Microfabrication of single-use plastic microfluidic devices for high-throughput screening and DNA analysis

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Abstract Modern drug discovery and genomic analysis depend on rapid analysis of large numbers of samples in parallel. The applicability of microfluidic devices in this field needs low cost devices, which can be fabricated in mass production. In close collaboration, Greiner Bio-One and Forschungszentrum Karlsruhe have developed a single-use plastic microfluidic capillary electrophoresis (CE) array in the standardized microplate footprint. Feasibility studies have shown that hot embossing with a mechanical micromachining molding tool is the appropriate technology for low cost mass fabrication. A subsequent sealing of the microchannels allows sub-microliter sample volumes in 96-channel multiplexed microstructures.

1 Introduction
Microfluidic devices fabricated by mass production offer an immense potential of applications such as high-throughput drug screening, clinical diagnostics and gene analysis [1]. The low unit production costs of plastic substrates make it possible to produce single-use devices, eliminating the need for cleaning and reuse [2]. The combination of small assay volumes and the possibilities of integrated capillary electrophoretic separation provide a powerful tool for rapid assay development.

Fabrication of microfluidic devices can be applied by microtechnical fabrication processes in combination with plastic molding techniques [3]. Basically, replication in plastics requires a hot embossing or injection molding tool. Various microfabrication technologies for the master fabrication are established, such as mechanical micromachining [6], micro electrical discharge machining (μEDM) [3] and the LIGA technique [4]. Depending on the specific requirements, the most suitable process can be selected. The availability of these technologies allows to generate robust metal molding tools which exhibit the inverse shapes of the intended microstructures.

This paper will show a low cost production of 96 channel plastic microfluidic devices including various microfabrication technologies to demonstrate the application of microtechnical fabrication processes for high-throughput screening and DNA analysis.

2 Master fabrication
The master fabrication holds a key position in plastic replication technology. Depending on the product requirements like structure dimensions, accuracy or fabrication costs, different master fabrication technologies are applied [5]. With mechanical micromachining [6] structural dimensions down to 50 μm are obtained. Micro electrical discharge machining [3] is a corrosive machining technique supported by an electrical potential. The smallest structural dimensions achieved with this technique are approximately 10 μm. Laser ablation can be applied to microstructure many materials. Structural dimensions down to 5 μm are achievable [7]. For the master fabrication with silicon micromachining [8] a subsequent electroplating step is required, because of the brittleness of the silicon material. Microstructures down to 2 μm can be produced with this technique. The master fabrication process with the highest structural resolution is the LIGA-technique [4]. Structural dimensions of approximately 5 μm are achieved with UV-lithography and down to 0.2 μm with X-ray lithography.

Mechanical micromachining is the least time and cost consuming master fabrication technology. In several cases complex masters are built up by combining the different microfabrication processes.

3 Plastic replication
Microfluidic devices out of plastic materials offer many advantages in comparison to microstructured glass or silicon devices. There is a huge diversity of resins available and the polymeric materials out of the shelf have reasonable prices. Additionally, the surfaces of plastic materials are biocompatible or can be treated or coated to achieve biocompatibility.

Plastic materials can be microstructured by a single master fabrication and subsequent replication by injection
molding or hot embossing. From one single master thousands of plastic replicates can be manufactured.

Hot embossing is a superior tool for mass production of plastic microcomponents (Fig. 1). In this process, a microstructured mold insert is pressed into a thermoplastic polymer film under vacuum, the film having been heated beyond its glass transition temperature. The polymer fills the mold insert, creating a detailed inverted replica of the microstructures. Subsequently, the entire molding setup is cooled down, and the replicated structure is demolded from the mold insert [9].

As a consequence of negligible flow lengths and the use of low molding speeds, this embossing process allows even filigree microstructures with very high aspect ratios to be produced. Most thermoplastic materials are eligible for this process like PMMA, PC, POM, PEEK, PVDF, and PSU. At the present, only this technology allows for a very precise generation of the filigree channel structures on large-area plastic substrates.

4 Fabrication and testing of a 96-channel plastic CE-plate
We have fabricated prototype single-use plastic microfluidic devices in a standard microplate format (Figs. 2, 3) by hot embossing with a mechanical micromachined molding tool and subsequent sealing of the microchannels (Figs. 7–10).

The molding tool is fabricated out of a large area brass plate by using various finger mills between 50 and 400 µm (Fig. 4). The microfluidic channels are embossed in plastic

![Hot embossing for replication of various plastics, like PMMA, PC, POM, PEEK, PVDF, PSU](image1)

![Design of a standard microplate with 96 CE-structures](image2)

![Sealed microplate with 96 CE-structures](image3)