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TECHNICAL NOTE

Adhesive bonding of microfluidic chips: influence of process parameters

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Abstract
In this note, the influence of process parameters for adhesive bonding as a versatile approach for the sealing of polymer microfluidic chips is investigated. Specifically, a process chain comprising pre-processing, adhesive transfer as well as post-processing is presented and parameter recommendations are provided. As a device for adhesive transfer, a modified laminator is utilized which transfers thin layers of adhesive onto the chip surface, only via a silicone roll. Using this device and a high temperature (Tg > 100 °C) epoxy adhesive, adhesive layers in the range of 2–4 μm can be reproducibly transferred (CV < 4%). For best bonding results, it is recommended to provide 2.5 μm thin layers of adhesive in combination with a subsequent evacuation step at 10 mbar for 3 h. Further, it is proposed to integrate capture channels near large, featureless areas to compensate for variations in processing and thus prevent clogging of channels.

(Some figures in this article are in colour only in the electronic version)

1. Introduction

So-called lab-on-a-chip systems for diagnostic technologies attract a growing interest due to their immanent benefits of reduced turn-around times, increased reliability and minimized costs [1]. For some time, there has been a strong trend towards disposable polymer labs-on-a-chip [2–4] specifically due to their amenability for low-cost mass production. The bonding of polymer substrates however can prove to be highly challenging and can ultimately decide on the functioning or even commercial success of the chip [5].

Multiple approaches for bonding of microfluidic chips like laser welding [6], thermal bonding [7] or adhesive bonding [6, 8–13] currently exist. Depending on the boundary conditions for lab-on-a-chip development, e.g. material used, different approaches are more or less feasible and providing a universal approach for different applications is a non-trivial task but still highly desirable. Laser welding for example requires an absorber at the interface between the chip and lid [6] while thermal bonding requires high temperatures or specific material combinations [7]. Thus, bonding via adhesives is still the most uniform approach as it primarily relies on the wetting of the chip surface by the adhesive and is therefore applicable on various polymer materials.

A standard approach for adhesive bonding is the coating of the lid with adhesive. This way however, a large amount of the adhesive gets in direct contact with the sample. Further, no bioreagents can be immobilized on the lid. Thus, different approaches to only selectively cover the chip surface with adhesive have been reported, namely contact printing [6, 9, 10, 13], the use of guide channels [8, 12] or by a laminator [11]. The so far presented work allows for selecting a
general approach for bonding. However, in most cases no quantitative data or in-depth investigation has been provided which prevents a head start in bonding development. This work therefore investigates the influence of different process parameters for the adhesive bonding of a microfluidic test chip while trying to abstract the parameters from the utilized device and chip geometry.

2. Materials and methods

2.1. Microfluidic test chip

The chip with outer dimensions of standard microscope slides comprises eight parallel channels with a sample volume of 7.5 μL each (figure 1). The reaction area features a width/depth of 500 μm while the supply channels exhibit a width/depth of 200 μm. The chips are currently fabricated by CNC-micromachining from a cyclic olefin polymer (COP, E480R, Zeonor, Zeonex Corporation). The chip assembly additionally comprises a lid (1 mm thick, made from E480R, not shown).

2.2. Pre-processing

Before bonding, the chip and lid are first ultrasonicated for 10′ in 2-propanol to remove debris from the channels. This is followed by a drying step utilizing pressurized nitrogen. Finally, the surfaces to be bonded are activated in an oxygen plasma for 4′ with a power of 200 W (Picollo, Plasma Electronic, Germany).

2.3. Adhesive

For adhesive bonding, reactive adhesives (two-component, e.g. epoxy) [6, 9, 10] and UV-curable adhesives [8, 11–13] are most frequently applied. However, the UV light in the bonding process of the latter can possibly denature stored bioreagents on the lid can thus be prevented. When the substrate comes into contact with the rotating transfer roll, about half of the amount of adhesive present on the roll will be taken up by the chip. Thus, the process is independent of the chip features. The transferred amount of adhesive depends on the distance between the definition roll and the transfer roll, the viscosity of the adhesive as well as the transport velocity. For a fixed distance, the layer thickness can be extrapolated according to [14] as \( d_{\text{adh}} \sim (\eta_{\text{adh}} \cdot v_{\text{roll}})^{0.64} \).

