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Processing of inorganic-organic hybrid material for microfluidic applications

Thesis for the degree of Master of Science in Technology.

Espoo, August 7th 2006

Supervisor: Professor Jorma Kivilahti
Instructor: Docent Sami Franssila

Preface

This work was done at the Microelectronics centre of Helsinki university of technology. The Micronova building provided excellent facilities to do the master's thesis.

First, I would like to thank Professor Jorma Kivilahti from laboratory of electronic production technology for supervising this thesis. I would also like to thank the laboratory of electronic production technology for giving me the opportunity to use their facilities for cell adhesion tests. My gratitude also goes to, docent Sami Franssila, for giving me the opportunity to do my master's thesis at Microelectronics centre. I would also like to thank him for his ideas and feedback throughout the work. My thanks also go to all of my co-workers at Microelectronics centre for the pleasant working atmosphere and for all the help they have given me.

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ABSTRACT OF THE MASTER THESIS

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Microsystem technology and as a part of it microfluidic is a fast growing field of technology, which produces e.g microscale analysis devices for analytical chemistry. Traditionally silicon and glass have been used for microfluidic device fabrication, but polymers are gaining ground mainly due to their easy processing.

In this master's thesis a new inorganic-organic hybrid polymer, ORMOCER®, is presented and its properties are evaluated from microfluidic point of view. Commercially available ORMOCER®material called ORMOCOMP®has been used throughout this thesis. Both UV-lithography and UV- embossing were tested to produce structures. The tests showed that ORMOCOMP is extremely UV-sensitive and for this reason fabrication of small, 100 μm structures is difficult. However, smaller structures can be produced by using a filter to reduce the intensity of the maskaligner. If the structure size is under 20 μm, the UV-embossing should be used since in this method the exposure dose is less critical.

The bonding process for enclosed channel fabrication has been developed. This techniques provides an easy and reproducible bonding. Chemical stability and cell adhesion of ORMOCOMP®were also studied. The chemical stability of ORMOCOMP proved to be relatively good, and it showed non-toxity in cell adhesion tests.

Keywords: ORMOCER, microfluidic

TEKNILLINEN KORKEAKOULU DIPLOMITYÖN TIIVISTELMÄ

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Mikrosysteemitekniikan yhtenä osa-alueena mikrofluidistiikka on nopeasti kehittyvä teknologia, joka tuottaa mm. erilaisia mikrokokoluokan analyysilaitteita analyyttisen kemian tarkoituksiin. Perinteisiä materiaaleja mikrofluistiikassa ovat olleet pii ja lasi, mutta erilaiset polymeerimateriaalit ovat valtaamassa alaa lähinnä niiden prosessoinnin helppouden vuoksi.

Tämä diplomityö esittelee uuden epäogaanisen-orgaanisen hybridi polymeerin, ORMOCER®in ja tarkastelee sen ominaisuuksia mikrofluidististen sovellusten kannalta. Kaupallisesti saatavilla olevaa ORMOCER materiaalia, ORMOCOMPia, on käytetty tähän diplomityöhön tehdyissä tutkimuksissa. Sekä UV-litografiaa että UV-embossingia on käytetty rakenteiden valmistamiseen. Tehdyt testit osoittivat että ORMOCOMP on UV herkkä materiaali ja tästä syystä pienten, alle 100 μm rakenteiden valmistus on hankalaa. Pienempien rakenteiden tuottaminen on kuitenkin mahdollista käyttäen suodatinta valotuslaitteen intensiteetin vähentämiseksi. Mikäli halutaan valmistaa alle 20 μm rakenteita, on syytä käyttää UV-embossingia, koska säteilyannos on tassä menetelmässä vähemmän kriittinen.

Kanavien sulkemiseksi on kehitetty bondausmenetelmä, joka tarjoaa helpon ja toistettavan bondauksen. ORMOCOMP®in kemiallista stabiilisuutta ja soluadheesiota siihen on myös tutkittu. ORMOCOMP®osoittautui kemiallisesti kohtalaisen stabiiliksi ja lisäksi se todistettiin myrkyttömäksi soluadheesiotesteissä.

Avainsanat: ORMOCER, mikrofluidistiikka

Contents

Abbreviations

BHF	Buffered hydrofluoric acid
CERAMER	Ceramic polymer
CNP	Combined nanoimprint and photolithography
DLC-PDMS	Diamond-like carbon poly(dimethyl siloxane)
EBL	Electron beam lithography
EUV	Extreme ultraviolet
HF	Hydrofluoric acid
HMDS	Hexamethyldisilazane
IC	Integrated circuit
ICP-RIE	Induced coupled plasma reactive ion etching
NIR	Near infra red
ORMOCER	Organically modified ceramic
ORMOSIL	Organically modified silicate
PAC	Photoactive component
PBS	Phosphate buffered saline
PC	Polycarbonate
PDMS	Poly(dimethyl siloxane)
PMMA	Polymethylmetacrylate
RIE	Reactive ion etching
rpm	Rotations per minute
SFIL	Step and flash imprint lithography
UV	Ultraviolet

Chapter 1

Introduction

Microsystem technology and, as a part of it, microfluidics are rapidly growing and developing fields. This relatively new technology has adapted most of its fabrication techniques from semiconductor technology. Along with these different techniques the most used material in semiconductors, silicon, has long been the core of microsystem technology as well. However, in recent years new materials have gained ground especially in microfluidic applications. One often used material in analytical chemistry equipment is glass and for this reason its use in microanalysis systems has been broadly studied especially for on-chip capillary electrophoresis [1, 2]. Even though glass has some good properties, for example it is chemically stable, the microprocessing of glass is difficult which makes its use somewhat impractical. One of the most attractive material class in today's microfluidic is polymers. Their easy processability and low price make them appealing materials [3]. The use of polymeric material has also led to development of totally new fabrication techniques, which provide both high throughput and resolution patterning. Major drawback of polymers is typically their poor thermal and chemical stability. For example often used polymer, poly(dimethyl siloxane) (PDMS) is not stable in contact with some organic solvents and at high temperatures [4].

In mid 1980's two independent groups reported on the preparation of new sol-gel based materials, inorganic-organic hybrids. Wilkes termed them as CERAMERs (ceramic polymers) [5] and Schmidt named these materials first as ORMOSILs

[6, 7, 8], organically modified silicates, but he later changed the name to ORMOCERs, organically modified ceramics, to emphasize their ceramic properties. In some articles difference between organic-inorganic and inorganic-organic polymers have been made. Inorganic-organic polymers have inorganic elements in their main chain and organic side groups. If their inorganic backbone is formed via traditional sol-gel processing of modified metal alkoxides and that is followed by organic cross-linking the resulting hybrid materials are called ORMOCERs. On the other hand, if the main chain contains carbon atoms and some inorganic side groups, they are called organic-inorganic polymers [9]. However this kind of categorization has not been well established and usually no difference is made between terms inorganic-organic and organic-inorganic polymer.

ORMOCER®s combine properties from several different material classes. Processing of ORMOCER is easy due to its polymeric nature. But at the same time it does not suffer from the same problems as typical polymers because of its inorganic network. ORMOCERs' easily modified properties have made them appealing material in different applications. ORMOCERs have been used as protective coatings, in micro-optic applications and as filling materials in dentistry. Their use in microfluidic applications have not yet been evaluated.

The main part of this thesis deals with the properties of ORMOCER and processing of microfluidic channels from it. Chapter 2 gives the background knowledge about different fabrication processes and chapter 3 concentrates on the material itself. In the experimental part the optimal processing parameters for microfluidic channel fabrication are presented for two different processes; UV-lithography and UV-moulding. In chapter 5 the use of ORMOCER in microfluidic applications is evaluated by testing its chemical stability. Some cell adhesion tests were also made. Finally in chapter 6 the enclosed channel fabrication is described. This bonding technique utilizes the polymerization properties of ORMOCER and leads to tight seal between bonded layers.

Chapter 2

Pattern transfer

There are several ways to transfer patterns onto different substrates. Lithography is a standard process, which utilizes photoresist and -mask. Microlithography is the core technology of semiconductor device fabrication [10].

Over the years the need for smaller linewidth and better resolution has led to use of shorter wavelengths. Different photolithographic systems can be divided according to their wavelengths. These include optical or ultraviolet (UV)-, deep-UV-, extreme-UV (EUV) and X-ray lithographies. Deep-UV uses 248/193/157nm wavelength, where as EUV and X-ray utilize 13nm and 6-40nm, respectively. Even though shorter wavelength leads to better resolution, there are some problems, which have so far prevented more extensive use of especially EUV and X-ray lithography. For instance reflective elements have to be replaced with multi-layer (Bragg) mirrors. Also with every reduction of wavelength the resist and mask materials used have to be redesigned. For these reasons optical lithography is still the most used method in research laboratories as well as in volume production. Optical lithography will be discussed in more detail in the next section.

Alongside with conventional lithography many new fabrication methods, often referred to soft lithography [11], have been developed. These techniques usually utilize some kind of stamp to form structures and they provide cheap and simple fabrication process. Some of these techniques are discussed in forthcoming section.

2.1 UV-lithography

Basic lithographic process contains three sequential steps; photoresist application, optical exposure to print an image of the mask onto the resist and resist development. Photoresist is usually applied by using spinner. Achieved resist thickness depends on spin speed and viscosity of photoresist. Patterns are transferred onto the resist by using mask that contains the desired image. Polarity of the mask depends on the type of the resist used.

Optical lithography can be made in three different modes: contact, proximity, or projection. In a contact mode mask and substrate with photoresist on top of it, are pressed tightly together. The resolution is determined by mask dimensions and diffraction at mask edges [12]. In the proximity mode small gap, usually from 3 to 50 μm, is left between the mask and the substrate. The resolution of proximity lithography is determined by the Fresnel diffraction and approximated by

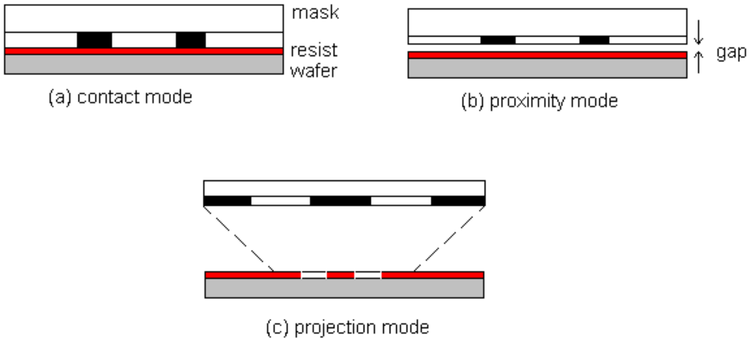
$$2b_{min} = 3\sqrt{\frac{\lambda}{n}\left(g + \frac{d}{2}\right)}, \tag{2.1}$$

where λ is wavelength of exposing radiation, g is gap between mask and photoresist, d is resist thickness and n resist refractive index [12].

Different modes of exposure have been illustrated in Figure 2.1. In a projection mode mask image reduction can be done. The reason for using projection mode is to make mask fabrication process easier and reduce cost along with it. In integrated circuit (IC) industry 4 or 5 times image reduction is used and linewidth below 1 μm can be achieved.

2.1.1 Photoresists

Photoresists usually consist of three different components; base resin, photoactive component (PAC) and solvent. Base resin determines the mechanical and thermal properties and photoactive component or photoinitiator the sensitivity to radiation. Photoinitiator is a molecule (usually organic), which absorbs light and forms reactive initiating species; radicals, H^+, or cation radicals. Photosen-



(a) contact mode (b) proximity mode

(c) projection mode

Figure 2.1: Different modes of UV-lithography.

sitizers are also sometimes used. Photosensitizer is a molecule, which has the ability to absorb energy and transfer it to photoinitiator. Solvents are used to control the viscosity of the photoresists. Viscosity has direct impact on achieved layer thickness. Problems may arise if the viscosity of the photoresist is high because it will flow on an uneven surface resulting non-uniform layer thickness. Resist materials have to fulfil some requirements in order to be useful. For example they have to be chemically and mechanically stable so that they can be used in forthcoming processes. These include etching and ion implantation in which resist acts as a mask material. Resist sensitivity can be altered to different wavelengths. Sensitivity is import for productivity. [12]

Photoresists can be divided into two categories; positive and negative resists. One of the most used positive photoresist is Novalac, which is insoluble in developers prior to exposure. Its photoactive component acts to inhibit the dissolution of the Novalac resin. Upon exposure photoactive component decomposes and releases carboxylic acid, which makes the exposed resist soluble in the developer solution, which are usually dilute alkaline solutions.

