A fast and simple method to fabricate circular microchannels in polydimethylsiloxane (PDMS)†

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Received 11th June 2010, Accepted 15th October 2010
DOI: 10.1039/c0lc00093k

A simple method to fabricate circular microchannels in polydimethylsiloxane (PDMS) is presented. A coating of liquid PDMS is applied on the walls of rectangular microchannels, fabricated using standard soft-lithography, by introducing a pressurized air stream inside the PDMS filled microchannels. Surface tension of the liquid PDMS forces the coating to take a circular cross-section which is preserved by baking the device to cure the coated layer. Diameters ranging from a few micrometres to a few hundreds of micrometres were achieved. The method was verified to work on microchannel networks as well as in straight channels. Different coating conditions were systematically tested. Design curves are reported for one to choose appropriate coating conditions for obtaining a desired diameter. A comparison between the performance of square and circular microchannels in trapping SiHa cells (cervical cancer cell line) is shown.

Introduction

In the past two decades, microfluidic and lab-on-a-chip (LOC) devices have enabled many biological advances, such as proteomics,[1] PCR,[2] cell manipulation,[3] and tissue engineering.[4] Microchannel networks for LOC devices are often fabricated using soft-lithography[5] or regular microfabrication techniques (photolithography followed by etching and bonding)[6–8] from which microchannels typically inherit a rectangular cross-section.

Although rectangular cross-sections are functionally adequate for many purposes, certain applications would benefit from microchannels with circular/round cross-sections. For example, in-plane microchannels are useful for immobilizing many cells for pharmacologic testing,[9] single-cell electroporation,[10] and cell–cell communication.[11] However, rectangular cross-sections (*vs.* circular/round cross-sections) form poor seals between a cell and a microchannel opening, requiring the application of large immobilization pressure that often undesirably causes cell lysis. Furthermore, circular microchannels are intuitively suitable for microfluidics-based cell electromechanical studies involving micropipette aspiration[12] and patch clamping[13,14] to achieve a satisfactory seal between the cell and the channel inlet.[15,16] Studies involving endothelial cell culture inside microchannels as an *in vitro* model for microvasculature can also benefit from the use of circular microchannels to more closely mimic blood vessels.[17,18] Rectangular microchannels limit cell growth on the channel bottom by exposing the cells to a non-physiological geometry. Cells grown on the bottom of a rectangular channel experience a varying shear stress which influences their alignment and elongation, differentiation, and gene expression.[19]

Circular microchannels can also increase the efficiency of light transmission inside on-chip waveguides for light-sensing and light actuation methods implemented in lab-on-a-chip devices.[20] Another advantage of circular microchannels is that they do not exhibit the flow stagnation phenomenon present in the corners of rectangular microchannels due to the symmetric velocity profile.[21] This stagnation zone in rectangular microchannels leads to dispersion of the analyte plug in separation processes, undesirably increasing the theoretical plate number.[22]

Recognizing the benefits of circular microchannels, several research groups were motivated to investigate new techniques for circular channel fabrication. For example, femtosecond laser pulses were used to increase the selectivity of HF etching in fused silica,[23] thus enabling etching circular passages with large aspect ratios; however, the longest channel achievable was limited to 1.5 mm. Arduous microfabrication recipes were also developed to produce circular microchannels. For example, forming circular microchannels required three deposited layers of silicon nitride, two reactive ion etching steps, and two wet etching processes.[24] A less complicated method involved etching a trench in silicon and filling it with a thick layer of doped silicon oxide that was later annealed to close the trench and form a circular channel.[15,25] However, this technique is only capable of forming very small circular microchannels (few micrometres in diameter) in silicon.

Researchers also explored methods involving the modification of existing soft-lithographic techniques to obtain circular

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† Electronic supplementary information (ESI) available: Variation of PDMS viscosity with shear rate, additional pictures of coated channels, and a video depicting a comparison between cell trapping using circular and square microchannels. See DOI: 10.1039/c0lc00093k

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channels. For example, photoresist annealing[26,27] and back side UV exposure[28] can produce semi-circular photoresist patterns which, after being transferred to PDMS, could be aligned and bonded to form circular microchannels. Nevertheless, the alignment and bonding of the two halves are problematic due to the flexibility of PDMS and the irreversible bonding of the two halves once they touch.

