A Rapid Prototyping and Mass-Production Platform of Microfluidic Devices

P.-J. Craig Kung[*], Yu-Long Kung[*], David Holcombe[*], Roger H. Grace[**],
Gerald Ungelenk[***], Enrico Piechotka[***], and Wolfgang Seiferth[***]

[*]Optotrack, Inc.
1070 Classic Road, Apex, NC 27539, U.S.A., ckung@optotrcak.com
[**]Roger Grace Associates, Naples, FL, U.S.A., rgrace@rgrace.com
[***]JENOPTIK Laser, Optik, Systeme GmbH, Jena, Germany, enrico.piechotka@jenoptik.com

ABSTRACT

Microfabricated devices have become an integral part of a variety of analytical, medical, and detection systems. As the applications of microfabrication are growing widely, a low-cost, rapid prototyping and mass-production platform has become essential. To serve this end, *Optotrack*, *Inc*. has developed a process of precision embossing, bonding, and surface modification to manufacture microfluidic chips, disposable biosensors, and micro-optical devices based on plastic materials. Multiple devices of the same or different designs are hot-embossed in a 4-inch or 6-inch plastic wafer. The wafer is then treated, bonded, diced, and inserted with interconnects. Discrete devices are tested for their quality prior to the integration with read-out schemes. It is estimated that from conception to mass production, this platform takes 50% less time and cost than its competing technologies. Microfluidic devices made from the present platform have been incorporated into automatic analyzers for drug discovery and bio-separation.

Keywords: microfluidics; hot embossing; bonding; plastic wafers; precision replication.

1 INTRODUCTION

Microfluidic chips, disposable biosensors, and micro-optical devices have been primarily manufactured from silicon or glass substrates for years [1 - 3]. This approach involves a variety of sophisticated production tools, tedious development process steps, and cleanroom working environments, which translates into heavy capital investments and a long lead time. Given today's fierce competition in the global marketplace, alternatives have to be implemented to achieve low cost, quick turn-around, and high product quality. In addition, because customers' requirements vary to great extent and are often application-specific, a manufacturer has to be flexible and responsive for its products and services to stay ahead the competition. Often, a prototype has to be tested, modified, and then retested to optimize its performance. All of these have to be carried out quickly and effectively. Therefore, "Speed-to-Market" is a critical success factor, and the research and development process itself needs to be duplicated reliably.

Although soft lithography has been used widely as an excellent alternative to silicon and glass photolithography [4 – 6], soft materials are not appropriate for manufacturing microfluidic devices when organic solvents have to flow inside the channels. These materials can swell in organic solvents, leading to a potential problem of device failure. Therefore, in this paper we introduce a rapid prototyping and mass-production technology platform based on plastic wafers to address the above issues.

2 MICROFABRICATION METHODS

There are several methods by which plastic devices or chips can be microfabricated. Process selection depends on the features to be created and the surface to be patterned. Laser micromachining uses a focused laser beam to ablate selectively a plastic sheet to create desired microstructures. Although this technology can be applied to make arbitrary device geometries automatically, the device is fabricated one at a time. It can easily take several hours to complete a complicated pattern. Injection molding, on the other hand, uses heated polymer pellets injected at high pressure into a closed cavity to replicate hundreds to thousands of plastic components; however, the die for injection molding is expensive. Therefore, it is best used for mass production of parts with a completed design.

Cold embossing, hot embossing, and UV embossing have recently been used to fabricate microfluidic devices and microelectrodes [7 - 9]. With improvements in the instrumentation of this field, we have developed a platform to fabricate precision-embossed, application-specific plastic wafers to pursue multiple market segments. These 4-inch or 6-inch wafers, which are imprinted with high-precision microstructures by a hot embosser (HEX03, Jenoptik), can be bonded and surface-treated for various applications. The bonded wafers are then diced into individual devices into which interconnects are inserted horizontally or vertically for device testing. This platform is a cost-effective and time-efficient approach with the flexibility of material selection and volume production. It definitely accelerates product development cycle times and leads to quick, iterative design changes for certain products currently based on silicon or glass wafers. As a result, the technology allows users to better cope with market dynamics and