On the other hand in negative photoresist, such as SU-8, unexposed areas are removed after exposure. Photoactive component of SU-8 reacts with UV-light and catalyses the cross-linking reaction, which continues in post exposure bake. After the post-bake, uncured areas are removed with suitable solvent. In Figure 2.2 the operation of negative and positive photoresists are illustrated.

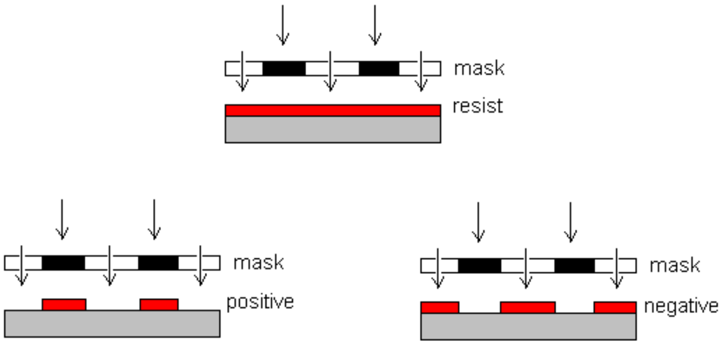


Figure 2.2: Operation of positive and negative photoresists.

2.2 Imprint techniques

Light wavelength reduction has traditionally been the method for achieving better resolution [13], but as mentioned before shorter wavelength brings some additional problems. Different fabrication methods that are based on electron beam can produce high resolution patterns but they suffer from low throughput. Imprint techniques were developed to provide high resolution and throughput patterning. There are many imprint lithography techniques, all having the same basis. The basic idea is to use stamp together with some curing process to pattern the surface.

Imprint lithography techniques can be divided into two categories, UV- and temperature -based methods, depending on the curing process used. In temperature based method, usually referred to hot embossing, used polymer is warmed above its glass transition temperature and the stamp is pressed in contact with polymer film using high force. For commonly used thermoplastic materials like polymethylmetacrylate (PMMA) or polycarbonate (PC) this temperature is in the range of 100-180°C. The embossing force is typically of the order of 20-30 kN [14] and it is held for few minutes. While still applying the force, both the stamp and the substrate are cooled to just below the glass transition temperature of the substrate. After that the stamp is detached from the patterned surface. Hot embossing process and its temperature and pressure cycles are presented in Figure 2.3.

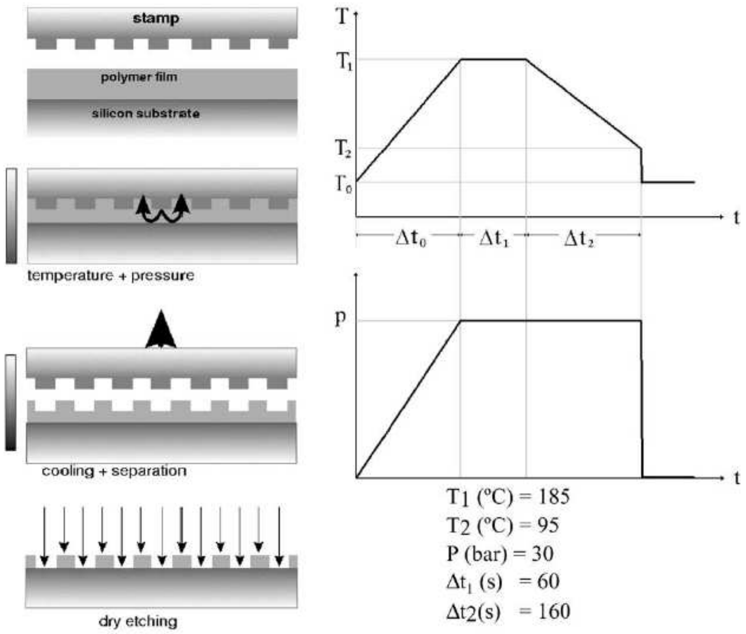


Figure 2.3: Schematic drawing of hot embossing process(left) and temperature and pressure cycles. [15]

Commonly used stamp materials in hot embossing are silicon and nickel. Replication errors may arise due to a mismatch between thermal expansion coefficient of polymer and that of the stamp material. Typical values for the thermal expansion coefficient of polymers are of the order of $7x10^{-5}/K$, while for silicon it is $2.6x10^{-6}/K$ and for nickel $1x10^{-5}/K$. For this reason the thermal cycle of the process should be as small as possible. Schematic drawing of the hot embossing equipment is presented in Figure 2.4.

In UV-based techniques, UV light is used to cure polymer film. In this method neither high pressure nor high temperature is needed. In UV - embossing [16] either transparent stamp or substrate is needed in order to perform photopolymerization. In case of a non-transparent stamp, backside illumination has to be used. In this section principles of UV-based techniques are examined. Also since feature sizes are highly dependent on stamp used, their fabrication is discussed in detail.

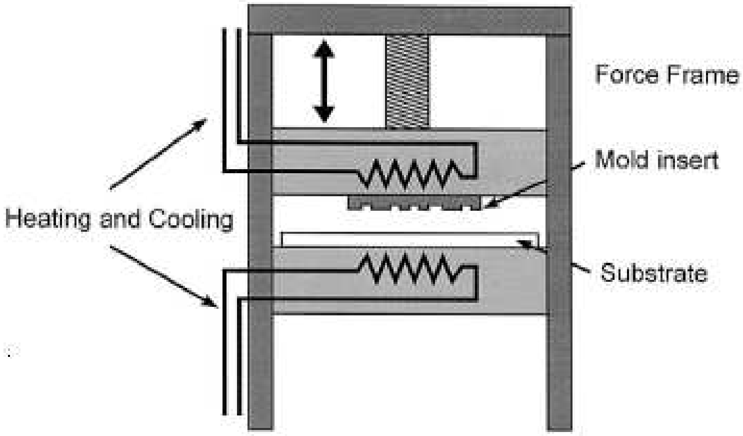


Figure 2.4: Schematic drawing of the hot embossing equipment. [14]

2.2.1 Elastomeric stamp fabrication

Stamps can be either elastomeric or some harder material for example silicon or quartz. Elastomeric stamps are widely used due to their good properties compared with common, hard, stamps. Due to their elasticity they, for example, conform to different substrates.

The most commonly used material in elastomeric stamps is poly(dimetyl siloxane) (PDMS) [17]. PDMS has several properties which make it a good material for high-quality pattern and structure formation. PDMS conforms to the surface of the substrate and it is released relatively easily. Due to its low interfacial free energy, it does not adhere irreversibly to or react with the polymers being moulded.

Even though there are several advantages of using flexible, elastomeric stamps, flexibility also brings some difficulties. Pairing is a problem that occurs when aspect ratio of relief structures is too large. Delamarche et al. showed that the aspect ratios (l/h, Figure 2.5a) of the relief structures on PDMS surface had to be between about 0.2 and 2 in order to obtain defect-free stamps [18]. Sagging occurs when features in the stamp are widely separated ($d \geq 20h$, Figure 2.5b). Also shrinking of PDMS during curing can lead into difficulties. Figure 2.5 illustrates these problems.

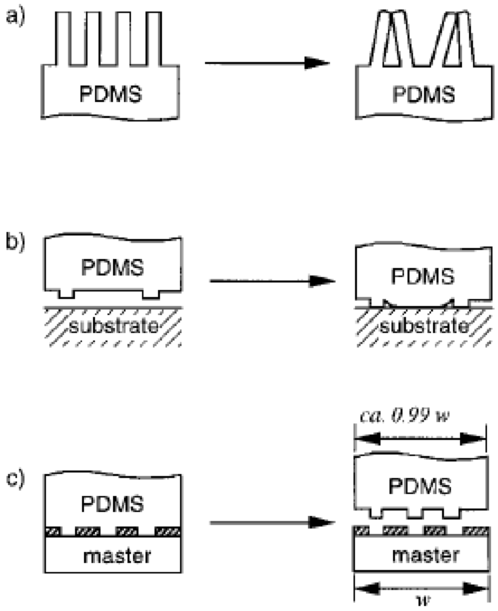


Figure 2.5: Deformation of elastomeric stamp. a)Pairing, b)sagging, c)shrinking [11]

In Figure 2.6b basic steps of a fabrication of elastomeric stamp are shown. First a master is prepared using some lithographic technique (Figure 2.6a). The choice of the fabrication method for the master depends on the desired feature size. Usually master can be fabricated using conventional UV-lithography, but if smaller, under 200 nm, structures are needed, the electron beam lithography (EBL) can be used. EBL provides high resolution but due to its low throughput it can not be used in mass production. Master material is usually silicon because of its well established fabrication process.

When the master has been fabricated, the stamp can be prepared by casting the liquid prepolymer of an elastomer against the master. The master, with uncured prepolymer on top, is then put into vacuum, so that all the air bubbles are removed from the elastomer. Then the prepolymer is cured for a period of time that depends on a temperature used. Temperatures between 20 °C and 80 °C can be used while the time required varies between 24 hours to 1 hour. Cured elastomer is peeled off the master. The same master can be used more than 50 times [11]. This is one of the advantages of UV-molding since fabrication of the master is slow especially if EBL is used. Coating of the master can also extend its lifetime. In one study the SU-8 master was coated with amorphous diamond-like carbon-poly(dimethylsiloxane) hybrid (DLC-PDMS-h) film [19]. It was shown that while uncoated SU-8 master could be used only for one or two PDMS casting, the coated one showed no degradation of SU-8 or DLC-PDMS-h coating after ten PDMS replication. Another coating method for master is to use a thin teflon-like film [20] as an anti-adhesive layer. This layer is deposited by using common reactive ion etching (RIE) machine. Depending on the feed gases, RIE can be used either for etching or for polymeric film deposition. For teflon-like film deposition CHF_3 can be used as feed gas. Fluorine-to-carbon ratio should be near two, but because there are hydrogen moieties present they will react with surplus fluorine producing HF. In this way the ratio will be approximately 2. The same kind of thin teflon-like film has been used to coat nickel stamp for hot embossing process [21]. As shown in Table 2.1 the surface energy of nickel is high, which causes problems of adhesion between surfaces. Teflon-like films are the most used coatings to reduce this adhesion.

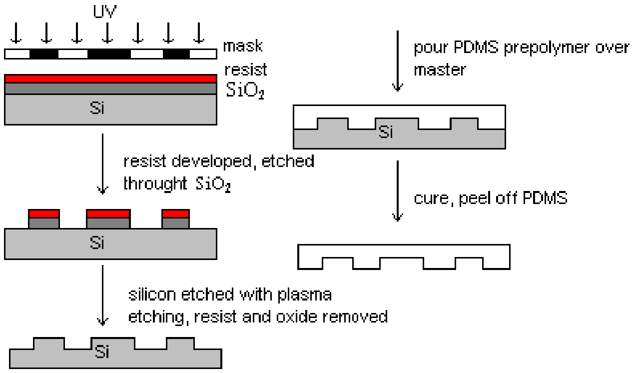


Figure 2.6: (a) Fabrication of hard, silicon stamp or master. (b)Fabrication process of elastomeric stamp. [11]

2.2.2 Step and flash imprint lithography

One relatively new imprint technique is step and flash imprint lithography (SFIL). In this technique photopolymerization chemistry and low processing pressure is

Table 2.1: Properties of different stamp materials

	Si	Nickel	Quartz	PDMS	SU-8
Density (g/cm^3)	2.33	8.9	2.6	0.97	1.2
Thermal expansion coefficient (ppm/°C)	2.6	13	0.5	310 [22]	52
Young's Modulus (GPa)	190 (111)	200	76	$3*10^{-3}$[17]	4[23]
Surface energy (mJ/m^2)	48	1900	980	21.6	43.6[24]

used to transfer patterns onto a substrate. The method differs from other imprint techniques by using a photocurable low viscosity organosilicon liquid and transparent, rigid template [25]. The template is fused silica, where patterns are fabricated by using electron-beam exposure. Due to its transparency, the layer-by-layer alignment is possible.

Liquid pre-polymer is dispensed onto the surface of the substrate. The substrate can be polymeric as well due to a low temperature process. The template is brought into contact with the pre-polymer, causing it to spread across the surface and conform to the structures defined by the template. UV light is used to polymerize the pre-polymer, after which the template is separated from the substrate. Pre-polymer solution must not change its composition significantly between dispensing and imprinting by for example solvent evaporation. Its viscosity has to be low enough for it to spread over the entire surface and to fill structures of the template. It should polymerize rapidly during exposure and shrinkage due to polymerization must be controlled. It should also detached from template easily after polymerization. [25]

Schematic process flow is presented in Figure 2.7. Last step shows the post-processing, which consists of etching through the thin residual layer of polymer and further etching through transfer layer using polymer as etch mask.

