ウェーハスケール・マイクロ流路デバイス製作のための感光性接着剤

Photo-Patternable and Adhesive Polymer for Wafer-Scale Microfluidic Device Fabrication

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ウェーハ・スケールでのマイクロ流路の製造を可能にする感光性マイクロ流路材料を開発した．この新しい材料は，シリコンウェーハ上に露光技術を用いてポリマーチャネルを作成することができるだけでなく，連続してチャネルの上に設置したガラスカバーとチャネルを熱圧着できる接着機能を合わせ持っている．IMECで設計した細胞分取（Cell Sorter）デバイスを使い感光性接着剤の材料特性評価を実施した．パターニング特性と接着強度の評価結果から，感光性接着剤；PAは，Si技術で作製したセンサデバイスとマイクロ流体をウェーハレベルで結合するために非常に有望な材料であることが分かった．

（本研究は，IMECとのJDP（Human++）の中で実施されたものである．）

A novel photo-patternable material with adhesive function for wafer-scale fabrication of polymer microfluidic devices has been developed. Not only this new material allows to fabricate polymer channels on a Si-wafer, using optical lithography, it also permits to thermically bond a glass cover on top of the channel in the same run. Evaluation of the photopatternable adhesive for wafer scale microfluidic device fabrication was done in collaboration with IMEC where an integrated microfluidic cell-sorter device was designed and processed. By studying the patterning properties and bondig strength of the new material, the photo-patternable and adhesive polymer; PA is a very promising material to combine sensor devices with microfluidics.

1 Introduction

In recent years, there is a growing interest in the development and fabrication of microfluidic Lab-on-chip（LOC）devices for a wide number of applications such as point-of-care and high-throughput screening. Material selection is a very critical step in the fabrication process of microfluidic systems. As summarised in Table 1, each of the traditionally known microfluidic materials has its advantages and drawbacks. When cheap disposable microfluidic devices are required, plastic is the material of choice. On the other hand,

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Table 1　Devices can be classified by substrate

Plastic	◆injection molded ◆low cost but also low complexity ◆Disposable ◆read-out requires separate device or instrument
Glass	◆some semiconductor processes ◆higher cost but also low complexity ◆important for sensitive fluorescent assays ◆read-out requires separate device or instrument
Silicon	◆CMOS compatible processing ◆perceived as high cost (true for low volume or prototyping) ◆potential for full integration or read-out

when more complex microfluidic devices are envisioned Si and glass are often selected. However, the process flow of both materials is rather costly and time-consuming.

Due to the increased complexity of LOC systems, where bio-sensors need to be integrated into the Si platform and need to be physically interfaced with fluid samples, there is a need for new microfluidic materials and processes which allows the easy integration of microfluidics with sensor chips (Figure 1).One of the most popular ways, until today, to combine microfluidics with sensor chips is making use of PDMS microfluidic channels

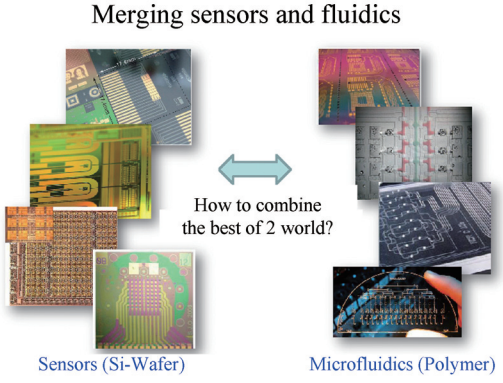


Figure 1　Material selection in the merging of sensors and microfluidics.

fabricated by soft-lithography[1]. Although PDMS has shown its value in microfluidics; it's transparent, cheap, biocompatible, it has some limitations as well, such as absorption of biomolecules, swelling in solvents, difficulties in surface modifications and mechanical stability[2]. Moreover, PDMS does not allow for wafer-scale process integration. To fulfill the need for materials allowing to merge microfluidics and sensor chips, we have developed Photo-patternable & Adhesive material; PA, which are suited to fabricate microfluidic structures directly on Si wafers. PA is highly compatible with "wafer-scale" processing, which enables the fabrication of smaller channel widths and allows for mass production.