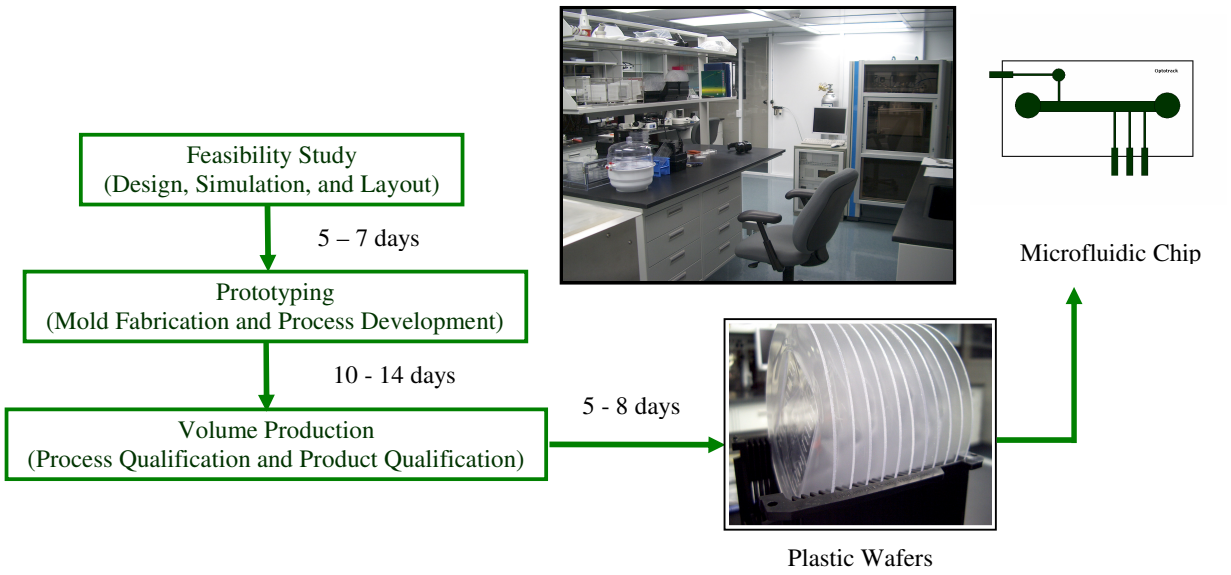

Figure 1. A typical workflow of precision embossing and replication at *Optotrack, Inc*.

technology platform transforming. In fact, surface-treated plastic microfluidic chips fabricated by the present platform have been used by a pharmaceutical company in fluorescent detection systems to measure the potency of inhibitors against target enzymes during its drug discovery tests, allowing an operation of 24 hours 7 days a week that is much faster than the current practice in the industry with 96-well plate-based assays and pipetting robots. It is estimated that this platform, in general, takes 50% less time and cost than competing technologies for microfluidic chip prototyping and production in today's marketplace.

As compared with injection molding, hot embossing manufactures components with less inner stress and is more appropriate for structures created in a thin sheet with high aspect ratios. It has a high degree of flexibility and a short tool exchange time. Figure 1 shows a typical workflow for prototyping and production implemented at *Optotrack, Inc*. We can transfer efficiently a surface relief profile with identical patterns in the resolution of sub-microns from a mold into plastic wafers of polystyrene, polycarbonate, polyethylene, PMMA, PTFE, etc. to fabricate microfluidic chips incorporated into a variety of analytical instruments. Such instruments, also known as lab-on-a-chip systems, manipulate μL and sub-μL volumes of samples and reagents to perform multiple biological and chemical reactions and analyses for automatic operation, fast validation, and real-time monitoring.

