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# Heterogeneous Technologies for Microfluidic Systems

GUNJANA SHARMA



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#### **Abstract**

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In this thesis, conventional and unconventional technologies have been studied and combined in order to make heterogeneous microfluidics with potential advantages, especially in biological applications. Many conventional materials, like silicon, glass, thermoplastic polymers, polyimide and polydimethylsiloxane (PDMS) have been combined in building heterogeneous microfluidic devices or demonstrators. Aside from these materials, unconventional materials for microfluidics such as stainless steel and the fluoroelastomer Viton have been explored.

The advantages of the heterogeneous technologies presented were demonstrated in several examples: (1) For instance, in cell biology, surface properties play an important role. Different functions were achieved by combining microengineering and surface modification. Two examples were made by depositing a Teflon-like film: a) a non-textured surface was made hydrophobic to allow higher pressures for cell migration studies and b) a surface textured by ion track technology was even made super-hydrophobic. (2) In microfluidics, microactuators used for fluid handling are important, e.g. in valves and pumps. Here, microactuators that can handle high-pressures were presented, which may allow miniaturization of high performance bioanalyses that until now have been restricted to larger instruments. (3) In some applications the elastomer PDMS cannot be used due to its high permeability and poor solvent resistivity. Viton can be a good replacement when elasticity is needed, like in the demonstrated paraffin actuated membrane. (4) Sensing of bio-molecules in aquatic solutions has potential in diagnostics on-site. A proof-of-principle demonstration of a potentially highly sensitive biosensor was made by integrating a robust solidly mounted resonator in a PDMS based microfluidic system.

It is concluded that heterogeneous technologies are important for microfluidic systems like micro total analysis systems ( $\mu$ TAS) and lab-on-chip (LOC) devices.

**Keywords:** actuator, biosensor, fluidic circuit board, heterogeneous technology, ion track, microfluidic, pump, stainless steel, super-hydrophobic, valve, Viton

*Gunjana Sharma, Department of Engineering Sciences, Microsystems Technology, 516, Uppsala University, SE-751 20 Uppsala, Sweden.*

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*To my son Pranshu*



# List of Papers

This thesis is based on the following papers, which are referred to in the text by their Roman numerals. Reprints were made with permission from the respective publishers.

- I      Myotube formation on micro-patterned glass: intracellular organization and protein distribution in C2C12 skeletal muscle cells, Yamamoto D L, Csikasz R I, Li Y, Sharma G, Hjort K, Karlsson R and Bengtsson T, *Journal of Histochemistry and Cytochemistry*, v. 56, 881-92 (2008)
- II     Printed fluidic board platform for pressure induced cell migration studies, Sharma G, Kolari K, Klintberg L and Hjort K, *Micromechanics Europe Workshop*, (Toulouse, France, Sept. 20-22) B19 (4pp) (2009)
- III    Stroke asymmetry of tilted superhydrophobic ion track textures, Spohr R, Sharma G, Forsberg P, Karlsson M, Hallén A and Westberg L, *Langmuir*, v. 26, 6790-6 (2010)
- IV    Viton-based fluoroelastomer microfluidics, Sharma G, Klintberg L and Hjort K, *Journal of Micromechanics and Microengineering* (Submitted) (2010)
- V      High-pressure stainless steel active membrane microvalves, Sharma G, Svensson S, Ogden S, Klintberg L and Hjort K, *Journal of Micromechanics and Microengineering* (Submitted) (2010)
- VI    High-pressure peristaltic membrane micropump with temperature control, Svensson S, Sharma G, Ogden S, Hjort K and Klintberg L, *Journal of Microelectromechanical Systems* (In Print) (2010)
- VII   Fabrication and characterization of a shear mode AlN solidly mounted resonator-silicone microfluidic system for in-liquid sensor applications, Sharma G, Liljeholm L, Enlund J, Bjurström J, Katardjiev I and Hjort K, *Sensors and Actuators A: Physical*, v. 159, 111-6 (2010)

# Comments on my contribution to the papers

- I Major part in fabrication. Small part in experiment and writing.
- II Part in planning, integration, experiment and evaluation. Major part in writing.
- III Part in fabrication, characterization and writing.
- IV Major part in planning, fabrication, evaluation and writing.
- V Part in planning and evaluation. Major part in writing.
- VI Part in experiment and small part in writing.
- VII Major part in integration and writing.

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# Abbreviations

CA	Contact angle
DNA	Deoxyribonucleic acid
EO	Electro-osmotic
F	Flourine
FBAR	Thin Film Bulk Acoustic Resonator
FCB	Fluidic circuit board
FFKM	Perfluoroelastomers
FKM	Fluoroelastomers
HTS	High Throughput Screening
IC	Integrated Circuit
LC-MS	Liquid Chromatography- Mass Spectrometry
LOC	Lab on Chip
μCP	Micro contact printing
μTAS	Micro Total Analysis Systems
PC	Polycarbonate
PCM	Phase Change Material
PDMS	Poly(dimethylsiloxane)
PE	Polyethylene
PET	Polyethylene terephthalate
PI	Polyimide
PMMA	Poly(methyl methacrylate)
PP	Polypropylene
Q	Quality factor
QCM	Quartz Crystal Microbalance
SAW	Surface Acoustic Wave
SH	Super hydrophobic
SMA	Shape Memory Alloy
SMR	Solidly Mounted Resonator
SOI	Silicon On Insulator
TH	Thermohydraulic
3D	Three Dimensional
2D	Two Dimensional

# 1. Introduction

This thesis focuses on presenting heterogeneous technologies for microfluidic systems. Heterogeneous technologies provide systems made from more than one material and processing platform. Research on heterogeneous micro-technologies demands a thorough understanding of each and every contributing technology, and how to combine them, resulting in complete 3D integrated systems. This is almost impossible with only one technology. In the research presented here, not only the well known technologies based on materials as silicon, glass and polydimethylsiloxane (PDMS) have been used, but also exotic and less frequently used technologies based on stainless steel, flexible foil and the elastomer Viton have been explored. To reach applicability, the work has been performed in close collaboration with different disciplinary expertise having thorough understanding in specific components or applications.

Microfluidics is a multidisciplinary field with a tremendous application potential for chemical analysis, bio-medicine, optics and information technology (Squires and Quake 2005, Dittrich and Manz 2006, Whitesides 2006). It comprises components such as fluidic networks, actuators, pumps and valves. By combining these components, complex systems can be formed, enabling applications where miniaturization, mitigating dead volume, ease of fabrication, low production cost, ease of integration, automation and parallelization are important. Micro total analysis systems ( $\mu$ TAS) or lab-on-chip (LOC) systems are combinatorial systems of one or several laboratory functions integrated on a single chip, which are only millimeters to a few square centimeters in size. For  $\mu$ TAS, fluid handling (sampling, transport of fluid, chemical reactions, separation and detection) along with the components needed for the fluid handling such as actuators, microvalves, micropumps, micromixers and their integration is important. Besides that,  $\mu$ TAS also involves surface modification and detection principles including, integrated detectors and integrated electronics. When dealing with  $\mu$ TAS, issues coupled to external components such as power source, interconnections, user-interface and hybridization of multiple chips also need to be considered. Developing this technology, demands that we combine different chips in a highly integrated system. In this thesis, silicon and glass technology, fluidic circuit board (FCB) technology, ion track technology and soft lithography have been used.

There are many ways of assembling different features of microfluidics in one chip. Monolithic integration (Burns *et al* 1998, LeMinh *et al* 2003), hybrid integration (Verpoorte *et al* 1994, Liu *et al* 2004), large scale integration (Melin and Quake 2007) and heterogeneous<sup>1</sup> integration (Yang *et al* 2002, Chediak *et al* 2004) are the most commonly used assembly techniques in microfluidics.

Microfluidic systems are most often realized by monolithic chips of silicon, glass, PDMS or thermoplastics. For large volumes and small areas, these are most often the best choices. In hybrid integration, several components can be integrated by pick and place assembly into a system to obtain benefits of combined materials or technologies. For example, monolithic sensors made by silicon technology can be integrated in polymeric fluidic networks, resulting in a highly sensitive detection system (**Paper VII**).

Due to the evolution of a wide range of materials for microfluidics, there is an increased interest for heterogeneous technologies, using several material combinations, and allowing an advanced 3D structure. There are several applications in microfluidics where less common materials and technologies are advantageous and often there is a need for heterogeneous technologies. In direct analogy to printed circuit board technology in microelectronics, FCB technology can give the advantages of low-cost and large-area systems. For example large metal sheets with fluidic networks and components can be manufactured at reasonable cost. FCB technology allows the integration of advanced small library components, which is only possible at reasonable costs, when produced in large numbers. It provides rapid prototyping, and small-scale series at reasonable production costs. In this thesis, heterogeneous FCB based on foils and membranes of stainless steel, polyimide (PI) and elastomers (PDMS and Viton) are presented. Hybrid integration of silicon on insulator (SOI) chip to a FCB is demonstrated by using a silicone gasket as a seal. Other techniques that have been used and can also be combined to make heterogeneous systems are ion track technology in polymers, soft lithography and surface coating of fluorocarbon polymers by plasma polymerization in vacuum.

Due to its ease in fabrication and low production cost in prototyping, PDMS is a commonly used material for microfluidic platforms. However, microfluidics often requires handling of fluids that are not compatible with PDMS, *e.g.* varieties of solvents, hydraulic oils and hydrocarbons (Lee *et al* 2003). This is most often resolved by transferring the systems into silicon, glass or thermoplastics. However, when stretchability is demanded, elastomers are the only options.

In this thesis Viton-fluoroelastomer has been explored as a novel material that can overcome some of the issues related to already existing solvent-

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<sup>1</sup> Heterogeneous integration evolved from hybrid integration and it refers to wafer level assembly of different materials, technologies or devices.

resistant elastomers. Permeability, sealing-force retention capability, high temperature and high pressure capability are some of the issues that can be resolved using Viton through its excellent mechanical and chemical properties abundantly tested in many macro-scale high-pressure and high-temperature environments. It is also possible to bond Viton-fluoroelastomer to Viton and stainless steel, allowing sufficient bond strength for several microfluidic systems, such as fluidic networks, actuators, valves and pumps. The described platform (**Paper IV**) can cover many applications, ranging from chemical synthesis and analysis at high pressure and temperature, to bio-medical applications where high elasticity and surface inertness is required.

When high elasticity is not required, often metals such as stainless steel can be a choice of material for highly integrated 3D microsystems (Agilent's LC-MS system). For example, in  $\mu$ TAS, highly integrated 3D microfluidic systems are needed comprising actuators, sensors and/or detectors, valves and pumps (Charlot *et al* 2008). Microfluidic systems made in steel are also suitable for chemical synthesis and analysis. True 3D microfluidics is obtained by using focused ion beam (FIB) technology and stereo-lithography. Also, stacking technology is considered as a 3D integration technology, which is used in stainless steel FCB technology (**Papers II and IV-VI**).

As previously mentioned, microfluidics has several applications in chemistry, and bio-medicine, but also in robotics, automation and information technology. In this thesis, microfluidics applications in biology and in hydraulics have been explored.

