Microthermoforming and Sealing of COP Films to Form Thin Walled Lab-on-a-chip Cartridges

D. Kosse[a], M. Focke[b], C. Müller[c], F. von Stetten[a,b] and R. Zengerle[a,b]

[a] *HSG-IMIT, Wilhem-Schickard-Straße 10, 78052 Villingen, Germany*
[b] *Laboratory for MEMS Applications, IMTEK, University of Freiburg, Germany*
[c] *Laboratory for Process Technology, IMTEK, University of Freiburg, Germany*

Abstract

This paper describes a process chain to form and seal thermoplastic films to obtain enclosed microfluidic cartridges with thin walls. Especially applications requiring fast thermocycling such as polymerase chain reaction (PCR) highly benefit from this lab-on-a-foil approach, due to an improved heat transfer. The cartridge fabrication is a two-step process comprising microthermoforming by soft lithography followed by a novel gas pressure assisted thermal sealing. As film material a 188 µm thick cyclic olefin polymer (COP) is used, which is microthermoformed over a male Polydimethylsiloxane (PDMS) mold to shape the intended thin walled microstructures. The process parameters have been optimized and feature sizes in the range of a few micrometers to millimeters with aspect ratios up to three are replicated. The forming of the thermoplastic film is caused by heating the film above glass transition temperature (T_g) and applying a gas pressure of 310 kPa. After cooling and demolding the COP structures are thermally sealed with a special coextruded COC film. The coextruded film consists of a temperature stable TOPAS COC 6013 (T_g ~ 135 °C) layer and a thin layer of TOPAS COC 8007 (T_g ~ 79 °C) acting like hot melt. An additional mold for bond support, which is commonly needed for positive thermoformed structures, has been eliminated by a gas pressure assisted bonding approach. The processes enable fast and flexible prototyping of thin walled microfluidic cartridges within 8 – 10 hours.

Keywords: Lab-on-a-Chip, Lab-on-a-Foil, microthermoforming, bonding, sealing.

1. Introduction

Within the past years a trend towards polymer film or sheet based lab-on-a-chip cartridges so called lab-on-a-foil systems can be observed [1, 2, 3]. Especially the need for thin walls for efficient thermocycling or the mechanical flexibility for new reagent release mechanisms and valving concepts favour film based lab-on-a-chip cartridges over rigid substrates structured by injection molding or hot embossing.

The presented prototyping approach to microstructure and seal thin walled lab-on-a-chip cartridges is inspired by the blister packaging technology, well known from pharmaceutical pill packaging. In contrast to the established macroscopic blisters, the microfluidic applications set much higher geometric requirements. Especially the inner fluidic channel or cavity geometries have to be shaped precisely to guarantee critical metering volumes or to avoid round corners at fluidic intersections or geometric valves.

Earlier approaches to form microstructures by microthermoforming have been demonstrated using negative (female) molds [4, 5]. While the outside of the film structures are defined by the negative mold, the critical inner channel geometry is additionally depended on the degree of film stretching. Sealing is done easily using the thermoform mold as bond support. The demand for defined inner fluidic geometries and sharply formed fluidic features limits the use of negative molds, though.

Alternatively positive male molds have been demonstrated for microthermoforming [6]. While the fluidic features can be formed precisely, the sealing afterwards is critically due to a lack of adequate bond support. In contrast to macroscopic blister which may tolerate unbonded areas in distance of one millimeter around each blister, microstructures have to be sealed tightly up to the very edge of each channel. A feasible fabrication method for bond molds for positive formed microstructures has not been shown, yet.

The presented two-step fabrication process over comes this challenge by introducing a novel gas pressure assisted thermal bond concept to bond positively thermoformed microstructures. An induced gas pressure eliminates the need for molds for bond support and is used to seal films structure independently.

