SURFACE MICROMACHINING OF POLYDIMETHYLSILOXANE (PDMS) FOR MICROFLUIDIC BIOMEDICAL APPLICATIONS

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ABSTRACT

A major technical hurdle in microfluidics is the difficulty in achieving high fidelity lithographic patterning on polydimethylsiloxane (PDMS). Here, we report a simple yet highly precise and repeatable PDMS surface micromachining method using direct photolithography followed by reactive ion etching (RIE). Our method to achieve surface patterning of PDMS applied an O_2 plasma treatment to PDMS to activate its surface to overcome the challenge of poor photoresist adhesion on PDMS for photolithography. Our photolithographic PDMS surface micromachining technique is compatible with conventional soft lithography and other silicon-based surface and bulk micromachining techniques. To illustrate the general application of our method, we demonstrated fabrications of large microfiltration membranes and free-standing beam structures in PDMS for different biological applications.

KEYWORDS

Microfabrication, microfluidics, PDMS

INTRODUCTION

Polydimethylsiloxane (PDMS) is one of the most frequently used structural materials in microfluidics, owing to its biocompatibility, optical transparency, gas permeability, mechanical elasticity, and electrical insulation [1]. The complexity of PDMS-based microfluidic systems is also increasing rapidly as sophisticated functions have been integrated into single microfluidic devices. Just as the surface patterning techniques using lithography and etching processes have been the major drivers for the successful development of micro-electro-mechanical systems (MEMS), there is an increasing demand in the field of microfluidics for highly reliable, repeatable and precise surface micromachining techniques to pattern PDMS for different microfluidic and bioengineering applications. However, till now, surface patterning techniques of PDMS using conventional photolithography and etching processes have not been achieved. In fact, PDMS has been largely considered incompatible with conventional photolithography, due to its low surface energy resulting in dewetting of photoresist on the PDMS surface [2]. Soft lithography is a popular micromachining technique for rapid fabrication of PDMS structures [1]. Yet, soft lithography is a bulk micromachining technique, and it largely relies on replica molding, which often leaves behind a thin residual PDMS layer on top of the mold features. Through holes in bulk PDMS are typically achieved by punching through the PDMS structures, which can only generate macroscopic openings in PDMS and is far from a precise patterning method. Here, we report a wafer-scale PDMS surface micromachining method to generate different PDMS thin film microstructures, with their critical dimensions ranging from sub-microns to tens of microns, using a combination of photolithography, reactive-ion etching (RIE), and convenient thin film releasing techniques.

EXPERIMENT

Our PDMS surface micromachining technique is illustrated in Fig. 1. A silicon wafer was first silanized with (tridecafluoro-1,1,2,2,-tetrahydrooctyl)-1-trichlorosilane to facilitate subsequent releases of patterned PDMS layers. PDMS prepolymer was then spin coated on the silanized silicon wafer and completely cured at 110°C for 4 hrs. Then we used a gentle O_2 plasma treatment to address the major technical hurdle for surface patterning of PDMS: dewetting of photoresist on the intrinsically hydrophobic PDMS surface. The PDMS surface was switched from hydrophobic to hydrophilic, allowing a uniform coating of photoresist in the following spin coating step (Fig. 1b&2a). Uniformly coated photoresist was patterned using conventional photolithography, and the exposed PDMS was etched with RIE using SF_6 and O_2 gas mixtures to transfer photoresist patterns to the underlying PDMS layer.
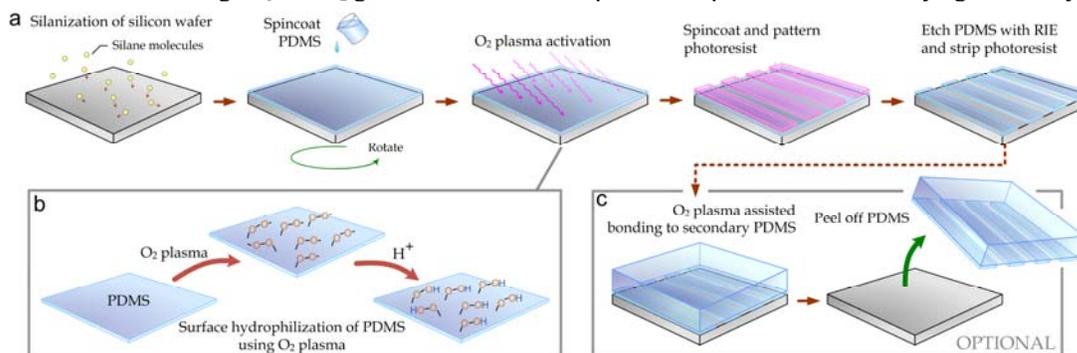
Figure 1: Schematic of surface micromachining of PDMS. (a) Fabrication process. (b) Surface hydrophilization of PDMS using O_2 plasma. (c) Releasing PDMS thin film structures using O_2 plasma assisted bonding to secondary PDMS structure.