Microfluidics is extensively used in life sciences for genomics (DNA amplification and analysis) (Khandurina and Guttman 2002), proteomics (extraction, separation, digestion and analysis) (Gao *et al* 2001) and cellomics (cell manipulation, cell-lysis and cell sorting) (Andersson and van den Berg 2004). In these applications, the interaction of proteins or cells with surfaces is of essential importance. Surfaces of materials can be neutral, hydrophilic or hydrophobic, depending on energy, charge and potential of the surface (Kirby and Hasselbrink 2004, Tandon *et al* 2008). Adsorption and bio-fouling are undesirable events in many applications, and these effects depend on surface properties such as surface charge and morphology. Surface inertness is essential in some applications *e.g.* biology, chemistry and medicine to avoid chemical reactions that will change the sample properties and consequently affect the results. Therefore, microfluidic devices are often surface-treated. By providing different surface treatments, textured and non-textured surfaces can be tuned from hydrophobic to hydrophilic states. Different functions can be performed such as cell culturing, valving, pumping, cell migration, droplet movement, self-cleaning (Lotus effect) and spatially confined chemical reactions. In this thesis different ways to create hydrophobic polymer coatings for cellomic studies and for creating super hydrophobic surfaces have been studied, which will be described in **Papers II and III**.

Hydraulics is the study of mechanical properties of water or liquids and their application to science and engineering. Hydraulics is used to generate, control and transmit power by the use of pressurized liquid. It mainly deals with the flow, flow control, flow measurement and fluid dynamics. Therefore the components related to fluid, such as pumps or valves are integral parts of hydraulics, and their applications at the microscale are equally important for  $\mu$ TAS.

The size of these components determines their use as integrable devices. Liquid manipulation in small capillaries, sometimes packed with porous material having nanosize pores in *e.g.* high performance liquid chromatography (HPLC) system, demands a valve that can withstand high back pressure. Reduction in size demands an actuator material that creates high force at low volume in valves and pumps (**Papers V and VI**).

Furthermore, microfluidic systems often require sensing of a flow rate, pressure, pH, temperature or viscosity. Sensors are used in microfluidic systems for system control. They are also used for signal read out, like in detection of bio-molecules or cells by a biosensor. Sensing of bio-molecules is gaining a lot of importance in bio-medical applications. For high-resolution detection of bio-molecules, in small sample volumes, biosensors are needed to be integrated in the system. Therefore, assembly becomes important when new devices are evolved, utilizing conventional and unconventional fabrication techniques (**Paper VII**).

The main focus of this thesis is on heterogeneous technologies for microfluidic devices or systems that require different fabrication techniques and materials in order to realize them as complete functional systems. Interesting features for microfluidics such as surface modification and high pressure application have been studied in depth. Different microfluidic platforms have been manufactured and evaluated.

## 2. Technologies for microfluidic platforms

Microsystem technologies based on silicon and glass may be considered as standard technologies. In some cases, other technologies are preferred due to a potential for large-scale production at low cost, or when silicon or glass simply cannot meet specific demands in  $\mu$ TAS. Fluidic circuit board technology, ion track technology, soft lithography, rapid prototyping and stacking technology are technologies studied in this thesis that may give advantages for heterogeneous technologies in  $\mu$ TAS.

### 2.1 Silicon and glass technology (Paper I, II, VII)

Silicon and glass have been dominant materials in microfluidics in cases where there are requirements of chemical resistivity and rigidity in the system. They are also preferred when surface inertness is required, ensuring that the surface itself doesn't interact with the samples or fluid. Silicon and glass have a wide range of uses in chemistry, biology and electronics. However these materials are brittle/stiff and cannot be used in liquid manipulations where high deformations are needed for some designs of valves, pumps and mixers.

Silicon (**Paper VII**) and glass patterning (**Paper I**) is often realized using photolithography and dry or wet etching. The fabrication of these devices requires a clean-room environment and is costly and time consuming.

In bulk micromachining the patterns are defined in the substrate itself. A process flow demonstrated in *Figure 2.1* includes substrate cleaning (step 1) and deposition (step 2) of a mask material, *e.g.* aluminium, on the surface. A photosensitive material is deposited on top of the sample and the desired patterns are transferred into it in a way similar to the technique used in developing old photos (steps 3-7). In turn, the mask material is etched away where exposed (step 8). These patterns are subsequently processed based on the desired application.

After etching openings in the mask material the substrate can be etched by either dry or wet etching (step 9 and 10). Dry etching involves ionized gases. Reactive gases like sulphur hexafluoride, octafluorocyclobutane, and carbon tetrafluoride ( $\text{SF}_6$ ,  $\text{C}_4\text{F}_8$  and  $\text{CF}_4$ ) can be used to etch both silicon and glass. The different parameters of the process, *e.g.*, temperature, pressure, and concentration of different gases, determines the etching rate. In **Paper I**, a borosilicate glass was patterned by bulk micromachining.

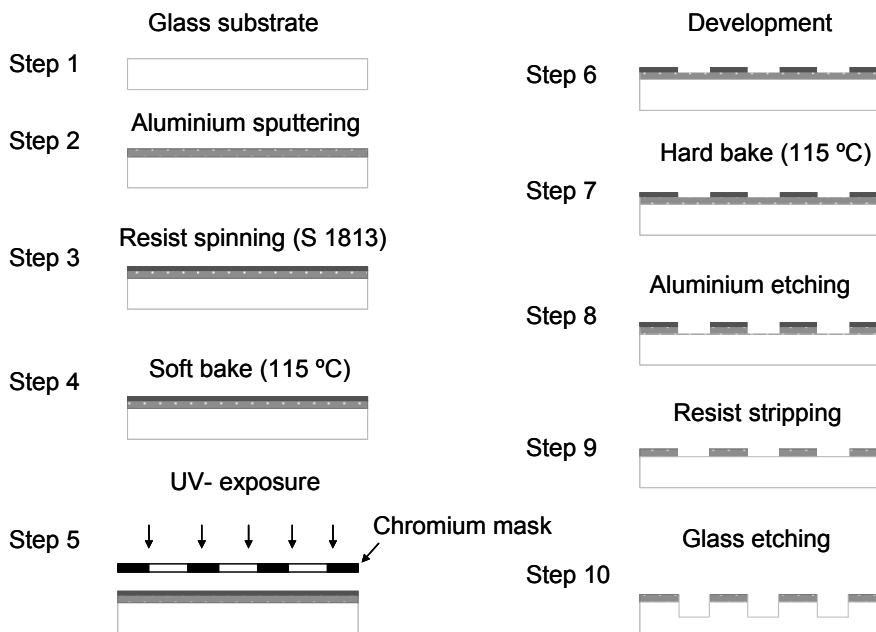


Figure 2.1. Schematic of bulk micromachining of glass showing the different processing steps. Adapted from Paper I.

Wet etching is performed by subsequently keeping the substrate in an etch solution, and can be isotropic or anisotropic. For example, wet etching of silicon in a mixture of hydrofluoric acid, nitric acid and ethanol (Björkman *et al* 1999) and wet etching of glass in hydrofluoric acid are isotropic (Iliescu *et al* 2005). Wet etching of silicon (Kendall 1990, Seidel *et al* 1990) in potassium hydroxide or tetra-methyl ammonium hydroxide is anisotropic. For anisotropic wet etching, the resulting patterns depend on the crystallographic orientation of a single crystalline material. Using anisotropic etching of silicon, thin membranes and suspended structures can be fabricated.

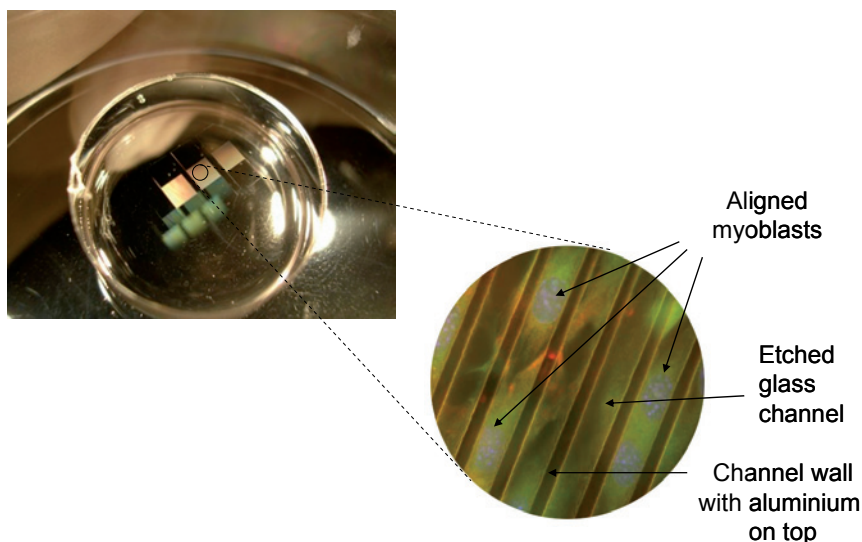
In surface micromachining, thin films (oxides, nitrides and polysilicon) are grown or deposited and patterned by selective etching. Several layers of different materials can be deposited by low-pressure chemical vapor deposition or plasma-enhanced chemical vapor deposition and utilized for devices such as membranes for pressure sensors.

The SOI machining used in **Paper II** utilizes both bulk and surface micromachining, and results in SOI type substrates with a buried oxide layer. SOI membranes are created by dry etching of bulk silicon, followed by etching of silicon oxide with hydrofluoric acid to release the structure. Deep holes and trenches with straight side walls can be made in silicon by deep reactive ion etching.

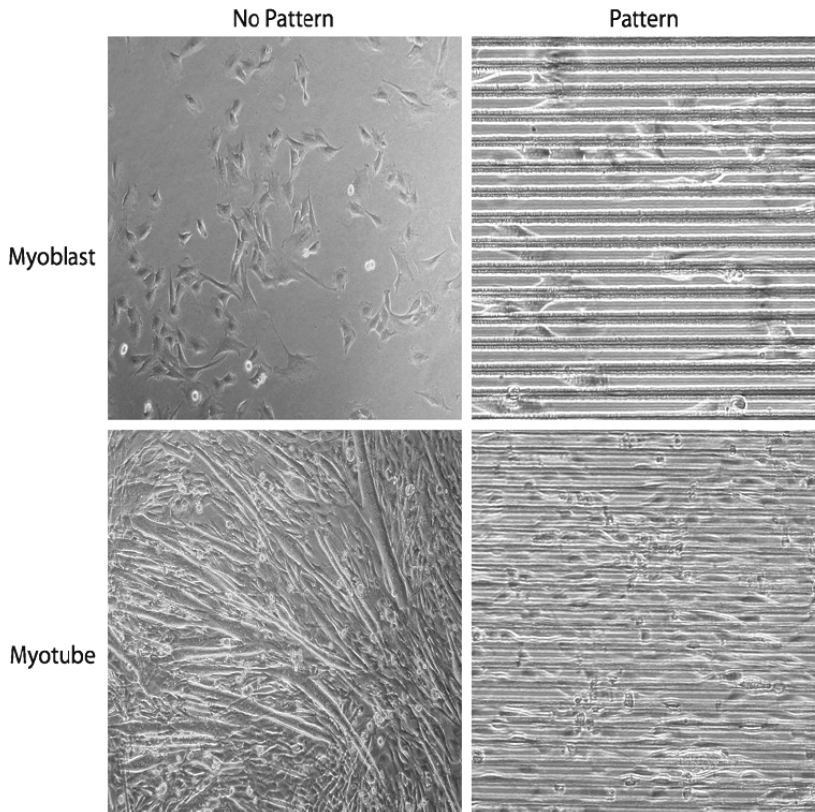
## Paper I

Cell proliferation (development and division) and fusion of myoblasts, which is a building block of skeletal and cardiac muscles, are needed for the generation and repair of multi-nucleated skeletal muscle fibers (myotubes) *in vivo*. Studies of myocyte (muscle cell) differentiation, cell fusion, and muscle repair are limited by an appropriate *in vitro* muscle-cell culture system. In **Paper I** mouse-derived C2C12 myoblasts were used for the study of skeletal muscle fiber development on micro-patterned glass. The result shows that the cultured C2C12 myoblasts proliferate, align, and fuse to neatly arrange in contractile myotubes in parallel arrays much like a muscle tissue.

