INTEGRATED MICROREACTOR FOR CHEMICAL AND BIOCHEMICAL APPLICATIONS

N. Schwesinger, L. Dressler, Th. Frank, H. Wurmus

Technical University of Ilmenau, Faculty of Mechanical Engineering,
Department of Microsystemtechnology

Abstract

A completely integrated microreactor has been developed, that allows the processing of very small amounts of chemical solutions. The whole system comprises several pumps and valves that are arranged in different branches as well as a mixing unit and a reaction chamber. The streaming path of each branch contains two valves and one pump between them. The pumps are driven piezoelectrically using pizoceramic elements mounted on thin glass membranes.
Each pump has a dimension of about 3.5mm x 3.5mm x 0.7mm. A pumping rate up to 25 µl/h can be achieved. The operation voltage is in a range between 40 V and 200V. A volume stroke up to 1.5µm is achievable for the membrane structures
The valves are designed as passive valves. The sealing is made by the use of thin metal films. The dimension of a valve unit is 0.8mm x 0.8mm x 0.7mm.
The ends of the separate streaming branches are arranged to meet in one point. This point acts as the begin of a mixer unit. The unit contains several fork-shaped channels. The arrangement of these channels allows the division of the whole liquid stream into partial streams and their reuniting. A homogeneous mixing of solutions and/or gases can be observed after having passed about 10 fork elements.
A reaction chamber is arranged behind the mixing unit to support a chemical reaction of special fluids. This unit contains heating elements placed at the outside of the chamber.
The complete system is arranged in a modular structure and built up of silicon. It comprises three silicon wafers bonded together applying the silicon direct bonding technology. The structures in silicon are made only by the use of wet chemical etching processes. The fluid connections to the outside are realised using standard injection needles that are glued into v-shaped structures of the silicon wafers.
An integration of further components, like sensors or electronic circuits, is possible due to the use of silicon as basic material.

1. Introduction

The development and synthesis of special agents and fine chemicals were connected in the past very often with a low efficiency. Big amounts of different chemicals and complicated processes were required to get a very small volume of a specific material. One of the basic reasons for that is the present state of the development of chemical devices. They are very often big, unable to work with small amounts of agents and not stable enough during process steps. Although they possess a relatively high accuracy with big amounts of inserted materials the accuracy is very low at insert volumes below 1µl. The handling of the devices is complicated, too. A direct control of the reaction

parameters is mostly not possible. A detection of the reaction products requires a great effort. These disadvantages lead to a strong increase in costs for new and specific products and methods in the field of chemistry and biochemistry.
The micromachining technology can open new fields in the area of chemistry and biochemistry. Different new modules, like pumps and valves have been developed during the last years [1-4]. These small devices are able in principle to handle very small amounts of fluids with a very high accuracy. Although these components have been characterised very often as individual components some of them were designed and manufactured as integrated systems [5-8]. The aims of these works were focused on the development of total analysis systems in microtechnology, so called μ-TAS. An integration of different components leads to an advantage of these systems in comparison to commonly used devices. In-situ measurements are possible due to the integration of specific sensor systems. Direct interconnections of these groups to electronic building groups are further advantages of these systems.
While the work of different groups world wide was focused on the development of specific sensor interfaces in μ-TAS devices, we tried to pay more attention to the design of micropumps, valves, mixing units and reaction chambers. We were mainly interested in integrated microreactor systems that can be produced by using related process technologies. We have designed and produced modular micropumps, valves, mixing units and reaction chambers to investigate their parameters. A technology for the production of completely integrated microreactor systems was developed.