Residual layer that remains after SFIL process can be problematic in some applications. Although the SFIL process itself only take few minutes, the residual layer removal with RIE can increase the process time relatively long, which limits the overall throughput. Also the residual layer thickness can be non-uniform due to a imprinting conditions or the pattern complexity. This makes it difficult to determine the time needed to etch through the residual layer. Etching too little will lead to some remaining residual layer and etching too much will reduce the

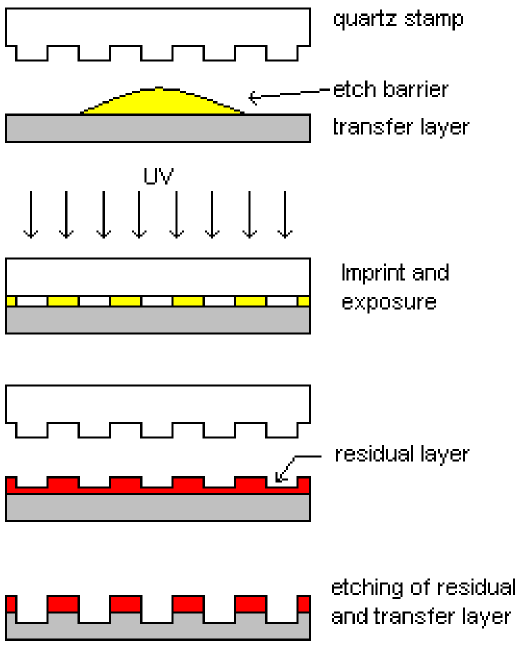


Figure 2.7: Schematic of the S-FIL process. Modified from[26]

aspect ratio of the structures.

Cheng et al. [27] introduced a combined nanoimprint and photolithography (CNP) patterning technique to overcome this residual layer problem. CNP process steps are illustrated in Figure 2.8. First, a stamp is fabricated from UV transparent material, but additional light-blocking metal layer is applied in protrusions of the stamp. When the UV exposure is done through the stamp, areas covered with metal layer are not exposured. When the stamp is removed residual layer still remains, but this time it can be removed with developing solution. This technique makes an additional residual layer removal with RIE unnecessary and shortens the processing time. Also, the aspect ratio of the structures does not suffer from this kind of approach and the aspect ratio of produced structures can be even higher than that on the stamp.

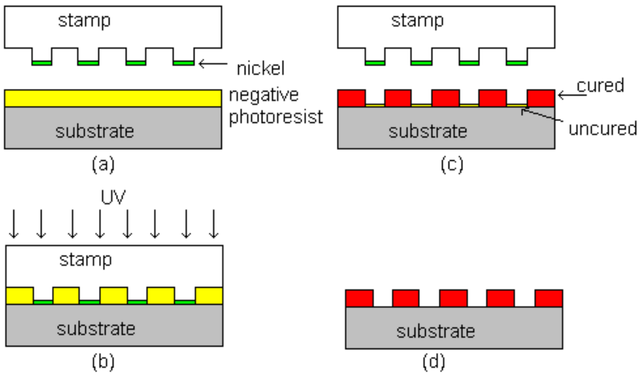


Figure 2.8: Main steps of combined nanoimprint and photolithography patterning. Modified from [27].

Chapter 3

ORMOCER®s

ORMOCER®s (ORganically MOdified CERamics, registered trademark of FraunhoferGesellschaft zur Förderung der angewandten Forschung e.V., Germany) are inorganic-organic hybrid polymers, which consist of inorganic backbone and organic side groups. Inorganic backbone is formed via sol-gel process followed by organic polymerization or crosslinking. Due to the formation process of ORMOCERs, their properties are easily modified.

ORMOCERs were first developed to optical [28] and electrical applications [29], but their easily adjustable properties have led to applications in many different fields. ORMOCERs combine several good properties from different material classes. In Figure 3.1 material relationship of ORMOCER is presented. They get e.g toughness and good processability from organic polymers, hardness and chemical and thermal stability from glasses and ceramics, and elastomeric and surface properties from silicones. Low process temperature of ORMOCER®s also enables the use of low cost polymeric substrates.

3.1 Structural units and network forming reactions

ORMOCERs are composed of four different structural units. All units are connected via strong covalent bonds. Structural units can be classified according to

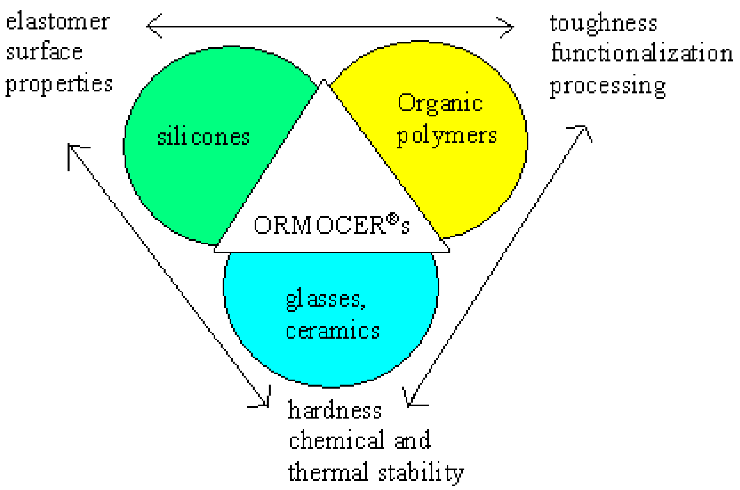


Figure 3.1: Relationship of ORMOCER®s to silicones, organic polymers, glasses and ceramics. [30]

their network forming or modifying roles.

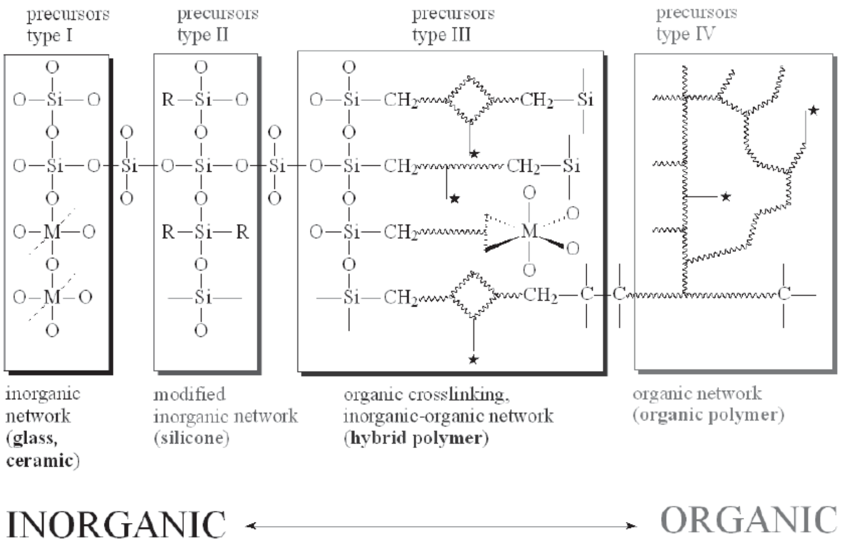


Figure 3.2: Structural units of inorganic/organic polymer. [9]

In Figure 3.2 structural units of ORMOCER are presented. Precursor type 1 is responsible for formation of inorganic network. Inorganic network of ORMOCERs are formed via classical inorganic sol-gel process. This process consists of two steps hydrolysis and polycondensation.

Hydrolysis:

$$\equiv SiOR + H_2O \rightarrow \equiv SiOH + ROH \tag{3.1}$$

Polycondensation:

$$\equiv SiOH + OH - Si \equiv \rightarrow \equiv Si - O - Si \equiv + H_2O \tag{3.2}$$

$$\equiv SiOH + RO - Si \equiv \rightarrow \equiv Si - O - Si \equiv + ROH \tag{3.3}$$

R in the reactions is either methyl, ethyl or propyl. These reactions are started and controlled by the addition of water and catalyst to an alcoholic solution of the precursors. Hydrolysis and polycondensation happen simultaneously, because polycondensation starts as soon as the first hydrolyzed species are present [30].

The size of these inorganic units can be influenced easily by modification of polycondensation conditions, e.g temperature, catalyst, concentration or solvent. The percentage value of inorganic network has major effect on material properties. The higher percentage will lead to higher elastic modulus, thermal and mechanical stability and lower thermal expansion coefficient and optical loss in the near infrared region (NIR).

Precursor type 2 modifies properties of ORMOCER. These are usually non-reactive aryl or akryl groups. Changing their percentage will for example modify density of the material. Adding arylic functions will raise the refractive index (up to 1.6). On the other hand alkyl or, even better, fluorinated alkylgroups will reduce the refractive index (down to 1.42). [30]

Precursor type 3 is a network connecting unit. The longer the chain the lower will be the elastic modulus and higher will be the thermal expansion coefficient. To achieve very high transparency in the NIR the connecting unit should be partially fluorinated.

Precursor type 4 forms the organic network. It has to be chosen considering the final use of ORMOCER. For example in thin film technology easily polymerize groups like methacryl or epoxy are needed. On the other hand these groups cause higher thermal expansion coefficient and optical loss in the NIR. [31]

3.2 Material properties

ORMOCERs are transparent and show thermoplastic behaviour due to the organic network. Because of their formation mechanism ORMOCERs are homogeneous materials. In electron microscopy and x-ray investigations no phase separation between organic and inorganic moieties was detected [30]. The conventional macroscale composites have domain size of micrometer or even millimeter scale, but in inorganic-organic hybrid materials they are of nanometer range, typically 1-100 nm [32].

As could be seen in previous section, properties of ORMOCER can be modified by varying reaction conditions or changing organic or inorganic groups. Therefore it is impossible to give exact numerical value for example Young's modulus or refractive index, and some number range is used instead. In Table 3.1 some of these properties are presented. The properties of commercially available ORMOCER material, ORMOCOMP, are also shown.

Table 3.1: Properties of ORMOCER (Modified from [9])

Property	value	comment
Density(g/cm^3)	1.1 - 1.6	without fillers
Thermal expansion coefficient (ppm/°C)	50 - 200 18 - 70	without fillers with fillers
Thermal stability	from 180 up to 400 °C	$<$ 5% weight loss (TGA)
Young's-modulus (GPa)	from 0.013 up to 18,6	high organic/ polymer content high inorganic content

ORMOCERs are dense and non-porous materials. As show in Table 3.1, the density of ORMOCER lies in between 1.1 to 1.6 g/cm^3 depending on the structure of ORMOCER material. Density of ORMOCER decreases with increasing amount of organic moieties.

Shrinking of ORMOCER during curing is probably the most major drawback of ORMOCER materials. Shrinkage can be as high as 50% when both solvent removal and curing are taking into account [30]. Shrinking causes problems because higher mechanical stresses are formed which will lead to bending and cracking of the ORMOCER layer. This problem can be solved by using (meth)acrylate alkoxysilane based ORMOCERs, which suffer from much less shrinkage than other ORMOCER materials. With these acrylate based ORMOCERs the shrinkage is reduced to 2-8 vol.%. Also by adding some fillers the shrinkage can be reduced even further. [30]

3.2.1 Mechanical and thermal properties

Variations in Young's modulus and thermal expansion coefficient between different ORMOCER materials are mainly due to differences in organic and inorganic contents and the spacer-length connecting the inorganic and organic sites. Young's modulus increases with increasing organic crosslinking density and thermal expansion coefficient decreases. As expected the Young's modulus increases as spacer-length decreases. A drastic increase of Young's modulus from 70 MPa to more than 2000 MPa can be detected by decreasing the spacer length from 20 to 11 atoms connecting inorganic and organic cross-linking sites [30]. With modification of alkoxysilane precursors thermal expansion coefficient can be from 50 to 200 ppm/°C and by adding some fillers the coefficient can be reduced to 18 ppm/°C [9].