2. Microthermoforming by soft lithography

2.1. Process description

The structuring of the thermoplastic films is accomplished by microthermoforming by soft lithography [7]

Proceedings of the 8th International Conference on Multi-Material Micro Manufacture
Edited by Heinz Kück, Holger Reinecke and Stefan Dimov

ISBN: 978-981-07-0319-6 :: doi:10.3850/978-981-07-0319-6_204

(see Fig. 1). Starting from a computer aided design (CAD) a master tool is fabricated, which shows the same structures as the intended lab-on-a-foil cartridge. Then an inverted male mold is cast with PDMS (Elastosil RT 607, Wacker Chemie). After curing at 80 °C for 30 minutes, the PDMS is demolded and additionally stored for 60 minutes at 200 °C for post-curing and outgasing. Afterwards the PDMS mold can be used to replicate the thermoplastic films.

For film replication a modified hot embossing machine (HEX01, Jenoptik AG, Germany) is used. The PDMS mold is placed into a lower tool holder and the film substrate is placed on top. In this case a cyclic olefin polymer film (COP ZF 14, Zeon Chemicals) is used with a thickness of 188 µm and a glass transition temperature of T_g ~ 135 °C. After heating up to an evacuation temperature T_e the setup is evacuated to avoid entrapped air between mold tool and the COP film, which can occur if the COP softens and sticks to the lower tool holder.

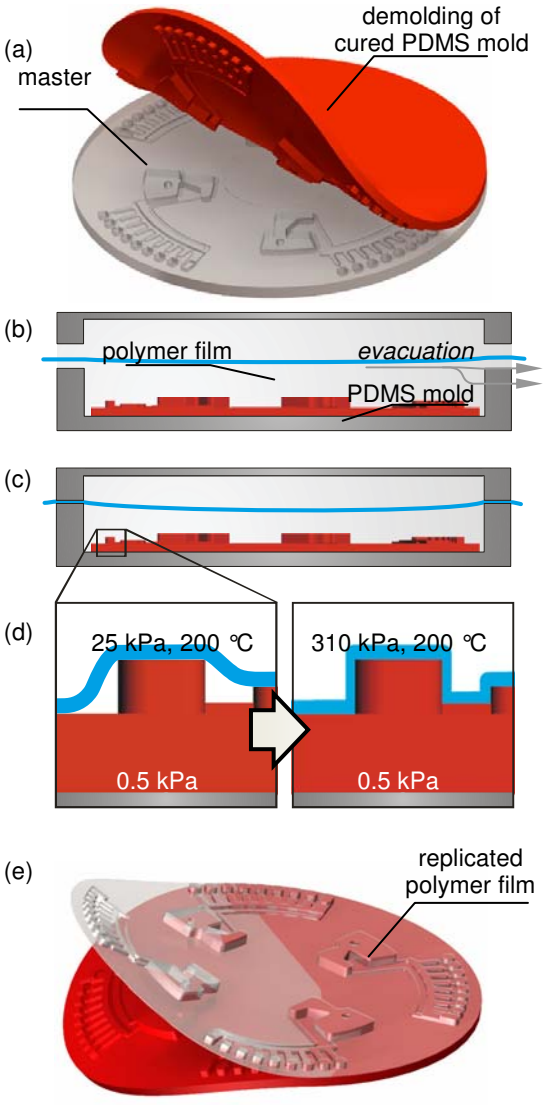

Fig 1. Microthermoforming process including mold fabrication. (a) Fabrication of the PDMS mold; (b) assembly in a modified hot embossing machine and evacuation; (c) clamping of the polymer film in vacuum; (d) molding of the film through application of a pressure difference at molding temperature; and (e) demolding after cooling, venting.

After evacuation the setup is heated up to molding temperature T_m and the film is clamped between the tool holder and an upper tool. T_m is material depended and has been evaluated for COP as 200 °C. After reaching T_m a pre-pressure p_1 is applied above the polymer film and held for a time t_1 to form the film onto the PDMS mold. A second main pressure p_2 assures the forming of critical structures such as sharp edges and corners and is held for a time t_2. Afterwards the setup is cooled down, vented and the thermoformed COP film is demolded. Afterwards the PDMS mold can be replicated again.