As a device, a custom-built laminator is utilized (NMI, Germany) [11]. It features an aluminum (Al) definition roll and a silicone transfer as well as a transport roll. The process is abstracted from the device by measuring the influence parameters, i.e. adhesive layer thickness, transport velocity and distance between the substrate and roll. Thus, the results are applicable for arbitrary laminators based on a soft (e.g. silicone or rubber) transfer roll.

2.4. Adhesive transfer

The applied technology is based on the previously presented transfer of an adhesive layer onto the microfluidic chip via rolls [11]. Any contact between the adhesive layer and bioreagents on the lid can thus be prevented. When the substrate comes into contact with the rotating transfer roll, about half of the amount of adhesive present on the roll will be taken up by the chip. Thus, the process is independent of the chip features. The transferred amount of adhesive depends on the distance between the definition roll and the transfer roll, the viscosity of the adhesive as well as the transport velocity. For a fixed distance, the layer thickness can be extrapolated according to [14] as \( d_{\text{adh}} \sim (\eta_{\text{adh}} \cdot v_{\text{roll}})^{0.64} \).

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2.5. Adhesive layer thickness

The amount of adhesive is measured gravimetrically using a high-precision microbalance (SC2, Sartorius, Germany) and the layer thickness is extrapolated based on these data. For a good wetting (i.e. activated) surface, a homogenous distribution of adhesive over the chip surface can be assumed.

2.6. Post-processing

After adhesive transfer, the chip is placed in an Al chip holder (not shown) comprising cavities for the chip/lid assembly. The depth of the cavities is 200 μm less than the total thickness of the assembly. Then, the lid is aligned on top of the chip. An Al plate is subsequently pressed on the holder via screw clamps (Bessey, Germany) which are able to exert a force > 1 kN. The chip holder is then evacuated to 10 mbar. Finally, the chip holder is put into a lab furnace (Binder, Germany) for 3 h at 70 °C for curing.

Figure 1. Microfluidic test chip featuring eight parallel channels comprising inlets, reaction areas and vents. The capture channels are discussed in section 3.3.
3. Experimental results

3.1. Adhesive layer thickness

With the selected adhesive and device, the minimum transferred layer thickness amounts to 3.5 μm. This can be explained by the incompressibility of the adhesive and the elasticity of the transfer roll. For achieving thinner layers, a larger amount is first transferred onto the chip surface followed by a second run through the laminator with no adhesive present thus effectively halving the amount of adhesive on the chip surface. Alternatively, an additional roll could be installed on the laminator. The results of the adhesive transfer, exhibiting a good reproducibility (coefficient of variation CV ⩽ 4%), are summarized in figure 2. Further, it has been evaluated that for a given transfer roll velocity of 20 mm s⁻¹, the transferred layer thickness is basically independent of the feeding orientation of the chip into the laminator (tested for one channel does not result in chip failure. Thus, the results of the selected adhesive and device, the minimum transferred layer thickness amounts to 3.5 μm. This can be explained by the incompressibility of the adhesive and the elasticity of the transfer roll. For achieving thinner layers, a larger amount is first transferred onto the chip surface followed by a second run through the laminator with no adhesive present thus effectively halving the amount of adhesive on the chip surface. Alternatively, an additional roll could be installed on the laminator. The results of the adhesive transfer, exhibiting a good reproducibility (coefficient of variation CV ⩽ 4%), are summarized in figure 2. Further, it has been evaluated that for a given transfer roll velocity of 20 mm s⁻¹, the transferred layer thickness is basically independent of the feeding orientation of the chip into the laminator (tested for a given transfer roll velocity of 20 mm s⁻¹). Additionally, the same amount of adhesive is transferred onto the smaller features (500 μm wide spacers between the channels in the center chip area) as well as on the outer chip area. However, a small adhesive meniscus may be present at the interface between channel and lid.