Our PDMS surface micromachining method can be integrated conveniently with other PDMS-based soft lithography methods and conventional silicon-based surface and bulk micromachining techniques to generate submicron-scale free-standing PDMS structures (Fig. 2). As shown in Fig. 2c-d, free-standing thin PDMS cantilever and beam structures (with a thickness of 500 nm) were successfully fabricated using XeF_2-based bulk silicon dry etching after surface pattering of PDMS on the silicon wafer. These free-standing PDMS cantilever and beam structures could potentially be utilized as sensitive mechanical biosensors based on mass- or force-based methods in microfluidic devices [3]. Free-standing PDMS microfiltration membranes (PMMs, with a thickness of 2-20 µm) with an array of through holes of different diameters (4-20 µm) and center-to-center distances (6-30 µm) were also generated using our PDMS surface micromachining method (Fig. 2e&f). Our PMM fabrication method allows generations of very large membranes (up to 3 cm × 3 cm) with great porosity (up to 30%), which could lead to a significant volume throughput for processing blood specimen without clogging. These PMMs can be integrated with PDMS support structures to provide a superior mechanical strength (Fig. 1c&2e). We envision that such hybrid micro/nanoscale components and devices could find a broad range of applications for different biological and biomedical applications, given the biocompatibility of PDMS and their extensive applications in microfluidics-based bio-sensing and -analytical devices. For instance, these PMMs could potentially be utilized for size-based separation of blood cells. There is a great current interest in devising efficient techniques to isolate and enrich the rare live circulating tumour cells (CTCs) from cancer patient blood as surrogates to understand the crucial early cancer metastatic process and discover new targets or new phenotypes in the CTCs that need to be targeted. We have started to utilize these PMMs for size-based separation of CTCs. Figure 2g-j show a filter device that can efficiently capture targeted CTCs or microbeads. Another application example shown in Fig.3 demonstrated an integrated microfluidic immunophenotyping assay (MIPA) device developed using PMMs for on-chip white blood cell isolation and enrichment and AlphaLISA-based detection of TNF-α secreted by stimulated immune cells. Using microbeads whose surface was functionalized with specific surface protein antibody, we can enlarge and isolate targeted sub-population of immune cells from blood. For example, the MIPA device can isolate monocytes conjugated to anti-CD14 antibody coated microbeads (diameter of 32 um) from blood for downstream analysis. The MIPA device can achieve rapid, quantitative detection of cell-secreted biomarker proteins with a low sample volume, and can be used for monitoring immune cell functions and hence advance cellular immunophenotyping techniques for diagnosis and treatment of infectious diseases.
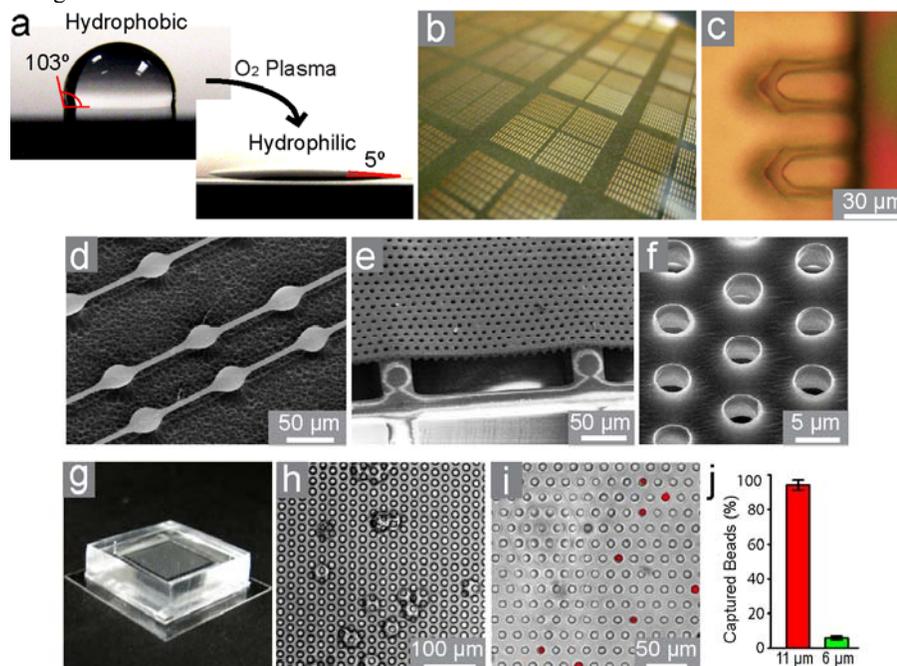
Figure 2: Surface micromachining of free-standing PDMS thin film structures. (a) Contact angles of a water drop on PDMS before (103°, left) and after (5°, right) 5 min treatment of O_2 plasma. (b) Optical image of patterned PDMS (with patterned photoresist on PDMS) on a 6-inch glass wafer. (c) Brightfield image of free-satnding PDMS cantilevers with a thickness of 500 nm, a width of 5-10 µm and a length of 30-50 µm. (d) SEM image of free-standing PDMS beam structures on a silicon wafer, with the beam thickness of 500 nm, total beam length of 800 µm and minimum beam width of 5 µm. (e&f) SEM images of a PDMS microfiltration membrane (PMM) bonded to a PDMS support structure. The PMM had a thickness of 10 µm, and it contained an array of hexagonally spaced through holes with a diameter of 4 µm. (g) Optical image of a microfluidic device containing PMM for capturing rare blood cells such as circulating tumor cells. (h) Phase contrast image of breast cancer cells (MCF-7) captured on the PMM with the through hole diameter of 8 µm. (i) Merged brightfield and fluorescence image and (j) quantified purity of microbeads captured on the PMM from a mixture of beads with different sizes (11 & 6 um). The PMM has a through hole diameter of 8 µm.