2.2. Process optimization and results

Process optimization was done using methods of design of experiments (DOE). Five defined critical geometric feature sizes within a set of microfluidic sample structures shown in Fig 2 have been evaluated for optimization purpose.

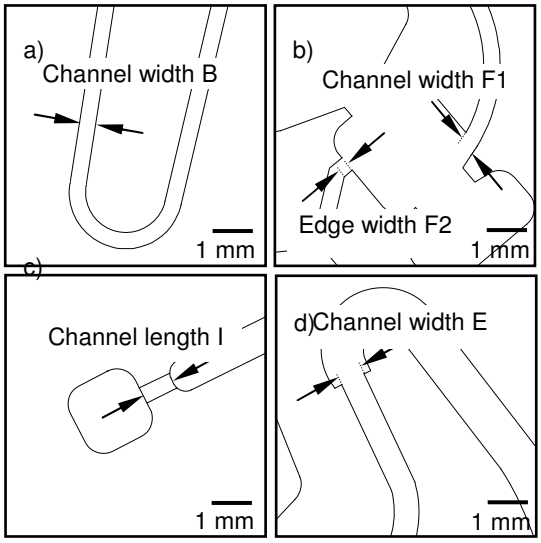

Fig 2. Defined microfluidic features sizes during DOE experiments; a) Channel width B of a straight channel; b) Forming of corners F1 and F2; c) Channel length l between two larger cavities, d) channel width E representing a sudden change in cross-section.

Within a first step a fractional screening design with a total of 30 runs was conducted with the parameters of a basic, suboptimal process as center level. Afterwards a response surface design with a full factorial design comprising 36 runs including a twelvefold iteration of the center point (12 runs) was conducted for parameter optimization. It was investigated that optimal process parameters may vary between designed structures. While shallow structures and straight channels, such as channel width B, are tolerant to shorter process cycles or varied gas

pressures, challenging structures with high aspect ratios or sharp corners, such as F1 and F2, could only be thermoformed with the following optimized process parameters (see table 1). The most relevant parameter has been molding temperature T_m with > 40 % relative impact.

Table 1. Optimized process parameters for microthermoforming 188 µm thick COP films.

T_e [°C]	T_m [°C]	p_1 [kPa]	t_1 [s]	p_2 [kPa]	t_2 [s]
130	200	25	722	310	145

The optimized microthermoform process takes about 30 minutes to mold microstructures with defined channel geometry and sharp edges and corners (see Fig 3). The process used for prototyping forms the films very gently due to a very low pre-pressure p_1. This enables forming of critical structures with high degree of stretching without causing holes.

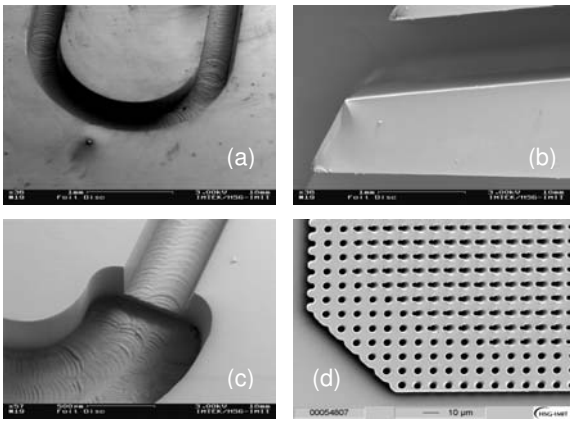

Fig 3. REM pictures of microthermoformed COP ZF 14 film. Sharp edges and corners and even small features in the range of a few micrometers are replicated.