In this paper, we demonstrate the use of PA, which can be used as microfluidic channel material and adhesive at the same time. Evaluation of the PA for wafer scale microfluidic device (cell-sorter) fabrication was done in collaboration with IMEC where an integrated microfluidic device was designed and processed.

2 Results and discussion

2.1 Guidelines for polymer microfluidics

When aiming for wafer-scale polymer microfluidics there are some important guidelines to follow. First of all, to ensure the uniform coating on Si-wafers, the polymer material should be of CMOS purity grade. Secondly, the channel walls should be as smooth as possible and should have a vertical profile. Thirdly, although strongly dependent on the application, an overall channel thickness of 20 μm to 100 μm is desired. Lastly, adhesion to heterogeneous substrates such as SiO_2 and metal films should be possible as well.

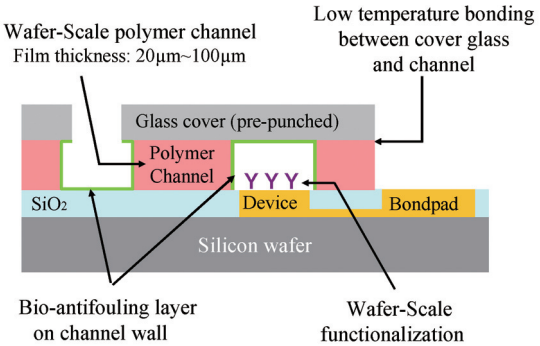
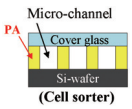
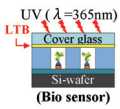
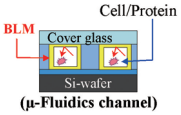


Figure 2　Requirements for polymer microfluidics.

To fabricate integrated LOC platforms according to the above described guidelines and schematically presented in Figure 2, we propose the use of three key materials as listed in Table 2. These are (1) PA for channel formation & bonding, (2) LTB (Low Tem-

Table 2 Key materials for wafer scale processing of microfluidic platforms

	(1) PA-Series	(2) LTB-Series	(3) ABF polymer
Key functions	Photo-patternable Adhesive	Low Temperature Bonding	Anti-BioFouling coating for cell/protein
	Channel & Bonding	UV cross-link	Surface change
Device Applications (Eg.)	 (Cell sorter)	 (Bio sensor)	 (μ-Fluidics channel)
Process temperature	200 ℃	<40 ℃	RT～37 ℃
Cytotoxicity evaluation	Passed	Passed	Passed

perature Bonding) to allow for low temperature bonding between the cover glass and the polymer channel, and (3) ABF polymer, an anti-biofouling coating to limit cell and protein adhesion. Depending on the device requirements a combination of these 3 materials will allow to fabricate wafer-scale polymer microfluidics. When aiming for a simple process flow, PA is the ideal material as the cover glass can be bonded to the channel directly after patterning. When using PA, channel depths are limited to 40 μm. If deeper channels, up to 100 μm, are required LTB should be used. LTB is a high transparent, solvent-free and UV-cure type polymer material. Consequently the LTB channel and cover glass can not be bonded in one-step. Therefore, and this in contrast to PA, LTB should be used again as an adhesive layer during bonding. Although the use of LTB implies a separate bonding step, bonding at lower temperatures (<37 ℃) has the big advantage that biomolecules can survive this step which happens by means of UV curing (i-line, wave length ; 365nm). Therefore, the immobilization of biomolecules for LOC based detection can be integrated into the fabrication process. To reduce the non-specific adsorption of bio-molecules to the channel walls, channels can be coated with ABF polymer which obtained by copolymerizing a hydrophilic and a hydrophilic monomer. This water soluble polymer can be flushed through the channels making them hydrophilic. Since ABF polymer is a water-based solution, coating is much simpler and faster compared to alternative coating procedures. To demonstrate the concept of wafer-scale polymer microfluidics, only the PA-series will be further explored within this paper.

