Platform for lab-on-a-chip systems based on integrated active valves made in polymers suitable for mass production

J. Rupp[1], M. Schmidt[1], B. Günther[1], M. Stumber[1], P. Rothacher[1], R. Zengerle[2], M. Daub[1]

[1] Robert Bosch GmbH, Corporate Sector Research Microsystem Technologies, Robert Bosch Platz 1, 70839 Gerlingen, Germany; Jochen.Rupp3@de.bosch.com
[2] Laboratory for MEMS Applications, Department of Microsystems Engineering (IMTEK), University of Freiburg, Georges-Koehler-Allee 106, 79110 Freiburg, Germany

Abstract

For the first time we present integrated pneumatically controllable valves realized with three layers consisting of two injection compression molded parts separated by a 25 µm thin elastic TPE (thermoplastic elastomer) membrane welded together in one step. The device shows excellent response time and sealing quality at a very low sealing pressure. The production technologies injection compression molding and laser welding fulfill the requirements of a high throughput production and have the potential to manufacture cheap and reliable lab on a chip systems. The elastic TPE membrane works as a joining layer between the two outer layers, each made of cycloolefinpolymere (COP), cycloolefincopolymere (COC) or polycarbonate (PC). Valving is realized by applying pressure in a displacement chamber above a microfluidic channel and deforming the elastic membrane. The materials used show a high chemical resistance against a broad range of commonly used liquids [1]. This consistent technological approach represents a flexible platform for µTAS applications with the active valve as a basic element for more complex applications, such as pumping and mixing on chip.

1. Introduction

The trend towards miniaturization and the flexible use of systems such as portable medical devices, micro fuel cells and even micro chemical reactors imposes strong requirements in terms of size, weight, accuracy and the capability for automation. Function integration is thus a key requirement, which leads to a growing demand for micro flow management components such as sensors, pumps and valves [2]. Polymer based lab-on-a-chip systems fulfill these requirements and have emerged the recent years. They promise cheaper and faster production cycles. Manufacturing very cheap lab on a chip systems by mass production should have great impact in biotech industries, pharmacology, medical diagnostics, forensics, environmental monitoring and basic research [3]. We developed a microfluidic platform based on polymers suitable for mass production with active valves as basic elements presented in this work.

2. Experimental

The integrated microfluidic device is made of an injection compression molded fluidic and control layer (both 600 µm thick) separated by a deformable TPE membrane (d_{TPE}=25 µm; **Fig. 1**) joined together using laserwelding. Valving is realized by applying a pressure $P_{control}$ inside the actuation chamber to deform the membrane which tightens the fluidic channel. This principle has been shown for several PDMS setups [4,5,6].

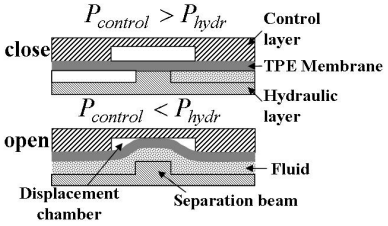

Fig. 1: **Working principle** of the pneumatically actuated valve. Schematic cross section of the setup and the working principle.

The so fabricated devices were then tested for their valving characteristics. We chose injection compression molding as a fabrication process in order to address the capability for mass production. Laserwelding as a joining technology was used to gain a mechanically stable part without negative influence on biochemical applications. During this production step no additional material such as glue is needed and the thermal energy is only irradiated locally. Other bonding processes like thermal bonding have an influence on biocontent.

2.1. Design

We investigated the characteristics of 12 different geometries as shown in **Fig. 2**. On the hydraulic layer each valve has a fluidic inlet and outlet connected by a channel. The valve is located in the middle of the channel consisting of a chamber with a separation beam. Each valve has a pneumatic displacement chamber the same diameter as the chamber in the hydraulic layer (**Fig. 3**). The geometric variations we investigated include the channel width w_{ch}, separation beam width w_{beam} and the chamber diameter $d_{chamber}$. The hydraulic channel length is 18 mm, channel depth is 100 µm for the fluidic and 50 µm for control layer. The in- and outlets were connected to PTFE tubes using glued metal adapters (**Fig. 4**). With these variations

978-3-8007-3183-1 © VDE VERLAG GMBH · Berlin · Offenbach

we investigated the influence on switching characteristics, flow rate and possible side effects.