3. Gas pressure assisted thermal bonding

3.1. Process description

To enclose the microfluidic cartridges the microthermoformed structures are sealed thermally. Thermal deformation is avoided by a special co-extruded film made of a temperature stabile TOPAS COC 6013 (T_g ~ 135 °C) and a low temperature grade TOPAS COC 8007 (T_g ~ 79 °C). While the COC 8007 softens and acts like hot melt the COP and the COC 6013 remain solid and preserves the shape. To avoid channel clogging by softened COC 8007, the layer thickness of the COC 8007 was set to be around 10 µm.

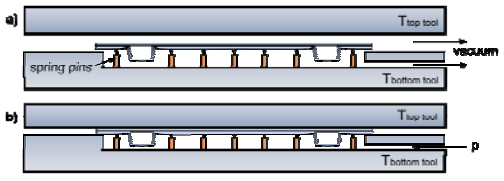

Fig 4. Setup for gas pressure assisted thermal sealing. a) The thermoformed structure is covered with a sealing film and placed onto spring pins, after evacuation b) the stack is clamped between the bottom tool and the top tool (sealing plate) and a bond pressure p is applied.

Due to the positive microthermoforming process the PDMS molds can not be reused for bond support. Alternatively a gas pressure is applied to induce the bond pressure independently from the shape. The bond stack of thermoformed structure and sealing film is placed into a special bond setup (see Fig. 4). The low temperature grade COC 8007 is facing COP. The whole setup is evacuated down to 0.1 kPa to avoid entrapped air between bond partners. Afterwards the films are clamped between the outer rim of the bottom tool and the upper sealing plate. The spring pins assure an overall contact with the sealing plate before clamping and avoid hanging of the films. The sealing plate is stationary preheated and the lower tool is cooled. Right after clamping a gas pressure is applied through the bottom tool, which presses the films onto to the sealing plate.

3.2 Process parameters and bond results

Best results have been achieved for sealing temperatures close to 135 °C and an applied gas pressure of 130 kPa (absolute pressure), which is hold for 10 seconds. Lower bond temperatures result in poor bond strength.

The gas pressure assisted sealing process scales best for microstructures. Fig 5 shows a 200 µm channel and a cavity of 1 mm. The channel shows no deformation. The cavity shows minimal bending of the sealing film and the bottom surface. During fluidic design it has to be noted that large chambers beyond a few millimeter may tend to show larger deformation. This can be reduced by special camber designs. Also the wall thickness should be designed to be thick enough to withstand the applied gas pressure without breaking or collapsing.

Fig 5. Sealed 1 mm cavity (left) and 200 µm channel (right). Both samples are bonded to the edge of the channel and show none to negligible deformation.

3.3. Bond characterization

The thin walled microfluidic cartridges have been tested for bond strength and minimal distance between channels without fluidic crosstalk. The test structure is

a water filled dead end channel (see Fig 6). In a varied distance to the dead end a second channel with a collecting chamber is placed. The distance between both channels has been varied between 200 µm and 1,5 mm. If the bond delaminates a filled collecting chamber can be observed with a stroboscope. The pressure is applied by centrifugation. The water filled dead end channel is rotated at different frequencies between 10 Hz to 100 Hz. This way the hydrostatic pressure can be varied up to 530 kPa.

It was shown that 500 µm spaced channels withstand 530 kPa (at 100 Hz) without leakage for at least an hour at ambient temperature (n = 10). Also for 200 µm, 300 µm and 400 µm leakage free bonding was observed at 530 kPa, if the bond was not weakened by particles.

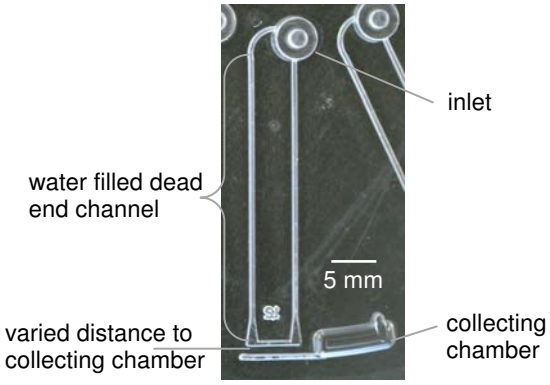

Fig 6. Test structure to characterize bond strength and minimum distance between channels. A water filler channel is rotated, which applies a hydrostatic pressure onto the dead end of the channel. The distance between dead end channel and collecting chamber has been varied between 200 µm to 1,5 mm.