2.2 Basic material properties

The successfull use of the presented materials for microfluidic applications highly depends on some basic material properties. Ideally, the materials should possess low out-gassing and low leaching properties. In case an optical detection system is being integrated in the LOC device the autofluorescence of the materials should be limited as well. However, one of the most important requirements is biocompatibility. To assess the biocompatibility of the materials, cytotoxicity tests according to ISO 10993 were conducted. Based on the results of these tests, PA was confirmed to be non-cytotoxic as shown in Figure 3, where the relative cell viability of fibroblast cells on PA was compared with the cell viability on a reference sample (polyimide), and a negative control sample (Cu).

2.3 Patterning properties of PA

To use PA as microfluidic channels, its patterning properties were thoroughly evaluated and optimized. PA is an alkali-soluble photosensitive (negative tone) epoxy acrylate material which is spin-coated in a first step on a Si wafer. Overall, the resulting film thickness is about 20 μm. The process is followed by a soft bake at 110 ℃ for 3 min. Following UV exposure (i-line aligner, 1,000mJ/cm^2 dosage) using a photolithographic mask, a post exposure bake; PEB (110 ℃/5 min) takes place. The final development (60 sec x 2 times) is done using 2.38 wt% TMAH, a standard developer in semiconductor lithography.

Figure 4 shows SEM images after development. Three different designs were processed: a short bar pattern of 50 μm x 250 μm, a square pattern of 200 μm x 200 μm, and a line pattern with 60 μm line width. All designs were successfully developed indicating the excellent resolution and patterning profile of PA.

2.4 Bonding strength evaluation

Following patterning of microfluidic channels, the channels should be bonded. To assess the bonding strength between the channels and a glass cover, both shear stress and pull stress evaluations were conducted. PA samples with a thickness of 10 μm were

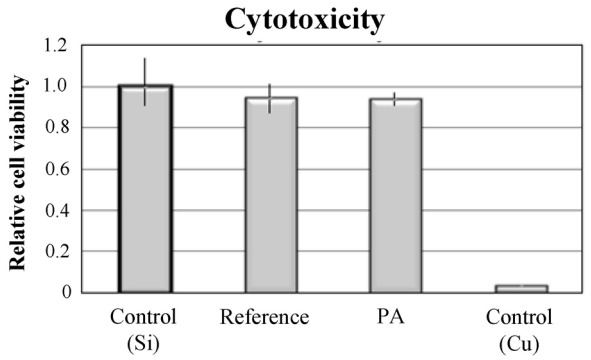


Figure 3 Comparison of the fibroblast cell viability on different materials.

Figure 4 Patterning properties of PA after development.

fabricated and bonded to a glass cover using following processing parameters:

-Soft bake: 110 ℃/3 min

-Exposure: 1,000 mJ/cm^2 (mask aligner)

-PEB: 110 ℃/5 min

-Development.: 60 sec x 1 puddle (2.38 wt% TMAH)

-Thermal bonding: 200 ℃/1.1 MPa/2 sec

-Final cure: 180 ℃/2 hours in N_2 oven

While Figure 5 schematically describes both test methods, Table 3 summarizes the results. After curing, the shear and pull strength were measured to be 22.1 MPa and 6.4 MPa, respectively. These values are considered high enough for most microfluidic system applications. The final curing step (2 hours at 180 ℃) was found to be beneficial as both the shear and pull strengths increased compared to the values before curing. It is expected that during this final curing step PA is hardenend out completely, improving the adhesion of PA to the glass cover.

2.5 Film properties of PA

Table 4 summarizes all PA film properties after final curing. Both the optical and thermal properties of PA were found to be very good. The optical transparency of 96% in the visible light region allows for the perfect alignment between the cover glass and the alignment mark on the substrate. The glass transition temperature (Tg) and the thermal decomposition temperature of PA were found to be 135 ℃ and 250 ℃, respectively indicating that PA is a promising material for microfluidic applications where a heat resistance of about 100 ℃ is required. The usability of PA for such applications will be described in the next section where PA is used for the wafer-scale processing of an integrated microfluidic cell-sorter device in collaboration with IMEC.