An interesting method for creating microchannels with semi-circular cross-sections was developed using capillary rise of liquid PDMS inside an open groove in a PDMS slab.[22] Yet, the requirement of making open grooves in thin layers of PDMS combined with aligning and bonding the two semi-circular halves together limited this method to forming channels of a few hundred micrometres in diameter. A simpler approach was reported, in which PDMS was cast on wires,[29–31] glass rods,[32] or nylon threads[33] instead of photoresist patterns to produce circular microchannels. However, welding microwires/rods together to form the desired network master rendered this technique non-practical for forming complex networks of microchannels. Additionally, having to pull the wires/rods out of the microchannel network after molding places restrictions on device design. Although using solder wires, which can be melted out of the channel, solved this problem,[18] it limited the minimum diameter achievable due to the large diameters of solder wires available (minimum of 300 μm).

Here, we present a rapid and simple technique to produce circular microchannels with diameters ranging from a few micrometres to hundreds of micrometres. Our technique uses a stream of pressurized air to displace[34,35] liquid PDMS filling a square microchannel fabricated using soft lithography. This leaves a thin coating of PDMS on the channel interior with a circular cross-section due to surface tension. Upon baking, this PDMS coating bonds to channel walls creating a circular microchannel. Although similar to the technique used by Abate *et al.*[36] who applied sol–gel coating on PDMS microchannels, our technique is more accessible and can be applied to square microchannels under any condition, contrary to the sol–gel method which requires coating to take place right after plasma bonding. We used this new method to make networks of circular microchannels with various diameters. We also report design curves for one to choose appropriate coating conditions to obtain a desired microchannel diameter. To demonstrate an advantage of the fabricated circular microchannels, we used them to trap cells at much lower pressures compared to square microchannels, which maintains the integrity of cells for further testing (*e.g.*, patch clamping, electroporation, and micropipette aspiration).

Experimental

Materials

All solvents were obtained from Fisher Scientific (Ottawa, ON) unless otherwise specified. SU-8 photoresist and SU-8 developer were from MicroChem Corp. (Newton, MA). Polydimethylsiloxane (PDMS) and Dow Corning Sylgard-184 kits were from Ellsworth Adhesives Canada (Burlington, ON). Silicone oil DMS-TO1 was obtained from Gelest Inc. (Morrisville, PA).

Fabrication of SU-8 masters

Channel masters were fabricated in the clean room facility of the Emerging Communications Technology Institute (ECTI) at University of Toronto. Glass slides were cleaned in acetone, methanol, and DI water, and dried on a hot plate (5 min @ 95 °C). A 5 μm thick seed layer of SU-8-5 was spin coated on a glass slide to enhance adhesion of the patterned SU-8 layer to the glass slide. SU-8-5 was spun on the slide (500 rpm for 5 s + 3000 rpm for 30 s), soft-baked (1 min @ 65 °C + 3 min @ 95 °C), and exposed to UV light (4 s, 16 mW cm^{-2}, 365 nm) through a transparency mask (Pacific Arts and Design, Toronto, ON) for large channels or a chrome-on-glass mask (University of Alberta Nanofabrication facility, Alberta) for small channels using a Karl Suss MA6 mask aligner (Garching, Germany). Slides were then baked on a hot plate (1 min @ 65 °C + 1 min @ 95 °C) to cross-link the exposed SU-8-5, developed in SU-8 developer for 20–30 s, and finally hard baked (2 hours @ 175 °C). The SU-8 layer carrying the channel pattern was prepared similarly according to the recipe summarized in Table S1 in ESI†.

PDMS molding and channel bonding. PDMS prepolymer and curing agent were mixed at a ratio of 10 : 1, degassed in a vacuum desiccator, poured on a channel master placed in an aluminium foil plate, and finally baked in a convection oven (15 min @125 °C). PDMS channels were then peeled from the SU-8 master and reservoir holes were punched through. Bonding to glass slides was done using a portable corona treater as described by Haubert *et al.*[37] where PDMS pieces and glass slides were treated with a BD20-AC corona treater (Electro-Technic Products Inc., Chicago, IL) for 30 seconds per piece, pressed together, and baked on a hot plate (1 hour @ 100 °C).