4. Outlook and conclusion

A two-step fabrication process for thin walled lab-on-a-chip cartridges was presented. Within a first step the thermoplastic films are shaped using microthermoforming by soft lithography. The thermoform process has been optimized for prototyping purposes and allows fast design iterations. Furthermore the process uses low pre-pressures to gently thermoform structures with high degree of stretching, which enables a high degree of design freedom during fluidic design.

The bond process is gas pressure assisted to eliminate the need for bond support molds. The bonded structures withstand more than 530 kPa with in a test structure, which makes the bond suitable for microfuidic applications.

The fabricated thin walled microfluidic cartridges are highly attractive for variotherm diagnostic such as genotyping. With the presented fabrication process, first prototypes for fluidic and biochemical testing can be provided.

Future works will focus on faster process cycles for the microthermoforming process. Especially the slow heat ramps and inefficient heating of the films limit faster process cycles.

Acknowledgements

This research project AIF-No. 15838N was funded by the German Federal Ministry of Economics and Technology via grants of the German Federation of Industrial Research Associations (AIF). The authors thank TOPAS Advanced Polymers GmbH and SML Maschinengesellschaft mbH for providing the co-extruded COC sealing film.

References

[1] M. Focke, D. Kosse, C. Müller, H. Reinecke, R. Zengerle, and F. von Stetten, Lab-on-a-Foil: microfluidics on thin and flexible films, *Lab Chip*, vol. 10, no. 11, pp. 1365-1386, 2010.

[2] T. Velten, H. Schuck, M. Richter, G. Klink, K. Bock, C. K. Malek, S. Roth, H. Scho, and P. J. Bolt, Microfluidics on foil: state of the art and new developments, *Proceedings of the Institution of Mechanical Engineers Part B-Journal of Engineering Manufacture*, vol. 222, no. 1, pp. 107-116, Jan.2008.

[3] R. Truckenmuller, S. Giselbrecht, N. Rivron, E. Gottwald, V. Saile, A. van den Berg, M. Wessling, and C. van Blitterswijk, Thermoforming of Film-Based Biomedical Microdevices, Adv. Mater., vol. 23, no. 11, pp. 1311-1329, Mar.2011

[4] R. Truckenmüller, Z. Rummler, T. Schaller, and K. Schomburg, Low-cost thermoforming of micro fluidic analysis chips, *J. Micromech. Microeng.*, vol. 12, no. 4, pp. 375-379, 2002.

[5] R. Truckenmüller, S. Giselbrecht, C. van Blitterswijk, N. Dambrowsky, E. Gottwald, T. Mappes, A. Rolletschek, V. Saileb, C. Trautmann, K. F. Weibezahn, and A. Welle, Flexible fluidic microchips based on thermoformed and locally modified thin polymer films, *Lab Chip*, vol. 8, no. 2008, pp. 1570-1579, July2008.

[6] A. Disch, C. Müller, H. Reinecke; Low cost production of disposable microfluidics by blister packaging technology; Proceedings of EMBC, 2007, pp. 6323-6326

[7] M. Focke, F. Stumpf, B. Faltin, P. Reith, D. Bamarni, S. Wadle, C. Müller, H. Reinecke, J. Schrenzel, P. Francois, D. Mark, G. Roth, R. Zengerle, and F. von Stetten, Microstructuring of polymer films for highly sensitive genotyping by real-time PCR on a centrifugal microfluidic platform, *Lab Chip*, vol. 10, no. 19, pp. 2519-2526, Oct.2010.