3D MICROFLUIDIC CARTRIDGES BY GAS PRESSURE ASSISTED THERMAL BONDING OF MICROTHERMOFORMED FILMS

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ABSTRACT

Microthermoforming of film substrates is an emerging technology to form thin-walled microfluidic Lab-on-a-Chip cartridges. We present a process chain to fabricate thin-walled 3D microfluidic cartridges by thermally bonding a stack of microthermoformed polymer layers. The three layer bond stack comprises an upper and a lower microthermoformed film substrate separated by a flat intermediate film layer. For thermal bonding the films are pressed together by gas pressure, eliminating the need for any structure dependent tools. The capabilities of the process chain are demonstrated by bonding a complex microfluidic LabDisk demanding two stacked fluidic layers on top of each other.

KEYWORDS

Lab-on-a-Foil; Gas pressure assisted bonding; Thermal bonding; 3D microfluidic cartridge; co-extruded film; Cyclic Olefine Copolymer; COC; Microfluidic LabDisk; SAXS-CD

INTRODUCTION

Inspired by the success of macroscopic blister packaging (e.g. pill packages) microthermoforming concepts have been presented in the past that are able to form microfluidic structures with a high geometric fidelity [1,2]. The technology enables to replicate structures ranging from sub-micrometer up to multiple millimeters in size. The thin walls for variotherm microfluidic applications and the minimal material consumption are unique features of the technology.

The published microthermoforming concepts heat polymer films above their glass transition temperature and apply a gas pressure to form the film onto a mold. Two different kinds of molds are commonly used, positive and negative molds. Negative molds have cavities in which the film is molded. Thus, the outside of the film is well defined by the negative mold, and the fluidic features on the inside depend on the stretching ratio of the film and the corresponding film thickness. In contrast, positive molds have elevated structures to shape the microfluidic features directly. This enables precise replication of microfluidic channels and cavities but results in less defined outer contours.

To create microfluidic channels sealing with a cover film is needed. For sealing of macroscopic blister packages special bond tools that serve as counterpart of the thermoformed film are used. In the microscale this approach is limited to negatively formed films only, which can be directly sealed within their mold. For positively molded films such counterparts are not feasible. To ensure proper bonding of all microchannels up to the very edge of each channel the bond tool has to match the outer contour of the films precisely. Instead of using costly microstructured bond tools the authors have introduced a novel approach that uses gas pressure as a structure independent counterpart for bonding of positively microthermoformed films [3]. So far bonding of one microfluidic layer with an unstructured cover film has been demonstrated successfully. More complex microfluidic applications, however, require two or more microfluidic layers stacked on top of each other. An example for such an application is the combinatorial dilution of liquids in different ratios [4]. Here we present a new method to realize 3D microfluidic cartridges by bonding two positively microthermoformed microfluidic layers to a third intermediate film. Functionality of the new method is demonstrated by fabrication of a 3D microfluidic LabDisk that automates the combinatorial dilution of three liquids.

3D MICROFLUIDIC LABDISK

A centrifugal microfluidic LabDisk for combinatorial dilution of three liquids serves as example for a complex microfluidic application that requires two microfluidic layers [4] (Fig. 1).

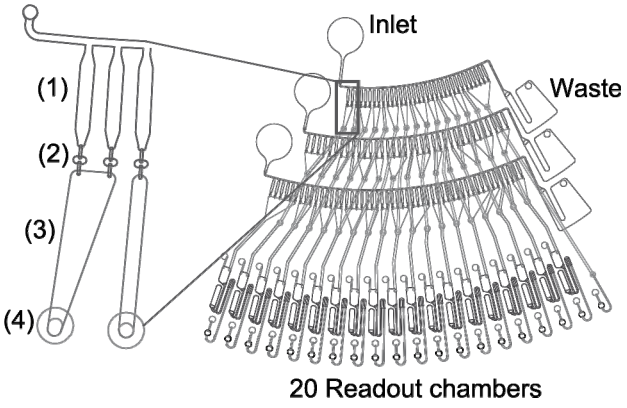

Figure 1: LabDisk for combinatorial dilution of liquids with two fluidic layers. Shown is one 60° segment. (1) 40 aliquoting fingers for each of the three liquids; (2) Geometric valves; (3) Fluidic structure combining aliquots to define mixing ratios; (4) Vias between first and second fluidic layer.

The LabDisk dilutes 3 µl of three liquids into 20 different ratios. First each of the three liquids is splitted into multiple 40 nl aliquots. Geometric valves are implemented to transfer the aliquots downstream, where they are combined and mixed. The mixing ratios are achieved by transferring six of the 40 nl aliquots into each of the 20 readout chambers.

