Plastic masters—rigid templates for soft lithography

Salil P. Desai, Dennis M. Freeman and Joel Voldman and

Received 9th December 2008, Accepted 4th February 2009 First published as an Advance Article on the web 5th March 2009

DOI: 10.1039/b822081f

We demonstrate a simple process for the fabrication of rigid plastic master molds for soft lithography directly from (poly)dimethysiloxane devices. Plastics masters (PMs) provide a cost-effective alternative to silicon-based masters and can be easily replicated without the need for cleanroom facilities. We have successfully demonstrated the use of plastics micromolding to generate both single and dual-layer plastic structures, and have characterized the fidelity of the molding process. Using the PM fabrication technique, world-to-chip connections can be integrated directly into the master enabling devices with robust, well-aligned fluidic ports directly after molding. PMs provide an easy technique for the fabrication of microfluidic devices and a simple route for the scaling-up of fabrication of robust masters for soft lithography.

Introduction

Soft lithography has emerged as the dominant technique for rapid prototyping of microfluidic devices as miniaturized platforms for experiments in biology and chemistry. Soft lithography employs the casting of elastomeric materials such as (poly)dimethylsiloxane (PDMS) and room-temperature vulcanizing (RTV) silicones on master molds fabricated from photoresists on silicon substrates.1 These silicon-photoresist masters (SPMs) offer excellent feature resolution (\sim 1 μ m) and the ability to fabricate complex devices using multiple layers of photoresist aligned to one another. However, photoresists perform poorly as structural materials in a two-material system such as SPMs due to delamination at the photoresist-silicon interface (especially when using the negative-tone photoresist SU-8 and silicon²⁻⁴). Hence, SPMs have a limited casting lifetime. Silicon micromachined masters (SMMs)5 can overcome the limitations of SPMs since the structural features are monolithic. SMMs, however, require specialized etching systems and carefully formulated etch recipes. Consequently, SMMs are more difficult to fabricate than SPMs. Given their fabrication complexity, SMMs are more limited in the geometries that can be realized and are consequently less widely used.

Soft materials, such as PDMS and RTV, can also serve as masters for molding. Previous work has leveraged the inherent flexibility of these elastomers to generate masters with curved surface topologies^{6,7} a feat that is challenging to accomplish using SPMs or SMMs. Additionally, elastomeric masters (EMs) serve as flexible molding platforms for molding high-aspect—ratio elastomeric structures.⁸ Such high-aspect—ratio elastomeric structures would be extremely difficult to unmold from rigid masters such as SPMs or SMMs. EMs play an important role in soft lithography in the ability to generate complex geometries

which are challenging to achieve using conventional master fabrication techniques.

EMs have also been used for the routine casting of rigid masters using UV-curable epoxies such as Epotek UVO-114 (Epoxy Technologies) and NOA 74 (Norland Optical Adhesives). Of these, Epotek epoxies have been the most widely employed and have been used in the generation of masters for optical wave-guides, 9,10 patch-clamp chips, 11 cell-sorting chips, 12 wavy cell culture surfaces,13,14 and for the fabrication of nanometer-scale features on curved surfaces.¹⁵ While photo-curable epoxies such as Epotek have previously been used to generate rigid masters from elastomeric devices, they pose some challenges—(1) they are expensive and require curing equipment and (2) large-area fabrication requires the use of uniform UV illumination systems. To overcome the limitations of both Epotek masters and standard SPMs we have developed a simple, costeffective process for generating rigid templates for soft lithography. Specifically, our process is much simpler than that required for photo-curable masters in that it replaces the UVcuring step (requiring a UV light source) with room-temperature curing (requiring no additional equipment), and there are no practical limitations on the mold sizes and thicknesses that can be achieved with our technique.

The plastic molding process starts with making a SPM using standard photolithographic techniques. Instead of casting PDMS repeatedly from this SPM, we cast PDMS once and then cast a new plastic master from that PDMS using a two-part polyurethane. The two casting steps re-create the negative SPM master geometries in a robust plastic master (PM). This simple three-step process (SPM to PDMS to PM) directly addresses the limitations of SPMs in that it generates a monolithic master mold that eliminates the failure-prone material interface of SPMs. Further, this molding process can be used to generate multiple PM replicas by casting multiple PDMS replicas, allowing for a cost-effective route to scaling up the production of masters. In this Technical Note, we provide the detailed methods for creating PMs along with the quantitative characterization necessary for researchers to immediately begin employing this technique in their own research.