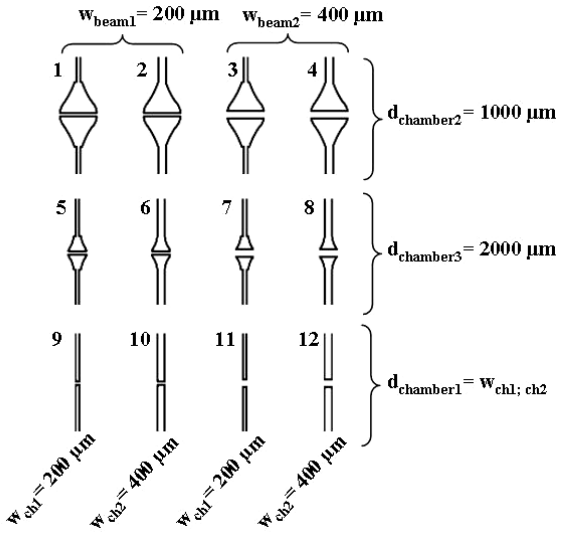

Fig. 2: Top view of the 12 different designs (hydraulic layer). Variation: inlet channel width w_{ch}, chamber diameter $d_{chamber}$, separation beam width w_{beam}.

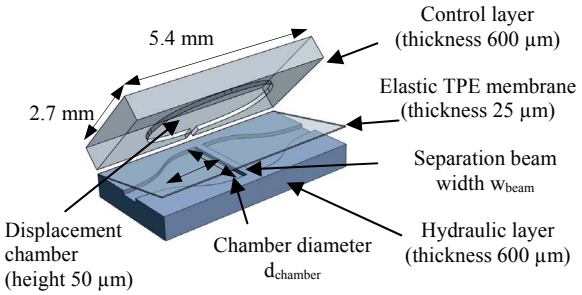

Fig. 3: 3D CAD schematic side view of the valve assembly consisting of two structured polymer parts separated by an elastic TPE membrane.

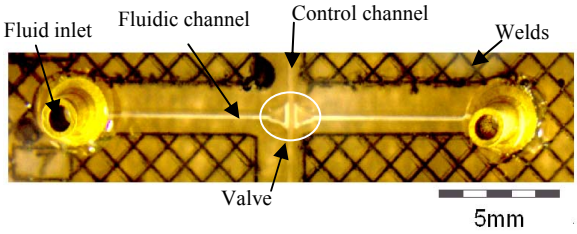

Fig. 4: Picture of the microfluidic valve (geometry 6) with the separation beam, the pneumatic control channel (vertical), 18 mm hydraulic channel (horizontal) and the glued metal adapters for tube connections.

2.2. Fabrication steps

For the injection compression molding process a metal tool with the desired structures was made in two steps. First step was to fabricate a master which contains the microfluidic structures. Second was to replicate the master to form an inverted metal tool which could be used for the molding. The master was manufactured using lithography on thick dry film resists laminated on a silicon wafer. A 50 µm negative resist (*Dupont WPR1050*) was laminated onto an unstructured silicon wafer with 20 mm/s at 85 °C and prebaked for 1 min at 100 °C. The structures were created with a UV 365 nm exposure for 40 s followed by developing supported by ultrasound and a hardbake step for 60 min at 145 °C. In order to create channel depths of 100 µm this step was repeated once. This master was replicated to form a metal tool for injection compression molding of PC (**Fig. 5**).

Fig. 5: Photograph of the control (black), the fluidic (transparent) PC disc and the stamp used in the DVD manufacturing process at *Arvato Digital Service*.

2.3. Joining technology

In order to create a mechanically stable and tight connection of the three layers a one step laser welding process is used. The material of the two bulk layers are weldable thermoplastics (T_G=140 °C) of which one layer is transparent for the applied laser wavelength (λ=1064 nm) and the other is absorbing. The welding process first was optimized by welding blank material varying laser speed and power. We welded different material combinations:

- PC – TPE – PC
- COC – TPE – COC
- COP – TPE – COP

We showed that the production technology is applicable for these materials. After testing milled devices to proof the principle of the joining technology the injection compression molded parts were fabricated in PC.

2.4. Valve characterization

There are numerous requirements miniaturized valves have to fulfill, such as minimum dead volume, low energy consumption, good sealing, short response times etc. [7]. In this work we investigate the basic functionality of a valve. The test bed used consists of a pressure regulator connected to a pilot valve which actuates the valve on chip. Three pressure sensors (*BOSCH SMD022*) read atmosphere, actuation pressure and hydraulic pressure. The resulting flow rate is measured by a mass flow sensor (*Sensirion Inc. ASL1600)*. The constant hydraulic pressure is generated by an elevated tank filled with DI water. Nitrogen works as actuation gas. Each of the 12 valves is tested separately. The characterization includes a **switching operation** and **switchover point.** Switching operation was investigated over a minimum number of 60 cycles of opening and closing the valve while measuring the flow rate. The switching characteristics were measured by in-

creasing and decreasing the control pressure above and below the fluid pressure level while measuring the flow rate. Four devices with 12 valves each were tested this way. One selected valve (design 1) was also tested at 95 °C, in order to simulate the circumstances many microfluidic applications work with, e.g. PCR on chip [8].