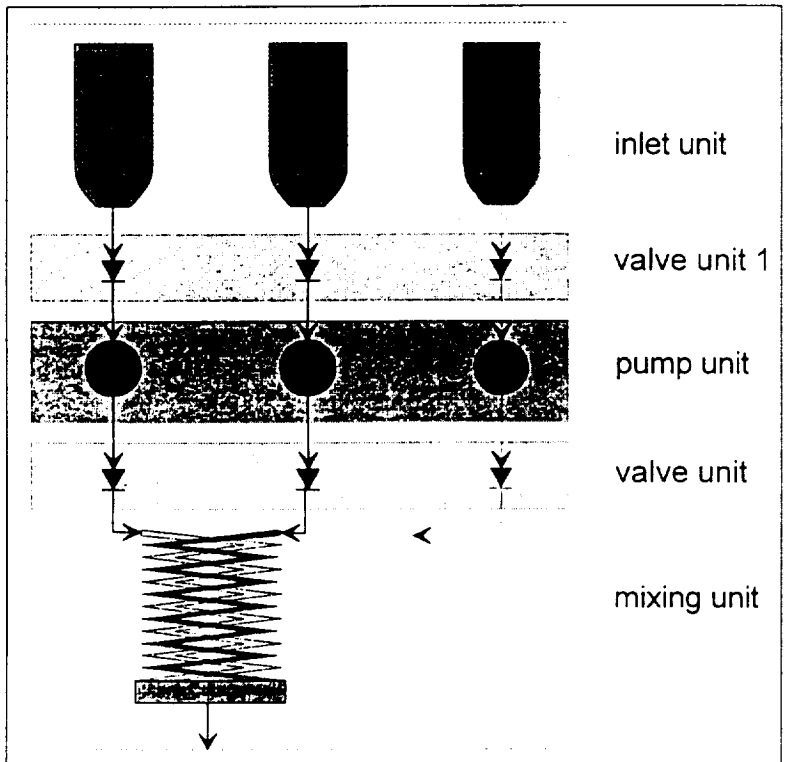

Figure 1: Integrated micrreactor

2. Concept of the microreactor system

The integrated microreactor system was designed to get the possibility of adding more microcomponents. The basic structure of a system consisting of five different groups is shown in figure 1.
The inlet unit is arranged on the top of the system. This unit connects the microsystem with the macroscopic environment. The best way to realise this is a direct connection of the microsystem with media to be observed.
The second group consists of valves. These valves prevent the reflow of the liquid. A reflow could happen when the pumps start their operation.
The pump unit is the next group of the system. The pumps drive the liquid flow from the inlet through the first and the second valve units and the mixing unit as well.
The valves of the fourth unit have to prevent a reflow of liquids into wrong branches of the system.

The fifth group of the system contains the mixing unit. The different liquids should be mixed or, if required, react during their flow through this unit.
The last group contains a reaction chamber and optionally a sensor unit or an outlet of the system. All groups of the system should be integrated. The basic material should be silicon. The number of process steps should be reduced to a minimum.

3. Micropump

3.1 Design of the micropump

The micropumps for application in microreactor systems were designed as piezoelectrically driven membrane pumps. The pump unit as shown in figure 2 consists of two silicon wafers bonded together by the use of a low temperature silicon direct , bonding technology. The wafer on the top is structured applying wet chemical anisotropic etching procedures. The thickness of the membrane is about 50µm. The membrane has a size of 4mm x 4mm. A piezo plate with a size of 3.5mm x 3.5mm x 0.2mm is mounted on top of the membrane. A voltage can be applied onto the top and the bottom of this plate. The silicon base plate covers the inlet and the outlet channels as well as the pressure chamber.

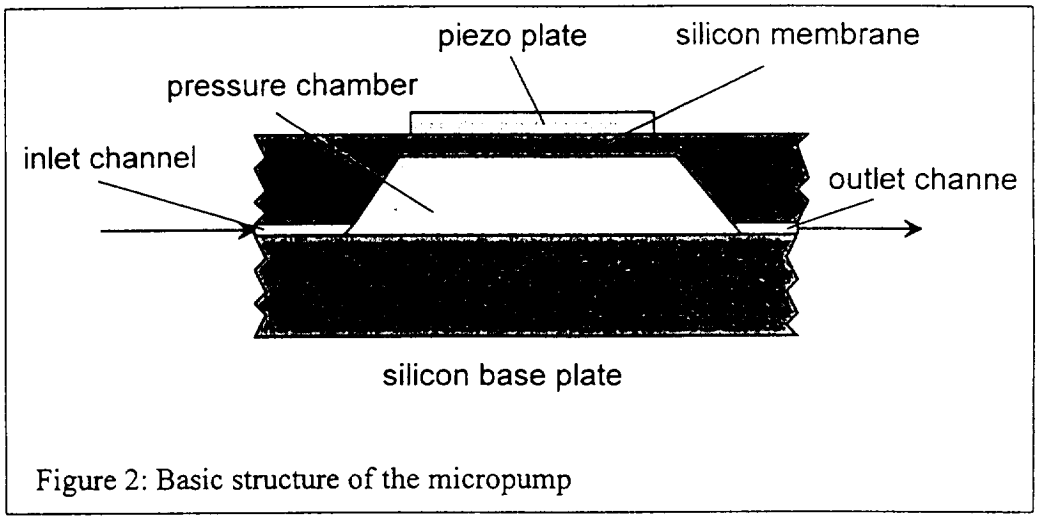

Figure 2: Basic structure of the micropump

3.2 Measurements on the pump

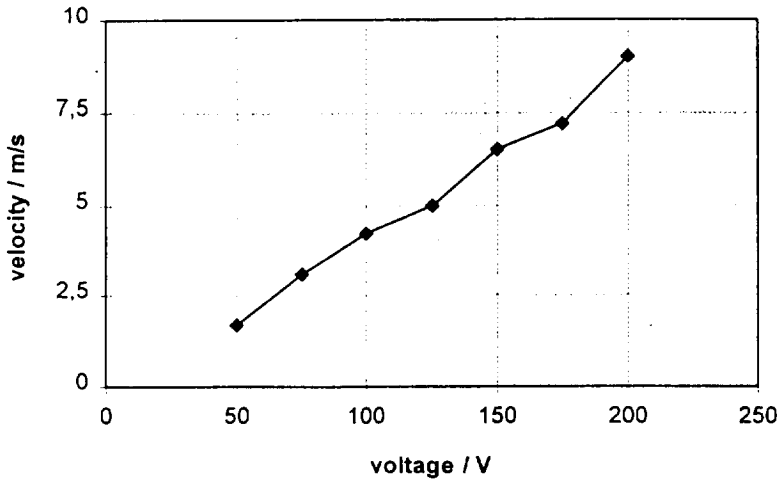

Figure 3: Velocity of the droplets in dependence from the height of voltage

To investigate the performance of the micropump we have prepared several examples according to the above principle. The inlet channel was directly connected with a fluid reservoir. The outlet channel was connected to a gaseous volume. Due to this arrangement it was possible to work without valves in the streaming path. Applying a voltage to the piezo plate one can observe a bending of the bimorph structure that consists of the piezo plate and the silicon membrane. This deformation causes an underpressure inside the