^aDepartment of Electrical Engineering and Computer Science, Massachusetts Institute of Technology, 77 Massachusetts Ave, Cambridge, MA, 02139, USA. E-mail: voldman@mit.edu; Fax: +1 617 258 5846; Tel: +1 617 253 2094

^bHarvard-MIT Division of Health Sciences and Technology, Massachusetts Institute of Technology, Cambridge, MA, 02139, USA

Materials and methods

PM fabrication

PMs are fabricated using a commercially available two-part polyurethane plastic (Smooth Cast 310, Smooth-On Inc.). The silicone device to be molded is first affixed to the bottom of an open-topped container constructed of PDMS (Sylgard 184, Dow Corning). Since the polyurethane plastic does not adhere to silicone surfaces, the open-topped PDMS container ensures that the plastic precursor is only in contact with silicone surfaces (except at the very top where it is exposed to air). Additionally, the inherent flexibility of the PDMS container allows for the hardened PM to be easily removed from the mold after curing. The PDMS container provides a reusable means for casting the PMs and obviates the need for any surface treatments (such as silanization) in the casting process. Depending on the device thickness and the type of mold desired, affixing the PDMS device into the PDMS container is done in one of three ways—(1) a thin seed layer of PDMS (mixed in a 10: 1 ratio and subsequently degassed) is poured in the bottom of the container and the device is placed on top of it, after which the container and device are

then placed in a 60 °C convection oven for 2 h to cure and hence bond the device to the container; (2) the device is double-sticky taped to the bottom of the container; or (3) for thin devices that are difficult to tape down, they are simply laid flat on the bottom of the container, allowing the native silicone seal to act as a bonding method. The device and container are then placed in a degasser for at least 30 min. In the meantime, the two parts of the plastic pre-cursor (parts A and B) are measured out in equal volumes and degassed separately for approximately 20 min. The low viscosity of the two parts (80 cps when mixed) ensures that they can be quickly and easily degassed. Parts A and B are then mixed together slowly taking care to avoid bubbles (the limited pot life of ~20 min of the mixed plastic precludes degassing the resultant mixture to remove air bubbles). The PDMS container with affixed device is removed from the degasser and the liquid plastic pre-cursor mixture is poured into the container. Microfluidic devices with micron-scale features typically have several entrapped air bubbles and these are summarily removed using a fine wire (taking care not to scratch the device surface). The plastic is then left to cure on a level surface for 2 h at room temperature. Upon curing the PM is removed from the

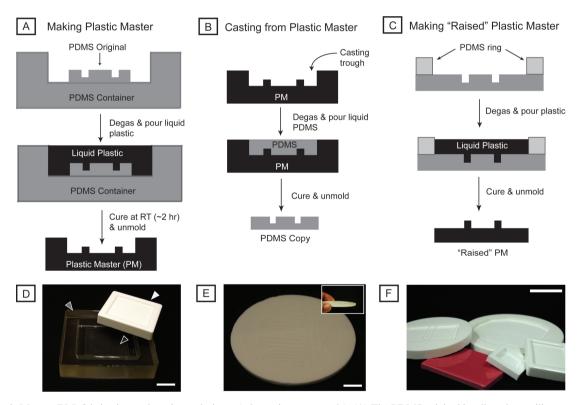


Fig. 1 Plastic Master (PM) fabrication and casting techniques (schematics not to scale). (A) The PDMS original is adhered to a silicone container and degassed for \sim 30 min. The two parts of the plastic are separately degassed and mixed, taking care to not generate bubbles. The liquid plastic is then poured into the degassed silicone container, bubbles are carefully removed with a fine gauge wire and the plastic is allowed to cure for \sim 2 h on a level benchtop. The hardened plastic master is then unmolded from the box and is ready for use. (B) Casting on the PM is analogous to casting on silicon masters except in that the PMs do not require silane treatment. PDMS devices are easily obtained by casting PDMS on PMs using standard soft lithography procedures. (C) "Raised" plastic masters are fabricated by placing a PDMS ring around a device and following the standard PM fabrication procedure outlined in (A). This technique yields PMs with features that are raised as opposed to recessed in a trough. (D) Images of fabricated plastic master (white arrowhead), PDMS container (gray arrowhead) and affixed PDMS device (black arrowhead). Scale bar 35 mm. (E) PM for spin-casting fluidic devices, features are raised without an outlying trough. Inset shows zoomed in view of thickness of PM, which is 2.5 mm. Scale bar 15 mm. (F) Collection of PMs. Image of several different white and red PMs ranging from a 150 mm mold with \sim 50 distinct devices to a mold with a single device. Scale bar 50 mm.