3.2.2 Optical and electrical properties

ORMOCERs are colourless materials which show no absorption in the visible spectrum. ORMOCER is optically transparent over the wavelength range from 400 nm to 1600 nm and it has refractive index of 1.52 at 588 nm. Its refractive index can vary from 1.42 up to 1.6 depending on the ORMOCER composition. It has a very low absorption loss at near infrared region (NIR) at 1310 nm 0.3 dB/cm and at 1550 nm ca. 1.5 dB/cm. If fluorinated ORMOCER is used, the optical losses can be reduced even further [33, 28].

ORMOCERs are usually highly dielectric materials. Their bulk resistivity is between 10^{13} and $10^{15} \Omega cm$. For this reason, and because of its good adhesion to different substrates, ORMOCERs have been used as interlayer dielectrics in electrical and optical interconnection technology [34].

3.3 Photopolymerization

Term photopolymerization means a chain reaction that is initiated by photochemical event. It differs from photocrosslinking because latter one requires photon for each chain propagation step. In photopolymerization every absorbed photon polymerizes a number of monomer units. This number of monomer units per absorbed photon is called quantum yield.

$$\Phi_m = \frac{R_p}{I_{abs}} = \frac{Rate\ of\ polymerization\ (in \frac{M}{s})}{Light\ intensity\ absorbed\ (in\ Einstein \frac{1}{ls})} \tag{3.4}$$

Photopolymerization can be divided into two groups; radical and cationic polymerization. As an example of cationic photopolymerization is a ring-opening reaction of epoxies, whereas acrylates are polymerized by radical reaction [35]. Both of these systems can be initiated by UV light source and both require photoinitiator. The major difference between these two reaction schemes comes from the differences in the chemistry of photoinitiator. Cure speed in free radical system is usually higher than in cationic polymerization. In both cases initiation happens usually through light exposure, but in cationic systems the properties of the cured film are improved by post-thermal treatment.

One of the things that need to be considered in radical photopolymerization is oxygen inhibition. Oxygen inhibition occurs in the photoinitiated radical polymerization of acrylate resin, which is a base monomer of many UV-curable resins. In this reaction the free radicals formed by the photolysis of the initiator react with oxygen molecules forming peroxyl radicals. Peroxyl radicals are not reactive towards the acrylate double bonds and can not therefore initiate or participate in any polymerization reaction. They usually attract hydrogen atoms from the polymer backbone to generate hydroperoxides. Inhibition effect of oxygen on the radical polymerization of acrylates is more pronounced in the top layer of the film in contact with the air [36]. When the film thickness increases, the influence of the oxygen inhibition decreases, since the thickness of the inhibition layer is proximately the same regardless of the film thickness. There are different possibilities to overcome this usually unwanted reaction. Probably the most used method is to perform the radical polymerization under inert gas atmosphere, e.g.

in nitrogen gas flow. The bonding process presented in later chapter is based on oxygen inhibition reaction.

3.4 Applications of ORMOCER®s

Numerous different applications utilizing inorganic-organic hybrid materials have emerged since their development. Nowadays applications cover several different fields from micro-optics to dental application. In this section some of these applications are presented.

3.4.1 Electrical and optical applications

Due to ORMOCERs good optical properties, it has been widely used in optical application. There are few commercial ORMOCER materials available; ORMOCORE and ORMOCLAD from Micro resist technology. They have been developed for planar optical waveguiding, ORMOCORE being the core material and ORMOCLAD the cladding material [37].

One of the most studied ORMOCER application is its use in microoptical components, such as gratings, holograms, waveguides, microlenses, etc. Usually these kinds of components can be fabricated with soft lithography. This provides several advantages over standard lithographic processes. These include fewer processing steps, very high resolution, typically in nanometer range and low cost, because of the possibility of mass production.

Microlenses are a vital part of today's optical systems. Lenses can be either refractive or diffractive and their size can be as small as 15 μm in diameter. Typical materials for microlens fabrication have been silicon and fused silica. In one study ORMOCER microlenses were fabricated on top of a cantilever using photoresist as sacrificial layer [38]. In Figure 3.3 process steps are illustrated. First the photoresist is spinned and patterned on a substrate. Then ORMOCER is applied and the patterning is done by UV-exposure using combined nanoimprint and photolithography.

In Figure 3.4 a SEM picture of obtained cantilever beams with microlenses on

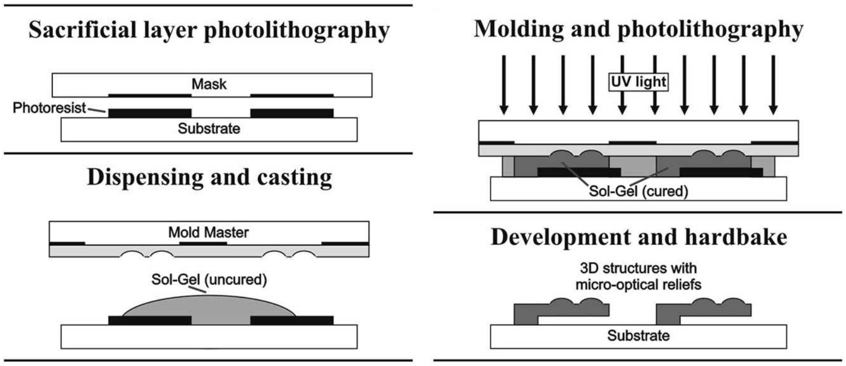


Figure 3.3: Process steps for the fabrication of replicated optical MEMS. [38]

top is presented.

Figure 3.4: Cantilever structures with microlenses on top. [38]

3.4.2 Protective and decorative coatings

Coatings are probably the first application field for ORMOCERs. They are attractive materials for coating application due to their transparency, their good adhesion to different substrates, chemical stability and good abrasion resistance. ORMOCERs provide many advantages over pure inorganic sol-gel coatings. A general problem with inorganic coatings is cracking of thicker layers. By using inorganic-organic material, layers up to 100μm and above can be fabricated with one spin coating step. Numerous ORMOCER based coating materials have been on market since the 1980s [29]. Basic application fields for ORMOCER coatings are [39]:

- abrasion and scratch resistance, decoration;
- barrier layers for packaging, corrosion resistant layers;
- antisoiling, antifogging, antistatic and antireflective applications.

There are numerous different methods by which the coatings can be applied. These include dipping, spinning and spraying, which is followed by UV and/or thermal curing.

Several different properties can be applied into the same ORMOCER material by using different additives. For example Haas et al. fabricated abrasion resistant antiadhesive and antistatic ORMOCER coatings [40]. Abrasion resistant antiadhesive ORMOCER coatings can be achieved by addition of highly fluorinated silanes during sol-gel synthesis. These oleophobic ORMOCER coatings show decreased adhesion of dust particles and they can therefore be cleaned much easier than the uncoated substrates. The abrasion resistance of these modified ORMOCER coating is not affected through the incorporation of fluoroalkyl silanes.

ORMOCER coatings can also be used for conservation of outdoor bronze sculptures, which are endangered by the environment that accelerates their corrosion [41]. In addition to corrosion protection there are also other requirements for coating materials. For example the adhesion between protective coating and the surface has to be good and the coating material should penetrate into the pores of the cast metal.

3.4.3 Dental applications and other medical applications

ORMOCERs can be used as filling composites in dental applications. Due to their hybrid nature, they shrink less in curing process than some conventional materials used in the same application. They are also easy to handle and are biocompatible. Other requirements for materials used in dental applications are reduced polymerization shrinkage, strong adhesion to dentine and enamel and they have to have high X-ray absorption. Traditional plastic filling composites have long-term adhesion problems and a high degree of polymerization shrinkage. The dual character of ORMOCER makes it more suitable as dental filling material. There are two commercially available ORMOCER filling materials; Definite®and Admira®, both of them are products of Fraunhofer ISC.

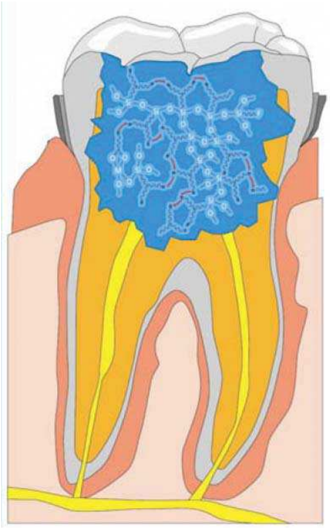


Figure 3.5: Application of ORMOCER as dental filling material. [29]

Drug delivery is one of the most studied area in today's medicine [42]. Usually oral administration of drugs is possible, but there are some exceptions. Some drugs do not absorb well enough or they suffer from enzymatic degradation in the gastrointestinal track or liver to be taken through mouth. This kind of drug is for example insulin, which is taken by using hypodermic needle. This is both painful and it causes an infection risk. Some drugs can also be taken transdermally by patch, but in case of insulin the rate of drug release and penetration through the skin is too slow. Slow penetration is mostly due to the great barrier imposed by skin's outer stratum corneum layer. Different solutions to increase skin's permeability have been investigated, one of them being the use of microneedles. The idea behind microneedles is their size that is small enough to remove the pain to the patient and to reduce damage at the injection site, but large compared to drug molecules. Furthermore their use does not require any medical training, but they can be used as a common transdermal patch. Microneedles have to fulfil several requirements in order to be useful. First of all, they must penetrate through the outermost 15 μm of epidermis and they should be strong enough so that they do not fracture during skin penetration.

Microneedles of different size, shape and of different material have been fabricated [43]. Ormocer microneedles have also been tested. Doraiswamy et al. [44] used two photon induced polymerization to produce hollow ORMOCER microneedle arrays. These arrays were fabricated on glass substrate. ORMOCER microneedles were tested against pork skin for penetration and fracture analysis studies. In preliminary studies it could be shown that mechanical properties of ORMOCER microneedles are sufficient to enable fraction free penetration through pork skin.

Chapter 4

Processing parameters

In the experimental part of this thesis the first ever microfluidic chips in ORMOCER were fabricated. Different processing parameters were tested. Both UV-lithography and UV-molding using transparent stamps have been tested. As a starting point for this study the parameters given by the manufacturer were used.

4.1 UV-lithography process

Table 4.1 present the steps of ORMOCER fabrication process. These steps are always needed when patterning ORMOCER layer. In this chapter each one of these are discussed in detailed.

Table 4.1: ORMOCOMP process steps

Process step	description
Surface pretreatment	dehydration in an oven at 120°C
ORMOCER application	Spinning, casting, dipping etc.
Soft bake	air bubble removal
Exposure	UV-light
Hard bake	on a hot plate
Development	unexposed areas are removed
Final bake	in an oven

In Figure 4.1 microchannels fabricated by using UV-lithography are presented.

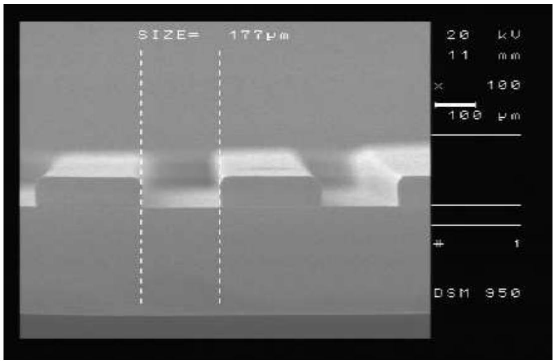


Figure 4.1: Lithographically patterned microchannel.

4.1.1 Surface pretreatment

Substrate was usually double side polished <100> silicon wafer. Wafers were RCA cleaned prior to use, and dehydrated in on oven at 120°C for at least on hour. (Convection oven used in the experiment is Heraeus UT 6200.) Dehydration should increase the adhesion. Shorter periods resulted in poor adhesion between silicon and ORMOCER layer. Another possibility is to use adhesion promoter. This process is wafer priming and it is widely used together with dehydration in an oven. Most commonly used adhesion promoter is hexamethyldisilazane (HMDS). The idea is to make the surface of the wafer hydrophobic and further reduce the moisture adsorption. In this study adhesion promoter was not used.

4.1.2 Resist deposition

ORMOCOMP was supplied from Micro resist technology as a ready-to-use mixture containing resist and photoinitiator. ORMOCOMP is solvent free. It can be deposited either by spinning or casting. Spin coater used in the experiment is BLE Delta 20 BM W8. Spin coating is done in two steps.

The wafer is initially accelerated from 0 to 500 rpm with 100 rpm/sec acceleration. Speed is kept at 500 rpm for 5 sec. At the second step the acceleration of 300 rpm/sec is used and the final speeds between 1000-6000 rpm were tested. This speed is kept for 30 sec. The spinning steps are presented in table 4.2.