pressure chamber. The liquid tends to stream into the pressure chamber. A turn back of the applied voltage leads to an overpressure in the chamber. The liquid will be pushed out of the chamber. If the outlet is connected directly with a gaseous volume, the streaming resistivity along this path is much lower than that one of the inlet path. By applying cyclic voltage one can observe a cyclic output of the liquid at the outlet. In dependence of the height of the applied voltage we have investigated the size and the velocity of the droplets formed at the outlet. One can see as shown in figure 3that an increase of the applied voltage leads to an increase of the droplet size and an increase of the velocity of the droplets respectively. Besides this we could also found that the volume of the droplets and their velocity depend on the frequency of the applied voltage. The droplet size can also be influenced also by the geometry of the outlet channel.
The best results were achieved in a voltage range between 50V and 200V. It was possible to work in a frequency range up to 6000Hz. The minimum amount that can be pumped was about 60 pl. A maximum flow rate of about 25µl/h is achievable. We have considered a maximum stroke of the bimorph system of 1.5µm. The power consumption of the micropump is lower than 10mW.

4. Microvalve - Design and fabrication

Pump operations in closed liquid systems require the existence of valves. Otherwise the flow and the reflow to the pressure chamber are the same for the inlet and the outlet channels. Microvalves have been well known for several years [3,4]. The integration of such individual devices into closed micro reactors can lead to different problems that are connected with sealing behavior, the dead volumes and the assembling technologies. Therefore we have designed a microvalve that is comparable to the known technologies of the other components and that possesses low dead volumes. The fabrication steps of the valve are shown in figure 4. By means of this fabrication technology it was possible to solve different problems. The valve body is made of a flexible metallisation tong that allows a nearly perfect sealing of the valve seat. Sticking effects of the valve body can be prevented due to the chosen material combinations. Direct bonding technologies can be carried out at low temperatures. .
We have prepared samples of the valves to investigate their behavior under different working conditions. The cross section of the orifice was varied from 300µm x 300µm to 1000µm x 1000µm. The metallisation layer was a sandwich structure that consists of 100nm chromium and 200nm gold.

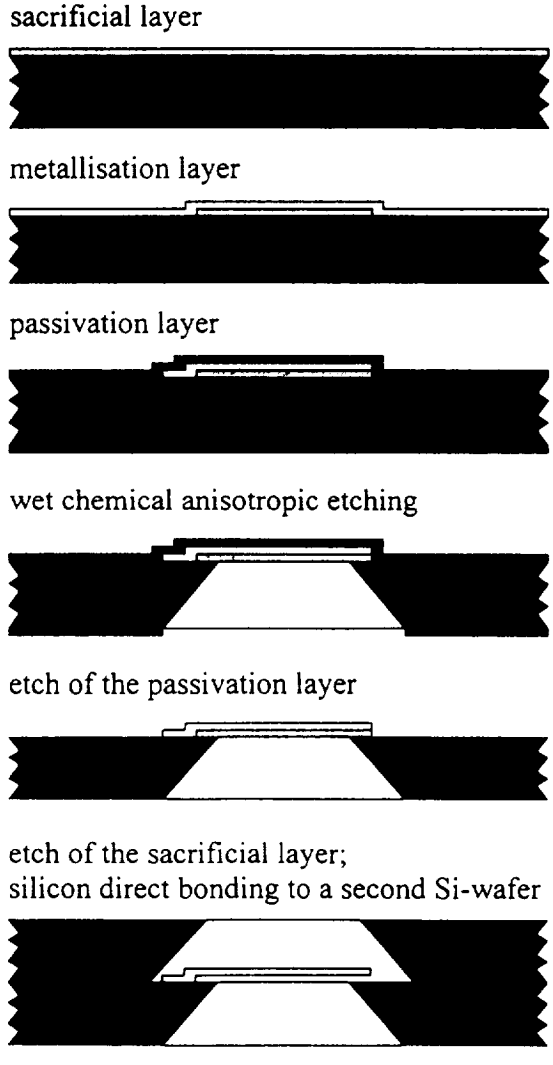

Figure 4: Process steps of the passive microvalve

Into the flow direction all valves were working perfectly up to a pressure of 1 bar. The opposite direction of the flow leads to a streaming breakdown at pressure differences greater than 5000 Pa. This low value indicates a mechanical instability. A better selection of the metals and noticeable thicker layers could lead to improved properties of the valve. An influence of the size of the valve body was not found. Due to the low streaming rate it was impossible to estimate the leakage rate of the valves below this limitation pressure.