container. The device is typically still embedded in the PM and is carefully removed using tweezers or a razor blade. The PM (without the need for silane treatment) is now ready for molding with silicon (an optional post-bake at 65 °C for 4-6 h can be performed to further harden the PM). A simplified process flow is schematically depicted in Fig. 1A. The use of an open-topped molding container results in a PM with an integrated trough in which PDMS is cast. In contrast, SPMs have a flat surface with raised features. In some cases, such as the generation of PMs for spin-casting PDMS/RTV and for elastomeric stencil fabrication, it is important that PMs have raised features and no molding trough. To generate such PMs, a silicone ring is placed around the rim of the master, allowing the native silicone seal to reversibly bond the ring and master. The ring now creates a reservoir for holding the liquid plastic precursor which is prepared as described above. The resultant PM now resembles a conventional SPM. This alternate PM fabrication procedure is outlined in Fig. 1C.

SPM fabrication

The SU-8 (SU-8 2015, MicroChem) resolution-test master with 20 μm tall features was fabricated using standard photolithographic fabrication techniques. Briefly, silicon wafers were cleaned and hard baked. SU-8 was applied and spin-coated at 1000 rpm for 30 s. Detailed fabrication procedures have been described previously. FSPMs for distortion tests were fabricated using similar techniques and have been previously described.

PDMS mold fabrication

PDMS devices were fabricated from SPMs and PMs using conventional soft lithography molding techniques which have been previously described in detail. Briefly, PDMS was mixed in a 10:1 base: hardener ratio and subsequently degassed in a vacuum chamber for ~ 30 min. Degassed PDMS was then poured directly on the PMs or silanized SPMs and then either left to cure at room temperature or at $60\,^{\circ}\text{C}$ for $2\,\text{h}$.

World-to-chip connections

PMs with integrated world-to-chip connections were fabricated by coring holes in the PDMS devices using commercially-available corers (Harris Uni-Core, Ted Pella, Inc.) prior to affixing them to the open-topped PDMS container (as shown in Fig. 2A). To integrate pins, stainless steel pins (Type 304, New England Small Tube) were press-fit in to the cored holes from the device-patterned side, prior to affixing them in the PDMS container (as shown in Fig. 2B).

Scanning electron microscopy

PMs were tape cleaned to remove dust and residual PDMS. SPMs were cleaned in a nitrogen stream to remove dust. A 5% solution (in deionized water) of 8 µm diameter (1% CV, cat. no. 64110, Polysciences, Inc.) and 30 µm diameter (1% CV, cat. no. 4230, Duke Scientific Corp.) NIST-traceable polystyrene microspheres were used as calibration targets. Approximately 50 µl of bead solution was pipetted onto each target (PMs, EMs and SPMs) and allowed to dry under vacuum. Individual SPMs, EMs

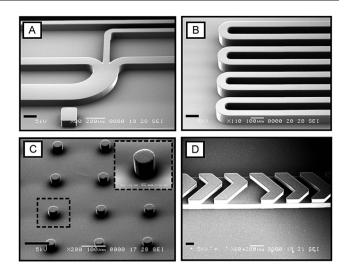


Fig. 2 SEM images of PMs molded from SPMs. Various microfluidic topologies have been successfully reproduced as PMs, ranging from standard single-layer , multiple-input channels (A) and serpentine channels (B). (C) Arrays of micro-scale posts (post diameter 40 μm), inset shows a high magnification view of a single post, exhibiting sharp sidewalls. Two-level structures have also been successfully replicated in plastic as shown in (D). Scale bars 100 μm .

and PMs were then sputter coated with 50 Å layer of gold in an argon plasma. The SPMs, EMs, and PMs were then mounted on a standard flat mount using conductive carbon tabs. Images were acquired at 5 kV acceleration and magnifications ranging from $50\times$ to $3000\times$.