The aim of this work was to develop a novel cell-culture technique to characterize different development and metabolic aspects of the sub-cellular organization during differentiation. To provide suitable *in vitro* cell-culture scaffolds, borosilicate glass was etched, resulting in a microtrench, using aluminium as a mask material. The width and the depth of the glass channel were approximately 20  $\mu\text{m}$  and 5  $\mu\text{m}$  respectively. The aluminium etch mask was not removed from the wall. Due to this, muscle cells tried to confine themselves inside the channel instead of on the top of the channel wall which is seen in *Figure 2.2*.



*Figure 2.2. Micro-patterned glass with aligned myoblasts (muscle cells). The cells were aligned and arranged within the 20  $\mu\text{m}$  wide channel. Adapted from Paper I.*



*Figure 2.3. Differences in cell alignment on non-patterned (left) and patterned glass (right). On non-patterned surfaces, cells spread in all directions, whereas in patterned surfaces, the cells were aligned like a muscle fiber. Adapted from Paper I.*

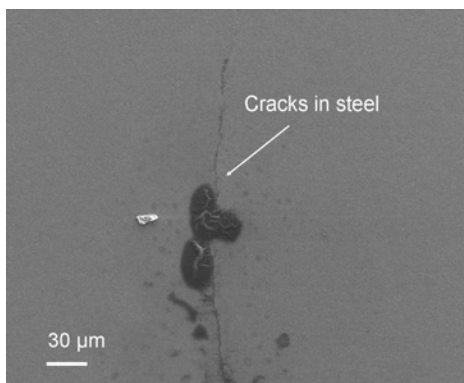
Figure 2.3 shows the difference in cell alignment between non-patterned and patterned glass surfaces. When the surface is not patterned, cells spread freely without proper alignment. With a micro-patterned surface, they are confined and aligned.

## 2.2 Metal fluidic circuit board technology (Paper II, IV - VI)

Microfluidic elements made from stainless steel have been used particularly for harsh environments, *e.g.* high pressures, high temperatures and aggressive chemicals (Agilent's HPLC chip, Janicke *et al* 2000). Stainless steel has a higher thermal conductivity compared to polymers, which is required in certain applications (Jensen 2001, Hessel and Löwe III 2003). Steel has been extensively used as a material for construction due to its stiffness and

strength. Chemical inertness and biocompatibility of steel is also utilised in many interesting applications like chemical reactors and implants.

There are special steel grades that are less susceptible to fatigue and that have been demonstrated as suitable membrane material for cyclic actuation at high pressure for several hours, *e.g.* 301, spring steel. This spring steel was used as a membrane in **Papers V** and **VI** because general stainless steel (X5CrNi1810 steel) cracked due to fatigue, as shown in *Figure 2.4*.



*Figure 2.4. Fatigue cracks in steel membrane due to cyclic actuation in a micro-pump for several hours.*

Computer numerical control machining, laser machining, microelectric discharge machining, and photochemical machining are some of the techniques utilized in patterning metal sheets. Different functional units such as fluidic channels, integrated heaters and sensors can be patterned in each stencil and the units can be stacked together to realize fully integrated 3D devices.

In *Figure 2.5*, an exploded view of a micropump is shown as an example of the stacking technology described in **Paper VI**. The metal sheets (in *Figure 2.5*, numbered as 1-4, 6 and 8) were patterned by utilizing FCB technology. These metal sheets having different functional units and polymer foils (numbered as 5 and 7) can be reversibly or irreversibly bonded by different bonding techniques (Yang *et al* 2002, Bodén *et al* 2008). In **Paper V** and **VI**, the metal stencils and PI foils were coated with parylene by chemical vapor deposition. Parylene C is an inert, bio-compatible thermoplastic often used in microfluidics, electronics and implantable devices (Specialty coating systems product information, Rodger *et al* 2006, Chen *et al* 2007). It also acts as an electrical insulator and is also solvent resistant. Coated stencils can be fusion bonded (Kim and Najafi 2005), resulting in a device consisting of different functional units combined.

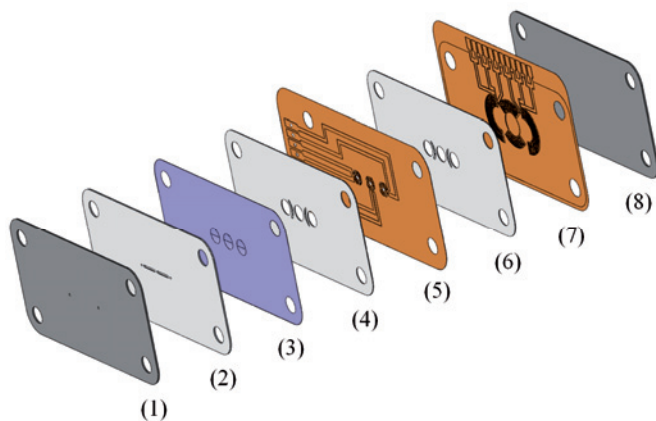


Figure 2.5. Exploded view of a stainless steel membrane pump. The numbers 1-4 and 6, 8 denote stainless steel sheets and 5, 7 denote copper-clad polyimide heaters and temperature sensors. Adapted from Paper VI.

The stainless steel valves and a micropump, which will be described in Section 4, were also made by utilizing stacking technology. In this case, this heterogeneous technology enabled reduced thickness and increased functionality.

In monolithic integration all components of the system are microfabricated by photolithographic technique and they are contained in one single substrate (Burns *et al* 1998, LeMinh *et al* 2003). There also exist examples of polymeric microfluidic systems monolithically integrated with integrated circuitry (Webster *et al* 2001, Chemnitz *et al* 2003). However, the cost for these systems increases with the length of the channel or surface area.

The hybrid approach is mature and has been used by several companies and groups (LioniX, Jösön *et al* 1991, Wagler *et al* 2003, Liu *et al* 2004, Sethu and Mastrangelo 2004).

In **Paper II**, heterogeneous technology was applied to integrate SOI chip into a stainless steel fluidic circuit board with the help of a microreplicated PDMS gasket.

## Paper II

A FCB platform was demonstrated where a silicon-based microfluidic component was integrated using a PDMS gasket. In *Figure 2.6a*, the FCB platform connected to the SOI chip using the PDMS gasket is shown together with an aluminium fixture. *Figure 2.6b* shows PDMS gaskets fabricated using a SU-8 mold. The SOI chip was positioned in a specially designed fixture with the help of a compression plate and four screws. The device was pressure-sealed. The SOI chip shown in *Figure 2.7* was prepared by bulk and surface micromachining techniques. It contains holes (sieves) for the

fluid and cells to move from one compartment to the other so called pressurized cell migration. PDMS gaskets provide leak-tight sealing for aquatic solutions. In this study we showed a migration platform capable of actuation of large pressures.

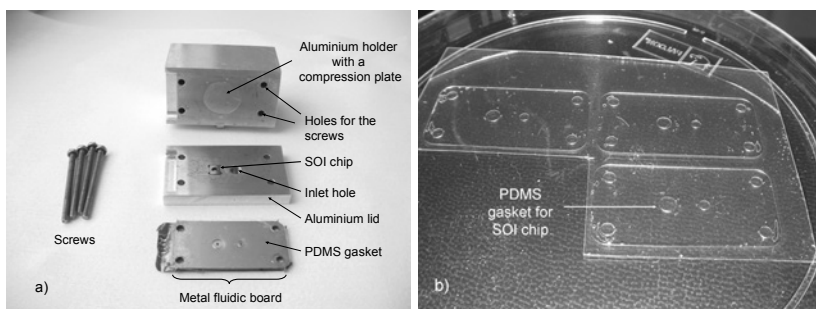
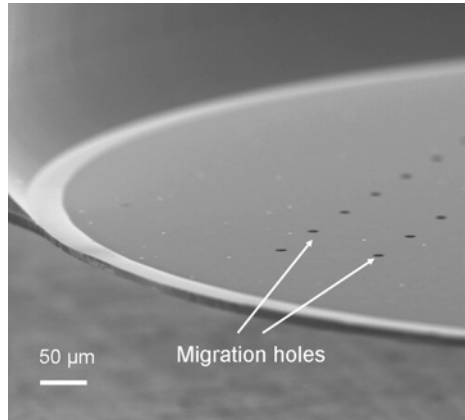


Figure 2.6. a) SOI chip placed in an aluminium fixture together with a PDMS gasket and a steel fluidic board b) Microfabricated PDMS gaskets.

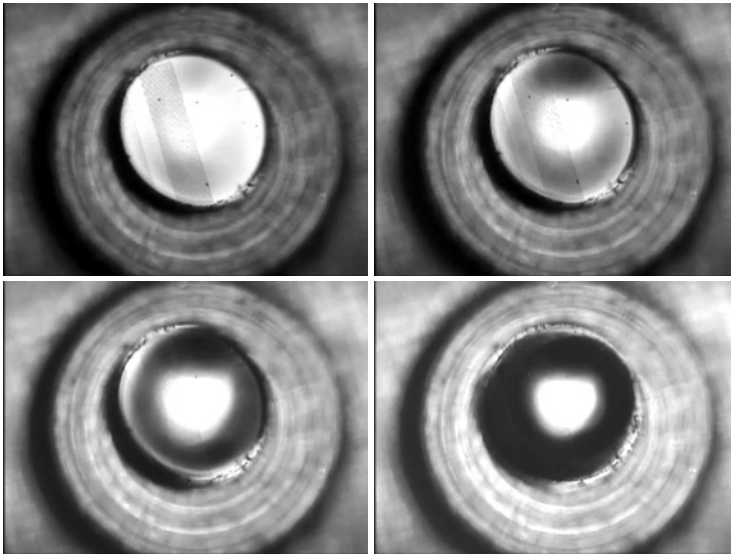
The pressurized cell migration offers potential for high throughput screening (HTS) in various biological processes such as embryogenesis, wound healing, immune response, tissue development (Nie *et al* 2007), and chemotaxis studies (Walker *et al* 2005). Cavities with sieve membranes can be used for cultivation and migration studies for cells and bacteria. While silicon offers the possibility of integration of complex spatial structures and thin film electronics, on a HTS cavity array, a water-repelling surface enables the use of elevated pressure to alter the cells' migration through the membrane (Buchholz *et al* 2008). The chosen plasma coating alters its cell adhesion and changes its biocompatibility (Kolari *et al* 2009). These features add the possibility of attracting the cells to cross the membrane with help of pressure and chemicals (Yassini *et al* 1994). However, there is a concern regarding the overpressure capability of such micromachined platforms with very thin membranes that at the same time have a large surface area. This was studied using the platform by utilizing pressure applied from an external syringe pump.

The measured hydrodynamic pressure needed to allow fluid penetration of the coated SOI membrane was observed to have a negligible dependence on the deposition time of the fluorocarbon ( $C_4F_8$ ) coating. However, the aging of the coating showed a reduced pressure tolerance before leaking. Fresh coatings were able to sustain water in the cavity until 1.2 bar overpressure, while 48 and 72 hours storage reduced this figure to about 0.4 and 0.2 bar, respectively.



*Figure 2.7. Micrograph of SOI chip with migration holes. The SOI chip was manufactured by bulk and surface micromachining.*

In *Figure 2.8* the bulging of a membrane due to applied pressure is shown, which corresponds to pressures 1.2, 1.7, 2.2 and 2.7 bars, respectively.