5. Mixing unit

5.1 Design principle

The mixing of fluids in small channels is a technical problem. The reason for that is the behavior of the liquids. In very small channels one can observe only a laminar flow of the liquid. This flow is not disturbed by any turbulences. During our experiments we found out that obstacles built in the channel do not lead to any turbulences in the flow. A good mixing of different liquids requires turbulences in the flow. Therefore the answer to the question "How is it possible to achieve a homogeneous mixing of different liquids in microsystems ?" is very important.
The integration of driven obstacles into tubes is known from the macroscopic area. Some rotating devices are known too in the microscopic area [9-11] . They are driven electrostatically and built up out of silicon. Unfortunately these systems were only observed in a gaseous atmosphere. The application with liquids is limited due to the high voltages required. A further disadvantage is the construction

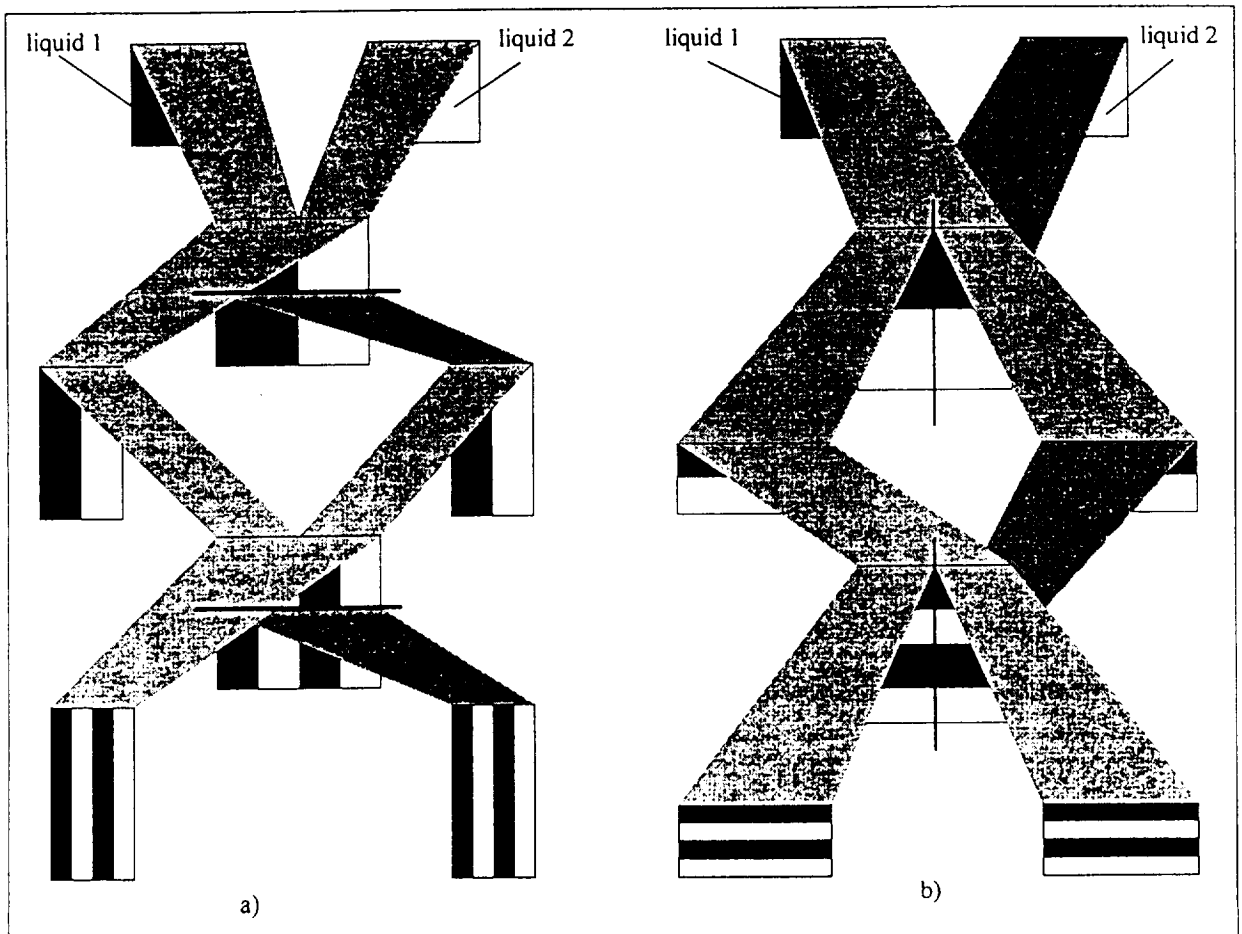

Figure 5: Mixing principles with an enlargement of the active surfacees
a) horicontal adding - vertical dividing - horicontal reuniting of two different liquids
b) vertical adding - horicontal dividing - vertical reuniting of two different liquids