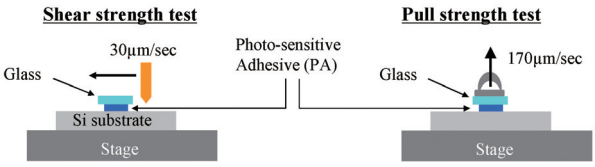


Figure 5 Schematic representation of both the shear and pull strength test.

Table 3 Shear and pull strength results before and after final curing

	Shear strength test		Pull strength test	
	Before cure	After Cure	Before cure	After cure
PA-S321	17.4MPa	**22.1MPa**	4.1MPa	**6.4MPa**

3 Wafer-scale polymer microfluidic using PA

3.1 Working principle of Imec's cell-sorter

A fully integrated LOC microfluidic device for high throughput analysis and sorting of rare cells such as CTC's (Circulated Tumor Cells) from blood was developed at IMEC. As schematically represented in Figure 6, the chip has 3 inlets, a central microfluidic channel and 3 outlets. The smallest channel width

Table 4 PA film properties after final cure

Item	Typical data
Transparency	96 % (λ= 500 nm)
Refractive Index	1.54 (λ= 408 nm)
Tg	135 ℃
CTE	93 ppm/mK
Tensile Strength	72 MPa
Elastic Modulus	2.3 GPa
Elongation	5.0 %
Decomposition temp.	250 ℃ (1 % loss)

within the design is 30 μm.

Following injection of the samples, cells will be imaged and identified within the microfluidic channel by lens-free imaging (i.e. in-flow cell tomography). Based on the identification data (i.e. red blood cell, cancer cell or other cells), the cells will be sorted into the correct outlet channel. For this purpose, two metal heaters are integrated together with the PA microfluidics on the silicon substrate as shown in Figure 6. These heaters are electrically controlled from the outside and will allow to create ultra-fast steam bubbles at hot spots which will control the fluidic action and will sort the cells on-chip. The wafer-scale processing of these devices using PA is described in the next section.

3.2 Patterning and process integration using PA

All steps for the wafer-scale processing of the device using PA are presented in Figure 7. Overall, similar processing parameters as described in section 2.3, are used. In a first step PA is uniformly spin-coated with a thickness of 30 μm across the Si wafer which is then prebaked for 3 min at 110 ℃ (A). After photo-exposure (Mask aligner) using the corresponding photo mask, a post exposure bake (PEB) (110 ℃/5 min) is carried out, after which the wafer is developed (60 sec in 2.38 wt% TMAH) resulting in the desired microfluidic pattern (B). Then, a cover glass is aligned to the alignment mark of the substrate (C). Finally, thermal bonding (200 ℃/5 MPa/2 sec.) using a pick & place tool, and curing (180 ℃/N_2/2 h) is carried out (D).

Figure 8 shows scanning electron microscopy (SEM) images of the created microfluidic channels after development. As can be seen on the pictures, the resulting PA pattern shows no residue in large openings such as the heater element area (A) or the bonding pad opening area (B). Moreover, the pattern profile looks steep (C) and the polymer surface looks smooth and clean.

Figure 9 shows a photograph of the final devices processed on a 8-inch wafer. Each die size is 2.2 cm x 4.2 cm and is covered by a 2 cm x 4 cm glass cover with pre-punched access holes. The glass cover is automatically bonded on the PA channels by a "pick and placement" bonding tool.

Using the proof-of-concept integrated cell-sorting de-

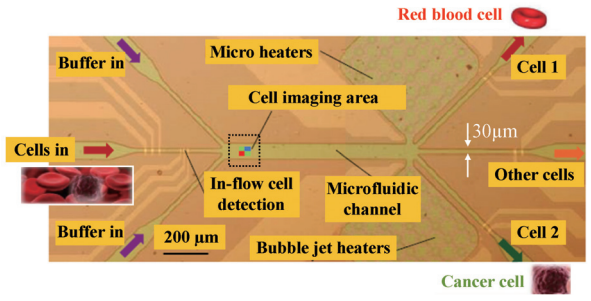


Figure 6 Schematic representation of cell sorter device.