3. Results and discussion

The dimensions of the polymer are approximately 20% smaller than designed. This possibly results from shrinkage of caused by the temperature steps during master fabrication and the injection compression molding process. The legends in the following figures are referencing the target values. **Fig. 6** and **Fig. 8** are results of design 1 and exemplary for the switching operation and flow rates of the setup.

3.1. Switching operation

The **basic functionality** for design 1 is shown in Fig. 6. A constant hydraulic inlet pressure induces a flow through the channel. The valve is opened and closed periodically with a frequency of 0.25 Hz. When a control pressure is applied the valve stops the fluid flow completely. The control pressure level was set to be at a constant of 10 kPa to make sure $P_{control} > P_{hydr}$. When released a flow starts immediately (Fig. 6).

All designs show this basic functionality over several minutes to hours without any loss of sealing quality. Although the resulting flow rate varies with bubbles trapped particularly in the wider valving chambers. A t**ime constant** for switching was measured to be 20 ms which leads to a maximum switching frequency of 25 Hz. Since the pilot valve used for actuation of the integrated valves has a switching constant of 20 ms the minimum switching time for the microfluidic valve couldn't be measured with this experimental setup but is considered to be shorter.

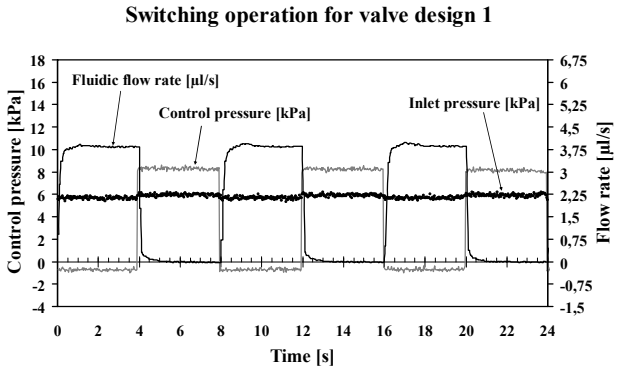

Fig. 6: Switching operation for valve design: w_{ch}=200 µm; $w_{chamber}$=w_{ch}; w_{beam}=200 µm.

The **average fluidic flow rate** varies depending on inlet pressure, channel width and chamber geometry. The broader 400 µm channels have flow rates almost two times than the flow rates of the smaller 200 µm channel. Wider **chamber diameters $d_{chamber}$** result in decreasing the fluidic resistance. The larger chamber causes more volume to push out the chamber resulting in an increasing overshooting peak during switching. This behavior is increased by a higher hydraulic inlet pressure. Large displacement chambers act as a bubble trap. When a bubble is trapped the main function of the valve is never affected but the decreased active channel cross section lowers the flow rate depending on the size of the bubble. The 200 µm **separation beam** is a smaller resistance to the fluid than the 400 µm beam which leads to an increasing average flow rate shown in **Fig. 7**.

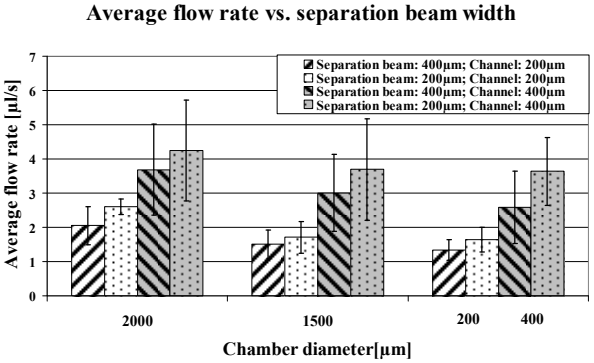

Fig. 7: Overview of the different average flow rates vs. the two separation beams for each chamber diameter.

