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Fabrication of a poly(dimethylsiloxane) membrane with well-defined through-holes for three-dimensional microfluidic networks

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Abstract
We report a simple method for the fabrication of a poly(dimethylsiloxane) (PDMS) membrane with through-holes by blowing a residual prepolymer away from a photoresist (PR)-patterned Si wafer. The fabrication method for the perforated polymer membrane is crucial to achieve both complicated three-dimensional microfluidic devices and polymer sieve sheets. This method has several advantages over the previous methods in that we can repeatedly make the well-defined holes on the PDMS membranes even if the excess prepolymer remains on the PR mold after spincoating at a relatively low rpm. In addition, the desired pattern can be selectively perforated from the whole wafer even if the mold is fabricated by single-step lithography.

(Some figures in this article are in colour only in the electronic version)

1. Introduction

Microfabrication techniques of soft matter including soft lithography have been intensively developed for various applications such as microfluidics and cell biology [1, 2]. In particular, the polymer membrane with through-holes has been usefully devoted to making multilayered microfluidic channels [3] and sieves for a cell culture [4, 5]. As the applications of these techniques expand to a multifunctional regime, the fabrication processes have become more complicated.

In recent reports, through-hole membranes have been achieved by exploiting various methods such as dry etching [6, 7], microdrill [8, 9], laser cutting [10], spin-coating [11], removing photoresist (PR) posts [12] and thermal compression [3, 13, 14]. Although we look for a simple method such as spin coating that does not require additional equipment as in dry etching, microdrill and laser cutting, spin coating alone is not enough to obtain well-defined holes in the poly(dimethylsiloxane) (PDMS) membrane [11] because the residual prepolymer on PR features after spinning at low rpm is inevitable, leaving the thin membrane on the top of the PR posts. Although the substantial difference in height between the protruding PR features and the thin PDMS film allows the clearly defined holes, it is not adequate for stacking the multilayer microfluidic channels because the PR structures over a PDMS film may prevent the upper PDMS slab from contacting the film [12]. In the case of the compression method, the narrow PR patterns on the wafer are obviously subject to the highly pressurized condition in the range of 10–50 kPa [3], resulting in crushed PR features. The intricate problem of the residual thin membrane over the mold still occurs. Moreover, avoiding bubble traps under uniform compression over the wafer should be assured for large-area fabrications.

The method of assembling cylindrical posts inside a microchannel to fabricate interconnects between channels in different layers has also been proposed, but it includes the complex procedure of making the SU-8 posts and interconnect holes and is not suitable for making sieve structures [15]. Assembly methods using the PDMS building

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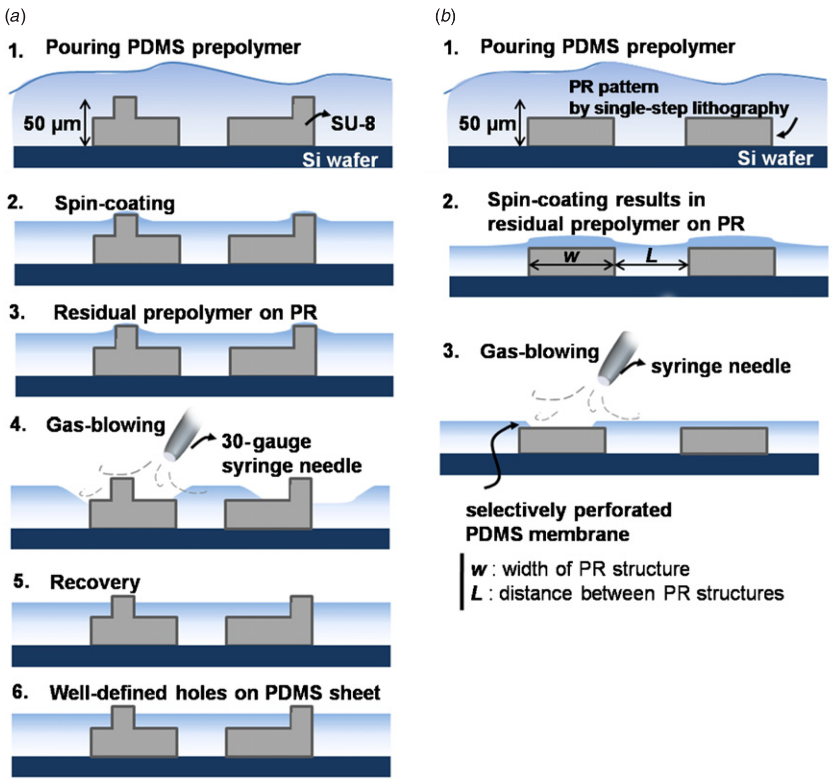