The speed of the final step determines layer thickness. 2 ml of ORMOCOMP is enough to cover the whole wafer when spin speed of 2000 rpm or higher is used. With 1000 rpm the amount of ORMOCOMP required is 3 ml. In Figure 4.2 a spin curve for ORMOCOMP is presented. The thickness of the ORMOCOMP layer was measured using DEKTAK 3 profilometer. Spin curve obtained from own measurements is identical to that received from the manufacturer.

Table 4.2: Spinning of ORMOCOMP

Process step	spin speed (rpm)	acceleration (rpm/s)	time (sec)
Step 1	0 to 500	100	5
Step 2	500	0	5
Step 3	500 to final speed	300	-
Step 4	final speed	0	30

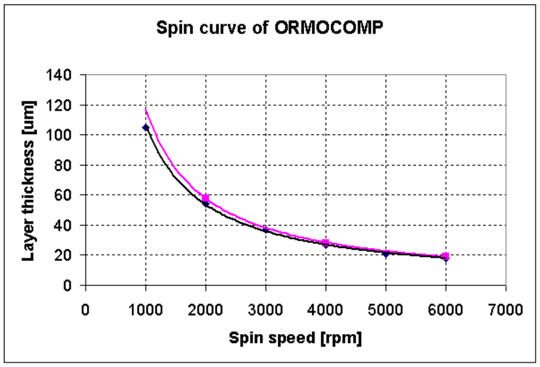
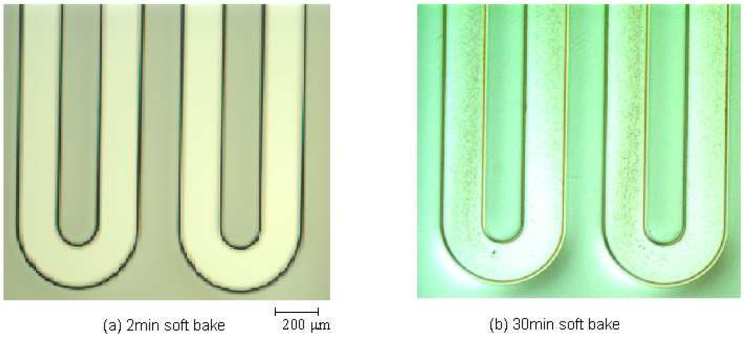


Figure 4.2: Spin curves of ORMOCOMP.[33]

4.1.3 Soft bake

Soft bake is usually done to vaporize surplus solvent from to resist material. It can be done either on convection oven or on a hot plate. In these experiments the soft bake is done on a hot plate at 80°C for 2min. Wafers were cut in four pieces to test different baking parameters. Soft baking times varied from no baking at all to 30 minutes. During the soft bake all the air bubbles inside the ORMOCOMP layer vanished. In Figure 4.3 the channels fabricated using different soft bake times are presented. No difference between these two pictures can be noticed. Because ORMOCOMP is solvent free, the main purpose of the soft bake is air bubble removal.



(a) 2min soft bake (b) 30min soft bake

Figure 4.3: Viscometer channels fabricated using 2 and 30 min soft bake times.

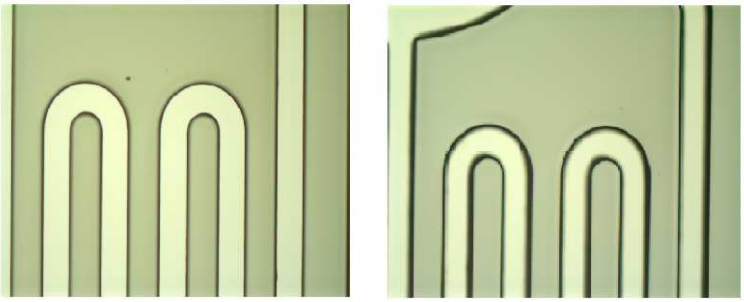
4.1.4 Exposure

Exposures were done with LOMO EM-5006 mask aligner. The wavelength of the light is 365nm and measured intensity about 17 mW/cm^2. Proximity exposure is used because ORMOCOMP is still sticky after soft bake. Exposure times between 1 to 110s have been tested. Due to an uneven intensity distribution of LOMO aligner, the exposure tests were all done within the same quarter of exposure. In Figure 4.4 200 μm channels with four different exposure times are presented. It can be seen that when using longer exposure times the width of the channels are reduced due to an overexposure.

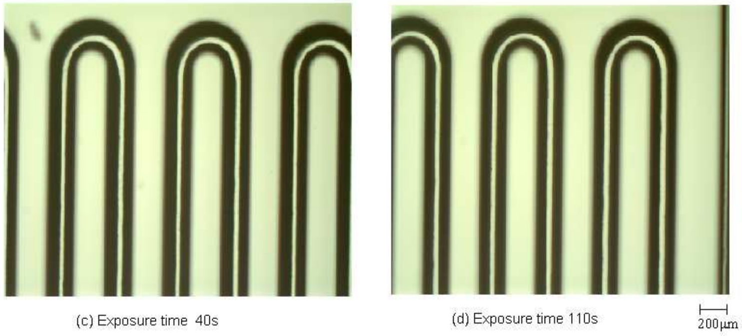
Even though shorter exposure times give better results, small, under 50 μm, structures were narrowed even with 1 s exposure. This indicates that ORMOCOMP is extremely UV sensitive. High UV sensitivity is a problem since 1 s is the minimum time that can be used with LOMO aligner. For this reason the possibility to use some UV - absorbing layer was examined.

UV intensity reduction

UV intensity of the LOMO aligner was measured with an intensity meter. Measurements were done with 3 mm thick PMMA sheet between UV - source and UV - detector and compared to the results achieved without PMMA. Intensity of LOMO varied between 15.84 mW/cm^2 to 17.99 mW/cm^2 without PMMA, and between 1.59 mW/cm^2 to 1.85 mW/cm^2 with PMMA. Exposure with PMMA



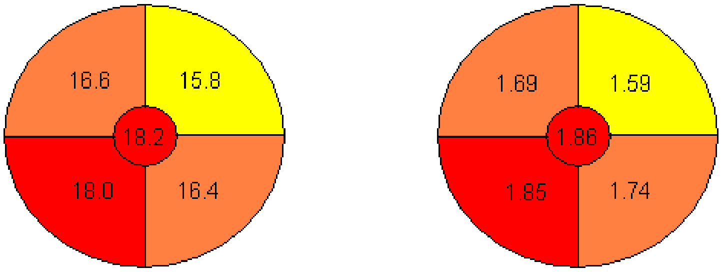
(a) Exposure time 5s (b) Exposure time 10s



(c) Exposure time 40s (d) Exposure time 110s

Figure 4.4: 200 μm channels with exposure times from 5 to 110 s.

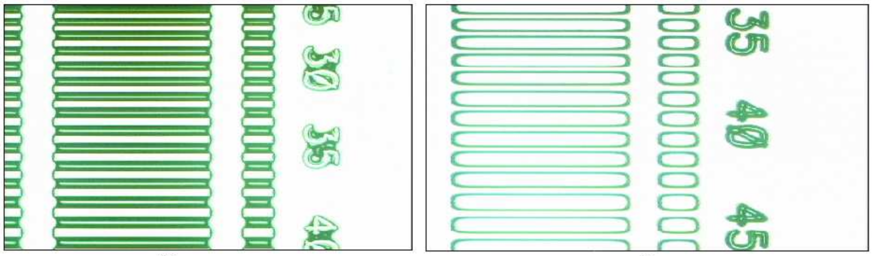
sheet reduced the intensity about tenth of the original value. It could therefore be seen that the PMMA absorbed a major part of the UV - light. PMMA sheet was used as UV - absorbing layer, so that smaller exposure dose could be tested. The results from UV -intensity measurements are presented in Figure 4.5. It can be seen that the intensity distribution is uneven, but the PMMA sheet does not effect to this distribution.



(a) Intensity of LOMO (mW/cm^2) (b) Intensity through PMMA sheet (mW/cm^2)

Figure 4.5: Intensity measurement of LOMO.

Exposure through PMMA sheet was tested with exposure times from 1 to 10 s. 1 s exposure with PMMA sheet corresponds to 0.1 s without it. It was noticed that with PMMA sheet, 3s and shorter exposure times led to poor adhesion between ORMOCOMP and silicon. This with uneven intensity distribution of LOMO can lead into difficulties. The exposure dose for one part of the wafer may be too little and the adhesion fails where as in others the overexposure may occur.In Figure 4.6 the difference between structures exposured with and without PMMA sheet is easily noticed. The minimum linewidth that has been able to produce so far is about 20 μm.



(a) (b)

Figure 4.6: (a) Structures formed with 10 s exposure without PMMA sheet. (b) Structures formed with 10 s exposure with PMMA sheet.

4.1.5 Hard bake

Hard bake can be done either on a hot plate or in an oven. The purpose of a hard bake is different for different resists. For example in case of SU-8 the actual crosslinking of epoxy moities takes place during hard bake, which makes this process step essential for epoxy polymers. Hard bake improves the film stability. In resists which utilize free radical polymerization, the curing happens during the UV exposure and the meaning of the hard bake is less significant.

In this study hard bake was usually done on a hotplate at 80 °C for 5 min. Different hardbake times were also tested but no significant differences between structures were detected. Results from different hard bake times are presented in Figure 4.7.

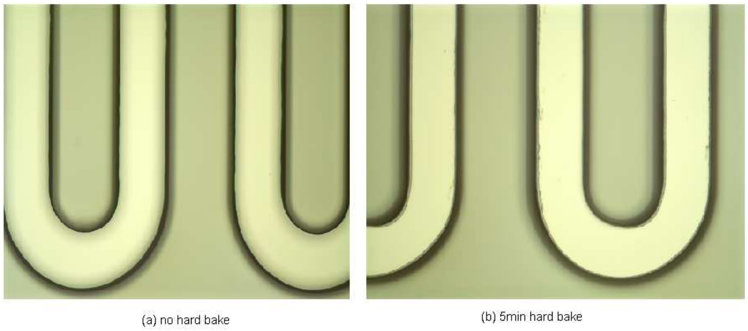

(a) no hard bake
(b) 5min hard bake

Figure 4.7: Viscometer channels fabricated using different hard bake times.

4.1.6 Development

Development was done with ORMODEV developing solution which contains isopropanol and methyl isobutyl ketone. Because ORMOCOMP behaves as negative photoresist, the unexposed areas are dissolved in developing solution. Different developing times, between 1 minute to over an hour, were tested. In principle the developing times are longer for deeper channels, but few minutes is long enough for structures tested by us. It was also noticed that there is practically no danger for overdevelopment. Even after over an hour development the structures on a wafer were unattacked. After development the wafers were rinsed with isopropanol and dried with nitrogen flow.

4.1.7 Final bake

Final bake was done to cure the ORMOCOMP layer completely. During the final bake the polymerization of epoxy groups take place. Also further condensation of alkoxy- and silanol-groups happen, which improves ORMOCER's thermal and chemical stability. The final bake will also significantly reduce the internal stress resulting from UV-exposure [45]. In this study final bake was usually done in an oven at 120 °C over night to ensure complete curing. Baking on a hotplate at 150 °C was also tested but no significant differences were noticed when compared with an oven bake.

4.2 UV-moulding process

UV-moulding process is presented in Figure 4.8. First, a standard silicon wafer was dehydrated in an oven for at least an hour. After that the wafer was put on a hot plate and ORMOCOMP was dispensed on top of it. The temperature of the hot plate was kept at 80 °C to spread the ORMOCOMP over the entire wafer. The stampping was also done on a hot plate and pressure was applied manually to remove the air bubbles between the stamp and the ORMOCOMP layer. After that the UV-exposure was done through the PDMS stamp. The exposure time was 10 s. In this process the overexposure is not extremely critical. After exposure the post bake is done on a hotplate for few minutes during which the PDMS stamp is detached almost by itself.