principle of these micromachines. A lot of more process steps would be necessary to build up completely integrated systems using these micromachines.
Static mixing units meet all requirements of the process technology and open the possibility to work with a small amount of basic materials in contrast to moveable obstacles .
The mixing of fluids in small channels can occur by a mechanical exchange of liquid elements due to streaming obstacles and / or by diffusion processes. To get a mixed solution after a short distance it is necessary to enlarge the boundaries between the fluids. A twisting of the fluid layers can not occur due to the laminar flow. An enlargement of the surface boundaries can be achieved in different ways. A simple solution is dividing of each flow into several partial flows. The partial flows of the different solutions will be stacked. Then the partial flows will be reunited. The disadvantage of this method is the size of the system. A lot of space is required due to the division of two or more flows into several partial flows. Therefore we developed a mixing principle that is suited for the use in microsystems and that requires only a small amount of space. Two basic principles of the mixing are shown in figure 5. In the first case (Figure 5 a)) the two liquids will be added together in a horizontal plane. The whole flow will then be divided along a vertical line. As result one gets two partial flows that are located in two different planes. They will be reunited again in a horizontal plane. Then the procedure starts again. In the second case all procedures are turned around 90°. In both cases only two planes are necessary. This mixing procedure allows the mixing of two different fluids. A mixing of more than two liquids is possible by a simple increase in the number of the inlets only.
We calculated the Reynolds-number for the streaming in the channels using water as a liquid. At a cross-section area of $1600\mu m^2$ we found a Reynolds number of about Re=18. To achieve a staple of fluid layers we took into account that the streaming resistivities in different parallel streaming channels should be in the same order. Otherwise one gets a streaming path through the system along the way of the lowest streaming resistivity. In such case no mechanical mixing can occur and the mixing effect is only caused by diffusion processes. We developed a mixing unit that consists of fork-shaped mixing elements. These forks are arranged in two layers. A liquid stream through such a unit will be divided perpendicular to the boundary layer, united in a stapled formation and separated again perpendicular to the boundary layers. Different cross sections of the channels in the fork lead to adapted streaming resistivities. A scheme of the mixing unit and a demonstration of its function is shown in figure 6. We have designed a mask that possesses several mixing units. The mixing units contain

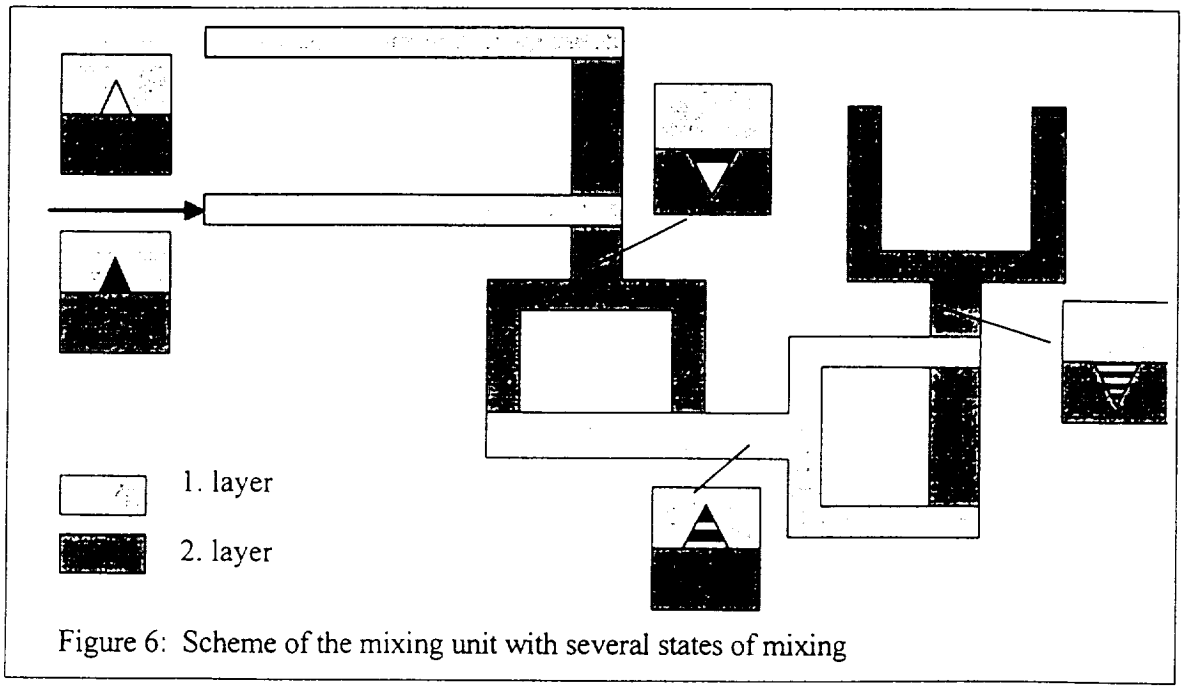

Figure 6: Scheme of the mixing unit with several states of mixing

either 5, 10, 15 or 20 mixing elements. The openings of the fluid channels of the mixing elements had a size of 150μm and 200μm respectively at the surfaces of the substrates.