3.2. Bonding influence parameters

For successfully bonding microfluidic chips, a high number of influence parameters have to be taken into account. The primary parameters for adhesive bonding, their influence and possible consequences are summarized in table 1 (in the order of processing). It should be noted that the chip design is the major influence parameter for bonding, i.e. chips featuring large (>1 mm) and deep (>500 μm) channels, only, will require less bonding process development due to the reduced risk of clogging than chips comprising small (⩽500 μm) and shallow (⩽200 μm) channels as well as isolated features. The other parameters of major influence are evaluated in the following section except for chip surface planarity and surface activation. The latter can be considered binary because either there is adhesion or not which depends on the wetting properties of the adhesive on the chip material. The chip surface planarity can be a major issue when using injection-molded chips specifically if the master exhibits two layers of different heights on the chip surface to facilitate fabrication. Then, the amount of transferred adhesive must be sufficient to compensate for the height difference. This however increases the risk of channel clogging.

For the parameters of minor influence, the rinsing, cleanliness of atmosphere as well as the alignment relate to the processing in general or handling. A variation in thickness, if existent, requires the bonding partners to be in intimate contact during post-processing and cure. For ideal substrates (e.g. silicon wafers), the basic adhesion between chip, adhesive and lid may be sufficient to result in a strong bond. The following can be seen as a rule of thumb for adhesive bonding: the less ideal the surfaces of the bonding partners, the more the pressure and/or adhesive is required.

3.3. Chip bonding results

In general, all successfully bonded chips did not exhibit any leakage even if operated for 2 h at 100 °C with an overpressure of 4 bar. Further, no cross-flow between channels could be observed (12 h @ 4 bar) when alternatingly priming the eight channels with dyed liquid and DI-water.

For the presented test chip, the different microfluidic channels can be seen as independent units, i.e. clogging of one channel does not result in chip failure. Thus, the results of the bonding have been classified in the following way.

![Figure 2. Extrapolated adhesive layer thicknesses. The three lower values were achieved by moving adhesive-covered substrates through the laminator without any adhesive on the transfer roll.](image-url)
of the capture channels should be equal to or smaller than the shallowest or least wide functional channel. Otherwise, excess adhesive would flow into channels exhibiting the highest capillary pressure and not into the capture channels. Additionally, it could be feasible to add a vent to each capture channel to further promote the adhesive flow and thus the collection of excess adhesive.

It should be noted that a yield $>90\%$ has not been achieved so far (table 2). Still, it should be possible by optimizing the position of the capture channels.

For the less viscous adhesive (Epo-Tek 302-3M), about the same layer thickness has to be transferred with respect to the primarily evaluated adhesive (Epo-Tek 375) to achieve perfect bonding results based on chips featuring capture channels. The failed chips correlate to the increased risk of channel clogging.

### 3.4. Process chain

- Ultrasonicate chips for 10’ in 2-propanol
- Dry with pressurized nitrogen
- Surface activation in O$_2$ plasma, 4 min, 200 W
- Transfer 2.5 $\mu$m of Epo-Tek 375 onto the chip surface
- Align the chip and lid in the chip holder
- Apply force $>1$ kN on chip assemblies
- Evacuate assembly for 3 h @ 10 mbar
- Cure assembly for 3 h @ 70 $^\circ$C

### 4. Conclusion

In this note, the influence parameters for the adhesive bonding of polymer chips have been evaluated. Consequently, a process chain with parameter recommendations is provided which can greatly reduce the time and costs for bonding development of a custom lab-on-a-chip. Further, the bonding principle in combination with the selected adhesive allows for applications where high temperature stability and reagent storage on-chip are required e.g. a solid-phase PCR.
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References