Figure 1. A scheme of fabrication processes for PDMS through-hole membrane using PR molds prepared by (*a*) two-step and (*b*) single-step lithography, respectively. Spin coating of the PDMS prepolymer on the Si wafer was followed by gas blowing which was followed by the recovery process to obtain the well-defined flat PDMS membranes.

blocks [9, 16] attract great interest, but they are currently inadequate for providing interconnections down to several tens of micrometers and require a stereolithography method [16] which is not available in a typical rapid prototyping process. Therefore, to enable easy access upon fabrication, the perforated polymer membrane should be developed for the rapid prototyping in the general laboratory environment.

In this paper, we report a simple method for the fabrication of the perforated PDMS membrane using gas blowing and successfully demonstrate the three-dimensional (3D) microfluidic device for generating 16-parallel concentration gradients. Advantages of this simple method include that we can repeatedly [12] and selectively make the well-defined holes on the PDMS membranes prepared at the low rpm [5] even with the PR mold fabricated by single-step lithography as well as two-step lithography.

2. Fabrication processes of the PDMS through-hole membrane and 3D microfluidic channels

The mold for the PDMS replica was prepared by conventional SU-8 patterning on a Si wafer. As depicted in figure 1, pouring prepolymer (Silgard 184, Dow Corning, MI) on the SU-8 mold fabricated by two-step lithography was followed by spin coating at 3500 rpm for 30 s resulting in about 40 μm PDMS membrane. The prepolymers of PDMS were left at the room temperature for 2 h before spin coating to increase the viscosity. That is because as-prepared PDMS prepolymers (10:1 mixing ratio) have a relatively low viscosity, which results in the large spoiled area when blown by the air gun. As presented in figure 1(*a*), an air compressor connected to a 30-gauge syringe needle (0.0055 inches of nominal inner diameter) generated a narrow jet of gas (air or nitrogen).[2] The prepolymer surface partially spoiled by gas blowing was restored spontaneously after we leave the wafer on the even plane for about 30 min. The pressure near the syringe needle (30-gauge) was 11 kPa and the needle was held around 2.0 mm above the PDMS surface. We mentioned the pressure rather than the velocity of the gas stream, because it is easier to follow the experimental condition according to the pressure change than the jet velocity. The air-blowing process through the nozzle continued for several seconds on the SU-8 patterns and the removal of the PDMS prepolymer from the pattern was simultaneously observed by a microscope. The air pressure above 15 kPa damaged the large area of the PDMS of 40 μm thickness and the pressure below 8 kPa was too weak to blow the residual prepolymer away from the PR post. Because these parameters do not require critical values for complete success, we can roughly use the parameter above to make well-defined through-holes.

Another approach of making the through-hole membrane of PDMS by gas blowing is to generate holes in the PDMS sheets selectively among the SU-8 patterns on the

[2] Pure gas without dust should be used. If neither an air compressor nor compressed nitrogen gas is available, a dust remover (gas sprayer) can be used. As a safety precaution, the connection of the stainless needle with the gas nozzle should be assured because the needle might be shot off from the gas nozzle.