Liquid PDMS coating to achieve circular cross-sections

To create circular cross-sections, the rectangular PDMS microchannels were filled with liquid PDMS (sometimes diluted with heptane or silicone oil) using a syringe connected to one reservoir. After filling the channels, excess PDMS was removed from the reservoir using a piece of tissue. The device was baked on a hot plate (10–60 s @ 75–150 °C) according to the final diameter desired (see Results section). A stream of compressed air *with constant pressure* was then pushed through the PDMS-filled microchannels from the other end for about 2 min using a spray gun (Innotech Products Inc., Minneapolis, MN) fitted with a blunt needle with the device still being baked on the hot plate. To fully cure the deposited PDMS coating, the device was left on the hot plate for at least 5–10 min. If compressed air tanks are not available, pressurized gas canisters, used for cleaning electronic circuits, can be used instead. However, since the pressure inside these canisters decreases with usage, they should be replaced regularly to achieve repeatable results.

Multiple coatings of the same channels can be performed to achieve smaller diameters. In such case, two or more layers of coating were applied consecutively using the method described above. Coating conditions (*e.g.*, baking time and temperature) for the latter coatings are different from the first layer to account for changes in channel diameter after each coating.

Results and discussion

When a viscous liquid filling a channel is displaced by a stream of gas, a portion of the liquid remains deposited on the microchannel walls due to its viscosity (Fig. 1a). At the microscale, where inertial effects are negligible compared to viscous and surface effects, this deposited liquid layer minimizes its surface energy by forming a stable cylindrical liquid–gas interface inside the microchannel. Using PDMS as the coating liquid and baking the devices while flushing air in the microchannel form a permanent coating with a circular cross-section (Fig. 1b and c).

The success rate for making circular microchannels using this method was 81%, based on coating 360 microchannels. Coating uniformity along channel length was tested and found to be consistent for microchannels as long as 16 cm long (channels were formed in the shape of a spiral to fit on a glass slide); see Fig. S1†. Moreover, coating conditions were tunable and could form circular cross-sections that are much smaller than the original size of the square microchannel; see Fig. S2†. When multiple coatings were applied, diameters as low as 0.26 of the original channel width were achieved (Fig. 1d). Thus, multiple coatings can be applied to convert large microchannels, including those produced by standard soft lithography or by rapid prototyping methods with limited resolutions,[38,39] to much smaller circular microchannels.

Coating conditions

Many studies[34,35,40] have investigated the use of a gas stream to displace a liquid filling a channel and reported that the amount of liquid deposited on channel walls increases with the Capillary number (Ca),

$$\mathrm{Ca} = \frac{U\mu}{\sigma} \quad (1)$$

where U is the speed of the gas–liquid interface, μ is the liquid viscosity, and σ is the liquid surface tension. For PDMS, the viscosity μ increases with time lapsed after mixing with the curing agent and baking temperature, and can be decreased by diluting PDMS with organic solvents[41,42] (heptane and silicone oil were used in this study). In addition to changing the viscosity, the speed of the gas displacing PDMS can be controlled by changing the pressure of the applied air stream at the microchannel inlet.

The effect of these 4 parameters (baking time, baking temperature, PDMS–heptane dilution, and air pressure) on the diameter of the resulting circular channel was systematically investigated. Microchannel diameter is denoted by the dimensionless ratio (D/W), where D is the resulting diameter, and W is the original microchannel width (Fig. 1a). A D/W ratio lower than one indicates a circular channel with a diameter smaller than the original microchannel width, whereas a ratio greater than one denotes coating of the channel corners only (Fig. S3†). The maximum value of D/W is $\sqrt{2}$ corresponding to no coating at all. Data shown in Fig. 2 were collected from coating originally square microchannels.

PDMS to heptane ratio. Diluting PDMS with heptane or silicone oil reduced its viscosity significantly, Table 1 and Fig. S4†, and resulted in lower Capillary numbers (Ca) and larger diameters for the resulting circular channels, Fig. 2. Besides reducing PDMS viscosity, heptane evaporation during baking, especially at high dilution ratios, helped increase the pressure of the applied air stream and the speed of displacing the liquid PDMS, thus forming a smoother coating. This effect was clearly observable when devices were preheated before filling them with the PDMS–heptane solution. In such cases, heptane evaporated from the diluted PDMS while it was introduced into the channel and opened a circular passage without the need for a pressurized air stream (Fig. S5†). Consistent with previous studies,[41] we did not notice