*Figure 2.8. Bulging of SOI membrane at different applied pressures: 1.2, 1.7, 2.2 and 2.7 bars. This shows the possibility of applying high pressure on one side of the membrane without rupturing the membrane, hence showing possibility of pressure induced cell migration studies.*

## 2.3 Polymers and ion track technology (Paper III - VI)

The use of microfluidics in biology, chemistry and medicine promotes the need for a fabrication technology that is fast, cost efficient and easy to use. These requirements favoured the use of polymers, in particular due to high demand in disposable devices. Commonly used polymers include PDMS (McDonald *et al* 2000, Sia and Whitesides 2003), poly (methyl methacrylate) (PMMA), polycarbonate (PC), polyethylene (PE), polyethylene terephthalate glycol, polyurethane, poly(vinyl chloride), polystyrene and polypropylene (PP) (Ng *et al* 2002, Shadpour *et al* 2006, Tsao and De-Voe 2009). Polymers are often inexpensive materials in comparison to silicon and glass and can be directly patterned by soft lithography, micro-contact printing ( $\mu$ CP) (Figure 2.12), replica molding or embossing. Polymer devices can be sealed thermally or by adhesives. However, most polymers are susceptible to organic solvents and low-molecular-weight solutes. Furthermore, the high-temperature sensibility of most polymers limits their use to applications used in moderate temperature (McDonald *et al* 2000).

PI possesses high-temperature compatibility, and can be patterned by standard processes and equipments that are normally used for silicon and glass when high precision is required. It is possible both to dry and wet etch PI using metal (copper) as a mask material. The Viton actuator in **Paper IV**, valves in **Paper V**, and pumps in **Paper VI**, all use copper-clad PI as a base material for heaters and temperature sensors.

Thin foils of PET can be metalized and patterned using UV lithography (Sharma *et al* 2005). Such foils showed biocompatibility and were used as a platform for single cell single ion irradiation.

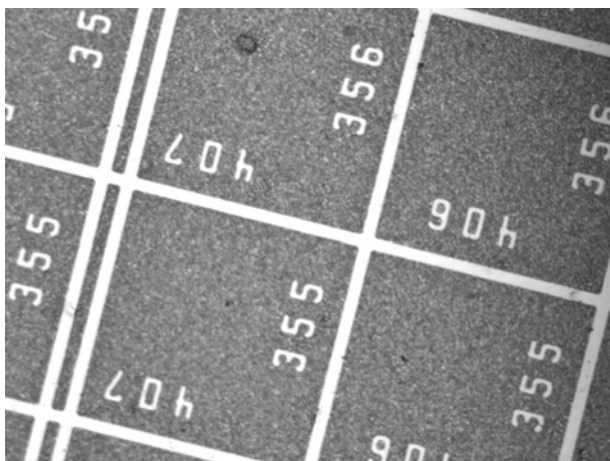


Figure 2.9. Gold grid with x and y coordinates on 6  $\mu$ m PET foil. The patterned foils are bio-compatible and were used for single cell single ion irradiation studies.

Figure 2.9 shows a gold grid with numbers that are 2  $\mu\text{m}$  wide on a PET foil with a thickness of 6  $\mu\text{m}$ . These patterned thin PET foils can also be used in making electronic circuitry. The foils can also be stacked together with metal stencils forming fluidic networks and other components and can in principle be used for microfluidic large-scale integration by further down-sizing the fluidic system.

#### *Ion track technology*

Polymers can also be patterned by ion track technology (Young 1958, Fleischer *et al* 1963, Spohr 1990). This technique uses swift heavy ions (such as Xe, Br, Ar, and I with energies above 10 MeV) impinging on a dielectric solid and leading to linear zones of about 10 nm diameter consisting of polymer fragments, (Figure 2.10). After irradiation, the material is subjected to chemical etching, removing preferentially the latent ion tracks. This method enables high aspect-ratio structures, which is desirable in many applications (Yousef *et al* 2007).

The technology can be used to fabricate channels with a diameter between 10 nm and 100  $\mu\text{m}$ . The latent ion tracks are revealed by a selective etching process, resulting in an array of nearly parallel channels. During etching, the size and shape of the etched ion track is determined. The most important experimental parameter is the track etch ratio, *i.e.* the ratio between the track etch-rate and the bulk etch-rate. The quality of the etch process depends on following parameters (i) the energy deposition density of the ion along its path, (ii) the radiation sensitivity of the material, (iii) the storage conditions of the ion-irradiated material before etching, and (iv) on the etchant.

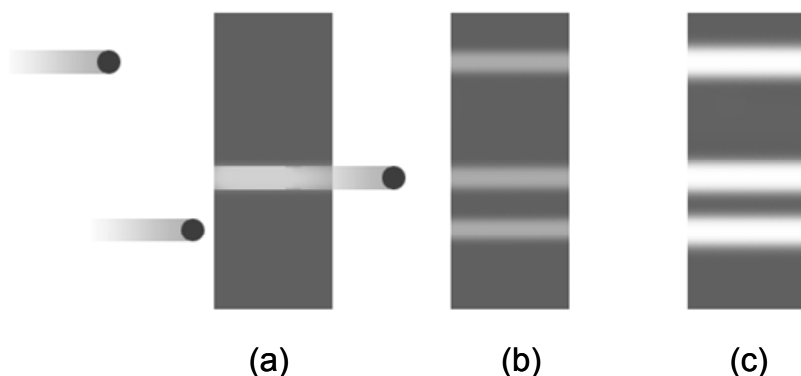


Figure 2.10. Principle of ion track technology. Swift heavy ions penetrate a dielectric solid (a), lead to latent ion tracks (b), and are revealed by selective etching (c). Courtesy: Reimar Spohr ([www.ion-tracks.de](http://www.ion-tracks.de))

Polymers such as PC, PET, PP, polyvinylidene-fluoride and PI are good materials for preparing high aspect-ratio ion track pores in free-standing membranes (<http://www.ion-tracks.de>). PC enables preparation of extremely

fine cylindrical ion track channels due to its extremely high track etch ratio of up to 1000 (Spohr *et al* 2009). Unfortunately, its long term use is limited to temperatures below 100°C. On the other hand, PI, due to its high temperature compatibility up to 300°C, is a good candidate for a microfabrication technology (e.g. bonding and soldering at high temperature). However, the generation of high aspect-ratio pores in PI requires a good control of pH during etching (Trautmann *et al* 1996). Figure 2.11 shows etched ion tracks in PC and PET. The pore size is approximately 60 and 80 nm for PC and PET, respectively.

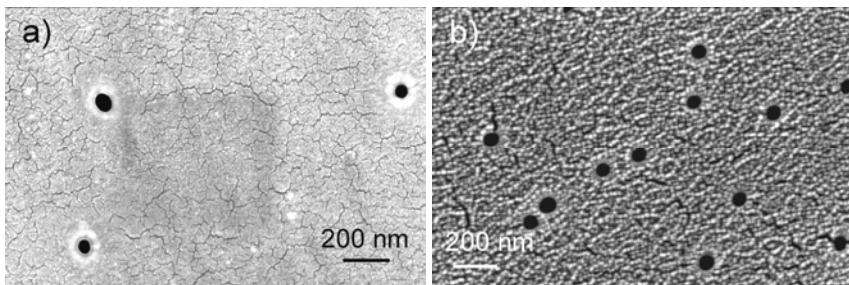


Figure 2.11. Ion track membrane in PC (a) and (b) PET with pore diameter 60 nm and 80 nm, respectively.

Ion track etched membranes may also be used in DNA sequencing (Chansin *et al* 2009) where control over pore size and pore density is important. The combination of a nanopore with single molecule fluorescence detection is also among the candidates for a “third generation” DNA sequencing instrument (Branton *et al* 2008).

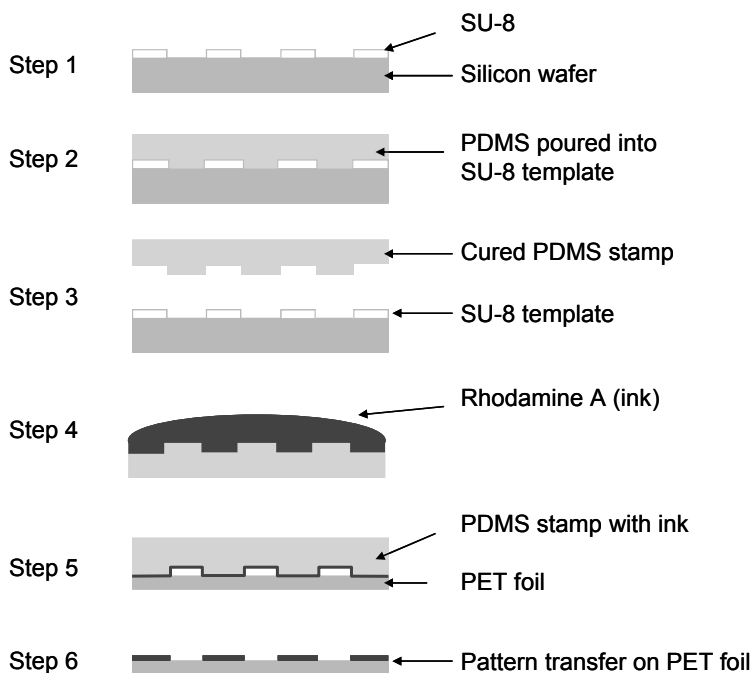
Ion track etched pores can be used in making vias by using screen-printing technology or electroplating technology. Nanowires can be made using ion tracks for sensing applications.

Using patterned foils or metal vias through ion track etched polymers, highly integrated, cost-effective electronic devices could be made. Track-etched membranes can also be integrated in microfluidics for filtration at different locations (Metz *et al* 2004) for 3D integration. Those membranes are also used in several biological applications (Hanot and Ferain 2009).

## 2.4 Elastomers and soft lithography (Paper II, IV, VII)

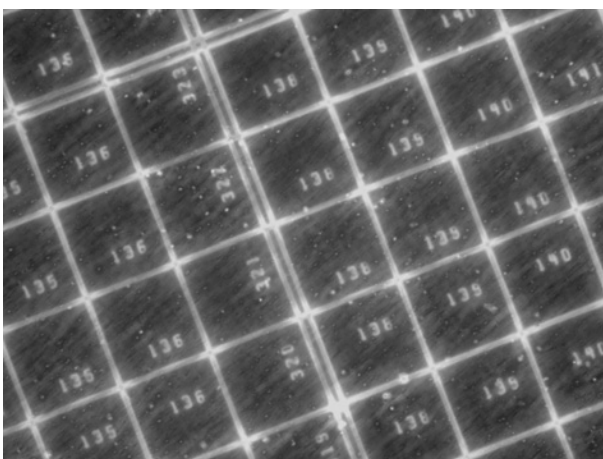
Elastomeric micro-molding was first developed at Bells Labs in 1974. The new concept of fabrication called soft lithography was developed as a tool for surface patterning via stamping, molding or embossing. In soft lithography, a master or a template is fabricated in a hard material such as silicon, SU-8 or metal. Then, a two-component liquid polymer is filled into the master and cured at elevated temperature or at room temperature. An example is the elastomer PDMS.

Soft lithography can also be used to describe  $\mu$ CP, replica molding and micro-transfer molding where molds made in elastomer (PDMS) are used to pattern other surfaces (Madou 2002). A detailed process flow of an imprinting technique is shown in *Figure 2.12*.