3 DISCUSSION

3.1 Mold Fabrication

Molds for hot embossing can be fabricated by several methods. Silicon molds with structures created into nitride or photoresist SU-8 coatings are fabricated by standard photolithography processes [10], and special attention is often needed to avoid mold damages during the hot embossing process. Although SU-8 has excellent chemical and mechanical properties, it can sometimes cause sticking problems during the demolding step. For rapid prototyping purposes, an excimer laser (λ = 243 nm) is used to etch anisotropically desired features such as channels and reservoirs in plastic sheets to make plastic molds. These molds are used to emboss plastic microfluidic chips to optimize chip designs. New molds with modified designs can be quickly made as necessary. Once the designs are validated and finalized, a metal mold will then be created for mass production. Figure 2 shows hot-embossed micro-

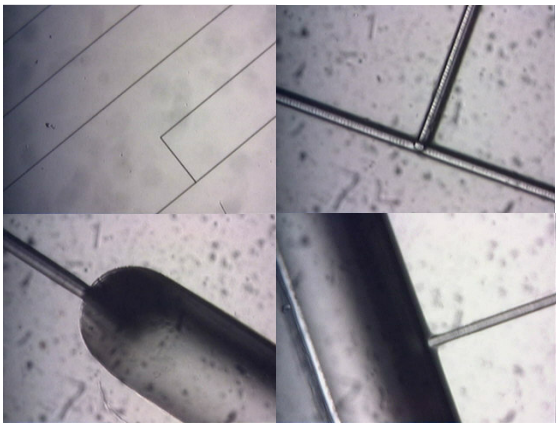

Figure 2. Polycarbonate microfluidic channels (10 – 250 μm in depth) embossed from an excimer-laser-micromachined mold.

NSTI-Nanotech 2007, www.nsti.org, ISBN 1420061844 Vol. 3, 2007

channels (10 – 250 μm in depth) fabricated from an excimer-laser-micromachined mold. As inspected using an optical microscope, structures are precisely replicated from the mold. These channels are used for mixing, separation, expansion, or flow control.

Heating, molding, and demolding are three key steps of the hot embossing process. Process parameters including molding temperature, embossing rate, embossing force, packing time, demolding temperature, and demolding rate have to be optimized. Material parameters play a big role in determining process parameters. Shrinkage differences between tool and substrate material can result in distorted, deformed, or torn-off microstructures. With simulation and optimization efforts, well-defined micro-features can be molded as shown in Figure 3.

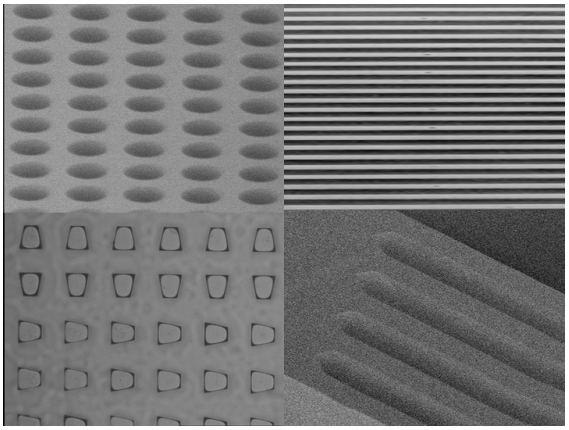

Figure 3. Various hot-embossed microstructures.

3.2 Bonding

Integrated microfluidic reactors and analyzers can be manufactured from a glass or silicon wafer with desired features bonded (anodic bonding or fusion bonding) with a readout silicon wafer. As to the microfluidic devices based on plastics, structures are first embossed into a plastic wafer, and channels or reservoirs are formed by sealing the embossed sheet with a plastic film on the top. Methods for such polymer-to-polymer bonding generally include gluing, ultrasonics, and thermal compression. In our approach, the same hot embosser used for embossing is employed to perform thermal bonding. In some cases, the bonded surfaces are carefully treated (coating or modification) prior to bonding to improve the bonding strength. Others, due to the application, require both the top and bottom plastic sheets to be embossed, carefully aligned, and then bonded (see Figure 4). Voids or trapped air bubbles can be avoided with proper procedures. Time, temperature, and pressure are the three main process parameters to be optimized. The bonded devices are tested in the pressure range of 100 psi to 800 psi and exposed to different solvents to check for their bonding strength and chemical resistance. Most devices can survive under continuous operation with a flow rate in the range of nl/min without leakage and delamination.