GAS PRESSURE ASSISTED BONDING

Preparation

Prior to bonding each of the two microfluidic layers of the 3D microfluidic LabDisk is microthermoformed by soft lithography (µTSL), using a positive silicone mold [5]. This ensures precise replication of micro and macro features inside microfluidic channels and cavities, as well as a defined and flat bond surface.

To realize the 3D microfluidic LabDisk the two microfluidic layers are bonded against an unstructured flat intermediate layer. The intermediate layer separates the fluidic layers and has CNC drilled vias. The vias transfer the fluids from one layer to another enabling the complex mixing paths required for the combinatorial dilution. The vias are 500 µm in diameter and up to 20 intermediate film layers can be stacked and drilled in one process step.

Bond concept

For bonding of the film substrates a thermal bond approach is selected. Thermal diffusion bonding allows high bond strengths and obviates the use of adhesives, which may interfere with the fluidic application.

Thermal bonding is achieved by (1) aligning the bond partners, (2) pressing them together and (3) applying heat, sufficiently low to not deform any microchannel.

In a first step alignment of all three layers is done using self-alignment structures. The alignment structures are designed as a pin and pinhole and are thermoformed into the film substrates. By clipping the films into each other the fluidic layers are aligned. The intermediate layer has through holes and also self-aligns with the pins.

The bond force is applied by a gas pressure. The gas distributes the bond pressure independently from the 3D geometry of the upper and lower microthermoformed film. Thus, one single bond setup can be used for different microfluidic designs within a predefined disk format or chip area. This renders the process to be ideally suited already for prototyping of microfluidic chips, which usually requires layout iterations with many different designs to be fabricated.

To avoid any channel deformation during thermal bonding a special selection of materials is required. Usually thermally bonded polymer substrates suffer from deformations, since they are heated above their glass transition temperature (Tg). By using co-extruded films as microthermoformed substrates, this issue can be avoided (Fig 2).

The selected 200 µm thick co-extruded Cyclic Olefine Copolymer (COC) film features a temperature stable Topas COC 6013 layer and a roughly 10 µm thin Topas COC 8007 layer on top. While COC 6013 with its higher glass transition temperature (Tg ~ 135 °C) preserves the shape, the lower melting grade COC 8007 (Tg ~ 79 °C) acts as hot melt. The co-extruded films are bonded against a pure 140 µm thick Topas COC 8007 intermediate film layer. Thus, all channel walls feature the same material. In case of the intermediate film deformation issues are not expected, since the film is unstructured and equal forces from both sides will level out during bonding.

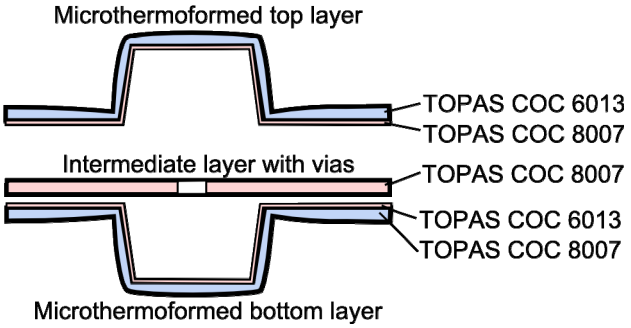

Figure 2: Bond stack comprising two microthermoformed co-extruded films and a flat intermediate layer; the low Tg material COC 8007 acts as hot melt, while the high Tg COC 6013 preserves the geometry.

Bond setup and parameters

The bond setup is depicted in Fig. 3 and comprises two bond tools. Both tools are made of aluminum and are mounted into a custom-made hot embossing machine (Wickert Maschinenbau GmbH, Germany). The top and bottom tool are designed to clamp the film stack at the outer rim of the disk and at unstructured areas. Additionally each tool is connected with a controllable gas pressure supply.

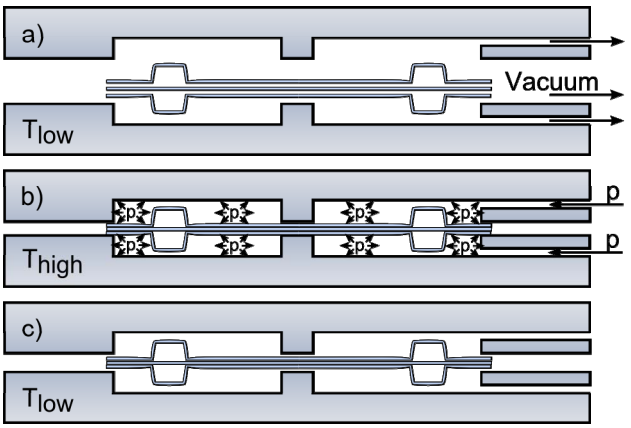

Figure 3: Bond setup; a) films are placed between an upper and a lower bond tool and vacuum is applied; b) after clamping, vacuum remains within the structures; a pressure p is applied to press the bond partners together and the setup is heated. c) After cooling, the bonded films can be retrieved.