5.2 Experimental investigations

For the experiments we used 3" - (100) oriented - p-doped silicon wafers. The wafers were cleaned in a standard cleaning procedure. A thermal oxide was grown with a thickness of about 1.2μm. After the lithography the oxide was etched. Then a anisotropic chemical etching was carried out in a 30% KOH solution at 80°C. All structures were etched until the natural etch stop at the (111) planes of the silicon were reached. The oxide was then etched away and the wafers were cleaned again. Then the wafers were pre-treated in an oxygen plasma for 30 sec. Immediately after this process they were rinsed in DI-water, aligned and prebonded. The bonding procedure was carried out at a temperature of 400°C for 4 hours. The wafer was severed into dies. Stainless tubes were slipped into the openings of the channels that were opened by the sawing process. Then the whole system was coated with an epoxy. The steel tubes were connected with transparent tubes made of polymers. To proof the efficiency of the mixers we used a micropump that delivers a cyclic flow rate of the fluids. The average flow rate of about 10 μl/h was constant during the experiments for both liquids. We observed the optical properties of the mixed fluids at the outlet of the mixer. This work was done by means of an optical microscope. We judged the homogeneity of the solution.

5.3 Experimental results and discussion

During our experiments we worked with mixing units that consist of different numbers of mixing elements. Four different types of fluids were used to examine the function of the micromixer.

1. 1 molar chloric acid + methylorange solved in water
2. water + air
3. oil + air
4. water + oil

1. The first liquids are soluble in each other. A mixing of these two fluids can be observed by a change of the colour of the solutions. Methylorange solved in water changes the colour from yellow to pink after a reaction with acids. We found a pink solution at the output of the mixing unit. The change of the colour was independent of the number of the mixing elements. Mixer units with 5 mixing elements show the same behaviour as units with 20 elements. In general the solution was homogeneous mixed. Due to the good solubility of the liquids it was not possible to estimate the real mixing process - diffusion or mechanical mixing.

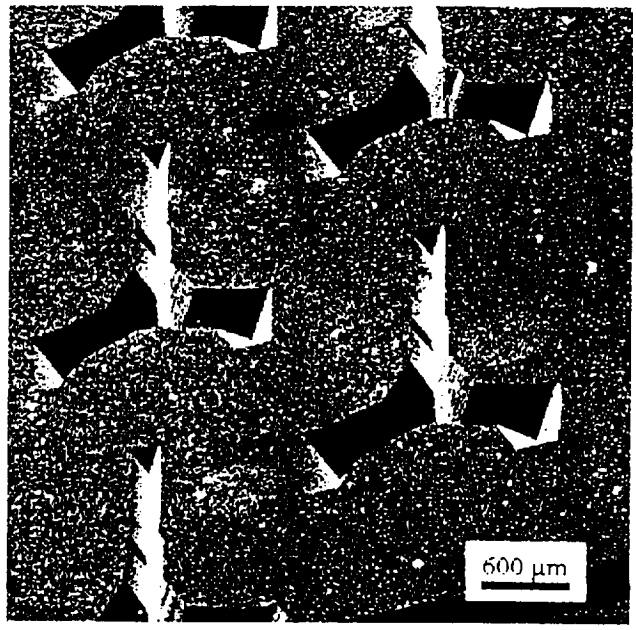

Figure 7: SEM micrograph of the fork-shaped channel structure of some mixing elements on top of one wafer

2. Air has a restricted solubility in water. One can observe bubbles of air in the water if the concentration of the air is too high. Mixing units with 5 elements show bubbles of air and between them columns of water. The volumes of the bubbles and the columns were nearly the same. The dimensions were in a range of 0.2-0.5mm. We observed a growing of an air bubble that was fixed for a short time immediately at the output of the steel tube. This bubble was removed from the outlet after it had reached a determined size. An increase in the number of the mixing elements leads to a change of the behavior. More than 10 mixing elements lead to a development of very small bubbles of air. These bubbles were not fixed at the edge of the tube. So the water became more frothy. The diameters of the bubbles were in a range of less then 0.1mm. The growing of bigger air bubbles was observed minutes after the mixing procedure. This new quality indicates a mechanical mixing of the two fluids. Due to the mixing principle the number of the fluid layers will be doubled and the thicknesses of the layers will be divided into half after each mixing element. Therefore the bubbles get smaller as more mixing elements are flowed through.

3. The mixing of air and oil leads to a similar behavior as described before. The growth of bubbles at the end of the steel tube was restricted due to the high viscosity of oil . The bubbles were removed from the edge of the tube if their diameter was in a range of about 0.1mm. The mixed liquid has changed the colour from yellow (colour of the oil) to a yellow - white. After the mixing unit the liquid was not transparent. A growth of bigger bubbles outside the mixer was observed, too. The oil mixed with the air by five mixing elements was nearly free of air bubbles after about 60 min. We got an oil free of air when the mixing was carried out in a 20 element mixer after 2-3 days. The velocity of the bubble growth was much lower than in water.

4. The mixing of oil and water is very difficult. There is no solubility of the fluids in each other. In a mixing unit with 5 mixing elements we found a growth of small water droplets at the edge of the steel tube. These droplets were surrounded by oil. The droplets were removed from the tube when they had reached a diameter of about 0.5mm. So we could observe an alternating raw of columns of oil and columns of water in the transparent tube. The liquids were separated very quickly inside a bottle made of glass. Fifteen or more mixing elements lead to a decrease of the diameter of the water droplets. These droplets are spherically shaped and surrounded by the oil. The solution is not transparent and seems to be in an emulgated state. A demixing of the two liquids was observed about 3-4 hours after the mixing procedure. This behavior indicates clearly a mechanical mixing of the two components.

