Published in final edited form as:
J Micromech Microeng. 2013 February 1; 23(2): . doi:10.1088/0960-1317/23/2/025009.

Characterization of freestanding photoresist films for biological and MEMS applications

D M Ornoff[1,2], **Y Wang**[2], and **N L Allbritton**[1,2,3,4]

[1]Department of Pharmacology, University of North Carolina, Chapel Hill, NC 27599

[2]Department of Chemistry, University of North Carolina, Chapel Hill, NC 27599

[3]Department of Biomedical Engineering, University of North Carolina, Chapel Hill, NC 27599 and North Carolina State University, Raleigh, NC 27695

Abstract

Photoresists are light-sensitive resins used in a variety of technological applications. In most applications, however, photoresists are generally used as sacrificial layers or a structural layer that remains on the fabrication substrate. Thin layers of patterned 1002F photoresist were fabricated and released to form a freestanding film. Films of thickness in the range of 4.5–250 μm were patterned with through-holes to a resolution of 5 μm and an aspect ratio of up to 6:1. Photoresist films could be reliably released from the substrate after a 12-hour immersion in water. The Young's modulus of a 50 μm-thick film was 1.43 ± 0.20 GPa. Use of the films as stencils for patterning sputtered metal onto a surface was demonstrated. These 1002F stencils were used multiple times without deterioration in feature quality. Furthermore, the films provided biocompatible, transparent surfaces of low autofluorescence on which cells could be grown. Culture of cells on a film with an isolated small pore enabled a single cell to be accessed through the underlying channel and loaded with exogenous molecules independently of nearby cells. Thus 1002F photoresist was patterned into thin, flexible, free-standing films that will have numerous applications in the biological and MEMS fields.

1. Introduction

Freestanding, micropatterned films for use as lab-on-a-foil devices is an area of emerging importance. These devices use flexible substrates less than 500 μm in thickness and are well-suited for a number of chemical and biological applications due to their rapid thermal transfer, low reagent use, laminar flow regimes, and flexibility - many of the same reasons that microfluidic-based lab-on-chip devices have become so attractive to the chemical and biological fields [1]. Freestanding, micropatterned films have been made using polydimethylsiloxane (PDMS) and parylene C. PDMS is frequently used in microelectromechanical systems (MEMS) and is inexpensive, optically transparent, and easily delaminated from the fabrication surface [2]. However, the fabrication of through-hole structures in PDMS is technically difficult, and thin PDMS films are mechanically fragile, limiting the range of useful thicknesses. Though a photopatternable PDMS-like silicone exists, it cannot be released from its fabrication substrate [3]. Thick PDMS films (100 μm) have been patterned by filling a microfluidic mold or by using an open photoresist mold followed by pressure application, but these processes require pre-existing molds and an overlying adhesive layer to prevent the PDMS from rising above the level of the mold surface [4]. Parylene C, a transparent poly(p-xylene) formulation, has also been shown to be

[4]nlallbri@unc.edu

amenable for forming micropatterned films and to be biocompatible, but its fabrication process is complex and requires multiple time-consuming steps including chemical vapor deposition, thermal evaporation, and reactive ion etching [5]. Thus, an inexpensive, biocompatible material that can be reliably patterned and quickly released to form a freestanding film, using a minimum of equipment and effort, would be a significant advance for the biomaterials and microfabrication fields.

Photoresists are light-sensitive resins used in a variety of industrial, chemical, and biotechnological applications. First used as protective layers in semiconductor patterning processes, photoresists have also found widespread use in recent years in a variety of applications outside the microelectronics industry [6, 7]. For example, patterned photoresists placed on a rigid substrate are often used as molds for soft lithography of PDMS [2, 8–10] and other polymers [2, 11, 12]. They also have application as protective layers during the etching of metals and silicon [13–16], as sacrificial layers to pattern silanes [17], polymers [18], and biomolecules [19–26] and as structural roles in microfabricated devices [27–33]. Pyrolysis of patterned photoresist films generates clear, microscale carbon electrodes [34–37]. Despite the many applications illustrated above, photoresists generally have been relegated to use as a sacrificial layer or as a rigid structural component remaining on its fabrication substrate (usually glass or silicon).

Though freestanding photoresist films have potential as lab-on-a-foil devices, little about such films has been reported in the literature. One reason may be that most commercially-available photoresists are not ideal for use in applications requiring a freestanding film, since these resists are brittle and inflexible [38–40]. Abgrall *et al.* detailed the fabrication use of freestanding films of the popular photoresist SU-8 for use in a lab-on-a-foil concept, but the film was laminated to a polyester support layer [41]. Other groups have fabricated and released membranes made of SiN, thin single-crystal Si, or a trilayer of metal, photoresist, and anti-reflective coating for various stenciling applications [42–44]. Wang and colleagues detailed the use of films of a negative photoresist to capture intact human colon crypts [45]. These photoresist films were detached from their glass fabrication substrates after completion of the lithography. McPherson and Walker recently showed that 1002F photoresist films could be released and used as mechanical sieves [46]. However, those reports did not characterize the release conditions for the films or the limits of film patterning. Thus, the ultimate patterning resolution and aspect ratio for such films, as well as the material properties, are not known.