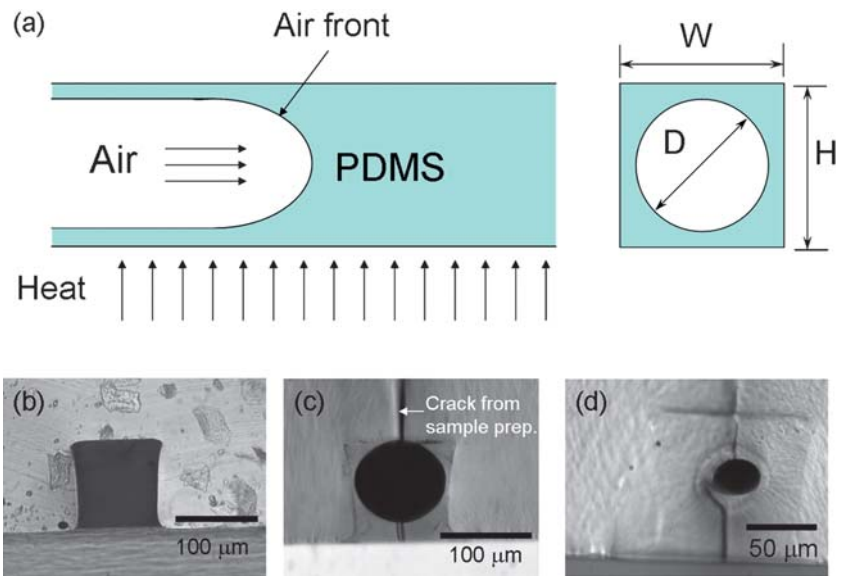

Fig. 1 (a) Schematic of the coating process. (b and c) Picture of a 100 μm × 100 μm microchannel before and after coating, respectively. (d) Picture of a 100 μm × 100 μm channel after coating it three times. Coating conditions were 125 °C baking temperature, 4 bar air pressure, 1 : 2 ratio of PDMS : heptane. First, second, and third coatings were baked for 50 s, 30 s, and 20 s, respectively. The resulting microchannel is 31 μm in diameter.

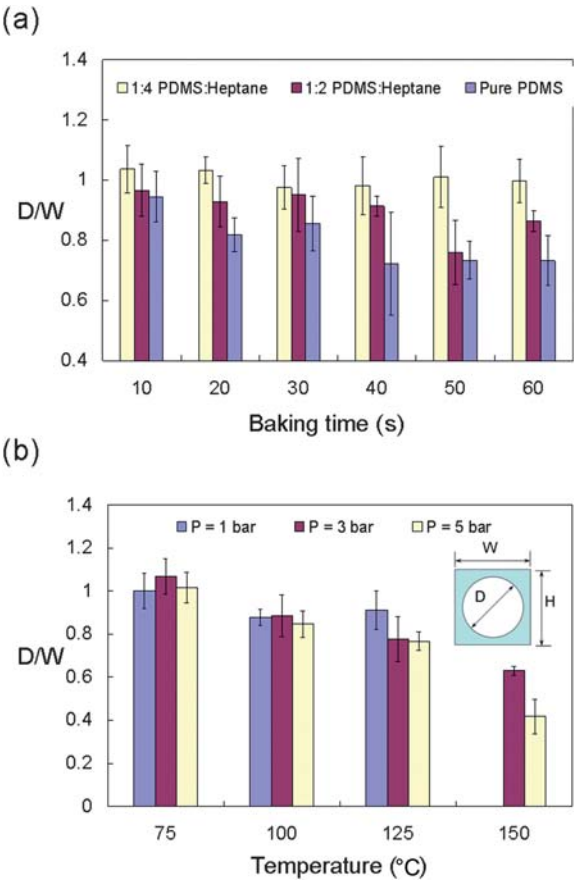

Fig. 2 Effect of different coating conditions on the resulting channel diameter, based on coating 360 microchannels. Outliers (15 points in total) have been removed using the Box-and-Whisker method; error bars are ±1 standard deviation. (a) Effect of baking time and PDMS : heptane ratio at a fixed air pressure of 4 bar and a baking temperature of 125 °C. (b) Effect of baking temperature and air pressure at a fixed baking time of 45 s and a PDMS : heptane ratio of 4 : 1. No data points exist for the 1 bar-pressure curve at 150 °C because this pressure is not high enough to open a passage in the almost hardened PDMS at such a high temperature. Viscosities of the different PDMS solutions are reported in Table 1 and Fig. S4†.