6. Reactor chamber

The mixing of reagents does not lead in all cases to a chemical reaction. A supply of energy is very often required to initiate chemical processes. This can be done by light, electricity, radiation or temperature. We chose an energy supply in form of temperature. An integration of a resistor network is simple and can also be done by the use of microtechnologies. Another advantage is the relatively low power consumption. To initiate a reaction of the mixed fluids a reactor chamber was designed. This chamber is directly connected with the output of the mixing unit. To prevent a chemical reaction or a catalytic influence of the resistor materials with the reagents the resistors were arranged outside the reactor chamber. For the heating elements we used platinum as material. The structures were prepared applying a sputtering technology for deposition and a lift-off-process to create the elements. Because of the very high thermal conductivity of silicon it is possible to increase the temperature inside the reactor chamber applying a current to the heating elements.

We carried out some experiments and found some disadvantages of this solution. The high temperature gradient caused by a heat up of the resistors leads to a spreading of temperature over the whole wafer. An increase in the temperature is observable not only inside the reactor chamber but also in the mixing unit, the micropumps and the microvalves as well. It was not possible to achieve the

preestimated temperature inside the reactor chamber due to the temperature losses in the whole system. Further investigations are necessary to reduce the temperature losses and the heating up of the whole system.

7. Design and process steps of the microreactor

The microreactor contains several individual components as shown in figure 1. All these components except the liquid reservoirs should be built up in an integrated form. The basic material for all components is silicon. All process steps should be compatible to commonly known microtechnologies. On the basis of this concept we designed and prepared an integrated microreactor module that meets all requirements in liquid handling and process technologies, respectively.
The microreactor consists of three structured wafers that are bonded together. The first wafer contains square deepenings. One kind of deepenings solves as coverage for the heating elements arranged on top of the second wafer. The other deepenings are required to get a membrane structure. Piezoceramic plates are mounted on top of the membranes. These plates act together with the silicon membrane below it as a bimorph structure. Applying a voltage to the piezoelectric element the whole bimorph structure will be bended. Due to this deflection a pressure will be built up in the chamber below the membrane. Caused by the pressure difference a directed flow of the liquids inside the chamber will be initiated. The directed streaming can be achieved by means of two passive valves. The second wafer contains the two valve units, a part of the mixing unit, the process chamber and the heating elements as well. The valves act as passive valves. They have thin metallic membranes as valve bodies. The flow of the liquid in one direction is possible due to holes etched through the wafer. The direction of the streaming is forced by the inverted arrangement of the holes and the valve bodies, respectively, in each streaming path. A part of the mixing unit is formed as an arrangement of "fork-shaped" v-grooves on the bottom of the wafer. A reactor chamber is arranged at the output of the mixing element. This chamber contains v-shaped grooves arranged in parallel. Deeply etched v-grooves act as partial shape for stainless steel tubes of the inlet and the outlet connections in this wafer. The third wafer contains an arrangement of v-grooves. These grooves act as channels for the streaming path, as second part of the mixing unit (fork-shaped) and as shape to take in the outside connections. The advantage of this design is the low consumption of basic materials, short ways of the flow inside the system and therefore very small dead volumes and only a few required process steps.

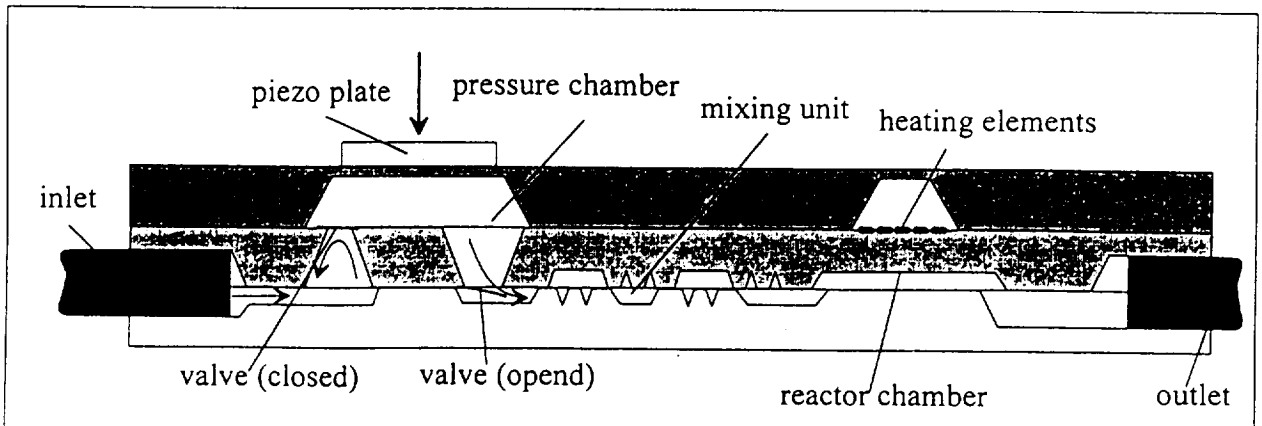

Figure 8: Cross-section of the microreactor

The microreactor can be realised by the use of silicon micromachining technologies. All three dimensional structures in the silicon can be etched anisotropically. The depth of the structures is defined by the natural etch stop at {111} planes of the silicon. Due to the etch stop it was possible to etch through the whole wafers in some required regions. The valve bodies of the passive valves and the

