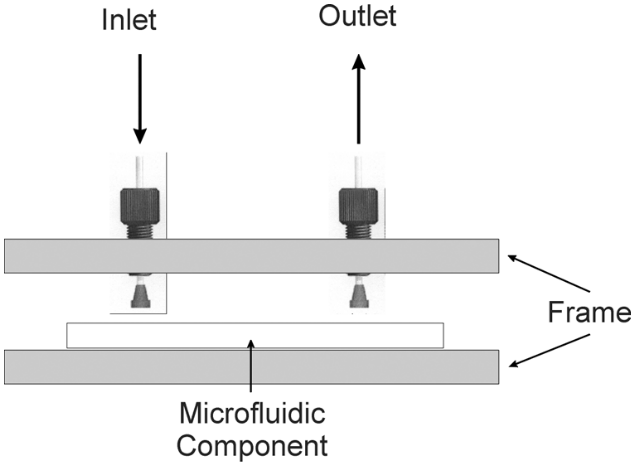

Figure 8. Connection technology for microreactors made out of glass.

3.3 Sensors

The electronic control unit can work only with the appropriate input. Therefore, different physical and chemical sensors are necessary.

To control a microchemical plant, sensors have to measure the temperature, the pressure, and the flow rates. The sensors have to be stable against aggressive chemicals. For this reason, e.g., glass encapsulated Pt100 temperature sensors and piezo ceramic pressure sensors are used. Together with Buerkert, mikroglas developed a sensor block to measure pressure and temperature. In addition, it contains safety devices like a pressure relief valve and a non-return valve.

Besides the physical sensors, chemical sensors for monitoring the chemical reactions are of great importance. There are different chemical sensors available which are specialized for specific compounds (like ChemFET's) or which detect a group of compounds (like optical measurements, e.g., IR detection). Unfortunately, there is no "universal" sensor, which can be used for all chemical reactions. The application determines which kind of sensor should be used.

4 Standardization

Presently, microreaction plants are offered by small and medium-size enterprises. These companies are specialists in certain microfluidic units and tend to rely on buying the remaining components for the microchemical plant from outside suppliers. The main problem is that commercially available components usually do not fit to each other and must be adapted each time. This approach is time consuming and expensive.

An important task for the future will therefore be to standardize the interfaces between the different components. This also has advantages for components to be produced and offered in larger quantities, therefore allowing different users to work with the same components. This should reduce the price of all microfluidic components substantially in the near future.

In Germany, an industrial consortium called "microchemtech", organized within the DECHEMA, works on this standardization. The German Federal Government has funded a project in which different institutions have already developed a so-called "Backbone" system. This system consists of standardized elements, which are able to connect microfluidic components from different manufacturers to form a microchemical laboratory plant. Some manufacturers have already adapted to these standards and offer appropriate modules. Using these elements, the Institute for Applied Chemistry in Berlin, the Karlsruhe Research Center and the IMM in Mainz have developed different plants (see Fig. 9). The first promising results are to be published in the near future.

5 Summary

It has been shown that microreactors made of glass for special applications are available and extremely productive. It emerged that the main advantages of these reactors are the chemical stability and the optical transparency.

Different modules (e.g., mixers, heat exchangers, dwell devices) are already in use. Further modules need to be developed. For example, no separation modules are available at the moment. There are some current activities in the field of phase separation and distillation, which however still need

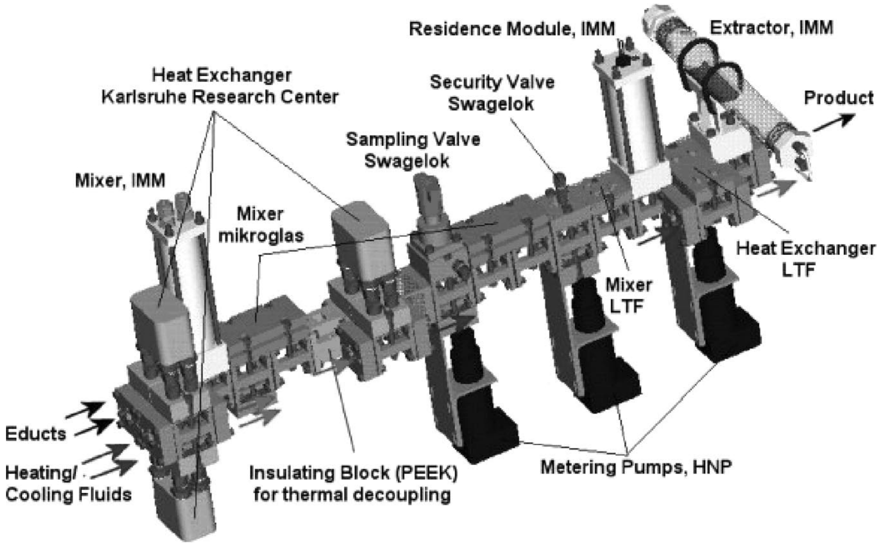

Figure 9. Test plant with backbone system.

some additional research to be commercially available. In order to build a whole chemical plant out of the available microreactors, a set of further components (e.g., sensors, pumps, safety devices, MSR components) is necessary. Because of the lack of standardized interfaces, it is difficult to connect different modules with different functions.

Different companies already offer plants ready for laboratory and/or small scale production. The chemical industry in Europe and Japan has already started to use this new technology, mainly for development and research, but it will still take some time until the advantages of this technology will lead to a significant change in the production of chemicals world wide.

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References

[1] T. R. Dietrich et al., *Microelectron. Eng.* **1996**, *30*, 497.

[2] J. Antes et al., *Proc. of the 4th Int. Conf. on Microreaction Technology, IMRET 4* (Eds: I. Rinard, W. Ehrfeld, U. Eul, R. S. Wegeng) ■publisher■ 5–9 March **2000**, pp. 194–200.

[3] T. Herweck et al., *Proc. of the 5th Int. Conf. on Microreaction Technology, IMRET 5* (Eds:M. Matlosz, W. Ehrfeld, J. P. Baselt) Springer, Heidelberg **2001**, pp. 215–229.

[4] S. Hardt et al., *Proc. of the 6th Int. Conf. on Microreaction Technology, IMRET 6* ■Eds/Publisher■ New Orleans **2002**

[5] T. Stief, O.-U. Langer, K. Schubert, *Chem. Eng. Technol.* **1999**, *21 (4)*, 297.

This paper was also published in German in Chem. Ing. Tech. ***2004****, 76 (6), 575.*
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