*Figure 2.12. Schematic of micro-contact printing as an example of a soft lithographic technique.*

A PDMS stamp was first prepared by molding and then ink was transferred on structured protruding surface. The inked PDMS is then pressed against the substrate to transfer the patterned ink. By using this technique a PET foil was patterned (*Figure 2.13*).



*Figure 2.13. Micro-contact printed PET foil with rhodamine. For biomedical applications where the device needs to be disposable, an imprinting technique will provide low-cost solutions. Adapted from Sharma et al 2005, unpublished.*

Since a decade, PDMS has become the dominant material due to its two major contributions: soft lithography and rapid prototyping. The combination of these technologies makes  $\mu$ TAS demonstrators possible, comprising completely integrated and functionalized systems (Wong and Ho 2009). PDMS is suitable for soft lithography due to its low interfacial energy and it is also considered as bio-compatible. PDMS has several other advantages making it suitable for biological applications, such as: high gas permeability, non-toxicity, and high transparency. However, many polymers including PDMS have disadvantages such as: (i) swelling of the polymer in contact with many solvents, (ii) extraction of impurities and (iii) chemical reactions between the polymer and solvent. It also has a low sealing capability at high-temperature and high-pressure and it is not suitable for hydraulic oils and hydrocarbons. *Table 1* shows a brief comparison between elastomers, neoprene, nitrile, silicone, fluorosilicone and Viton, for its chemical compatibility. It presents Viton as an excellent material of choice for solvent-resistant microfluidics. Compared to other elastomers such as neoprene, nitrile, PDMS and fluorosilicone, Viton has higher chemical resistance and is compatible to hydrocarbons and hydraulic oils. It is a sealing material with a broad chemical resistance and temperature range, and thus minimizes contamination and production problems.

The high permeability of PDMS can be a drawback in some applications. For example, PDMS cannot be used in vacuum systems. Therefore, there is a need for a material with elastomeric properties similar to PDMS, but applicable in vacuum systems and possessing moderate to high solvent resistance for valving and pumping in association with, *e.g.*, paraffin-based actuators.

*Table 1 Chemical resistance of elastomers. Adapted from  
http://www.dupontelastomers.com*

Common name	Neoprene	Nitrile	Silicone	Fluorosilicone	Viton
Alcohols	1	1	2	1, 2	1
Aliphatic hydrocarbons	2	1	4	2	1
Alkalis	1, 2	2	1, 2	2	4
Aromatic hydrocarbons	4	2, 4	4	2, 3	1
Concentrated acids	4	4	4	3	1, 2*
Dilute acids	2, 3	3, 4	4	3	1
Fireproof hydraulic fluids	2	3	3	4	4
Hydraulic oils	2	1	2, 3	1	1
Ketones	3, 4	4	4	4	4
Lubricating and fuel oils	2	1	4	1	1
Water (>80°C)	3	1	1	1	1
Key: 1 = Excellent 2 = Good 3 = Fair 4 = Not recommended					
*Rating is type dependent					

Elastomers such as tetrafluoroethylene propylene copolymers and terpolymer fluoroelastomers (FKM), and perfluorinated elastomers (FFKM) are considered to be highly solvent-resistant. In particular, perfluorinated fluorocarbon, possess excellent solvent resistance due to the strength of the carbon-fluorine bond. (Logothetis A L 1989) For example, castable solvent-resistant photocurable perfluoropolyethers and fluorinated-norbornene (Roland *et al* 2004, van Dam 2006, Huang *et al* 2007) have been demonstrated to form the bulk in microfluidics with solvent resistance capability similar to that of Teflon. However, they are similar to PDMS with regard to their high gas permeability.

FKMs such as Viton are materials suited for systems that are stretchable. FKM is not only solvent-resistant, but it also possesses improved long-term sealing performance at high temperature compared to silicone and its counterparts (nitrile and polyacrylate). Sealing force retention (force under constant stress) and compression set are standard test methods used to predict seal longevity. In *Figure 2.14* the sealing force retention capability of four different elastomers are shown. In this set, Viton is the best material of choice when sealing is required at high temperature for a longer time.

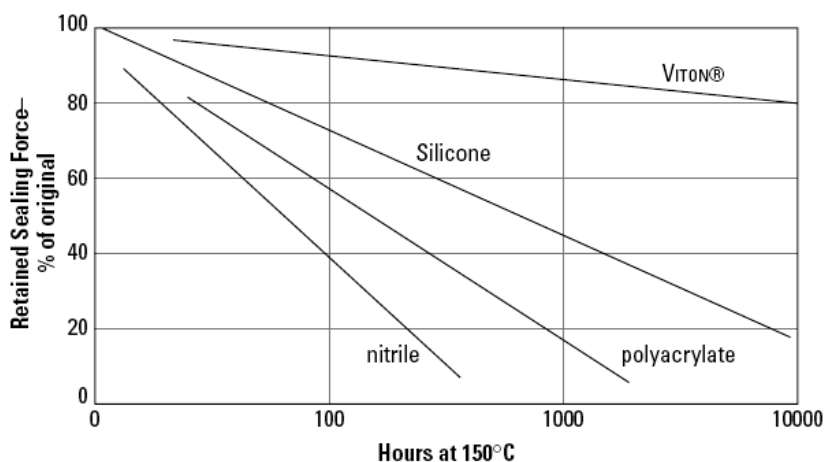


Figure 2.14. Retained sealing force of four elastomers as a function of time. Adapted from <http://www.dupontelastomers.com>

Compression set is defined as the percentage of a measure of deformation remaining after a certain period of time for a given load and temperature, which is an important factor for the capability of an elastomer to seal. Viton has a compression set of 18%, which is lower than that of FFKM. The tensile strength of Viton is 11 MPa (much higher than fluorosilicone and silicone but comparable to FFKM). In this context, Viton is a well-suited material for high-pressure applications. However, Viton is not suited for ketones, carboxylic acids and acetic acid.

On macroscale, Viton is a highly developed polymer with a wide application in cars. Examples are: fuel pump seals, fuel pump couplers, filler neck hoses, fuel tank cap seals, fuel line hoses and tubings, check valves, fuel pressure regulator diaphragms, O-rings and gaskets.

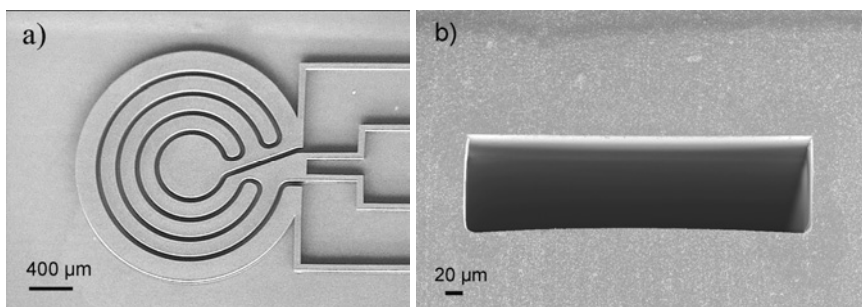
There are different grades of Viton that have been developed with different degrees of solvent resistivity and operation temperatures. Higher fluorine contents improve the solvent resistivity and upper temperature limit.

In **Paper IV** novel Viton-fluoroelastomer-based microfluidics and a Viton-encapsulated paraffin actuator was manufactured by imprinting technique and evaluated.

Still, in many applications PDMS is an excellent elastomer, which survives larger strains than Viton. In cellomics, where aqueous solutions are used, it is most often a better material of choice and is much faster and easier to fabricate. Hence, it is used both as the sealing material in **Paper II** and confining the microfluidic system in **Paper VII**.

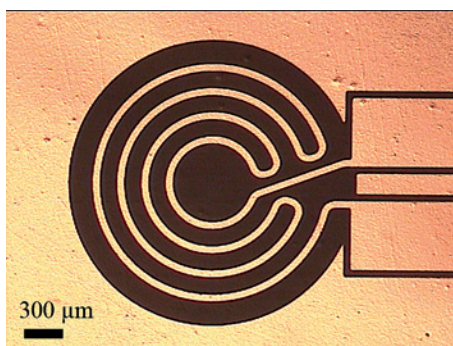
#### Paper IV

A solvent-resistant Viton-fluoroelastomer was imprinted, metalized and bonded to Viton, steel and glass. Its compatibility with hydrocarbons was demonstrated by making a Viton-encapsulated paraffin actuator.



*Figure 2.15. Viton (a) imprinted by using soft lithography (b) partly cured and bonded under applied pressure.*

In *Figure 2.15*, imprinted and bonded Viton is shown. Viton was first imprinted by soft lithography under applied pressure. It was further metalized and patterned by using standard UV lithography that is often used in patterning silicon and glass. A metalized gold pattern on Viton sheet is shown in *Figure 2.16*. Partly cured Viton was also bonded to partly cured Viton, stainless steel and glass, resulting in a fluidic channel with different interfaces. Viton-Viton and Viton-stainless steel gave sufficiently high bond strength (above 0.2-0.3 MPa) suitable for various applications in microfluidics.



*Figure 2.16. Viton metalized and patterned with gold film by using standard UV lithography.*

### 3. Surface Modification (Paper I - III)

In microfluidics, effects such as laminar flow, diffusion, fluidic resistance, surface area to volume ratio and surface tension become dominant (Beebe *et al* 2002). Hence, with decreasing size, surface properties become increasingly important (Huang *et al* 2006). Silicon is hydrophobic while oxidized silicon and quartz are hydrophilic. Many polymer surfaces such as PP, PE, polysulphone, or PDMS are hydrophobic. Most polymer surfaces can be rendered hydrophilic by oxygen plasma treatment. Such surfaces temporarily remain hydrophilic and can be further modified by other methods to obtain desired surface properties.

In **Paper I**, Section 2.1, Aluminium layer deposited on top of micro-machined glass channel wall restricts the cell growth, confining the cell to grow along the channel and not on the surface.

Wettability is an important parameter in surface technology. Therefore, control of this property is necessary in various applications. Paint technology, glass engineering, corrosion protection, separation processes, and self-cleaning panels are few examples at macroscale. Micro- and nanoscale applications include examples such as frictionless motion of droplets in microfluidics, tuning of biocompatibility, and protection against protein and cell adsorption. (Vourdas N *et al* 2007, Forbes 2008) Often, hydrophilic surfaces enable liquid pumping by capillary action (Kolari *et al* 2005). Wetting or water repellency (hydrophilicity or hydrophobicity) is governed by both surface chemistry and surface topography (d'Agostino *et al* 2005).

In **Paper II**, a surface modification technique was used to create a Teflon-like hydrophobic coating by carbondifluoride radicals ( $\text{CF}_2$ ), resulting from the decay of octafluorocyclobutane,  $\text{C}_4\text{F}_8$ , in an inductively coupled plasma reactor. The hydrophobic surfaces obtained by fluorocarbon polymer coating on silicon can be tuned and be made hydrophilic at desired locations by  $\text{O}_2$  plasma (Kolari and Hokkanen 2006). Since the fluorocarbon coating is possible in the plasma reactor, which is used in the process of etching silicon and glass, different surfaces (silicon, glass and PC) can be tuned in a simple way.