The bond process starts with aligning the films by clipping the self-alignment pins into each other. Afterwards the stack of (1) a thermoformed film at the bottom, (2) an unstructured flat intermediate layer with vias in the middle, and (3) a second thermoformed film on top are placed into the bond setup. The whole setup is

evacuated, avoiding entrapped air between the bond partners. After clamping the bond stack between the bond tools an overpressure is applied at both tools. In this stage vacuum is still entrapped within the fluidic structures. The applied gas pressure of absolute 2 bars induces the required bond force. By heating the setup from 80 °C to 125 °C within 90 second the low Tg grade COC 8007 softens and bonds. The temperature is held for 2 min and cooled down to 80 °C subsequently.

Bond results and discussion

A bonded segment of the combinatorial dilution LabDisk is shown in Fig. 4. The optically absolutely clear appearance indicates good thermal bonding. Large cavities such as inlet structures and waste chambers remained their geometry. Small features such as aliquoting fingers with a spacing of 200 µm between each other are also bonded without leakage.

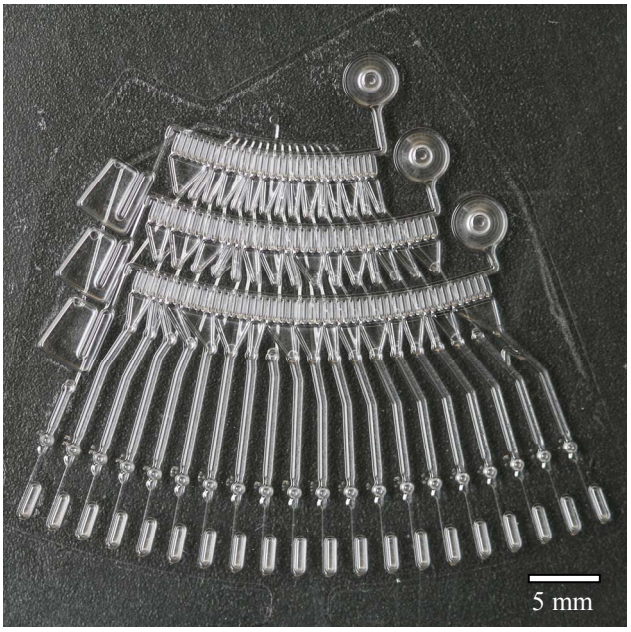

Figure 4: Bonded 3D microfluidic LabDisk for combinatorial dilution of three liquids. Liquids are aliquoted in a first fluidic layer, routing of the liquids to obtain the defined mixing ratios in the reaction chambers takes place in a second fluidic layer on the backside.

To evaluate the gas pressure assisted thermal bonding concept four aspects are assessed: (1) proper alignment of the fluidic layers, (2) robustness to channel deformation, (3) bond quality of overlapping channels and (4) the microfluidic functionality.

The alignment of the bonded fluidic layers is achieved by self-alignment structures. The two fluidic layers on top and bottom line up precisely with an alignment error of less than 20 µm. The 500 µm vias within the intermediate layer connect the 200 µm channels of the two fluidic layers (Fig. 5). Smaller vias could be implemented, but smaller drills limit the amount of intermediate film layers which can be drilled at the same time.

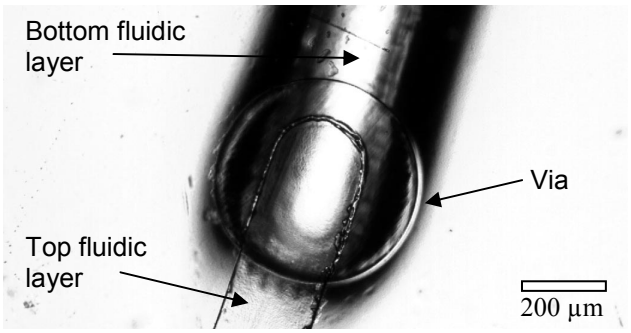

Figure 5: One of the aligned interconnections between first and second fluidic layer.

Possible channel deformation has been studied by examining cuts of different fluidic structures. As characteristic features the cross sections of the aliquoting fingers, the geometric valves and the fluidic structures for defining the mixing ratios are chosen.