Table 1 Viscosities of the different PDMS solutions used to coat microchannels measured at a shear rate of 0.15 s^{-1}. See Fig. S4† for the effect of shear rate on viscosity

Solution	Viscosity/Pa s
Undiluted PDMS	3.521
1 : 2 PDMS : Silicone oil	0.0766
1 : 4 PDMS : Silicone oil	0.008
1 : 2 PDMS : heptane	0.0202
1 : 4 PDMS : heptane	0.0125

effects of heptane-diluted PDMS on the morphology or viability of biological cells. However, the biocompatibility of heptane-diluted PDMS deserves more systematic characterization.

Baking time. Increasing baking time resulted in smaller diameters because of the increase in PDMS viscosity (Fig. 2a). Larger channels were found to require longer baking time for curing the larger amount of PDMS filling the channels.

Baking temperature. Similar to the effect of baking time, increasing the baking temperature results in smaller diameters due to the rapid increase in PDMS viscosity (Fig. 2b). It was found, however, that the resulting diameter dependence on baking temperature was much stronger than on baking time, which makes the latter an easier parameter to control for achieving a desired diameter. Moreover, at higher baking temperatures we found a higher tendency for PDMS to rupture under the applied air pressures.

Air pressure. Increasing the velocity of the air stream used to flush liquid PDMS out of channels by increasing the air pressure was expected to increase Capillary number (Ca) and decrease the resulting diameter. However, as seen in Fig. 2b, air pressure (which was kept constant throughout the coating process) had no significant effect on the diameter except at high baking temperatures when low-pressure air streams were not able to open a passage altogether in the almost hardened PDMS filling. This insignificant effect of air pressures could be due to the fact that pressure was measured in the piping upstream of the spray gun which had a filter installed in it (0.45 Micron Filter, Innotech Products Inc., Minneapolis, MN). The filter may have reduced the pressure significantly and mitigated effects of the applied pressure differences.

Effect of channel size and aspect ratio

Circular channels were best obtained using originally square channels (1 : 1 aspect ratio). We were successful in making circular channels ranging from 200 μm to 5 μm in diameter (Fig. S6†). Smaller channels usually require shorter baking times and are sometimes difficult to fill with undiluted PDMS because of its high viscosity. For channels smaller than 50 μm, silicone oil is preferred to heptane for diluting PDMS to avoid the swelling effect of heptane on the PDMS channels.[42]

When rectangular channels were used, the resulting channels were elliptical as expected (Fig. S7a†). However, sometimes at high width-to-height aspect ratios within a rectangular channel, the air stream broke into two streams forming two small circular channels instead of a single elliptical one (Fig. 7b†). This phenomenon agrees with what previous modeling studies predicted when a gas displaces a liquid from wide flat channels.[43,44]

Microchannel networks

Lab-on-a-chip devices usually comprise networks of microchannels that are formed in various geometries to serve an intended application. These networks can contain branching points, bends, and sudden changes in channel width. We tested devices with such connections to determine how these complex geometries affect our method of forming circular channels. We found that airflow conformed well to such geometrical changes, and circular channels were formed regularly. Fig. S7c–e† show top views and cross-sections of circular channels formed around sharp turns, sudden increase in channel width, and branching points, respectively. It should be noted that the coating process may require modifications in the layout of microchannel networks to allow for proper venting of the pressurized air. Coating can be applied to literally any network of microchannels

as long as it is designed to allow for unidirectional flow of the air stream from one port to all other ports on the device.

If the microchannel network comprises channels of different widths or heights, hydrodynamic resistance will vary across channels. This variation may result in different air velocities and sometimes different coating thicknesses (*i.e.*, different ratios of D/W). We successfully coated networks of microchannels comprising channels as small as $5 \times 5\ \mu m^2$ and as large as $50 \times 25\ \mu m^2$ on the same device without having the small channels blocked. The coating thickness may have been different, but all channels were opened.

