BLOW MOLDING OF POLYMER FOILS FOR RAPID PROTOTYPING OF MICROFLUIDIC CARTRIDGES

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ABSTRACT

We present a novel process for small-lot manufacturing of microfluidic lab-on-a-chip cartridges made of thin polymer foils within 8 hours starting from a CAD layout. A master tool is micromilled and then casted with polydimethysiloxane (PDMS) to obtain an elastic replication mold. This is used for blow molding of thermoplastic foils in order to manufacture lab-on-a-chip cartridges with very thin sidewalls of 100 to 180 µm. These are suited for microfluidic applications requiring fast heat transfers, most prominently thermocycling for polymerase chain reactions (PCR) as demonstrated with our technology.

KEYWORDS: Rapid prototyping, thermoforming, polymer films, Lab-on-a-chip

INTRODUCTION

The time of sample-to-result in diagnostics is critical. Hence, the complete handling of reagents can be automated by using lab-on-a-chip systems like the centrifugally driven Bio-Disk [1]. Duration of assays that require thermocycling between approximately 50° and 95° C can be further reduced by fast heat transfer. This is enabled by use of blow molded polymer foils with thin sidewalls. These cartridges can then be used as lab-on-a-chip systems.

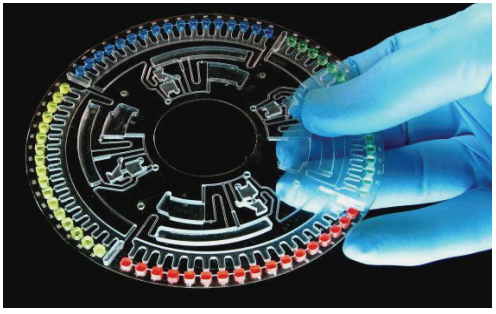

Figure 1. Image of a thermoformed cartridge with four sectors of microfluidic structures for a Real-Time PCR.

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TECHNOLOGICAL PRINCIPLE

A master mold is micromilled in polymethyl methacrylate (PMMA) and afterwards casted in PDMS to obtain an inversed mold insert. For replication, the insert is placed into an aluminium tool holder and covered by a COP foil (Zeon Industries) with typical thicknesses between 100 and 200 µm (fig. 2). Then the complete process chamber is evacuated and the tool holder is tightly sealed with a clamping force of 15 kN. After heating beyond the glass transition temperature of the polymer foil, nitrogen is pressurized to blow mold the softened foil onto the PDMS mold. Finally, the process chamber is cooled and vented [3],[4]. Demolding is uncritical due to sufficient elasticity of the PDMS mold. This thermoforming process suits also for other thermoplastic materials such as PMMA, polypropylene or polyethylene. The thermoformed foil cartridges can be sealed with an adhesive film (for example Sarstedt 95.1994) where applicable.

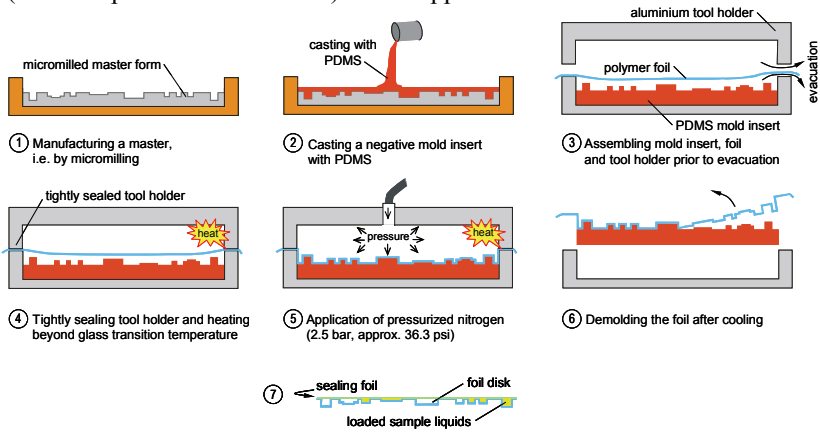

Figure 2. Cross-sectional view of the process scheme. After demolding the cartridge can be sealed and filled with reagents.

EXPERIMENTAL RESULTS

We manufactured a foil-based centrifugal microfluidic cartridge exhibiting a previously described aliquoting structure [2] and reaction cavities for Real-Time PCR (fig. 4 & 5).

Contour and replication accuracies were determined by an optical-tactile measurement machine (Werth Videocheck IP400). The dimensional variation of thermoformed foils is very low (CV 0.4%). On a typical 3-mm wide chamber located on the outer perimenter of a 130-mm cartridge, we measured a contour precision of 18 µm (full width at half maximum). We observed a dilation factor between master and thermoformed foils of +1.35% which is due to thermal expansion of the heated PDMS mold. The master does not require draft angles, thus accelerating its construction. We realized aspect ratios of up to 3 and sharp corners of up to 60° (fig. 3), thus allowing the integration of geometry controlled capillary effects.

Finally we successfully tested the functional capability of a microfluidic foil cartridge with a complex aliquoting structure [2] operated on a centrifugal platform.

The CV of aliquoting a 10.5-µl volume to 17 peripheric cavities was 5% - compared to 3% obtained for a similar, milled structure [2]. Thermocycling and fluorescence detection were demonstrated by Real-Time PCR of a dilution series of the Exfoliative A gene (fig. 5).

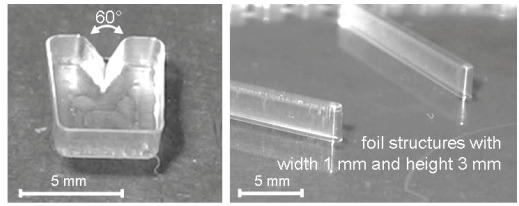

Figure 3. Sharp corners with 60° (left) and aspect ratios up to 3

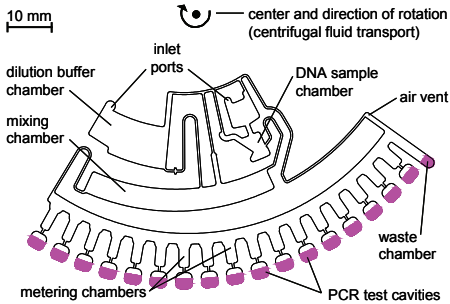

Figure 4. Schematic of the structure that was blow-molded and tested. The metering chambers hold aliquots of 10.5 µl before filling the test cavities for Real-Time PCR.

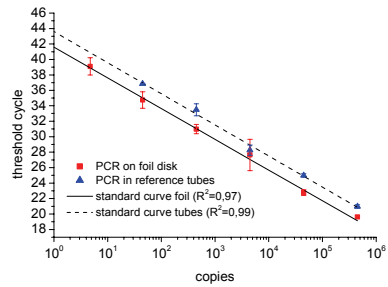

Figure 5. A standard curve of a Real-Time PCR dilution series (Exfoliative A gene) determining the DNA sample concentration in a given sample volume. Comparison with conventional PCR in tubes confirms compatibility of fluorescence read-out applications.

CONCLUSIONS

We developed a rapid prototyping method for replication of foil-based microfluidic cartridges that is fast, precise and reproducible. Among hot embossing and injection molding, the here presented blow molding of foils is the only replication technology that allows to replicate structures with thin sidewalls by applying only one mold tool.

ACKNOWLEDGEMENTS

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