In **Paper III**, the same coating technique in combination with ion track technology was used and a unique technique of achieving super-hydrophobic (SH) surfaces was demonstrated. A water-repellent surface was studied that consisted of a large number of pin-like features protruding from the surface. Modification of surface property can be expressed in terms of change in

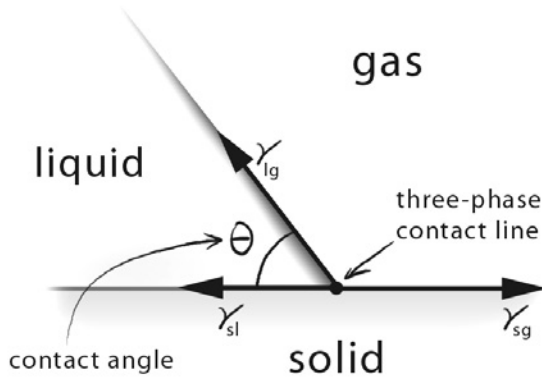
contact angle (where the droplet's surface meets the material). The contact angle ( $\theta$ ) of a water droplet on an arbitrary flat surface is shown in *Figure 3.1*.

The three basic models, namely the Young, the Wenzel and the Cassie-Baxter models, describe three possible equilibrium states of a droplet sitting on a surface, and give design guidelines to fabricate hydrophilic ( $\theta < 30^\circ$ ), hydrophobic ( $\theta > 90^\circ$ ) and SH surfaces ( $\theta > 150^\circ$ ).

For a flat surface, Young's equation (Young 1805) is valid and is described by

$$\cos \theta = \frac{\gamma_{sl} - \gamma_{sg}}{\gamma_{lg}} \quad (1)$$

where  $\theta$  is a contact angle (CA)  $\gamma_{sg}$ ,  $\gamma_{sl}$  and  $\gamma_{lg}$  are interfacial free energies of solid-gas, solid-liquid and liquid-gas.



*Figure 3.1. Contact angle described by Young. (Courtesy: Pontus Forsberg 2010)*

For non-flat surfaces, Young's equation is modified and is called as Wenzel (Wenzel R N 1936) equation, which is described by

$$\cos \theta_w = r \cos \theta \quad (2)$$

where  $\theta_w$  is the contact angle of a rough surface and  $r$  is a roughness factor, defined as the ratio of the actual area of a rough surface to the geometrical projected area, as shown in *Figure 3.2a*.

In equation 2, when  $r$  is larger than unity, the intensity of hydrophobicity increases. According to Johnson and Dettre (1963), above a certain critical value  $r (r_c)$  CA continues to increase with a decrease in hysteresis, (fluctuations of the contact angle) which leads to a slippery surface. Air can remain

trapped below the drop, which leads to a super-hydrophobic behaviour, because the drop sits partially on air. The droplet doesn't stick to the surface but instead rolls like a water droplet sitting on a lotus leaf.

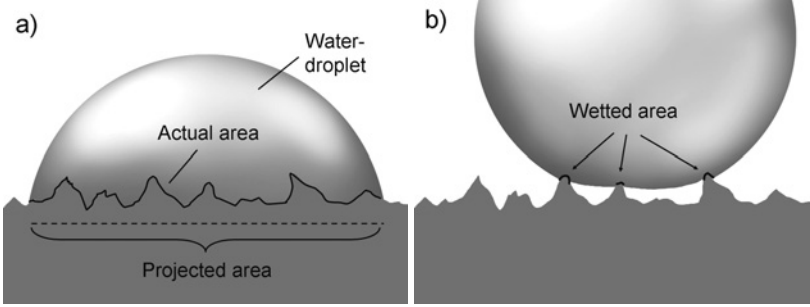


Figure 3.2. Droplet sitting on a rough surface in the Wenzel state (a) and in the Cassie-Baxter state (b). (Courtesy to Pontus Forsberg)

The droplet in this state is called Cassie-Baxter state and is shown in Figure 3.2b which is further described by the Cassie-Baxter equation (Cassie and Baxter 1944):

$$\cos \theta_{CB} = r_f f \cos \theta + f - 1 \quad (3)$$

where  $r_f$  is the roughness factor of the wetted area and  $f$  is the fraction of the projected area of the solid surface that is wetted

Therefore, according to the Wenzel and Cassie-Baxter, the hydrophobicity can be increased by nano-structuring of the hydrophobic surfaces. To create SH surfaces, surfaces with high aspect-ratio topography need to be coated with low surface energy coatings, *e.g.* Teflon.

Plasma processes have attracted the attention in being a means of fabricating SH surfaces, and examples include: 1) plasma polymerization and plasma etching of polytetrafluoroethylene (Morra *et al* 1989), 2) plasma etching of glass surface followed by a F-silane deposition (Ogawa *et al* 1993), 3) plasma etching of PP (Youngblood and McCarthy 1999), 4) silicon pillars from lithography (Callies *et al* 2005) or without lithography (Lejeune *et al* 2006) followed by plasma etching, 5) plasma-enhanced deposition of nano-structured, ribbon-like Teflon-like coatings (Favia *et al* 2003), 6) plasma etching and plasma deposition on PET (Teshima *et al* 2003) and 7) PMMA etching with an ion beam and subsequent deposition of fluoroalkyl silanes via thermal evaporation (Kaless *et al* 2005).

### Paper III

A stroke asymmetry of contact angles for water drops was demonstrated. Textured nanostructures (ion track etched) combined with surface treatment lead to hydrophobic or super-hydrophobic surfaces (SH).

Polymer foils can be irradiated at different angles based on the application and requirements. In order to get oblique structures like animal fur, each individual ion track is tilted by an arbitrary angle with respect to the surface plane.

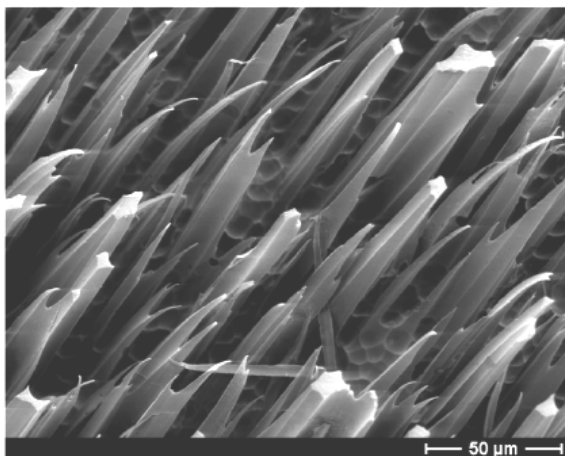


Figure 3.3. Ion track texture in polycarbonate. Adapted from Paper III.

Comparable to animal fur, a direction of reduced friction exists (from bottom left to top right in Figure 3.3). We defined this as the “stroke direction”.

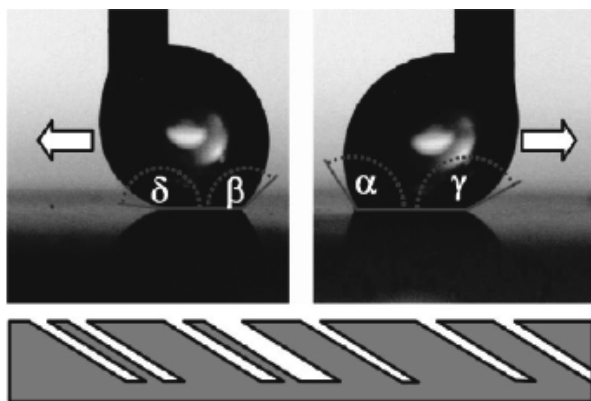


Figure 3.4. Stroke asymmetry of water droplet on top of tilted textures. Adapted from Paper III.

In *Figure 3.4*, a stroke asymmetry of moving water droplets suspended on the tip of a syringe needle is demonstrated. White arrows indicate the direction of the pulling force applied to the drop via a syringe needle. The movement is in the stroke direction (left) and against the stroke direction (right). The bottom of the *Figure 3.4* shows a schematic view of the tilted texture. The low-friction direction of stroke (*i.e.*, the stroke direction) is here from right to left.

To fabricate the textures in **Paper III**, we irradiated polycarbonate with bromine (having a range of about 20  $\mu\text{m}$  in polycarbonate) at a tilt angle of  $30^\circ$  with respect to the sample surface and etched the latent ion tracks selectively.

In rough agreement with Cassie-Baxter theory, the cosines of the four contact angles depend linearly on the wetted area fraction. The etched inclined tracks are randomly distributed on the surface of polycarbonate disks, where the aspect-ratio of individual etched cones is higher than 10. The morphology of the resulting surface is characterized by randomly shaped flat tops overhanging on one side and gradually falling off on the other side. The area fraction of the supporting tops can be calculated from the number of impinging ions per unit area and the cross section of the etched ion tracks. The top layer of the texture consists of flat, horizontal and irregularly shaped tops supporting water drops in the Cassie-Baxter state (*Figure 3.2b*). With increasing etching time, the texture becomes increasingly clefted. The textured surface was made hydrophobic by  $\text{C}_4\text{F}_8$  coating, in a plasma reactor.

Special features like directional wetting can also be achieved by micro-structured surfaces (Jokinen *et al* 2009).

## 4. Microfluidic components (Paper IV - VII)

To perform fluid manipulation in microfluidic system actuators, valves and pumps are required, either at high or low pressure. Also, different kinds of chemical reactors, sensors and analytical systems are needed for performing a  $\mu$ TAS. The thesis studies the challenges in downsizing these components and integrating them heterogeneously, to enable highly integrated systems with different functions and functionalities paving a way towards  $\mu$ TAS. Especially, it is a contribution to an increase in the high pressure capability of such systems.

### 4.1 Actuators

Actuators are either the motors or, more often, the muscles of a microsystem, and in microfluidics they are used for fluid or particle manipulation. There are several different materials and principles used for actuation (Bell *et al* 2005). Piezoelectric materials can exert high forces with short response times but their strain is less than 0.1%. Phase change materials like shape memory alloys (SMA) on the other hand, possess high strain of 6-8% (for TiNi alloys) but they often suffer from large thermal hysteresis and are also difficult to use in planar technology. Solid-to-liquid phase change materials (PCMs), like paraffin, are sometimes the best suited materials in miniature actuators due to their high force capability and conformability. Paraffin can generate 10% volume expansion in its solid-to-liquid transition and its response time is often in the range of seconds, similar to SMA. The response time varies with the design in both SMA and in paraffin-based actuators. Paraffin has low thermal conductivity as well as a high (specific) heat capacity which makes it slow to respond to thermal changes. Still, by having a proper cooling, the response time can be reduced to less than a second. Paraffin actuators have been applied to microsystems for various purposes (Carlen *et al* 1999, Klintberg *et al* 2002, Klintberg *et al* 2003).

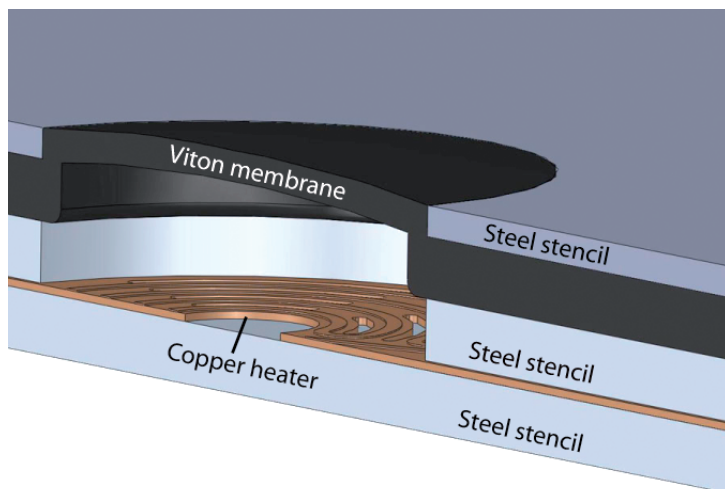
According to De Volder and Reynaerts (2010), pneumatic and hydraulic actuators can be divided into three different kinds: elastic fluidic actuators, piston-cylinder actuators, and drag-based fluidic actuators. Elastic fluidic actuators are more common in microsystems whereas piston-cylinder actuators are common as large-scale actuators due to high actuation force. These two kinds of actuators utilize a direct action of a pressure difference. On the

other hand, drag-based fluidic actuators utilize the viscous (drag) force exerted by liquid or gas flow and are less popular due to their low actuation force compared to the other two actuators.