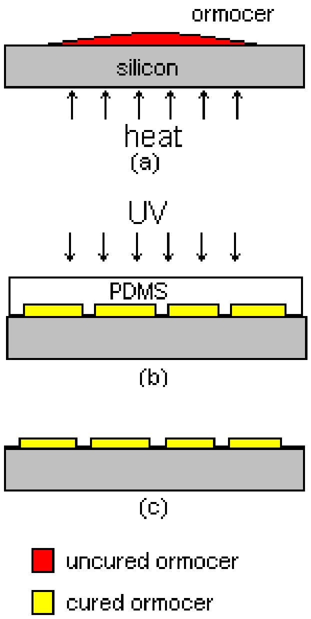


Figure 4.8: UV - embossing with PDMS stamp. (a) dispensing ORMOCER (b) UV exposure (c) demould ORMOCER structure

The SEM picture of stamped ORMOCER is presented in Figure 4.9

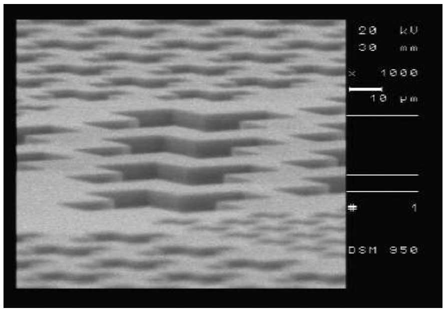


Figure 4.9: PDMS stamped ORMOCER.

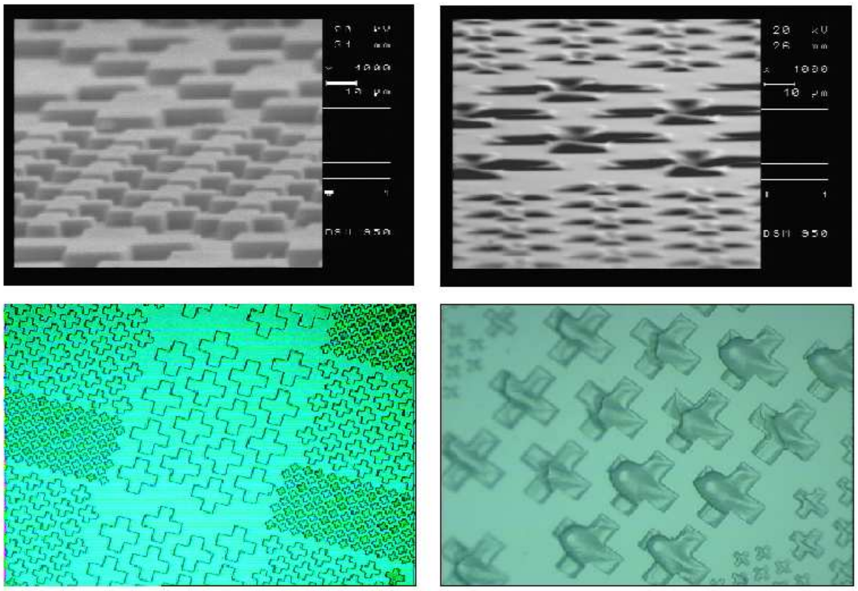
4.2.1 Stamp fabrication

Before the actual PDMS stamp could be fabricated, the silicon master was made. Silicon master was fabricated using UV -lithography. Standard <100> wafers with 200 nm silicon dioxide layer on top were used.

First, wafer was baked in an oven at 120 °C for 10 min in order to remove any moisture. After baking, the wafer was HMDS treated to make the surface hydrophobic. Positive AZ5214 photoresist was dispended and the spin coating parameters were 4000rpm for 25 sec. Wafer was soft baked in an oven at 90 °C for 20 min. Exposure was done with Electronic Vision AL6-2 aligner. Exposure time was 4 sec. After 60 sec development, wafer was hard baked in an oven at 120 °C for at least 30 min. In a next step photoresist was used as an etchmask in BHF etching of silicon dioxide. Other option is to use RIE etching of silicon dioxide, which leads to anisotropic etching profile. After the etching step, resist was removed with acetone in ultrasonic bath and continued with IPA rinse. The silicon etching was done with ICP-RIE which makes high aspect ratio structures possible. Etching time of 5 min led to 21 μm deep structures. After ICP-RIE etching, an additional surface treatment was done to facilitate the stamp release from the master. Thin teflon-like film was grown in conventional RIE etching machine [46]. 100 sccm of CHF_3 gas was used with the power of 50 W to grow the film. The deposition time was 5 min. After deposition the water droplet was placed onto surface and according to this test the surface seemed hydrophobic. The thickness of the film could not be exactly evaluated, but Jaszewski et al. estimated the deposition rate of about 1Å/s in the similar process [47].

PDMS stamp was fabricated by mixing two components; base and curing agent in 10 to 1 ratio. The mixture was placed in a vacuum to remove all the air bubbles from the pre-polymer solution. After half an hour the pre-polymer was poured on top of a silicon master, which was in a petri dish. The polymerization was done in room temperature where it was left at least for 24 hours. Different times and temperatures were also tested but no change in stamp structure were noticed. The main rule is that higher the tempareture faster is the curing process, although not higher than 100 °C should be used. After curing PDMS stamp was separated out from the master.

The stamp was easily detached when using teflon-like coating on top of a silicon master. In Figure 4.10 the difference between PDMS stamps that are fabricated with teflon-like film coated and uncoated master can easily be seen. Without coating, high aspect ratio structures were caught into the master and structures seemed collapsed.



(a) (b)

Figure 4.10: PDMS stamps (a)master teflon-like film coated (b) master not coated

Another method for stamp fabrication is the use of hard PDMS (h-PDMS) together with common PDMS to form a so called composite stamp [48]. The idea is to use h-PDMS, which has the higher elastic modulus than common PDMS, to make the stamp more rigid. This is expecially favorable when structures in a stamp are far from each other and sagging is likely to occur. With h-PDMS the sharped-edge structures are also easier to produce. Because h-PDMS is relatively brittle material, common PMDS is used to support structures and make the stamp easier to handle.

The composite PDMS stamps composed of a thin h-PDMS layer supported by the thick soft PDMS layer. In this study the composite stamp was fabricated using silicon master above which the h-PDMS was spin coated. The process flow for h-PDMS preparation is presented in Figure 4.11. First, 3.4 g of vinylmethylsiloxne-dimethylsiloxane (VDT-731, Gelest) was mixed with 17,5 μl of platinumdivinyltetramethyldisiloxane (SIP6831.1, Gelest) and 5 μl of 2,4,6,8 - tetramethyltetravinylcyclotetrasiloxane (87927, Fluka). This mixture was degassed for 1-2 min after which 1 g of methylhydrosiloxane (HMS-301, Gelest) was gently stirred into a mixture. Immediately after that the h-PDMS was poured on top of the silicon master and a home-made spincoater was used to spread the mixture onto silicon master. Because there was no tachometer on spin coater it is impossible to say anything about the layer thickness, but by spinning the h-PDMS instead of simply pouring it, more uniform layer thickness can be achieved. H-PDMS layer was cured at 60 °C for 30 min. After that the standard formulation PDMS was poured on top of the master. PDMS was prepared as described before.

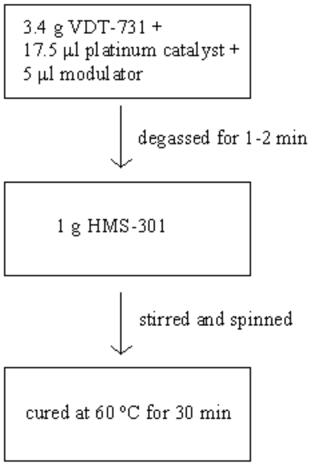
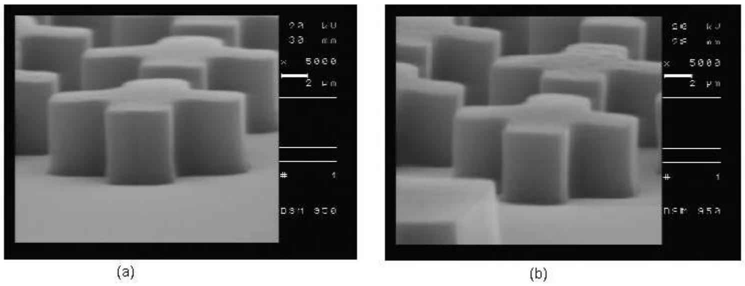


Figure 4.11: Process flow for h-PDMS preparation.

The fabrication of composite PDMS stamp was tested with and without the teflon-like film on top of silicon master. When no anti-adhesive layer was used, the h-PDMS layer cracked easily and peeling off was impossible. But as with the common PDMS stamp, the teflon-like film made peeling off easy and defect free stamp was obtained. In Figure 4.12 a common PDMS and hybrid stamp are presented.



(a) (b)

Figure 4.12: PDMS stamps (a) a common PDMS stamp (b) hybrid stamp

Stamping of ORMOCOMP was also tested with this composite stamp. The moulding procedure was the same as with standard PDMS stamp and nice looking structures could be achieved.

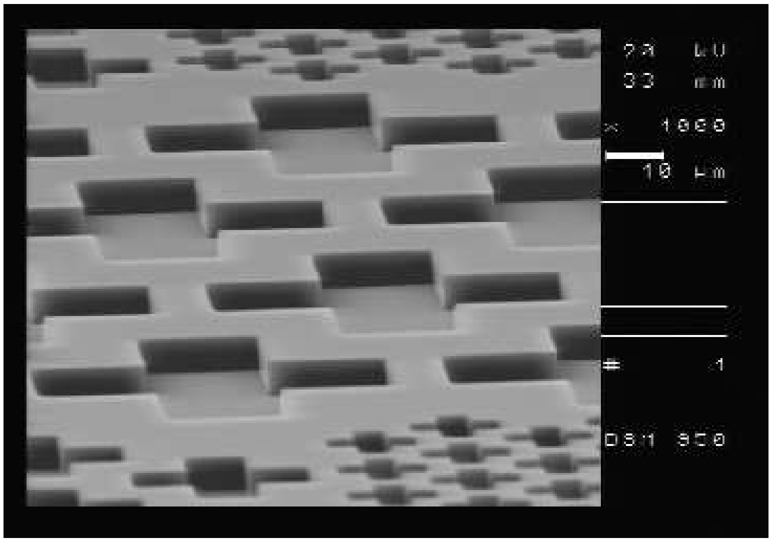


Figure 4.13: h-PDMS stamped ORMOCOMP.

Chapter 5

Stability and adhesion tests

Chemical stability of materials used in microfluidic channel fabrication is crucial because different kinds of solvent and acids or bases are used either as a buffer or cleaning purposes in analytical devices. In this chapter chemical stability of ORMOCOMP is evaluated.

Another important factor to be considered is the toxity of the material. In many microfluidic applications it is enough to have a material that is non-toxic, but in others the biocompatibility is requisite [49]. Biocompatibility involves two principal areas. First, it has to be biosafe, which means that the material should not be harmful to the organism. It should not be cytotoxic, mutagenesis or carcinogenesis. The second factor is biofunctionality which means that the material should have the ability to perform with an appropriate host response in a specific application [50].

In microfluidic application where cells and other biological agents are in contact with the material, the non-toxicity is the main requirement. The interaction between the biological environment and the microfluidic device leads to various challenges that have to be taken into account. For example proteins have tendency to adsorb to surfaces and these protein layers tend to create undesired behaviour of the device. Biofouling is the main reason why in vivo glucose sensors have been difficult to make [51, 52]. Protein adsorption also mediates cell adhesion which can lead to catastrophic flow problems due to the comparable size of the cell with the microfabricated device [53]. In the second part of this chapter the cell adhesion to ORMOCOMP surface was evaluated.

5.1 Chemical stability

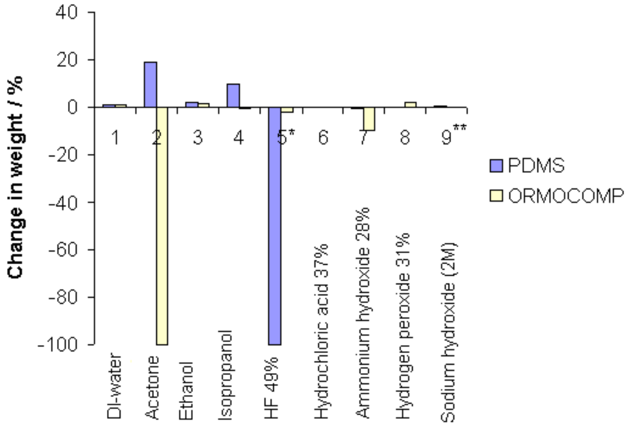
Chemical stability of ORMOCOMP was tested with various commonly used solvent, acids and bases. PDMS was used as a reference material. PDMS has been used in many different microfluidic devices, including capillary electrophoresis [54]. For this reason the solvent compatibility of PDMS has been evaluated [55]. It was noticed that PDMS is compatible with water and most alcohols, but its stability is poor in non-polar solvent. PDMS did not swell considerably in any acid and bases tested but it is incompatible with those that dissolved it, for example sulfuric acid.