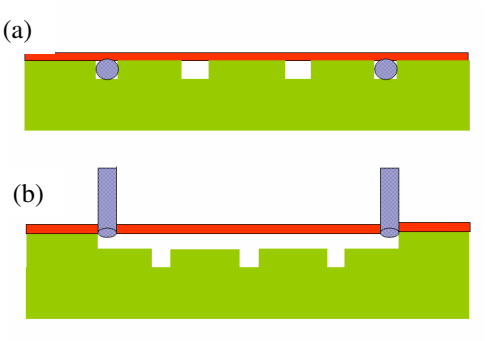

Figure 4. Interconnects are inserted (a) horizontally and (b) vertically after a microfluidic chip is treated and bonded thermally.

3.3 Surface Treatment

It is widely known that reagents introduced into microfluidic chips often have adsorption issues, namely, they are stuck to the chip surface, which causes carry-over problems and results in experimental errors. If such a system is used to screen compounds for drug discovery, it can mislead the conclusion about drug potency and enzyme kinetics. Therefore, different surface coating and treatment protocols through liquid or gas phase interactions have been developed for various applications to minimize compound adsorption to the surface. In general, ionization of a molecule leads to the accumulation of the hydrophilic form in aqueous phase. The logarithm of the participation coefficient, LogP, of a compound observed between water and n-octanol thus can be used to measure the compound's hydrophilicity, though it is a time-consuming process. Alternatively, we measure contact angles prior to and after surface treatment to check for hydrophilic or hydrophobic characteristics. For most applications, a surface with its surface energy similar to that of water has to be created. Figure 5 shows variations in the contact angle of polycarbonate chips that are surface-treated under different conditions. We can modify a surface from hydrophilic to hydrophobic and vice versa. In some cases, features are embossed into metal-coated plastic wafers to create special devices of interest.

It is noticed that surface treatment may weaken the bonding of the devices if not applied appropriately. The behavior of macromolecules near the surfaces and interfaces, therefore, plays a vital role in the application of surface treatment. X-ray photoelectron spectroscopy (XPS) is used in our study to analyze the surface compositions after the treatment. The existence of fluorine and oxygen at the surface was confirmed in devices treated with fluorine and oxygen, respectively.

4 MICROFLUIDIC SYSTEMS

Microfluidics-based systems allow accurate control and manipulation of minute fluids in microchannels. They can

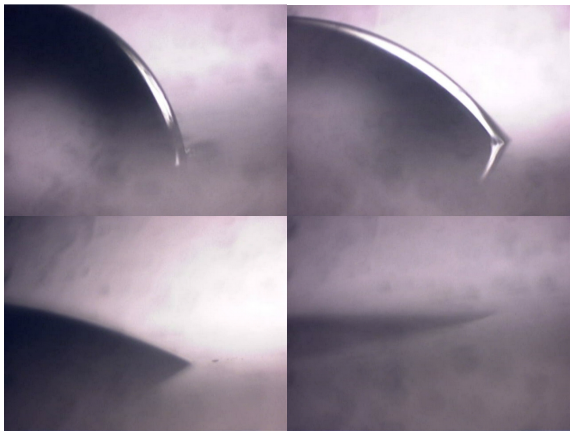

Figure 5. Contact angle measured on polycarbonate chips that were surface-treated by different methods.

process and identify fluid-based cells, molecules, or particles that are transported from an inlet area to a detection area and then to a disposal area. They transport μL and sub-μL volumes of samples and reagents and perform multiple reaction and analysis techniques for automatic operation, fast validation, and real-time monitoring. Therefore, it offers portability and facilitates cost savings, low consumption of reagents, reduction in sample preparation, and higher throughput. The systems can be custom-designed and custom-assembled to meet application needs and yield significant benefits across a variety of fields including forensic analysis, genome mapping, clinical therapy, and medical diagnostics.