Elastic fluidic actuators are of great interest due to their straight-forward fabrication technology. They generally consist of membranes or another elastic component that expands under an applied pressure. This expansion or deflection can be used to grasp objects or as an active element in microvalves and micropumps for fluid manipulation. With no sliding parts, this kind of actuators doesn't contribute to friction wear and sealing issues.

Elastic actuators can be of different types such as membrane, balloon, bellows, and artificial muscles. Membrane actuators consist of a flat or corrugated membrane that can be deflected by a driving pressure. Due to their planarity, fabrication is easy and it is possible to make large-scale integration. In a membrane-based micropump the stroke volume and the frequency of operation determine the amount of liquid transported by the pump. The main limitation of membrane actuators is their stroke volume, *i.e.* its deflection in one stroke, which depends on the Young's modulus, Poisson's ratio, thickness, and diameter of the membrane.

In **Paper IV**, a paraffin-based actuator was manufactured and evaluated with Viton elastomer acting as a membrane. In **Paper V** and **Paper VI**, paraffin-based actuators have been used with stainless steel as membrane material.



*Figure 4.1. Viton membrane actuator manufactured by stacking technology. The Viton membrane was pressed by using a PDMS pillar in order to create a cavity approximately 500  $\mu\text{m}$  deep.*

Viton is a good membrane material for paraffin-based actuators due to its compatibility with hydrocarbons. A Viton membrane actuator was fabricated by utilizing a principle of stacking technology (see Section 2.2) and the cross-section of such actuator is shown in *Figure 4.1*.

The Viton actuator was manufactured by imprinting technique where a PDMS stamp was used to create a cavity for paraffin encapsulation. The depth of the cavity was about 500  $\mu\text{m}$ . The two stainless steel sheets were bonded by placing an uncured Viton membrane in-between. The paraffin filled cavity was closed by a backing stencil with a copper-clad PI heater glued on top. The actuator was evaluated by measuring the deflection of the Viton membrane during heating and cooling.

The most important characteristics of an actuator are its load-bearing capacity and its response time. Therefore, the load-bearing capacity of the Viton actuator was evaluated, and the deflection was found to be around 115  $\mu\text{m}$  at unloaded condition. As the load increases, deflection decreases. The Viton actuator has a response time of 2-3 s. It was concluded that Viton is better used to carry homogenous pressures rather than point loads.

This kind of actuator may find application in fluid handling of gases and oils in chemical reactors and analytical systems.

## 4.2 Valves

Valves are one of the essential components of micropumps, micromixers, microdispensers and can be either active or passive. Passive valves do not require energy to change their state, whereas active valves need energy. They can be designed to be normally open or normally closed, based on the demands in different occasions. In some applications there is a need of fluid manipulation at high pressures *e.g.* pneumatics and hydraulics, cryo-coolers, certain types of microreactors and HPLC systems. It is challenging to make leakage-free microvalves for high-pressure applications.

Paraffin-based thermohydraulic (TH) actuators are good candidates for membrane valves. When melted, it will be easier for the membrane to conform to the valve seat, and thus make a leak-tight seal. Furthermore, liquid paraffin has a very low compressibility, enabling it to carry large loads with only small deformations. Therefore, sealing is easily accomplished at high pressure compared to solid material that doesn't conform to the counter surface such as SMA and piezoceramics, or pneumatic actuators that yield when the load is higher than the actuation pressure.

In **Paper V**, a stainless steel microvalve for high-pressure applications is presented.

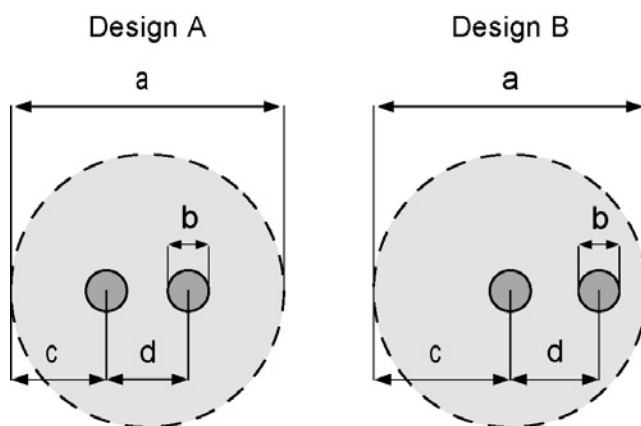
## Paper V

To meet the need of high pressure valving in microfluidics, stainless steel microvalves were designed, fabricated and evaluated. The influence of clamping, and the orifice placement and size were studied explicitly.

The valve was evaluated for high-pressure applications with two different designs, symmetrical design (A) and asymmetrical design (B) (*Figure 4.2*). The symmetrical and asymmetrical designs vary in the positioning of their inlet and outlet orifices relative to its center. These valves provide mechanical stability and ease in fabrication at low cost. The leakage rate was less than 0.05 nL/min.

The valve with asymmetrical design was able to withstand back pressures of 200 bar both for water and air. The maximum power needed to seal when pressurized with water was 0.5 W and 0.4 W for symmetrical and asymmetrical design, respectively. The valve has a response time of less than 0.6 s.

An interesting behaviour was found for the asymmetrical design at small orifice diameters: after reaching a pressure of 200 bar for water, the valve did not open as the power was turned off. Instead, it continued to seal until the pressure was released from the other parts. This behavior was observed already at pressures slightly above 15 bar. Below this pressure it acted like a normal valve. We believe that this interesting phenomenon that we termed “self-sealing” can be utilized in making safety valves for exothermal reactions.



*Figure 4.2. Orifice designs: symmetric (left) and asymmetric (right). Adapted from Paper V.*

Paraffin-actuated valves can seal from 1 to 200 bar, and since stainless steel is used as a membrane material, this kind of valve can be used for fluid sampling at high pressures, chemical reactors and HPLC.

## 4.3 Pump

Pumping schemes incorporate many different physical principles (Laser and Santiago 2004, Woias 2005, Zhang *et al* 2007, Iverson and Garimella 2008, Nisar *et al* 2008), and they can be mechanical and non-mechanical based on their construction (Laser and Santiago 2004). Pumps are often characterized by flow rate, stability, efficiency, power consumption, and the ability to pump against a back pressure. The majority of the micropumps referred to above operate at low pressures (up to 1 bar), and very few up to 10 bar.

Large-scale integration of microfluidics demands pumps that are integrable and small in size. Decrease in the channel size, increases the fluidic resistance and the demand for liquid manipulation at high pressure increases consequently. Pumps that can manipulate fluid against high pressure are needed for HPLC (Reichmuth *et al* 2005). For microscale applications, based on actuation principles, pumps are categorized as electromagnetic (EM), piezoelectric (PE), electrohydrodynamic (ED), pneumatic (P), thermopneumatic (TP), electroosmotic (EO) and thermohydraulic (TH). A comparison of different mechanical and non-mechanical micropumps in terms of their pressure and flow rate is shown in Figure 4.3.

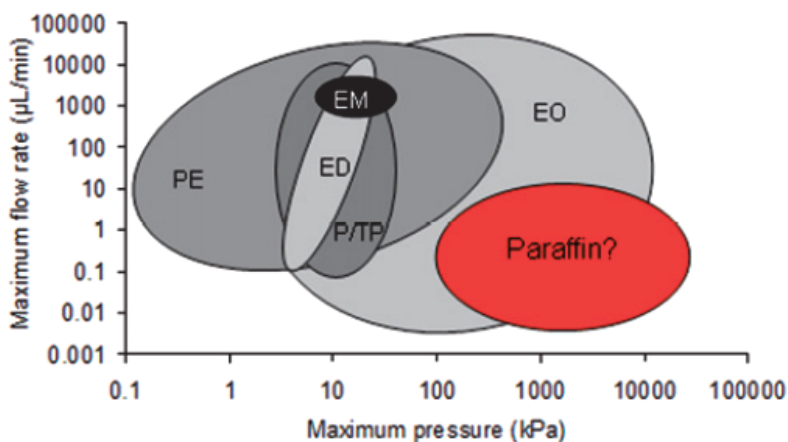


Figure 4.3. Characterization of various micropumps by their maximum flow rate and pressure. EO pumps are popular for the application where high flow rate and high pressure is needed. Adapted from Roger Boden's PhD thesis.

For high-pressure applications (in the order of megapascals), EO micro-pumps provide higher flow rates compared to paraffin-actuated pumps (Chen *et al* 2008). However, the application of the EO actuation principle is based

on the nature of the pumped liquid (polar or polarisable), and may not be applicable to many liquids. The EO actuation principle also requires high voltage (in kV range) and stable zeta-potentials. Unlike EO pumps, paraffin-based micropumps can operate at lower voltages (a few volts), and can be used with any kind of liquid. Depending on the application, the low flow rate capability is a problem or a feature, giving paraffin-based micropumps a niche in high-pressure applications that demands low flow rates.

This stainless steel micropump was a substantial improvement compared to the previously described micropump by Bodén *et al* (2008). It provides positive flow rates at much higher pressures, but most importantly with a long-term stability in pumping. It was also possible to monitor the temperature of the paraffin wax during melting and solidification by an integrated temperature sensor, which offers a more efficient way to operate the pump.

**Paper VI** describes design, manufacturing and evaluation of a peristaltic micropump with integrated paraffin-based actuators and temperature sensors for high-pressure applications.

## **Paper VI**

A high-pressure peristaltic membrane micropump was designed and evaluated, capable of pumping liquid at a constant flow rate of 0.4  $\mu\text{l}/\text{min}$  against a back pressure up to 130 bar. A peristaltic pump is a displacement pump where liquid is pumped out by sequential movement of the membranes, bending upward and downward, upon melting and solidification of the paraffin, respectively. An exploded view of such a pump is shown in *Figure 2.5*. The main focus was to maintain the flow characteristics also at high back pressures. The micropump was able to pump liquid with a positive flow rate up to 150 bar.

The pump was manufactured by fusion bonding of parylene-coated stainless steel stencils, copper-clad polyimide heaters and temperature sensors, and stainless steel membranes, as described in Section 2.2. The large volume expansion due to solid-to-liquid phase transition in paraffin was used to move 10  $\mu\text{m}$  thick stainless steel membranes.

The pump was evaluated by using two different driving schemes, a 6-phase and a 4-phase cycle, which is shown in *Figure 4.4*. The 4-phase cycle had lower power consumption since its active duty for all three valves was only 50% where in 6-phase the active duty was 67%.

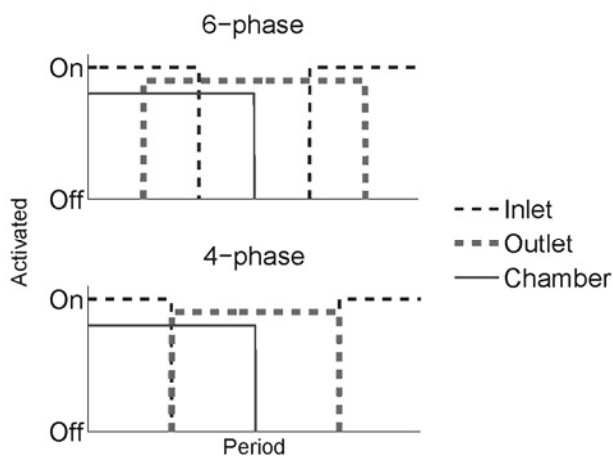


Figure 4.4. A 6-phase and a 4-phase cycle. These two cycles were used for evaluating the pump. The 4-phase cycle is more energy efficient compare to 6-phase cycle. Adapted from Paper VI.