Profilometry

SMs and PMs were cleaned with nitrogen and placed on the stage of a vibration-isolated profilometer (P-16, KLA-Tencor). Linear scans were performed with a 2 μm diameter tip at 50 μm s $^{-1}$ scan speeds and a 200 Hz data sampling rate. Care was taken to calibrate the profilometer with a known step-height (4.5 nm calibration step, VLSI Standards) prior to each set of measurements on a given sample.

Results

PM Fabrication

Images of a typical PM and open-topped container are shown in Fig. 1D. PM fabrication techniques can be used to generate masters of varying thickness and area, including 2.5 mm-thick masters for spin-casting thin silicone films (Fig. 1E). Thin masters (with form-factors similar to traditional SPMs) are necessary for spin-casting as thicker PMs cannot be easily held with typical vacuum chucks. Thin PMs provide both reduced weight and size compatibility with related processing equipment, such as aligners. We have also created plastic masters of a single device the size of a standard microscope slide and masters encompassing an entire 6" wafer with several devices (Fig. 1F). PMs fabricated using this technique have a shore D hardness of 70 and ultimate tensile strength of 3000 psi and are robust during normal handling. In addition, the PMs are resistant to moisture,

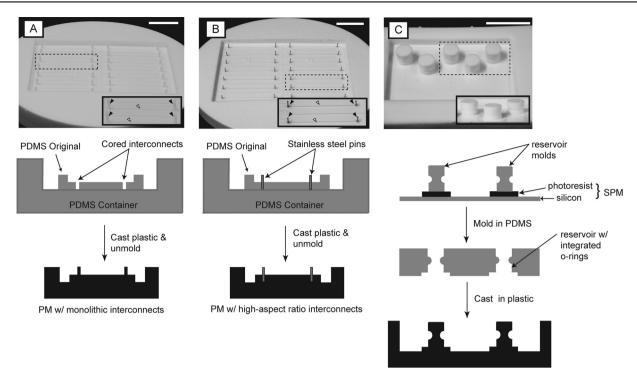


Fig. 3 World-to-chip connections (schematics not to scale). (A) Master containing high-aspect-ratio posts molded in plastic provide a method for molding world-to-chip connections directly into devices without the need for punching or coring holes. Inset shows zoomed in view of two parallel channels (white arrowheads) with high aspect-ratio structures (black arrowheads) at the input and output. Scale bar 25 mm. (B) Master containing integrated pins for denser world-to-chip connections with narrower tubing interfaces. Inset shows zoomed in view of two parallel channels (white arrowheads) with pins (black arrowheads) at the input and output. Scale bar 20 mm. (C) Master with integrated molds for o-ring-type connections. The groove mid-way between the posts (as shown in the inset) when cast in PDMS resembles an o-ring and forms a robust, press-fit fluidic seal. Such masters can be generated starting from either SPMs or PMs. Scale bar 15 mm.

many solvents (with the exception of acetone and toluene), weak acids and can withstand temperatures up to 75 °C. Post-curing the master at 65 °C for 2–4 h further enhances physical property performance.

Various microfluidic topologies have been successfully reproduced as PMs as shown in Fig. 3. Microfluidic devices ranging from standard single-layer multiple-input channels (Fig. 3A), serpentine channels (Fig. 3B), micro-post arrays¹⁸ (Fig. 3C) and micromixers¹⁹ have been successfully reproduced as PMs. The micro-post arrays, especially, provide a more robust alternative to similar features replicated in photoresist, which are prone to delamination during PDMS molding. Creating a monolithic master eliminates the common failure mode in SPMs whereby the tall and narrow photoresist posts delaminate from the silicon wafer during molding. The SEM images show excellent fidelity in reproduction from PDMS originals and exhibit sharp sidewalls.

World-to-chip connections

We have also found that PMs are well suited for the direct molding of world-to-chip connections of devices. PMs allow for the integration of—(1) rigid, high-aspect—ratio posts (as shown in Fig. 2A), (2) stainless steel pins (as shown in Fig. 2B), and (3) o-ring-style press-fit interconnects (as shown in Fig. 2C). These devices allow for the generation of reliable fluidic connections and prevent failures resulting from poor interfaces to device inlet/outlet ports.