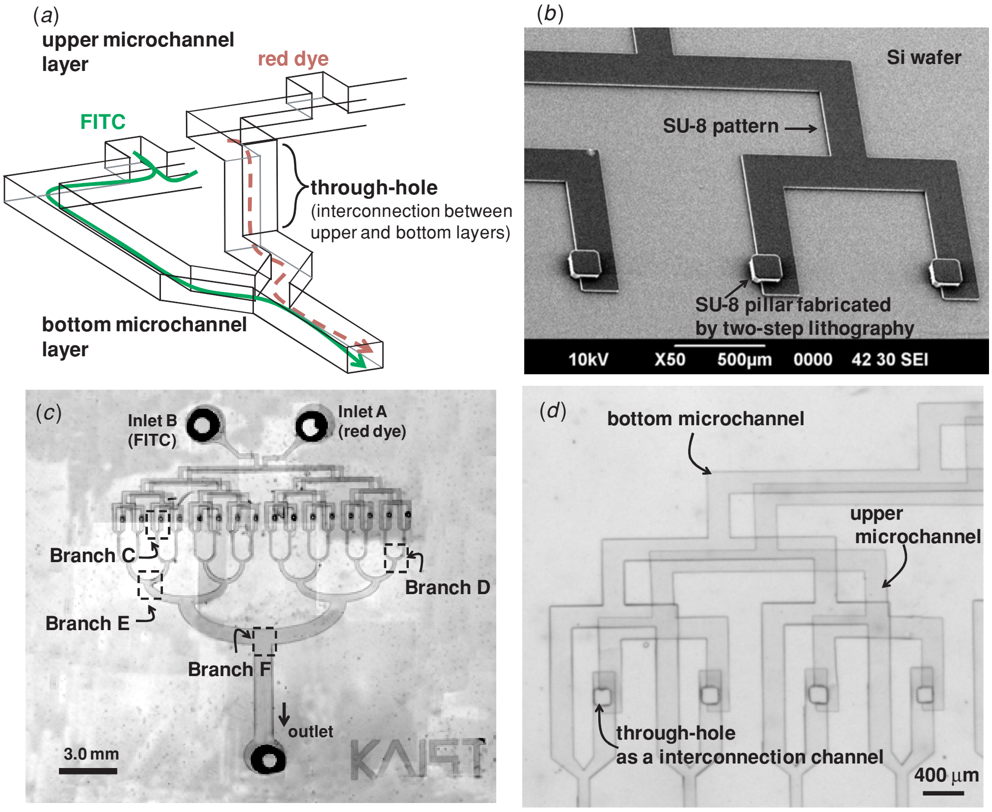

Figure 2. A 3D microfluidic device for generating 16-parallel concentration gradients. (*a*) A scheme of the interconnection part (Branch C in panel (*c*)) in the microfluidic device for 16-parallel concentration gradients. (*b*) SEM image of the SU-8-patterned Si mold fabricated by two-step lithography. The squared SU-8 posts from the PDMS holes on the membrane for interconnecting two microfluidic layers. (*c*) Microscopic image of a two-layered microfluidic device. The entire image of the device was obtained by superposing each compartmental image of the device. Dark spots in the middle of the microchannel branches are the through-holes for interconnecting the microchannels in both bottom and upper layers. (*d*) A magnified view of the microchannel area around Branch C in panel (*c*). The bottom and upper microchannels are connected by the through-holes.

wafer fabricated by single-step lithography. Although this method eliminates the need for multistep lithography, there is a limitation that it requires a sufficient distance (several millimeters of L in figure 1(*b*)) from the PR patterns to be preserved in PDMS if we want to achieve a selective perforation. If L is less than 1–2 mm, the blowing of the prepolymer on one pattern may also affect the mold beside the target. L is dependent on the intensity of blow, viscosity of prepolymer and the needle gauge. However, if the purpose is to fabricate the PDMS sieve, the distance L will not be a problem because the entire prepolymer covering the through-holes should be blown away from the PR posts. A shrinkage problem of the upper PDMS substrates was reduced by curing the PDMS prepolymer at a low temperature (60 °C) for 2 h. The microchannel dimension was designed in consideration for shrinkage of the PDMS substrate to completely align the through-holes with the microfluidic channels patterned on the upper PDMS slab. The alignment of the microchannels and the through-holes was manually carried out as we observed the patterns using a microscope.