In chemical stability tests the thick layer, about 100 μm, of ORMOCOMP was spun on top of a silicon wafer. ORMOCOMP was cured and the wafer was cut into pieces. Pieces were weighed with the Sartorius CP224S scale, with a relative accuracy of 0.1 mg. Pieces were put into a petri dish that contained the liquid examined. Pieces were kept in petri dish for seven days. After seven days, the pieces were weighed again and the change in weight was calculated.

Results are presented in Figure 5.1. ORMOCOMP experiences very little weight changes in mineral and acid solutions, but its stability is poor in acetone. It should also be noticed that ORMOCOMP is incompatible with HF, even though its weight does not change, its structure change dramatically. The main problem for the evaluation of the chemical stability of ORMOCOMP was the use of substrate material. In this case when the substrate was silicon, only chemicals that do not react with silicon could be tested. For example silicon is etch by sodium hydroxide, which made it impossible to measure the weight loss of ORMOCOMP.

5.2 Contact angle measurements

Contact angle with water was measured with KSV Instruments' CAM100 goniometry, which is shown in Figure 5.2 (a).Contact angle is geometrically defined as the angle on the liquid side of the tangential line drawn through the three phase



* Structure of ORMOCOMP changes
** Weight loss of ORMOCOMP couldn't be measured

Figure 5.1: Solvent compatibility of ORMOCOMP measured by procentual changes in weight of ORMOCOMP pieces. (PDMS used as reference)

boundary where a liquid, gas and solid intersect [56]. Contact angle is measured by placing a drop of water onto material surface. The picture of the drop is taken, after which the curve is fitted around the droplet. The curve fitting is based on Young & Laplace equation. In Figure 5.2 (b) a drop of liquid is shown on a flat solid surface. The triple interface is formed between solid, gas and liquid and it will move in response to the forces arising from the three interfacial tensions until the equilibrium position is established [56]. The surface is said to be hydrophilic if the contact angle with water is below 90° and hydrophobic if the contact angle is above 90°. In general, adhesion of cells on a material is determined by the hydrophilic property of the material. Cells tend to adsorp better to more hydrophilic materials [49].

Contact angle of several often used materials, as well as ORMOCOMP, were measured and results were compared with those obtained from literature. Results from these measurements are presented on Table 5.1. All the own results are average values from five measurements. It could be seen that the contact angle of ORMOCOMP is significantly lower than PDMS. It is also lower than PMMA and PC when compared with our own measurement. However, in literature the contact angle of PMMA and PC is smaller than those obtained from

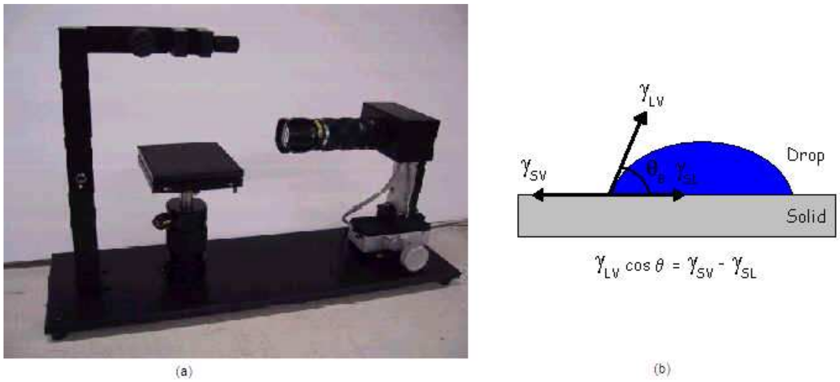


Figure 5.2: Contact angle measurement.

our measurements.

Table 5.1: Contact angle measurements

	This work	Literature	Reference
ORMOCOMP	66.4 ± 0.4	> 76	[45]
PDMS	99.9 ± 1.8	102.5	[49]
PMMA	71.5 ± 1.0	62.7	[49]
PC	83.7 ± 1.4	70.1	[57]
Silicon dioxide	46.8 ± 1.8	30	[58]

5.3 Cell adhesion

In this section the cell adhesion and survival on ORMOCOMP surface was evaluated. The patterned and unpatterned ORMOCOMP surfaces were used in cell culture tests. Patterned surfaces were tested to assess the cell adhesion between ORMOCOMP and silicon surfaces. Unpatterned silicon surface was used as reference. Because silicon is often used material in different MEMS applications, its biocompatibility has been evaluated before [59].

5.3.1 Substrate patterning

The samples used in cell adhesion tests were patterned in cleanroom by using conventional UV-lithography. About 20 μm thick ORMOCOMP layer was spinned on top of a silicon wafer. The mask used in substrate patterning contained structures from 5 to 50 μm.

5.3.2 Cell culture

Before the actual cell culture was done all the samples were sterilized in ethanol. Samples were dipped in ethanol and dryed carefully in air flow. In this work a three day old mouse fibroblast like 3T3 cells were used. First the culture medium was removed after which the cell culture was washed with 2.5 ml of PBS-EDTA solution. The washing the culture is important because this way the amount of old culture medium is minimized. Old medium for example inhibits the enzyme activity in next stage. The 0.5 ml of trypsin-EDTA solution is applied. Trypsin is an enzyme produced by pancreas and it brakes effectively extracellular proteins and this way assists the cell release from the walls of the petri dish. The petri dish is put into the incubator, which temperature is 37 °C and CO_2 content 5 %, for few minutes. Trypsin, as well as other entzymes, is most effective at 37 °C. After that the cells are suspensed carefully to 4 ml of culture media. Then cells are devided into four petri dish, which contain the material samples and 4ml of culture media is added into each dish. The dishes are put into incubator for 4 days. The process flow for cell culture is presented in Figure 5.3.

5.3.3 Sample preparation

After incubation the samples have to be prepared for visual analysis. The preparation method is chosen depending on the visualization method. If optical microscope is used the cells are usually stained to make different parts of cell visible. When using scanning electron microscopy (SEM), as in this case, the samples need to be dried properly since very high vacuum is used.

Sample preparation starts by removing the culture medium. Then samples were rinsed with phosphate buffer to remove all the unattached cells and the remaining medium. Rinsing should be done carefully so that the attached cells would not be removed as well. After rinsing the glutaraldehyde is applied to attach cell into the sample more permanently. Samples are kept in glutaraldehyde for 30 min.

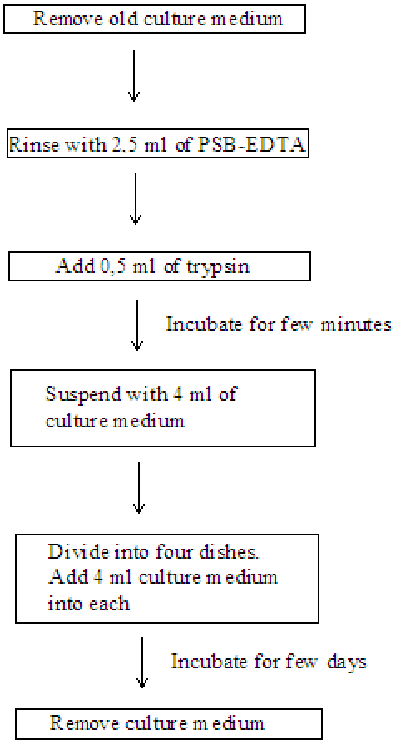


Figure 5.3: Cell culture.

The ascending ethanol rinse is used to dry the samples. Rinsing is started with 50% ethanol and finished nearly 100%. Samples are kept in each concentration for 2 min. Ethanol will replace the water in cells. The reason for ascending rinsing is that if too strong ethanol is used in the beginning the cells might collapse. Finally, samples are rinsed with HMDS, which will dry the samples complitely. HMDS is led to evaporate over night.

5.3.4 SEM analysis

SEM analysis was done with Zeiss/Opton DSM scanning electron microscopy. Prior to SEM study a thin, about 20 nm thick, layer of gold was sputtered, with Balzers SCD-05 sputter, on top of the samples to make them conductive.

In Figure 5.4 the SEM pictures of cells on top of ORMOCOMP ridge is shown. And in Figure 5.5 an optical microscopy image of unpatterned silicon and OR-

MOCOMP substrate are presented. It can be seen that the density of cells on top of a both substrates is quite high. This proves that the ORMOCOMP is non-toxic. The dense cell adhesion may be a problem in some microfluidic applications and some kind of surface passivation may need to be used. On the other hand in many microfluidic applications the fluids are flown through the channel and the cell adhesion is dramatically reduced [53]. Also in some applications the cell adhesion is not just favorable but also requirement. If microdevise is used as cell seeding scaffold, the material itself should promote cell grow [49]. Doraiswamy et al. also showed previosly that ORMOCOMP demostrates acceptable cell viability and cell growth for tissue engineering scaffolds [44].

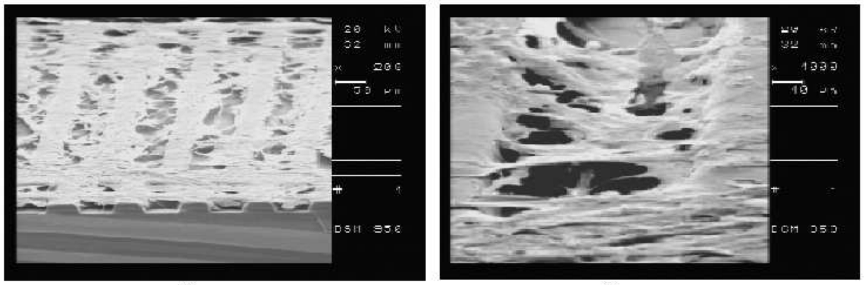

(a) (b)

Figure 5.4: Dense cell grow on ORMOCOMP ridge.

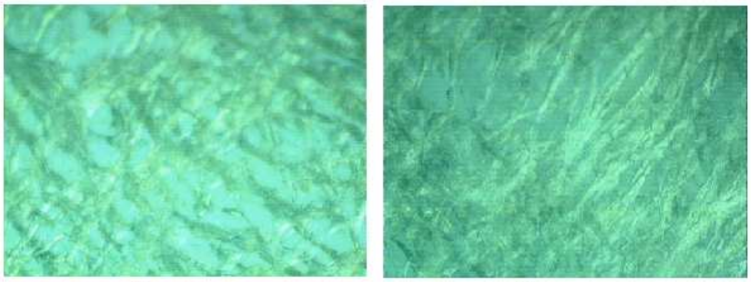

(a) (b)

Figure 5.5: Optical microscopy pictures from (a) cells on silicon surface and (b) cells on ORMOCOMP surface.

Chapter 6

Fluidic chip fabrication

In this chapter the fabrication of microfluidic chips has been presented. One of the most difficult part of microchannel fabrication is the bonding of the channels. In this chapter different bonding methods have been evaluated and their pros and cons are listed. The fabrication of enclosed ORMOCER microchannel is presented. Fabrication of inlets in ORMOCER channels is also evaluated.

6.1 Bonding methods

Several different bonding methods for enclosed microchannel fabrication have been used. The selection of a bonding method is primarily dependent on the materials being bonded. The bonding methods can be devided into two classes; direct bonding and indirect bonding with intermediate layers. The direct bonding can result in strong bond between substrates. Indirect bonding uses adhesives and the strength of the joint depends on the materials and methods used. Many different materials can be used as adhesives such as metals, glass or polymers [60].

One of the direct bonding methods is fusion bonding. This method is used bonding silicon to silicon. First two wafers are brought together at room temperature. Then a high temperature, between at 700-1100 °C is used to form a permanent bond between two wafers. Due to very high temperatures, this technique is most commonly used to bond two similar wafers. If two different materials with very different coefficient of thermal expansion need to be bonded, some other method should be employed. Another major problem with the fusion bonding is related to the non-contacting areas called voids. The voids are mainly caused by particles, organic residues, surface defects such as scratches and inadequate contact prior to bonding [61].

Another direct bonding method is anodic bonding. The anodic bonding of silicon to glass is the oldest method in microfabrication [60]. This bonding method utilizes a heater block that is heated approximately to 400 °C. At this themperature the glass decomposes locally to sodium and oxygen ions. A voltage of -300 to -1000 V is applied to the glass wafer. Sodium ions move towards the glass top surface and oxygen ions towards the silicon wafer. This will create a electrostatic force which pulls glass and silicon wafers together. Schematic picture of anodic bonding process is presented in Figure 6.1. Even though temperatures are lower than in fusion bonding, the difference in coefficient of thermal expansion need to be taken into account. The glass wafer used should be selected so that its coefficient of thermal expansion is as close to that of silicon as possible [62].