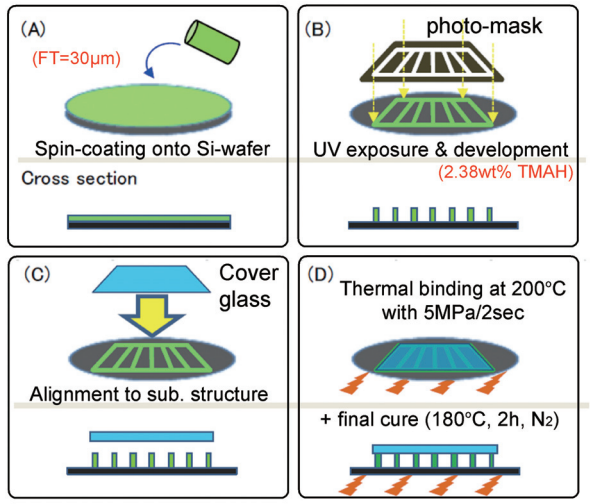


Figure 7 Wafer-scale process integration for IMEC cell sorter.

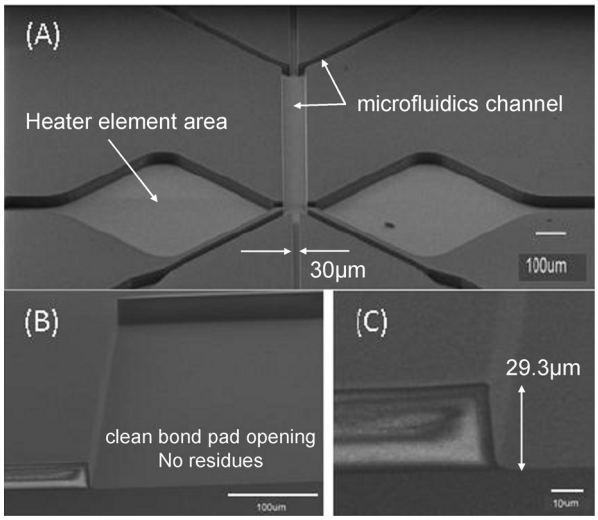


Figure 8 SEM pictures of patterned PA microfluidic channels.

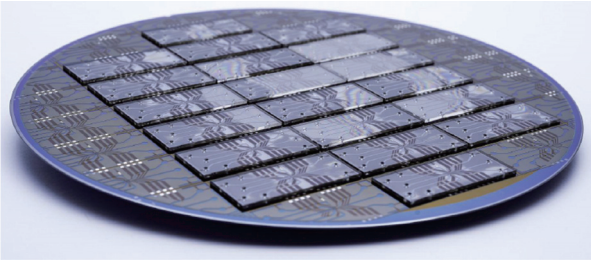


Figure 9　Picture of bonded wafer-scale (8-inch) processed PA cell-sorter devices.

vice, it was able to sort 2,000cells/sec. Currently further improvements in the design are being implemented to improve the performance of the device.

4 Conclusion

To combine the best of 2 worlds namely sensors and microfluidics, new materials were described and evaluated in this study. The use of these materials for wafer-scale microfluidic device fabrication was demonstrated using PA. Basic material evaluation showed that PA fulfilled all requirements to be used as microfluidic material(i.e. non-cytotoxic, heat resistant, transparency, low out-gassing, low leaching, and no unwanted interaction with biochemistry). The resolution and patterning properties of PA was found to be excellent as well. As a proof-of-concept, PA was succesfully used to process a fully integrated LOC microfluidic cell-sorter device in collaboration with IMEC. Cell-sorting experiments using these devices, show that wafer-scale polymer microfluidics as described in this report, offers an easy, fast solution for the mass fabrication of LOC microfluidic devices.

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