To demonstrate the 3D microfluidic channel using the perforated PDMS membrane, we designed multilayered microfluidic channel networks, consisting of two inlets and a single outlet. 3D microflows are depicted in figure 2(*a*) and the fabricated SU-8 mold and the PDMS microfluidic device are presented in figures 2(*b*)–(*d*). The heights of the PR patterns for microchannels and through-holes are 20 μm and 50 μm, respectively. The perforated PDMS bottom layer is irreversibly bonded with the upper PDMS slab using an air plasma treatment (200 mTorr, 1 min, 200 W) by an expanded plasma cleaner (PDC-002, Harrick Science, Ossing, NY). Although the diameter of the syringe needle (about 140 μm of I.D.) is similar with that of SU-8 pillar structures (130 μm), the range that an ejected air jet influences becomes quite larger than that of the actual needle size. Consequently, the prepolymer surface area spoiled by gas blowing reaches to 1–2 mm. However, regardless of the spoiled area, the prepolymer is completely recovered and microholes are generated on the PDMS surface.

3. Results and discussion

The well-defined through-hole membrane was obtained by peeling off the PDMS sheet from the SU-8 mold after bonding with the upper PDMS substrate. To confirm the well-defined through-holes, the PR mold on Si wafer and the PDMS membranes peeled off from the PR mold were observed by scanning electron microscopy (SEM)

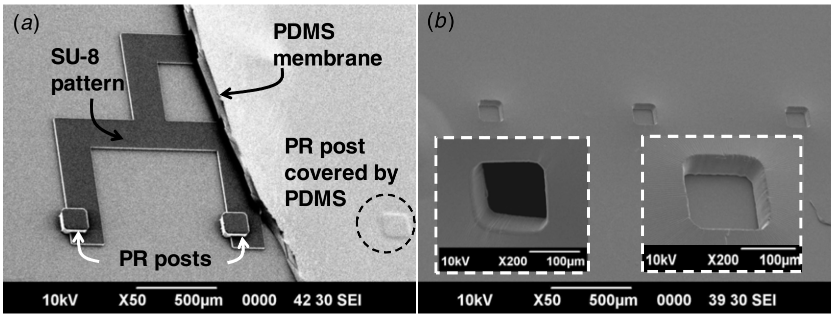

Figure 3. SEM images of the experimental results for perforating PDMS membrane using SU-8 Si mold prepared by two-step lithography. (*a*) While the spin-coated PDMS membrane shows no openings in the PDMS membrane (see dashed-circle line), (*b*) the perforated PDMS membrane can be obtained by blowing the residual prepolymer away from the PR posts. Insets in (*b*) are the magnified images of the through-hole captured from a different view. Panel b shows the top side that was open to the air except the inset right which is the bottom side in contact with the SU-8 mold.

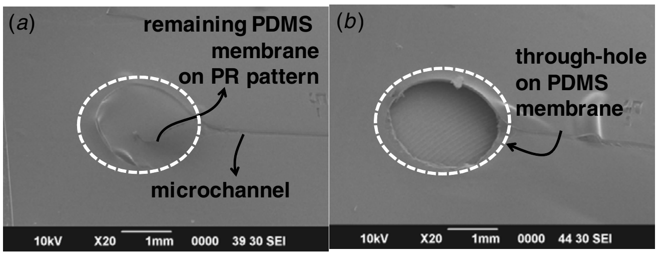

Figure 4. SEM images of the experimental results using SU-8 Si mold prepared by single-step lithography. In similarity with the results using the mold obtained by two-step lithography, (*a*) we were not able to obtain the PDMS membrane with through holes; (*b*) however, the perforated PDMS membrane can selectively be generated by the method described in this report.