Quantitative characterization

We used a standard photolithographic resolution test target (USAF 1951) to fabricate an SPM (using SU-8) and then formed a PM from that master (via PDMS). The SPM and PM were then imaged via an SEM to compare fidelity. The SEM images (Fig. 4) show slight shrinkage ($\sim 4\%$) of the PM features with respect to the original SPM. The SEMs also show that features of 2 µm can be reliably replicated (Fig. 4, right column). This shows that PMs provide resolution comparable to SPMs (and would faithfully replicate even the smallest features realized with SPMs, typically ~ 1 um). Profilometer measurements showed an average roughness of the PM of 5.9 nm (n = 5), rougher but comparable to that of the SPM of 3.4 nm (n = 5). We also quantified distortions arising from replications from EMs across large arrays of structures (Fig. 5). These measurements show that there is a distortion of $\sim 10 \, \mu m$ over a 1 mm² area of interest (this area of interest was chosen as it was amenable with highresolution electron microscopy). Finally, PMs can be selfreplicated through repeated castings in PDMS and plastic, providing a cost-effective route for the scaling-up of fabrication of masters. We quantified the ability of PMs to replicate by casting the resolution test target twice-over and compared the first generation PM to the third generation. Comparisons of these two PMs (shown in Fig. 6B) show that there is again a slight shrinkage of features (\sim 3%) over these successive replications, demonstrating that PMs can be self-replicated

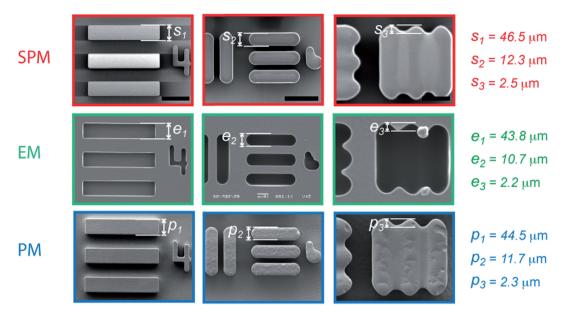


Fig. 4 PM replication fidelity. Each row shows SEM images of a standard photolithographic resolution target (USAF 1951) fabricated in SU-8 (top row), cast in PDMS (middle row) and subsequently cast in plastic (bottom row). Columns from left to right show features of decreasing linewidth; the smaller features are not replicated properly in the starting SPM. On the right we show measurements made from the SEM images indicating that the PMs are analogous to the SPMs in terms of resolution (\sim 4% change). Scale bars 50 µm (left column), 25 µm (middle column), and 5 µm (right column). SEM images taken at high magnification (3000×), right column, indicate that feature sizes of 2 µm can reliably be replicated in plastic.

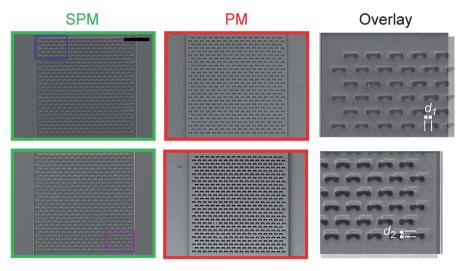


Fig. 5 Distortion in PM fabrication process. SEM images of EMs (left column and PMs (middle column) of arrayed features from two different (top row and bottom row) devices on an SPM (the two devices were separated by \sim 3 inch). Overlays of the arrays (right panel) where top overlay corresponds to boxed region of the first device, and bottom overlay (bottom panel) corresponds to boxed region of the second device. Overlays quantify distortions, with in-plane distortions of \sim 10.5 µm ($d_1 = 12.51$ µm, $d_2 = 9.49$ µm) measured across a 1 mm² area. Scale bar 200 µm.

with minimal loss of fidelity. This 3% shrinkage represents a worst-case scenario as to scale-up the fabrication of PMs a single PDMS device would be used repeatedly to make multiple PMs (with no loss of resolution) as compared to the scheme depicted in Fig. 6A where a single PDMS device is used once to make a single PM.