Figure 4.5 shows the flow rate at different frequencies where the flow rate increased with increased frequency.

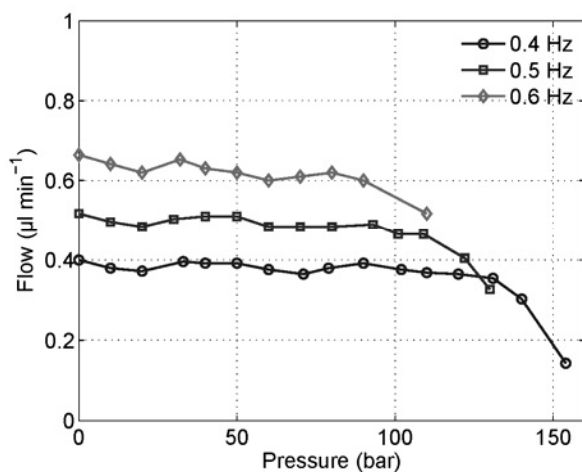


Figure 4.5. Flow rates at three frequencies using 6-phase cycle. Adapted from Paper VI.

Since the pump was thermally activated, a temperature sensor was integrated to control the melting and solidification of paraffin. This pump had a total thickness of about 1 mm. The pressure range covered by this micro-pump was within the range needed for, e.g., HPLC systems.

## 4.4 Sensors

Microfluidics often requires sensing and measuring capabilities in micro-scale range. For example, in a micropump, we often need to know the output of the device, such as flow rate by using a flow sensor. The measurement of pressure build up inside the channel is also important, and can be measured by a pressure sensor. In **Paper VI**, the temperature inside the pump is measured by a resistive temperature sensor.

Biosensors are one of the most important types of sensors for applications where precise and selective detection of target molecules are required. Reduction in device size means a reduction in the amount of reagents and samples volume. This means that there will be small amounts of material to detect and consequently, a sensor that has a high sensitivity is needed.

Piezoacoustic devices are known for their excellent frequency stability, and have therefore been used in quartz crystal resonators as a tool for high-precision determination of frequency and time in clocks or electrical transmitters. Their use has also been extended to mass sensing applications (Sauerbrey 1959).

Based on the transduction principle, sensors used in bio-chemistry can be of various types such as: 1) thermal sensors: for sensing temperature changes due to biochemical reactions, 2) optical sensors: for sensing changes in optical properties due to a change in biochemical reactions, 3) electrical sensors: for sensing electrical potential or current change due to biochemical reactions.

Similarly, electro-acoustics (QCM, SAW, FBAR and SMR) deals with the transformation of acoustic energy into electric energy or vice versa. Usually, this transformation is conducted within a piezoelectric material. So far, the most common configurations have been bulk acoustic wave (BAW) devices and surface acoustic wave (SAW) devices. These devices are used in almost all time and frequency control applications.

In recent years, thin film bulk acoustic-wave resonators (FBARs) have been used as filters (Ueda *et al* 2008), and as high-sensitivity mass sensors (Zhang and Kim 2005, Gabl *et al* 2003, Gabl *et al* 2004) and are considered to be promising candidates for biochemical sensor applications (Link *et al* 2006, Wingqvist *et al* 2007). FBARs are better than quartz-based technology in terms of mass resolution and cost effectiveness. (Resolution is the smallest detectable signal and is often limited by noise and sensitivity. Sensitivity is the sensor output per unit of measurand). The main advantage of using thin-film technology is that the process is IC compatible and has a much higher operational frequency. The higher operational frequency, >1 GHz, offers much higher sensitivity compared to thick QCM sensors (5-10 MHz). Quality factor (Q), is also an important parameter for a resonator. It is defined as the ratio of stored energy to the energy lost by the device. When

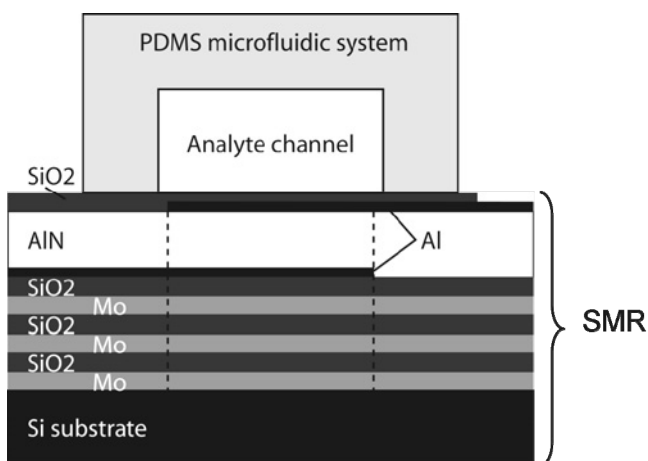
operated in liquid environment, the FBAR resonators reduce their Q-factor compared to their operation in air.

A surface mounted resonator (SMR) is a kind of electro-acoustic device that is more robust in fabrication than FBARs, since it doesn't contain a free-standing membrane. But it still needs acoustic isolation, which is solved by using impedance matching Bragg reflectors (*Figure 4.6*). An electro-acoustic resonator can be excited either in longitudinal mode or in shear mode, based on the application. Shear mode excitation of piezoelectric films exhibit significantly lower energy dissipation in water and therefore has potential as a high-frequency resonators operating in a liquid environment. Hence, it has potential use as highly sensitive biochemical sensors.

**Paper VII** describes a detection principle combining polymer and silicon technology. This can be considered as a hybrid assembly where an elastomer (PDMS) and a silicon sensor chip with SMR configuration was bonded irreversibly.

## Paper VII

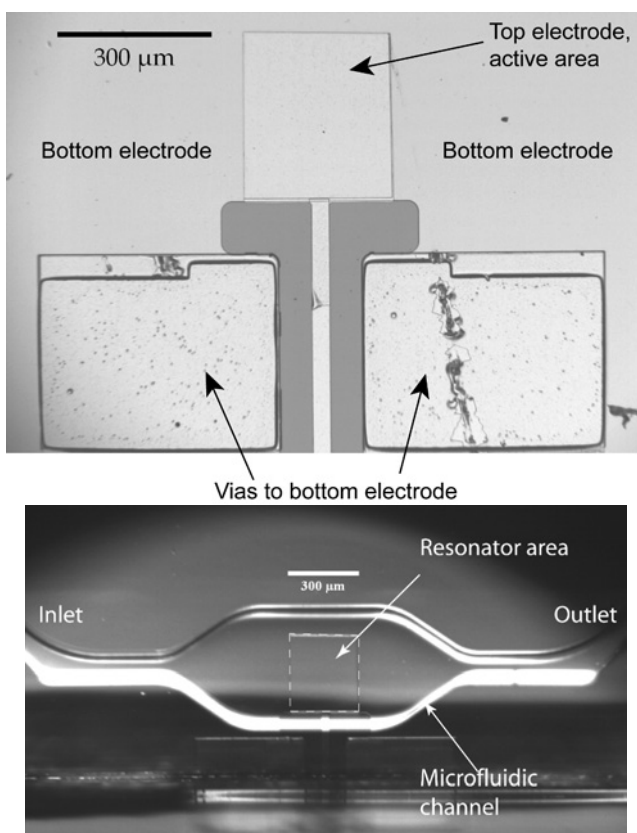
The proof-of-principle of a complete microfluidic sensor system with a shear mode SMR chip was presented. The SMR chip was irreversibly bonded to PDMS microfluidic system by using oxygen plasma treatment and the schematic is shown in *Figure 4.6*.



*Figure 4.6. Schematic of SMR bonded to PDMS microfluidic system. The top layer consists of a  $\text{SiO}_2$  layer which makes irreversible bonding with PDMS after being exposed to  $\text{O}_2$  plasma. Adapted from Paper VII.*

A shear-mode aluminum nitride (AlN) SMR microfluidic sensor system was fabricated and characterized. The AlN SMR fabrication process is fully IC compatible, and uses reactive sputtering to deposit piezoelectric AlN thin films.

The top of the SMR structure (*Figure 4.6*) contained a thin layer of SiO<sub>2</sub>, which after oxygen plasma treatment, was bonded to the PDMS microfluidic system to transport the analyte as well as to confine the flow to the active area of the sensor chip (*Figure 4.7*). The sensor operation in air, water, glycerol and acetone was characterized. The resonator had a resonance frequency of around 1.2 GHz and a Q value in water of around 100. The results indicated a potential of highly sensitive low-cost microfluidic sensor systems for applications in, *e.g.* point-of-care testing.



*Figure 4.7. SMR (top) and SMR bonded to PDMS microfluidic system (bottom). The SMR was manufactured by IC technology and PDMS was manufactured by soft lithography. This is an example of hybrid integration. Adapted from Paper VII.*

## 5. Conclusion

In order to enable complex 3D microfluidic systems, heterogeneous technologies are essential. Combining materials such as silicon, glass, steel, polymer foils, and elastomers means that different material properties can be utilized in terms of solvent compatibility, flexibility, surface inertness and sealability. Fluidic circuit board technology, including stacking technology described in the thesis is one of the techniques that allow heterogeneous systems.

Stainless steel serves well as a bulk and membrane material for high pressure applications. Most importantly, steel can be stacked together to form 3D microfluidics systems. Polymer flexible circuit board foils, such as copper-clad PI, are patternable and can be used as integrated heaters and temperature sensors in heterogeneous microfluidic systems. They can be combined with FCB technology using the same bonding techniques as for stainless steel. Elastomers, such as PDMS, allow low production cost by utilizing a fast, rapid imprinting technique called soft lithography.

Surface modification, either by metalizing a micro-patterned glass surface or by depositing a Teflon-like hydrophobic coating on textured and non-textured surfaces of silicon or PC, has potential applications in cell-culture, pressure-induced cell migration and several other applications related to self-cleaning windows and confined chemical reactions.

The fluoroelastomer Viton that was explored, utilized and tested has a potential for applications that demands sealing against hydrocarbons. Viton-fluoroelastomer has shown many important characteristics, such as compatibility with hydrocarbons, solvent resistivity and sealing capability at high temperature and pressure, which may be needed to solve some of the issues in microfluidic large-scale integration. This material is good for bonding against metal and glass and is also a potential candidate for heterogeneous microfluidics.

Paraffin-based actuators have a potential for use in integrated valves used in high-pressure applications. Stainless steel valves, that can withstand high pressure up to 200 bar without leakage, can be a potential candidate for liquid manipulation in high-pressure applications such as HPLC systems, chemical reactors and nanofluidics. They can be used for both air and water. Similarly, paraffin high pressure peristaltic pumps with integrated temperature control can solve some of the issues related to microfluidic large-scale integration by reducing the total size of actuator and pump systems. Viton-

encapsulated paraffin actuators have potential in making stretchable systems such as artificial muscles.

Hybrid integration allows a PDMS fluidic network to be incorporated with IC technology. A SMR, made by IC technology was successfully combined with a PDMS fluidic network to achieve a highly sensitive detection system for bio-sensing.

I believe that the technologies developed and demonstrated in this thesis have potential applications in many areas of microtechnology, and especially in heterogeneous microfluidic systems.

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