To have wide utility, freestanding photoresist films should have several characteristics. First, the resist should be easily patterned by conventional methods. Second, the material must be amenable to facile release from the fabrication substrate without harsh solvents. Third, a material that is transparent in the visible wavelengths and possessing little autofluorescence would insure compatibility with light and fluorescence microscopy techniques. Fourth, the material used should be structurally resilient and flexible in a range of thicknesses. The photoresist 1002F meets the above criteria possessing excellent flexibility, low autofluorescence, and high biocompatibility [47]. In this report, we characterized the release of 1002F films from an underlying substrate over time in the presence of a variety of solvents. Fabrication parameters for a variety of film thicknesses, patterned with through-holes of a variety of shapes and sizes and in multiple layers, were measured. Properties of the films such as the patterning aspect ratio and resolution as well as the Young's modulus were assessed. Lastly, two applications of the films, the use as stencils for achieving patterned deposition of metal onto a substrate and the study of single cells atop a micropore, were demonstrated. This is the first quantitative description of the fabrication of freestanding films using a photoresist. These results established the utility of flexible, freestanding1002F photoresist films for use as an industrial, chemical, or biological tool.

2. Experimental Details

2.1 Materials

EPON resin 1002F photoresist (phenol, 4,4′-(1-methylethylidene)bis-, polymer with 2,2′-[(1-methylethylidene) bis(4,1-phenyleneoxymethylene]bis-[oxirane]) was obtained from Miller-Stephenson (Sylmar, CA). UVI-6976 photoinitiator (triarylsulfonium hexafluoroantimonate salts in propylene carbonate) was purchased from Dow Chemical (Torrance, CA). SU-8 photoresist was obtained from MicroChem Corp. (Newton, MA). γ-Butyrolactone (GBL) and developer (propylene glycol methylether acetate, PGMEA) were obtained from Sigma-Aldrich (St. Louis, MO). PDMS (Sylgard 184 silicone elastomer kit) was purchased from Dow Corning (Midland, MI). Chrome photolithography masks were designed in-house using TurboCAD software and printed by FineLine Imaging (Boulder, CO). Dulbecco's modified Eagle's medium (DMEM), fetal bovine serum (FBS), and penicillin/streptomycin were obtained from Invitrogen (Carlsbad, CA). H1299 cells were obtained from American Type Culture Collection (ATCC, Manassas, VA).

2.2 Fabrication and release of single-layer films

1002F-10, 1002F-50, and 1002F-100 negative photoresists were prepared by dissolving EPON 1002F resin and triarylsulfonium hexafluoroantimonate salts in GBL (described previously)[47]. Films of 1002F photoresist of various thicknesses (4.5–225 μm) were obtained by spin-coating 1002F-10, -50, or -100 on precleaned glass slides[47]. The coated slides were then soft-baked at 95°C in an oven to remove organic solvent. After cooling to room temperature, the slides were exposed to UV light from an Oriel collimated UV light source (1.68 mW/cm^2, Newport Stratford, Inc., Stratford, CT) through a patterned chrome photomask. A two-step post-exposure bake, first at 95 °C and then at 120 °C, followed UV exposure. After cooling to room temperature, unpolymerized monomer was removed by developing the slide in propylene glycol methylether acetate (PGMEA), rinsing with 2-propanol, and drying under a nitrogen stream. Films were hard-baked at 120 °C for 2 h. Unless stated otherwise, films were released from the glass substrate by incubated in water for 12 h on a laboratory shaker (60 rpm, Bellco Biotechnology, Bellco Glass, NJ) at 23°C. Films were detached from the glass slide by sliding a razor beneath the film at its corner and using tweezers to gently peel the film away from the glass slide. Detached films were dried under room air.