3.2. Switching characteristics

During this test the control pressure $P_{control}$ is increased above the fluidic inlet pressure level P_{hydr} and then decreased to zero. This way the switchover pressure and hysteresis are investigated (**Fig. 8**). This ramp is done two times for each valve while measuring the flow rate. The ramp duration was four minutes for two cycles. The **switching interval** between complete open and complete closed is below 3 kPa. The **minimum closing pressure** shown in Fig. 8 is 2.3 kPa below the fluidic inlet pressure. This could be caused by the TPE membrane being prestressed counteracting against the fluidic pressure without any applied control pressure. For all tested devices an average minimum closing pressure of 0.72 kPa higher than P_{hydr} is necessary for complete sealing. Because of the low Young's modulus (6-9 MPa) and a membrane thickness of only 25 µm the setups' minimum closing pressure is 40 times lower than in comparable PDMS setups where a typical closing pressure of 40 kPa above P_{hydr} is needed [4]. **Hysteresis** (direction clockwise) appears in all designs varying between 0.5 and 1.5 kPa. One possible reason for this effect could be the foil sticking to the separation beam increasing the energy needed for the flow to start. We showed that with this setup several parallel conjoined valves work properly over several hours without cross interaction. The setup was tested with pressures applied up to 70 kPa without bursting. The valve was tested for behavior at elevated **temperature.** Valves were heated to 95 °C and actuated while measuring the flow. The valve showed similar functionality like the ones tested at room temperature although we observed slightly higher flow

rates. A reason could be the temperature dependency of the stiffness of TPE membrane which decreases at elevated temperatures decreasing the fluidic resistance. Also an increased bubble creation caused by heating occurred causing the same effect as explained in 3.1.

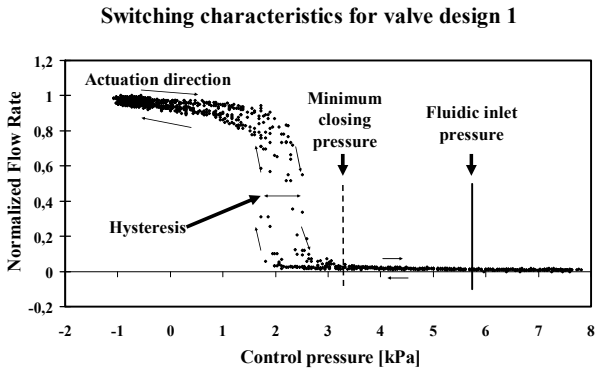

Fig. 8: Normalized switching characteristics for valve design 1.

4. Conclusion

We presented integrated pneumatically controllable valves realized with three layers consisting of two injection molded parts separated by a 25 µm thin elastic TPE (thermoplastic elastomer) membrane welded together in one step. The production processes were chosen to be suitable for mass production, namely injection compression molding and laser welding. We investigated 12 different valve designs and tested them for functionality and characteristics. Short switching times of only 20 ms were measured. Thus the minimum switching time could not be evaluated because of limitation from the used actuating pilot valve. The integrated valve shows excellent sealing quality at very low closing pressures of only some kPa. The setups' minimum closing pressure is 40 times lower than in comparable PDMS setups where a typical closing pressure of 40 kPa above P_{hydr} is needed [4]. At elevated temperatures the valve showed full functionality. Different designs have been characterized in order to fulfill different requirements for several applications. The small chamber dimensions of only 0.5 mm allow a high integration of the valves for µTAS applications. The integrated and planar setup enables the lab on a chip designer to put the valve freely on chip with the actuating pilot valves remaining off chip. This way designs for different applications can be realized with one off chip equipment that addresses various valves on chips. This technological approach leads to a microfluidic platform with a valve as a basic element and materials suitable for mass production.

5. Acknowledgement

The present study is supported by the German Federal Ministry of Education and Research (01EZ0709). We want to thank Mr. Steinbrecht from *Arvato Digital Services* for the support and discussion during this work.

Literature

[1] Stoyanov, I. Tewes, M. et.al. (2005): Proceedings Material Research Society Symposium, 872.

[2] Micro fluid management, a key enabling technology of the future, (2008)Yole Micronews October, Issue n°73

[3] Bruus, H. (2007): Microfluidics and lab-on-a-chip technology, MIC –Supplementary lecture notes, 2nd edition, Department of Micro and Nanotechnology, Technical University of Denmark

[4] Unger, M.A. et.al. (2000): Monolithic Microfabricated Valves and Pumps by Multilayer Soft Lithography. Science 288 113-116.

[5] Groover, H.W. et.al. (2003): Monolithic membrane valves and diaphragm pumps for practical large-scale integration into glass microfluidic devices. Sensors and Actuators B 89 315-323.

[6] Stoyanov, I. et.al. (2006): Microfluidic devices with integrated active valves based on thermoplastic elastomers. Microelectronic Engineering 83, 1681-1683.

[7] Hardt, S.; Schönfeld, F. (Hg.) (2007): Microfluidic Technologies for Miniaturized Analysis Systems. Boston, MA: Springer Science+Business Media LLC Springer.

[8] Li, Dongqing (Ed.) (2008): Encyclopedia of Microfluidics and Nanofluidics, Springer, pp1619.