Taken together these results demonstrate that the PMs serve as excellent replicas of SPMs. The $\sim 4\%$ in-plane accuracy is comparable to typical in-plane photolithographic tolerances of $\sim 10\%$, making PMs ideal candidates for use in a wide variety of applications for soft lithography.

Discussion

Polymer molding has been previously employed in the generation of masters for soft lithography, most notably in the use of UV-curable epoxies such as Epotek and NOA.⁹⁻¹³ UV-curable epoxies have also been used to create rigid molds for microcontact printing applications.^{20,21} While these techniques have used epoxies for molding and mastering, the fidelity of these UV-cured masters (UVMs) has not been described. Also, the generation of UVMs with integrated world-to-chip connections and the ability of self-replicate UVMs have not been previously

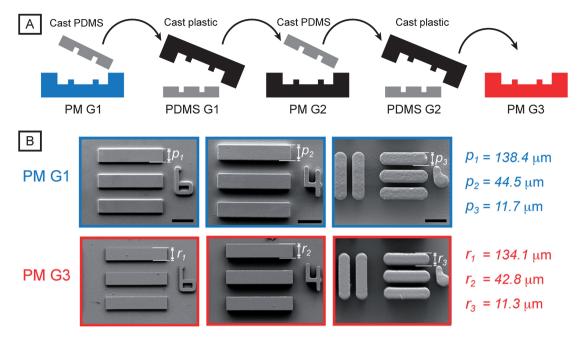


Fig. 6 PM self-replication fidelity. (A) Self-replication process schematic, first-generation PM (PM G1) is cast in to PDMS then plastic (and repeated once again) to yield a third-generation PM (PM G3). (B) SEM images of test targets replicated as in the scheme shown in (A). PM G1 (top row) and PM G3 (bottom row) imaged at a range of magnifications. Measurements indicate that the masters do not degrade significantly in fidelity. Scale bars 150 μm (left column), 50 μm (middle column), and 10 μm (right column).

reported. By quantitatively characterizing our plastic molding process and demonstrating its self-replication capability we have provided the necessary information for the dissemination of our simple technique.

PMs provide a simple approach for PDMS-based molding with a number of advantages over UVMs. First, they do not require UV-curing systems or lamps and can be readily produced in any lab that already employs soft lithography. Second, the PM fabrication process is performed at room temperature and hence the generation of large-area masters does not require additional process optimizations such as adjusting UV dosage which would be required for UVM fabrication. Finally, PMs can be fabricated at the fraction of the cost of UVMs and hence provide a more reliable route to the scale-up of master fabrication (and subsequent device fabrication).

PMs also have distinct advantages over the SPMs from which they are derived. The PM fabrication process creates monolithic molds and hence delamination between the features and the substrate is no longer a limiting factor. Consequently, PMs can be re-used practically indefinitely. In our hands, we have molded from PMs up to 50 times without apparent degradation of the master. The inherent fragility and failure-prone material interface of SPMs can make repeated castings at times challenging. PMs also simplify the fabrication of elastomeric devices in that they do not require silanization, a required step for use of SPMs. Additionally, PMs with raised features have been demonstrated for the spin-casting of PDMS/RTV for the generation of microfluidic valving control layers, providing for more costeffective and robust masters for multi-layer soft lithography as compared to SPMs. PMs have integrated troughs in which PDMS is cast which makes for a cleaner, more reliable fabrication procedure compared to SPMs which are either placed in

a secondary container (such as a Petri dish) or have a secondary container fashioned around them (typically from aluminium foil). Since PMs do not require additional equipment for fabrication they can be readily fabricated in a standard biology or chemistry laboratory and hence can facilitate the dissemination of technologies from engineers to scientists. Finally, due to their low-cost and ease-of-fabrication PMs are better suited to the scale-up of fabrication of masters and devices than both UVMs and SPMs. Indeed, we have used PMs extensively for large-scale production of devices for educational projects.²² The ability to easily fabricate large numbers of devices is also important for single-use devices, and hence PMs have important implications for microfluidics fabrication outside of the realm of academic research.