Notice that the ratio of surface area to volume in microfluidic systems is many orders of magnitude larger than what is found in conventional analytical tools. Small variations in channel dimensions can lead to significant experimental errors if such systems are used to measure the concentration of a molecule or enzyme kinetics. However, with dedicated designs, simulations, and validations, an integrated microfluidic system can accurately control small volumes of fluid to perform a wide range of functions including sampling, mixing, dilution, separation, reaction, crystallization, and detection.

In our platform, the replication error between the mold and the final embossed and bonded structure is controlled within the range of 2% to 5%. With the objective of offering quality foundry services, we are now in the process of streamlining our workflow and developing the protocols of proprietary surface modification and coating (oxidation, fluorination, nitridation, metallization, and polymerization) for various applications, which is considered as a critical process step to provide a biocompatible or non-sticking surface in many microfluidic chips and systems. All this will influence the quality of data that can be obtained from the experiments conducted within a chip. Noise due to thermal fluctuation and mechanical damping as well as deviation in real reagent concentrations caused by carry-over or diffusion shoulders should always be minimized. The incorporation of special geometries into the chip design, the effective treatment of achieving a hydrophilic surface in plastic chips, and the ability of fabricating multilayer plastic chips would definitely help the advances in microfluidic systems to great extent.

5 CONCLUSIONS

The rapid prototyping and mass-production platform of plastic microfluidic devices has been developed using hot embossing, thermal bonding, and surface treatment. Metal, silicon, and plastic molds, with positive or negative patterns, are employed to emboss many isolated and dense features precisely into plastic wafers and metal-coated plastic films. The process shows high repeatability from wafer to wafer. These chips can be incorporated into various microfluidic systems that are often used to screen chemical compounds, detect chemical and biological warfare agents, deliver precise amounts of prescription drugs, and conduct in-vitro diagnostics. As compared with silicon and glass microfluidic chips, the use of surface-treated plastic wafers as the chip material allows us to make small parts disposable, cost-effective, and yet with greater configuration flexibility. As estimated, this platform takes 50% less time and cost than its competing technologies, which implies that it may eventually change the nature of competition in the biotech and life science industry.

REFERENCES

[1] J. Ouellette, *The Industrial Physicist*, August/ September, pp. 14 – 17, 2003.

[2] Z. H. Fan and D. J. Harrison, *Anal. Chem.*, vol. 66, pp. 177 - 184, 1994.

[3] H. Zhao, J. H. Montgomery, N. S. J. Mitchell, and H. S. Gamble, *J. Microlith., Microfab, Microsyst.*, vol. 3, pp. 493 – 500, 2004.

[4] D. C. Duffy, J. C. McDonald, O. J. Schueller, and G. M. Whitesides, *Anal. Chem.*, vol. 70, pp. 4974 – 4984, 2003.

[5] A. D. Stroock, S. K. W. Dertinger, A. Adjari, I. Mezic, H. A. Stone, and G. M. Whitesides, *Science*, vol. 295, pp. 647-651, 2002.

[6] J.N. Lee, C. park, and G.M. Whitesides, *Anal. Chem.*, vol. 75, pp. 6544 – 6554, 2003.

[7] S. C. Wang and M. D. Morris, *Anal. Chem.*, vol. 72, pp. 1448 - 1452, 2000.

[8] H. Schift, R. W. Jaszewski, C. David, and J. Gobrecht, *Microelectronic Eng.*, vol. 46, pp. 121-124, 1999.

[9] J. P. Rolland, R. M. Van Dam, D. A. Schorzman, S. R. Quakes, and J. M. DeSimone, *J. Am. Chem. Soc.*, vol. 126, pp. 2322-2323, 2004.

[10] F. E. H. Tay, J. A. van Kan, F. Watt, and W. O. Choong, *J. Micromech. Microeng.*, vol. 11, pp. 27 – 32, 2001.