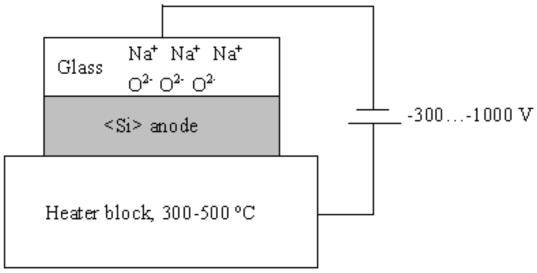


Figure 6.1: Anodic bonding. Redrawn from [12]

An indirect bonding method called polymer adhesive bonding uses polymer as intermediate layer to attach two wafers together. The advantages of this bonding technique are low processing temperature, which can be below 100 °C depending on the adhesive material. Different substrates materials can also be joined together. Since polymers are soft materials they conform to particles, which reduces the problems with voids. High bonding strengths can be achieved with relatively low price. Main disadvantage is that bonding with intermediate layer does not lead to a hermatic seal. Also the limited thermal stability of most polymers may be a problem in some applications, since only few polymers have glass transition temperature higher than 400 °C. Polymeric materials also have limited long-term stability, which can weaken the joint. [63] Adhesive bonding is also used when polymers are bond together. In this method the polymer used as intermediate layer can be the same as the bulk material.

6.2 Fabrication of enclosed ORMOCER microchannels

Different fabrication methods for enclosed microchannels have been tested for other negative resist material, SU-8 [23, 64, 65]. In Figure 6.2 two of these bonding methods are presented. In Figure 6.2 (a) fabrication of embedded SU-8 microchannel is done using a direct write proton micro machining. In this method a two different exposure are needed to form the microchannel. First, the 0.6 MeV protons are used to make the cover for embedded channels. The thickness of this cover will be about 10 μm. Second, another exposure with the 2 MeV protons is used to produce the walls of the channel. With this method the channel with wall angle of 89.6° can be produced. Main drawback of this method is that only very short channels can be fabricated since the development of the enclosed microhannels is difficult.

In Figure 6.2 (b) another method for enclosed microchannel fabrication is presented. In this process Riston®film is used to close the channel. Riston®is a photoimagable dry film for a simple and low-cost process. Main advantages of Riston®are film layer thickness uniformity and possibility of high thicknesses and multi-layer structures. On the other hand the chemical stability of Riston®is relatively poor [66]. It should also be noticed that if the channels are fabricated using Riston®film, the roof of the channel is different material as rest of the walls, which may be disadvantage in some applications.

In this work bonding method is similar to that described by Tuomikoski et al. [65]. In Tuomikoski's method the SU-8 channel wafer is fabricated prior to bonding. After that the soft baked SU-8 layer is bond to a channel wafer. Problem of this method could be that SU-8 flows inside the channel and this way changes its di-

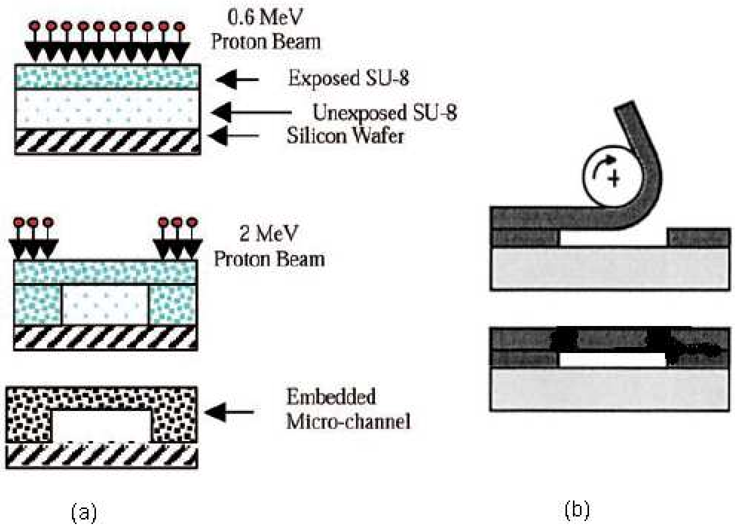


Figure 6.2: Two processes for enclosed microchannel fabrication. (a) two proton beam exposure [23] (b) channels enclosed by lamination[66]

mensions or even block the channel complitely. However with optimal processing parameters this problem may be overcome.

In Figure 6.3 a bonding process used in enclosed ORMOCER microchannel fabrication is presented. First, ORMOCER is spun on top of a transparency, which is attached to a silicon wafer with double-sided tape. This ORMOCER layer is soft baked at 80 °C for 2 min. After that the blanket ORMOCER layer is UV -exposed to polymerize it. Exposure time of 2 s is used. Because UV -exposure is not performed under inert gas atmosphere, a thin (ca. 1 μm thick) uncured ORMOCER layer remains on top of the wafer [33]. The blanket ORMOCER wafer is baked for few minutes and the transparency, with ORMOCER on top, is then detached from silicon wafer. The channel wafer and blanket ORMOCER are brought together on a hotplate (Figure 6.3b). Wafers are bonded by pressing with tweezers. After joining the wafers, the second exposure is used to bond two ORMOCER layers (Figure 6.3c). The exposure time of 10 s was used. At this point the overexposure is not a problem since no structures are being formed. Finally, the bonded wafer is baked on a hotplate for few minutes and then the transparency is removed. Removing the transparency by simply pulling it off is easy since the adhesion between the transparency and ORMOCER is weaker than between two bonded ORMOCER layers.

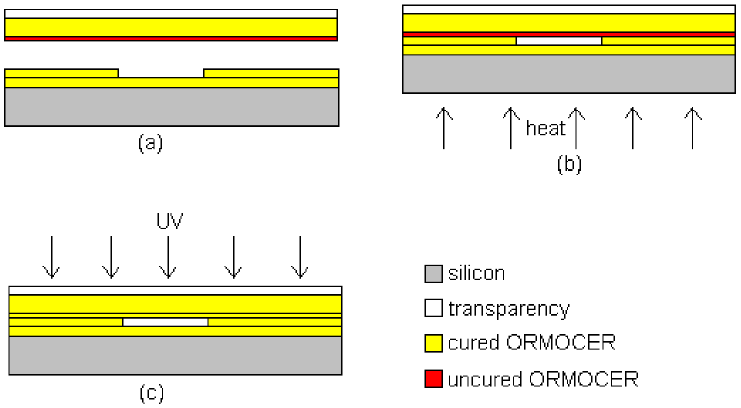


Figure 6.3: Bonding ORMOCER microchannels.

The SEM picture of bonded ORMOCOMP microchannels fabricated with UV-lithography is presented. The bonded interface looks tight. The bonding was tested by putting water into a microchannel and a evaluated with optical microscopy. The water did not leak from the channel at any point so the bonding proved to be good.

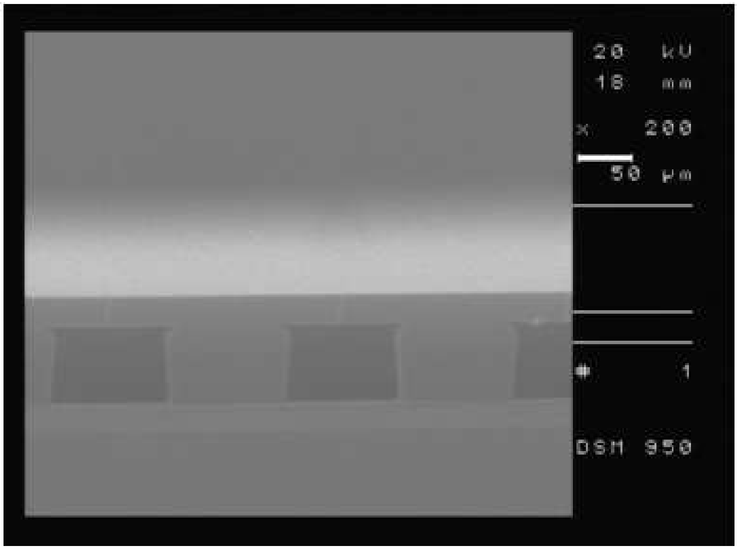


Figure 6.4: Enclosed 100 μm ORMOCER channels.

6.3 Inlet fabrication

Another difficult part in microfluidic chip fabrication is the production of inlets. There are several different possibilities for inlet fabrication. The approach used in this study was similar to that introduced in Tuomikoski's article [65]. In Figure 6.5 the schematic picture of the bonded channel wafer is presented. First, an aluminium layer is sputtered on top of a silicon wafer. This layer should be relatively thick, here 300-400 nm was used. Then the first ORMOCOMP layer is spun and inlets are patterned into it. The actual channels are in the second ORMOCOMP layer. After the second exposure the development is done. Finally, channels are closed by bonding as descibed in previous section.

The ORMOCER channel structure have to be released from the silicon wafer to release inlets. This is done by wet etching. In case of SU-8 structures, instead of using aluminium as sacrificial layer, silicon dioxide is used. To etch silicon dioxide HF has to be used. For ORMOCOMP this approach is not possible since ORMOCOMP is incompatible with HF. Aluminium is used instead and etching both with NaOH and phosphoric acid were tested. Phosphoric acid was heated to about 50 °C and the wafer was put into a solution for few hours. Areas where the aluminium was directly exposed to phosphoric acid were etched away quite rapidly. However for some reason the underetching was insignificant and the ORMOCOMP layer was not released. When using 10 M NaOH solution, the etching of exposed aluminium layer was extremely fast, but again underetching was slow. However, the NaOH solution proved to be better choice than phosphoric acid and releasing could be possible with this method. This is because the etching of aluminium was faster with NaOH and the ORMOCOMP seemed to stand it better than phosphoric acid.

Other possible method for inlet fabrication would be through wafer etching and sacrificial etching of entire wafer. Etching entire silicon wafer could be done either in NaOH or KOH solutions. The time required to etch the wafer is relatively long since the etch rate of silicon in 20% KOH, which is warned to 80 °C is about 1 μm/min. Another method, where only inlets are etched through the silicon wafer is also somewhat problematic. The etching time is naturally long, and there are some shape limitations when using wet etching.

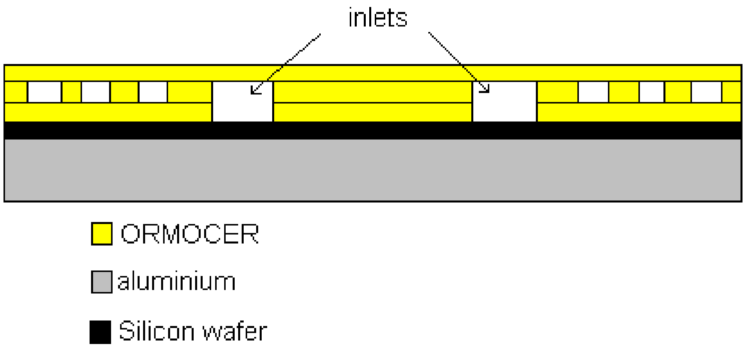


Figure 6.5: Enclosed microchannels on top of an aluminium layer.

Chapter 7

Conclusions

The processing parameters for enclosed ORMOCER microchannels have been presented. Both UV-lithography and UV-embossing have been studied to assess their possibilities and limitations. The UV-lithography has been used to produce patterns down to 20 μm. Due to high UV-sensitivity of ORMOCER no smaller patterns were able to produce with UV-lithography. UV-embossing was tested as a method to produce smaller structures. Because ORMOCOMP is solvent free it is very suitable for UV-embossing process. The structures of 5 μm in width were produced. This is small enough for most microfluidic devices.

A novel bonding method for ORMOCER channels was invented. The bonding utilizes the oxygen inhibition effect that occurs when ORMOCOMP is cured under air. Due to the nature of this bonding technique the thickness of the bond area is self-limited.

In the chemical stability tests ORMOCOMP showed suitability for several applications and its biocompatibility was tested in cell adhesion tests. The chemical stability of ORMOCOMP was good in most of the solutions tested, but it was poor in acetone and HF. Cell adhesion to ORMOCOMP surface was relatively high, which can be problematic in some applications. However, in flow channels the adhesion is significantly smaller than in static environment. ORMOCOMP could also be suitable for cell seeding scaffolds.

The inlet fabrication was also studied. Sacrificial etching of aluminium with NaOH was prooved to be the best method of those tested. However, there are still some modifications that need to be done before it can be used for dependable inlet fabrication.

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