2.3 Measurement of film properties

Photoresist thin films were imaged with a Nikon Eclipse TE2000-U inverted fluorescence microscope under brightfield conditions and the image recorded with a cooled CCD camera (Photometrix Cool Snap *fx*, Roper Scientific, Tucson, AZ) controlled by NIS Elements software (Nikon, Melville, NY). Films were also imaged using an FEI Quanta 200 FEG scanning electron microscope (SEM) with a Shottky field emission gun, operated under low-vacuum conditions (0.38 torr) (Chapel Hill Analytical and Nanofabrication Laboratory (CHANL)). Film thickness was determined using SEM and profilometry (KLA-Tencor P-15 Profilometer, KLA-Tencor, San Jose, CA). Aspect ratios were measured by cutting films and measuring the film thickness and dimensions of through-holes using SEM. 1002F films were subjected to tensile strength testing using dogbone-shaped films 50 μm in thickness and 0.3 cm wide and 2.4 cm long using an EnduraTEC Smart Test Series tension loader. Films were subjected to axial stress using a 5-lb load cell and pulled at a rate of 0.01 mm/s until failure. The Young's Modulus was determined to be the slope of the best-fit line in a plot of the axial stress versus strain, as measured photographically over the course of the tensile strength test, and the ultimate tensile stress determined as the axial stress in the film just prior to mechanical failure.

2.4 Characterization of photoresist thin film release kinetics

The release of photoresist thin films from glass substrates was assessed using different solvents over a 24-h time course. Twenty square-shaped photoresist thin films 50-μm thick with dimensions of 25 × 25 mm were fabricated and immersed in either acetone, 75% ethanol, deionized laboratory water, or a 1% detergent solution (Contrex Labware Detergent, Decon Labs, PA) (5 films per solvent dish). Films were shaken for 24 h in covered dishes. The dishes were observed after 1, 8, 12 and 24 h for spontaneous detachment of films. After 24 h, slides were removed from solvent dishes and assessed for the attached films assessed for their ability to be removed. Three independent trials were conducted, each on a separate day.

The time needed for release of a film incubated in deionized laboratory water was also measured. Twenty films with dimensions identical to those described in the above paragraph were fabricated and immersed in water in covered laboratory dishes on a shaker for 1, 2, 4, 8, and 12 h. At each time point, the films in each dish (5 films per time point) were observed for spontaneous detachment. The ability of undetached films to be released from the glass substrate using a razor blade was also assessed. Three independent trials were conducted, each on a separate day.

2.5 Patterned metal deposition

Patterned deposition of metal through photoresist film stencils was accomplished using a Cressington 108 Sputter Coater (Cressington, United Kingdom), which was monitored using an MTM-10 thickness monitor. Between 10 and 20 nm of Au:Pd was deposited on substrates under an argon gas plasma. Sputtering was performed on glass substrates using un-released and released films as stencils and on PDMS substrates using released films as stencils. Released films used as stencils were attached to the surface of new glass substrates using clamps or placed on PDMS using manual pressure. All substrates were imaged before and after deposition and after removal of the photoresist stencil by brightfield microscopy.

2.6 Cell culture on a film with a single pore

H1299 lung adenocarcinoma cells were cultured in Dulbecco's modified Eagle's medium (DMEM) supplemented with penicillin/streptomycin and 5% fetal bovine serum. 1002F photoresist films with a single through-hole 10 μm in diameter were fabricated, released, and attached to a support column so that the film separated an upper and lower fluid chamber. After microscopic evaluation to ensure that films contained only one pore and were free of defects, films were plasma treated and the surface of the upper chamber was coated with 100 μg/mL collagen (type I from rat tail) for 1 h. H1299 cells were cultured in the upper chamber on the film until the cells were confluent on the film surface (24 h). Media in the basal (lower) compartment was replaced with DMEM containing calcein AM dye (10 μM). The film was imaged at the site of the pore after 5 min using a Nikon TE300 inverted epifluorescence microscope.

3. Results and discussion

3.1 Fabrication of 1002F films and release from glass substrates

Films of 1002F photoresist (25 mm × 25 mm × 50 μm, ℓ × w × h) were fabricated on a glass substrate with a 100 × 100 array of 75-μm diameter through-holes spaced 20 μm apart (figure 1). The films were incubated in four different solvents: acetone, 75% ethanol in water, water, and 1% detergent in water. The ability of the films to be released from the substrate was then assessed over time and all released films were visually inspected for defects. All films incubated in acetone spontaneously detached from the glass substrate by 1 h, but were distorted and rigid. At 24 h, films in ethanol, water, and detergent remained

adhered to the glass substrate but could be detached by inserting a razor blade between the film and substrate. Films incubated in 75% ethanol curled upon release and could not be flattened. By contrast, all films placed in either water or detergent appeared undistorted and remained flat upon release (figure 1(b), S1). Representative images of films removed in each of the four solvents are shown in figure S1. Since the highest quality films were released after incubation in water, this solvent was selected for all subsequent characterizations of film release.