The PM fabrication process uses two distinct polymer chemistries (PDMS and polyurethane) with different cure dynamics and properties and hence it is important to characterize the inherent distortions involved in the fabrication process. Distortions in soft lithography have been the subject of considerable past study²³ and show ~ 500 nm lateral distortion over a ~ 1 cm² area (for a ~ 0.1 mm thick PDMS sample). Distortions can be challenging to measure and are dependent on the thickness of the structures, the curing conditions and the compositions of the polymer used for casting. Our measurements indicate that PDMS masters closely match the SPMs (from Fig. 4) and that the inherent distortions from SPMs to PDMS will be unavoidable.

Here we show the use of a certain plastic chemistry (SmoothCast 310, Smooth-On, Inc.) for molding applications; however, we have used other room-temperature-cure plastic chemistries (such as TASK 3, Smooth-On, Inc.) as well (not shown). These higher performance plastics with 6600 psi tensile

strength, Shore D hardness of 80, and compressive strength of 8300 psi may be desirable for certain applications (such as the generation of even thinner masters for spin-casting). Thus the plastic-molding method is a general technique and can be used to generate PMs with a range of material properties. Since this technique uses liquid pre-cursors of plastics, a number of additives can be incorporated to alter both the appearance and cure dynamics of the masters themselves. Pigmentation dves can be added to the master (as shown in Fig. 1F) to color-code masters. Metallic powders can be added to increase the optical contrast of masters (particularly useful for masters for spin-casting where bulk-cast chips are to be optically aligned to the thin, spin-cast membranes to realize multilayer microfluidic devices). A variety of cure accelerators can be added to the liquid plastic pre-cursors to further reduce the fabrication process time (at the very least by a factor of 2).

PMs greatly simplify world-to-chip connections. As microfluidic devices gain in complexity and with the trend towards more fully integrated devices, ²⁴ world-to-chip connections play an increasingly important role. PMs provide significant ease-of-use and flexibility in the integration of world-to-chip connection ports directly on the master, thus limiting time-consuming and tedious coring/punching of interconnects by hand. Moreover, PMs enable the realization of new types of interconnects, such as those integrating o-ring-style connections (as detailed in Fig. 2C). These o-ring type connections could easily be further miniaturized for a number of tubing dimensions (and directly integrated on PMs) to allow for robust, scalable, press-fit interconnects for integrated microfluidic systems.

While PMs provide significant ease-of-use and distinct advantages over SPMs and UVMs, they do have a few limitations. PMs cannot be directly generated using photolithographic techniques and hence at the very least require the fabrication of PDMS chips from SPMs. Similar to many other plastics, PMs have limited resistance to certain solvents; acetone and toluene will degrade the features on a PM. PMs also have limited temperature resistance and cannot withstand temperatures higher than 75 °C. This precludes the use of certain protocols for flash-curing PDMS devices at high-temperatures (~150 °C).²⁵ The fabrication process for the PMs could be further optimized, for example, the degassing of the PDMS container and device could be eliminated altogether by using a plastic with a longer pot life, allowing for the plastic precursor to be degassed after being poured in the PDMS container. This would make the PM fabrication process analogous to the standard soft-lithography process for the fabrication of PDMS devices.

In all, the ability to make (1) robust and scalable interconnects, (2) masters for spin-casting, and (3) large-area masters, represent distinct conceptual advances by PMs compared to previous rigid template mastering techniques such as those employing UV-cured materials (such as Epotek and NOA).

Conclusions

We have presented a simple, cost-effective technique for the fabrication of rigid plastic masters for the use in soft lithography. This technique allows for the easy creation of robust monolithic molds that faithfully reproduce micron-sized features and are suitable for repeated casting. By combining conventional SPMs

with posts and other three-dimensional structures, PMs can create monolithic three-dimensional structures from the size scale of microns to centimeters, a feat that is difficult to achieve with either photolithography-based microfabrication or conventional machining techniques.

Acknowledgements

The authors would like to thank the W. M. Keck Imaging Facility at the Whitehead Institute for the use of the SEM and the Center for Material Science and Engineering (CMSE) for the use of the profilometer. We thank Brian M. Taff, Hsu-Yi Lee, Adam Rosenthal and Alison Skelley for the fabrication of SU-8 masters. This work was supported in part by the NIH (RR199652 and EB005753), the Singapore-MIT Alliance, and the d'Arbeloff Fund for Excellence in Education.