(JSM-6390LV, JEOL Ltd., Tokyo, Japan) as shown in figures 3 and 4. They present the clearly defined through-holes for interconnections in 3D microfluidic channels (130 μm × 130 μm × 50 μm), while the membrane prepared only by the spin-coating process shows no openings on the surface. Even in the PDMS membrane spun on the Si wafer mold produced by single-step lithography, we were able to observe a large through-hole that was selectively perforated by the air gun (figure 4). As shown in figure 4(*b*), we can selectively perforate the PDMS membrane when L is large enough, and distinguish the clearly defined holes from the PR features covered by prepolymer by reflecting light on the prepolymer surface. In addition, we can take into account of a small curvature around the edge of the through-holes, which results from the surface tension between the prepolymer and the surface of the SU-8 posts during the recovery process. This meniscus around the through-holes may prevent the contact of the PDMS film to the upper PDMS slabs. However, the PDMS slab is flexible enough to bond and adhere to the curvature of the meniscus. Also, the effect was negligible in this experiment because the through-holes are generally aligned and bonded with the upper channel patterns, which were slightly larger than the pattern of the hole and the meniscus.

This technology was also applied to the 3D microfluidic device for generating 16-parallel concentration gradients.

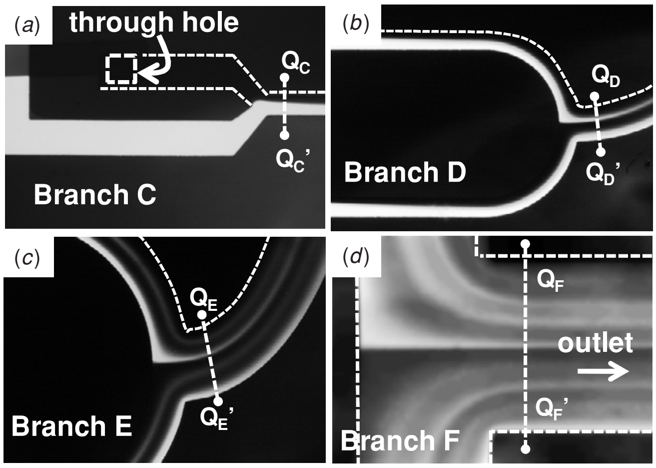

Figure 5. When we injected the red dye and FITC solution through the inlets A and B, respectively, the parallel concentration gradients were observed in each microfluidic compartment. (*a*)–(*d*) show branches C–F of figure 2(*c*), respectively.

The perforated PDMS membrane was bonded with the microchannel-patterned PDMS substrate to complete the 3D microfluidic device for generation of the parallel concentration gradient. The air bubbles trapped in the microfluidic channels were completely removed by permeation through the PDMS wall [17]. As shown in figures 5 and 6, the concentration gradients of the red dye and fluorescein isothiocyanate (FITC, 3.0 mM) solutions were successfully generated throughout the two-layered PDMS microchannels using a syringe pump (Pump 11 Pico Plus; Harvard Apparatus, Inc., MA). The fluorescent intensity peaks were measured at each branched channel of Branch C–F in figure 2(*c*) using the ImageJ software (W. Rasband, ImageJ 1.34s), where the intensity decreases in every other peak (figure 6). This result is caused by the flow of red dye in the upper PDMS channel applying pressure to the lower channel of FITC through the thin membrane. Because the channels with the red dye are overlapped with every other channel of FITC among the four channels of branch C (figure 2(*d*)), reduction of the volumetric flow rate occurs in those channels.