Surface micromachined device for on-chip cell isolation and Alpha-LISA detection
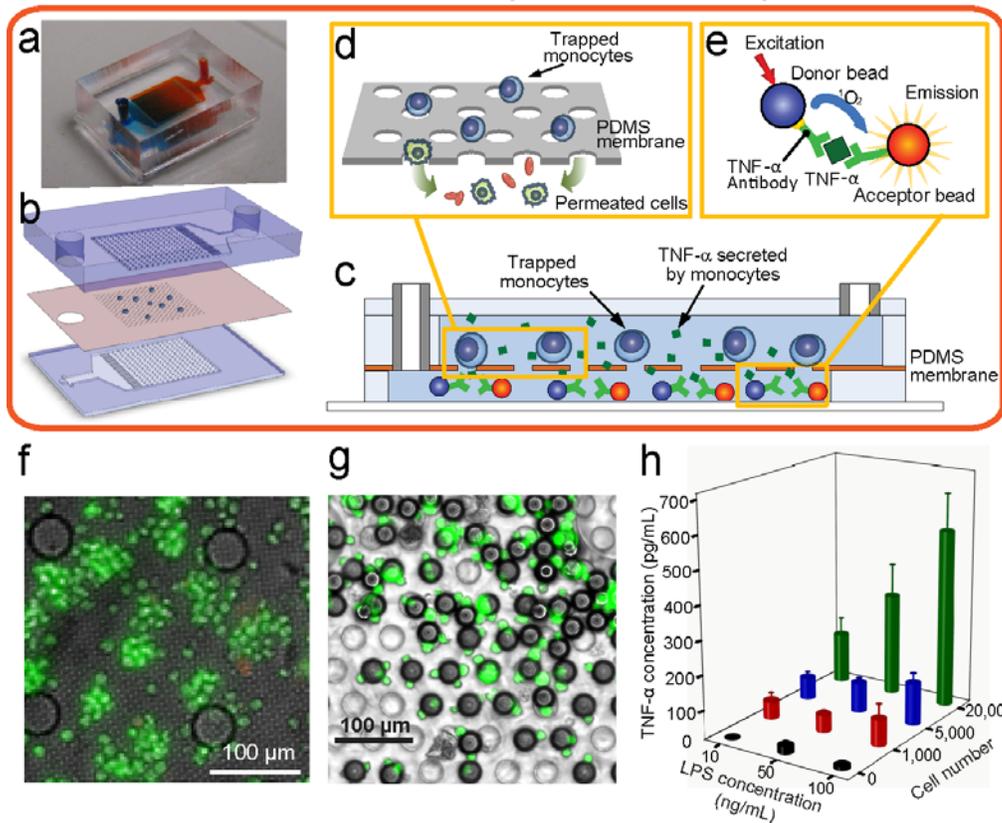
Figure 3: Microfluidic immunophenotyping assay (MIPA) device for on-chip cell isolation and Alpha-LISA detection. (a) Optical image and (b) schematic of the multilayered MIPA device. (c) Schematic of cell loading on the PMM and AlphaLISA beads loaded in the MIPA device for immunoassays. (d) Schematic of isolated monocytes on the PMM. (e) Schematic of detection of TNF-α secreted by LPS-stimulated monocytes using AlphaLISA. (f-g) Merged brightfield and fluorescence image showing trapped THP-1 monocytes (f) and THP-1 monocytes conjugated to anti-CD14 antibody functionalized microbeads (g). The cells were stained with CellTrack Green showing green color. (h) Plot of measured TNF-α concentration secreted by LPS-stimulated monocytes as a function of cell number and LPS concentration.