The aliquoting fingers represent a set of small chambers with a volume of 40 nl and a spacing of only 200 µm between each other. Deformation of these chambers would reduce the metering accuracy. For the same reason bond defects between the fingers are not tolerable. Fig. 6 (a) shows the fluidic layer prior to bonding (left) and a cross section after bonding (right). The aliquoting fingers are bonded to the very edge of each channel wall and maintained the rectangular channel cross section.

The geometric valve is the smallest feature. A 50 µm x 25 µm channel is widened instantaneously (Fig. 6 (b)). Capillary forces then stop the liquid at the sudden expansion. Clogging or deformations of the valve would cause failure or a shift in the centrifugal microfluidic frequency protocol. The cut in Fig. 6 (b) shows no visible deformation of the valve geometry after bonding.

Third, larger features have been investigated. While the small features so far are well supported by the surrounding film material, larger shallow features are more likely to bend. However, the selected 200 µm deep fluidic structure with an aspect ratio of 0.2 does not show any visible deformation of the cross section either (Fig. 6 (c)).

Besides the geometric stability of the bonded films the bond quality of overlapping channels has been investigated. Fig. 6 (a) and (c) show 200 µm x 50 µm microchannels on the bottom layer which are right underneath of fluidic structures on the top layer. Optical inspection and fluidic tests with colored fluids approved leak tight bonding. In case of the overlapping channels it needs to be pointed out, that the bond pressure to press the intermediate layer against the bottom layer cannot be distributed through the hollow top film layer directly. For the tested features with small dimensions of 200 µm x 50 µm this was not an issue, though. The indirectly distributed forces have been strong enough to bond the COC-films. For larger cavities in the range of a few millimeters this effect could be more critical.

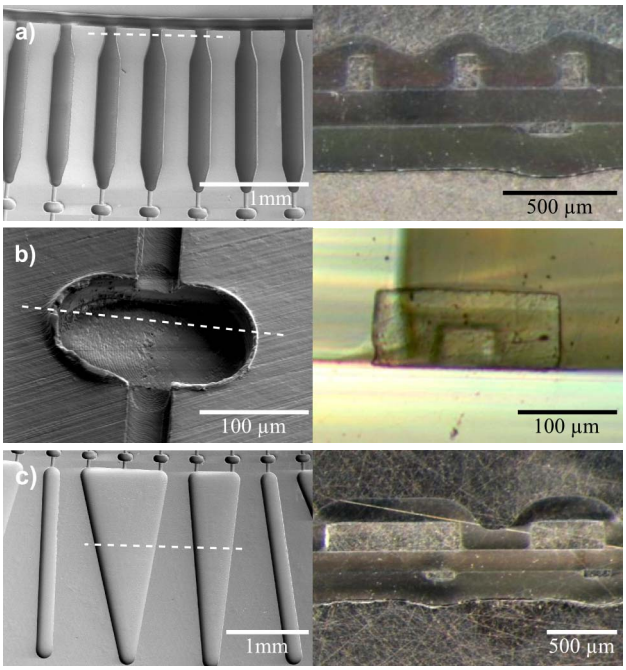

Figure 6: SEM micrographs of fluidic structures (left) and optical microscope pictures from cross sections of bonded films at the dashed lines (right); a) aliquoting fingers; b) geometric valve; c) fluidic structures for combining aliquots in pre-defined mixing ratios.

In a last step the bond quality has been proven by demonstrating a microfluidic application. The inlets of the 3D microfluidic dilution LabDisk are cut open with a scalpel. Thus, the vacuum within the structures is vented and the liquids can be pipetted into the system. The three fluids are aliquoted and routed in different ratios towards the reaction chambers, without any leakage. The maximum fluid pressure was calculated to be 0.2 bar. The fluidic processing of the film based 3D microfluidic cartridge showed similar behavior as previous micromilled substrates [4]. Time consuming milling steps which exceed 24 h for each LabDisk with the demonstrated design can be eliminated with the new fabrication approach.

CONCLUSION

We presented a bond process which enables to fabricate thin-walled 3D microfluidic cartridges. Two microstructured polymer layers have been bonded with a planar intermediate layer to form microfluidic cartridges with 3D geometries. The bonding force has been applied via gas pressure which bonds the films independently from their shape, eliminating the need for individual design-specific bond tools.

The process chain facilitates fabrication of small prototyping series and allows fast design iterations without any tool adaptations. As a proof of concept a complex microfluidic LabDisk for preparation of combinatorial dilutions was manufactured and tested. Successfully bonded features have been in the range of 50 µm up to several millimeters.

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