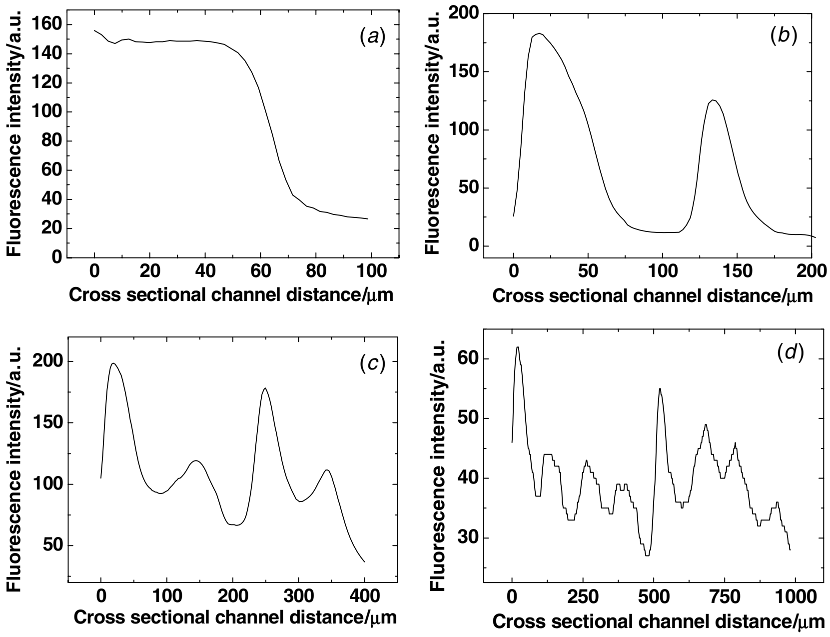

Figure 6. The fluorescence intensity was measured, (*a*)–(*d*), at each branched-channel area through branches C–F, respectively. The fluorescence intensity peaks are observed in repeated patterns however they show irregular peaks, which result in the PDMS membrane deformation due to asymmetric fluidic resistance. As shown in (*d*), we are able to measure the eight peaks of FITC intensities, which are simultaneously generated by 16-parallel FITC-red dye gradients. FITC intensity in (*d*) contains inherent noises, which are caused by a long diffusion time along the microfluidic channel (branch F), compared to the other measurement sites (branches C–E).

This simple method offers several advantages over the conventional perforating methods. First, it allows us to fabricate the perforated membranes with various thicknesses and through-hole sizes. In previous works, the PDMS membrane with well-defined through-holes of which the thickness is over 100 μm at around 1000 rpm is not achievable using only a spin-coating process because the slow speed of spin coating (2000–3000 rpm) often results in the residual PDMS membrane on the PR posts [5]. Since the size of the fabricated through-holes depends on that of the patterned PR structures, we can make them with various sizes and many kinds of shapes such as round, square and other figures we can design, while the microdrilling process is not applicable [8]. Another advantageous point is that we can selectively perforate the membrane by the blowing technique. The general methods for making through-holes of the PDMS membrane, including thermal compression, spin-coating and etching, simultaneously provide the holes on the whole Si mold, on which we cannot choose the particular perforating positions. This selective perforation capability eliminates the need of multi-step lithography for making various heights of PR structures, which means that, in other words, we are able to make the holes on the membrane even if we have PR patterns of the even height using this technique. However, in certain cases, the selectivity of perforation can be restricted because the gas blowing often provides the spoiled area of 1–2 mm. In current gas-blowing resolution for the selective perforation using the even height PR patterns, we need to design the patterns to be at least 1–2 mm apart from each other not to affect the PDMS patterns nearby the through-hole. Moreover, while the chemical etching method requires its appropriate etchant depending on the kinds of polymer, this method needs neither additional chemicals nor equipment except for the air gun and the syringe needle, as long as we use any kind of polymers that can be spin-coated on a wafer. Although we used a single syringe needle for perforating the PDMS membrane on the wafer in the current demonstration, if nozzle arrays for simultaneous ejection of the air jet is assembled, they will reduce the required time and labor, and achieve automated systems for increasing throughputs of the through-hole fabrication.

4. Conclusions

We reported a simple and easy method to fabricate PDMS membranes with well-defined through-holes using gas blowing. Despite the success of conventional PDMS through-hole techniques, it requires complicated and additional setups, confining the PDMS microfluidic techniques mainly in the two-dimensional fluidic networks. With the aid of two-step lithography, we achieved a three-dimensional channel network, which can produce 16-parallel concentration gradients of two solutions with only two layers of the PDMS substrates. Because this perforation method of gas blowing enables the selection of patterns, we could also select though-hole patterns partially from the whole wafer simply with single-step lithography. In addition, this blowing method is applicable in the various thicknesses of the polymer membranes, which is determined by the spin-coating rate (rpm) of the prepolymer.

Acknowledgments

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