Cell trapping using circular channels

As a demonstration of the advantage of having circular channels in microfluidic applications, we have compared the performance of square and circular microchannels in single-cell trapping. Cells were difficult to be aspirated into square microchannels even at vacuum pressures as low as −2 kPa due to the lack of a good seal between the cell and the channel entrance, which results in a leaking flow through channel corners, Fig. 3. When pressure was decreased further, cells were aspirated inside the microchannels, but were lysed directly due to the large elongation resulting from the high vacuum applied. This high vacuum requirement coincides with previous studies, which reported that vacuum pressures as high as −2 psi (∼−14 kPa) were needed to trap cells at the channel entrance.[10] On the contrary, cells sealed circular microchannel inlets completely at vacuum pressures as low as −100 Pa. When the pressure was removed, trapped cells were released from the microchannels, and the deformed cells were able to return to their original state over time. A movie depicting trials of cell trapping in both square and circular microchannels is included in the ESI†.

Conclusion

Circular microchannels ranging from a few micrometres to a few hundreds of micrometres in diameter were created by applying PDMS coating to square microchannels fabricated by soft-lithography. Coating can be completed within a few minutes and does not require special chemicals or sophisticated equipment. Coating parameters have been tuned to achieve diameters as small as 30% of the original channel width with the ability to further reduce the diameter by applying multiple coatings. This method can be useful in forming microchannels of small diameters by coating large channels fabricated by rapid prototyping techniques with limited resolutions. Our method was also demonstrated to be effective in channel networks with complex geometries, such as around branching points, sharp turns, and sudden changes in channel width. We also demonstrated circular microchannels' superior performance over square ones in single-cell trapping experiments where circular microchannels achieved a better seal and required lower pressures for cell trapping. We expect this technique for forming circular microchannels to be useful for many microfluidic applications, such as those requiring cell immobilization.

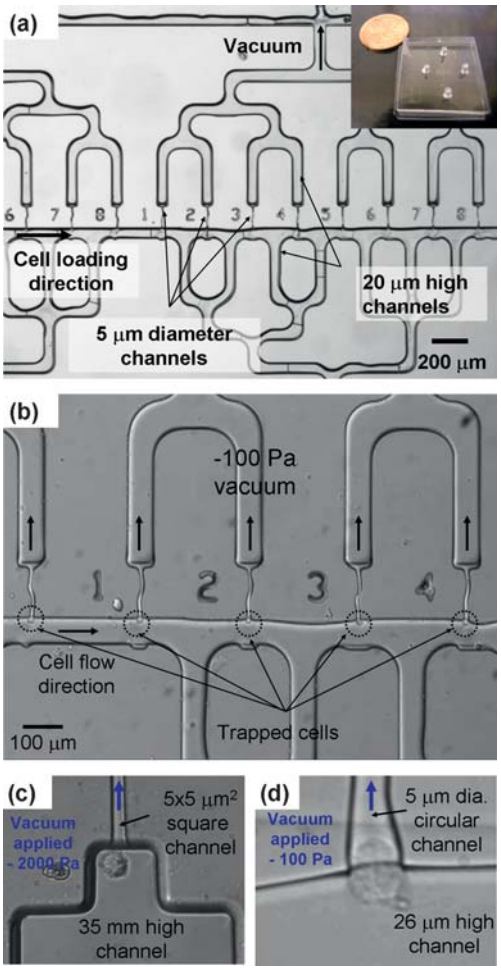

Fig. 3 Comparison between square and circular microchannels in single-cell trapping. (a) Picture of the microchannel network used for cell trapping after coating with PDMS, inset is a picture of whole device. (b) Closeup showing 5 cells trapped at inlets of circular microchannels at a vacuum pressure of −100 Pa. (c) A SiHa cell cannot be trapped at the entrance of a 5 μm × 5 μm square channel at a vacuum pressure of −2000 Pa. (d) A cell is trapped at the entrance of a circular channel at a vacuum pressure of −100 Pa. See ESI† for a short video showing the difference between square and circular microchannels in cell trapping.

Acknowledgements

We thank Dr A. Abate from Prof. Weitz group at Harvard University for helpful discussions on the coating conditions and Chris Moraes from Prof. C. Simmons group at University of Toronto for providing useful tips on SU-8 master fabrication. We also thank Lindsey Fiddes from Prof. E. Kumacheva group for the suggestion of using silicone oil for PDMS dilution. We acknowledge financial support from the Natural Sciences and Engineering Research Council of Canada (NSERC) for a Strategic Grant, an NSERC post-doctoral fellowship to M. Abdelgawad, and the Canada Research Chair in Micro and Nano Engineering Systems to Y. Sun.

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