CONCLUSION

In summary, we have demonstrated a PDMS surface micromachining strategy using a combination of photolithography, RIE, and convenient thin film releasing techniques (O_2 plasma assisted PDMS bonding or XeF_2 Si etching). By using a gentle treatment of O_2 plasma for the PDMS surface prior to spin coating the photoresist, the long-standing challenge of photolithography on the PDMS surface was successfully addressed. Our PDMS surface micromachining technique was compatible with existing Si-based surface and bulk micromachining techniques, thus opening promising opportunities for generating different novel hybrid devices for highly integrated bio-sensing and -analytical applications. Our PDMS surface micromachining method can provide an efficient method for fabricating well-defined PDMS thin film microstructures, fulfilling the current technical demands of PDMS surface micromachining in microfluidic and bioengineering applications.

ACKNOWLEDGEMENTS

REFERENCES

[1] Y. N. Xia and G. M. Whitesides, *Annu. Rev. of Mater. Sci.,* 28 (1998), pp. 153-184.
[2] K. S. Ryu, X. F. Wang, K. Shaikh and C. Liu, *J. Microelectromech S.*, 13 (2004), pp. 568-575.
[3] J. L. Arlett, E. B. Myers and M. L. Roukes, *Nat. Nanotechnol.*, 6 (2011), pp. 203-215.

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