References

- 1 Y. Xia and G. M. Whitesides, Angew. Chem., Int. Ed., 1998, 37, 551-553.
- 2 M. P. Larsson, R. R. A. Syms and A. G. Wojcik, J. Micromech. Microeng., 2005, 15, 2074–2082.
- 3 H. S. Khoo, K.-K. Liu and F.-G. Tseng, J. Micromech. Microeng, 2003, 13, 822–31.
- 4 A. Bubendorfer, X. Liu and A. V. Ellis, *Smart Mater. Struct.*, 2007, **16**, 367–371
- 5 Y.-C. Toh, C. Zhang, J. Zhang, Y. M. Khong, S. Chang, V. D. Samper, D. van Noort, D. W. Hutmacher and H. Yu, *Lab Chip*, 2007, 7, 302–309.
- 6 Y. Xia, E. Kim, X.-M. Zhao, J. A. Rogers, M. Prentiss and G. M. Whitesides, *Science*, 1996, 273, 347–349.
- 7 K.-H. Jeong, J. Kim and L. P. Lee, Science, 2006, 312, 557-561.
- 8 J. L. Tan, J. Tien, D. Pirone, D. S. Gray and C. S. Chen, *Proc. Nat. Acad. Sci.*, 2003, 100, 1484–1489.
- 9 Y. Huang, G. T. Paloczi, J. K. S. Poon and A. Yariv, *Appl. Phys. Let.*, 2004, **85**, 3005–3007.
- 10 Y. Huang, G. T. Paloczi, J. K. S. Poon, A. Yariv, X. Zhang and L. R. Dalton, J. Phys. Chem. B, 2004, 108, 8606–8613.
- 11 K. G. Klemic, J. F. Klemic, M. A. Reed and F. J. Sigworth, *Biosens. Bioelec.*, 2002, 17, 597–604.
- 12 Y. Chung, X. Zhu, W. Gu, G. D. Smith, and S. Takayama, *Methods in Molecular Biology*, ed. S. D. Minteer, 2006, 321, 27–244.
- 13 X. Jiang, S. Takayama, X. Qian, E. Ostuni, H. Wu, N. Bowden, P. LeDuc, D. E. Ingber and G. M. Whitesides, *Langmuir*, 2002, 18, 3273–3280
- 14 M. T. Lam, W. C. Clem and S. Takayama, *Biomater.*, 2008, 29, 1705–1712
- 15 K. E. Paul, M. Prentiss and G. M. Whitesides, Adv. Func. Mater., 2003, 13, 259–263.
- 16 S. P. Desai, B. M. Taff and J. Voldman, *Langmuir*, 2008, **24**, 575–581.
- A. Skelley, O. Kirak, R. Jaenisch and J. Voldman, *Proc.* μ*TAS*, 2007, 2007, 581–583.
- 18 A. D. Rosenthal, A. MacDonald and J. Voldman, *Biomater.*, 2007, 28, 3208–3216.
- 19 H.-Y. Lee and J. Voldman, Anal. Chem., 2007, 79, 1833–1839.
- 20 Y. Xia, J. J. McClelland, R. Gupta, D. Qin, X.-M. Zhao, L. L. Sohn, R. J. Celotta and G. M. Whitesides, Adv. Mater., 1997, 9, 147–149.
- 21 J. C. Love, D. B. Wolfe, H. O. Jacobs and G. M. Whitesides, *Langmuir*, 2001, 17, 6005–6012.
- 22 D. M. Freeman, A. J. Aranyosi and M. Gray, HST.410J/6.07J Projects in Microscale Engineering for the Life Sciences, Spring 2007, Massachusetts Institute of Technology, MIT OpenCourseWare, http://ocw.mit.edu (accessed March 10, 2007). License: Creative Commons BY-NC-SA.
- 23 J. A. Rogers, K. E. Paul and G. M. Whitesides, *J. Vac. Sci. Technol. B*, 1998, 16, 88–97.
- 24 S. Einav, D. Gerber, P. D. Bryson, E. H. Skan, M. Elazar, S. J. Maerkl, J. S. Glenn and S. R. Quake, *Nat. Biotech*, 2008, 26, 1019–1027.
- 25 A. O'Neill, J. S. Hoo and G. Walker, Chips and Tips, 2006.