heating elements were produced by a metallisation process before the etching procedure. The wafers can be bonded together after structuring using the silicon direct bonding technology. This process step was carried out after a short treatment of the wafers in a pure oxygen plasma for about 30s. The bonding temperature was 450°C. The advantage of this low temperature is the possibility of an integration of microelectronic circuits. The piezoceramic plates were mounted after the bonding process with a glue on the top. The tubes of the inlet and the outlet were slipped into the deeply etched channels and fixed by the use of an elastic glue. All open surfaces of the system are made of silicon. For special chemical reagents it is possible to cover the surfaces with inert materials, like SiO_2 or Si_3N_4.
Having applied a voltage to the piezo plates a flow rate up to 20µl/h was observed.

8. Conclusion

An integrated microreactor was developed that consists of several individual components. Each individual component was investigated separately. The pumps can force a flow rate up to 25µl/h applying a voltage of 200V. Passive valves offer resistance in closed state up to 5000 Pa. The behavior of the mixing unit was proved by the mixing of different fluids. The possibility of the mixing of liquids with liquids as well as the mixing of gases with liquids was shown. A homogeneous mixture can be achieved for liquids that are soluble in each other after 5 mixing elements. Fluids that are not soluble in each other will be emulgated after more then 10 mixing elements. The mixer possesses a very high efficiency in the mechanical mixing of two fluids. The process chamber was arranged with heating elements on their outside. Due to the temperature losses in the whole system it was not possible to achieve the preestimated temperature inside the chamber. Furthermore investigations are required to find out a better energy supply inside this component. The integrated microreactor was designed and built up using commonly known process steps of the microtechnology. A total flow rate at the output of 20µl/h was observed. The microreactor is suited in principle for applications in the chemical and the biochemical area. The advantages of the system are low reagent consumption, very high accuracy, low power consumption, small and light and the possibility to integrate sensors and microelectronic circuits.

9. Acknowledgement

The authors would like to acknowledge the guidance and help of the researchers in the Laboratory of Microstructuring Technologies, particularly J. Burghold for discussions about the streaming behavior of liquids in capillaries; M. Fischer for discussions about the design of micropumps;
O. Marufke for the direct bonding procedures; B. Hartmann and G. Harnisch for preparing various types of micropumps, microvalves, mixing units and integrated microreactors.

10. References

[1] Zengerle, R.; Kluge, S.; Richter, M.; Richter, A.
A bidirectional silicon micropump
Procceding MEMS'95, Amsterdam, p. 19-24

[2] v.d. Pol, F.C.M.; van Lintel, H.T.G.; Elwenspoek, M.; Fluitman, J.H.J.
A thermo-pneumatic micropump based on micro-engineering techniques
Sensors & Actuators, A21-23, 1990, p. 198-202

[3] Esashi, M.; Shoji, S.; Nakano, A.
Normally closed microvalve and micropump fabricated on a silicon wafer
Sensors & Actuators, 20 (1989), p. 163-169

[4] Miles, R.; Weber, W.
Thermopneumatically actuated microvalves and integrated electro-fluidic circuits
4. Int. Conf. on new Actuators "Actuator 94" Bremen 1994, p. 56-60

[5] Branebjerg, J.; Fabius, B.; Gravesen, P
Application of miniature analyzers: from microfluidic components to μTAS
Micro Total Analysis Systems, Enschede 1994, Proceedings, p. 141-151

[6] Elwenspoek, M.; Lammerink, T.S.J.; Miyake, R.; Fluitman, J.H.J.
Towards integrated microliquid handling systems
Journ. of Micromech. and Microengineering vol. 4(1994), no. 4, p. 227-245

[7] Mensinger, H.; Richter, T.; Hessel, V.; Döpper, J.; Ehrfeld, W.
Microreactor with integrated static mixer and analysis system
Micro Total Analysis Systems, Enschede 1994, Proceedings, p. 237-243

[8] van der Schoot, B.; Verpoorte, E.; Jeanneret, S.; Manz, A.; de Rooij, N.
Microsystems for analysis in flowing solutions
Micro Total Analysis Systems, Enschede 1994, Proceedings, p. 181-190

[9] Fan, S.-L.; Tai, Y.-C.; Muller, R.S.
Integrated Moveable micromechanical Structures for Sensors and Actuators
IEEE Tr. on ED, vol 35(1988), no. 6 p.724-730

[10] Tai, Y.-C.; Muller, R.S.
IC-processed Electrostatic Synchronous Micromotors
Sensors & Actuators 20(1989), p. 49-55

[11] Fan, L.-S.; Tai, Y.-C.; Muller, R.S.
IC-processed Electrostatic Micromotors
Sensors & Actuators 20(1989), p. 41-47