The time required for the release of photoresist films from fabrication substrates was assessed by immersing the films in water for varying times. Film releasability was then assessed. All films were visually inspected and characterized as "releasable without damage," "released but damaged," or "not releasable" (Table 1). Released films with any defect observed either visually or via brightfield microscopy were considered damaged. The most common defects observed were tearing and/or irreversible bending of the films. By 2 h of water immersion, all films were releasable but 60% were damaged during the release process (Table 1, figure S2(c)). By 4 h, 87% of the films were released without damage and by 12 h, all of the films were released undamaged (Table 1). Thus the 1002F photoresist films were easily released without damage by 12 h using simple solvent systems and without the need for an underlying sacrificial or water-soluble layer.

3.2 Mechanical strength of freestanding 1002F films

To study the mechanical strength of freestanding 1002F films, the Young's modulus and ultimate tensile stress were measured. Dogbone-shaped films of 1002F were fabricated, released, and subjected to tension testing. The Young's modulus for 1002F films was determined to be 1.43 ± 0.21 GPa, and the ultimate tensile stress determined to be 54.5 ± 3.1 MPa (final elongation 105.1 ± 0.5 %). By comparison, the Young's modulus of SU-8 has been reported as 2.2 ± 0.1 GPa [48], and, the Young's moduli for parylene and PDMS were reported to be 3.2 GPa and 0.75–4 MPa, respectively [49–52], suggesting that 1002F photoresist is mechanically similar to parylene and SU-8 but more resilient than PDMS. In addition, 1002F films were shown to be flexible (figure S3) and amenable to mechanical manipulation without damage to the films, in contrast to films fabricated with the more brittle SU-8.

3.3 Fabrication of micropatterned freestanding 1002F films

The potential to fabricate freestanding photoresist films of a variety of thicknesses with features that faithfully replicated a master was assessed. 1002F photoresist films of varying thickness (4.5 – 225 μm) were first formed on a glass substrate and incubated in water for 24 h. All films, regardless of thickness, were released without damage. Representative electron micrographs of films with thicknesses of 4.5 μm and 225 μm are shown in figure 2(a). To determine whether a mask pattern through which the photoresist was exposed with UV light could be faithfully reproduced in the free-standing films, features in a variety of shapes and sizes were photopatterned into the 1002F. The 1951 USAF Resolution Target was used as a standardized feature target. Figure 2(b) shows replication of level 3–3 of the 1951 USAF Resolution Target. Rectangles 247.5 μm long and 49.5 μm wide were recreated as rectangular through-holes 248.9 ± 2.9 μm in length and 51.0 ± 3.1 μm in width on the film. Areas of this standard mask that were visible to the unaided eye could also be fabricated, such as the features 2.5-mm in length (figure S4(a)), without loss of film integrity.

In addition to using the 1951 USAF Resolution Target, other masks, custom-designed in the lab, were tested. Faithful replication of the mask pattern was observed for a variety of designs ranging in dimensions from 645 to 25 μm in 50-μm thick films exposed to a UV dose of 350 mJ / cm^2. For example, mask circles (75 μm diameter) yielded circular through-

holes on the film of diameter 74.3 ± 2.5 μm (mean ± standard deviation) (figure 1(b)). Mask spirals with a 645 μm in height and a 42 μm line width were reproduced in the film as spirals 644.8 ± 3.0 μm in height and 42.6 ± 1.7 μm wide (figure 2(b)). Mask squares of either 25 or 250 μm to a side yielded square film holes of dimensions 24.4 ± 1.4 μm and 250.1 ± 3.2 μm on a side, respectively (figure 2(c)). The smallest through-hole that could be reliably fabricated into films 50 μm thick was 10.1 ± 0.6 μm in diameter, using a mask with circles 10-μm in diameter (figure S4(b)). The smallest through-hole that could be reliably fabricated overall was 5.1 ± 0.5 μm in diameter, fabricated in a film 4.5 μm-thick film using a mask with 5-μm circles (figure 2(c), Table S1).

The maximum ratio for the film thickness-to-hole width (aspect ratio) that could be fabricated in a freestanding film was also measured. The 1951 USAF Resolution Target was again used as a standard mask. Features with an aspect ratio of 6:1 were easily formed when fabricating rectangular holes into the film (figure 2(d)). Using custom masks, the maximal aspect ratio for circular features was shown to be 4.5:1 (figure S4(b)). By comparison, we have previously fabricated freestanding 1002F micropillars at an aspect ratio of 4:1. A higher resolution mask and alignment system may further enhance the aspect ratio and resolution.

3.4 Fabrication of multilayered, micropatterned freestanding 1002F films

The potential to generate photoresist films with multiple layers, each carrying a different pattern of features, was explored. An initial layer of 1002F photoresist was photopatterned onto a glass slide. After hard-baking and plasma treatment, a second layer of 1002F was then spin-coated over the initial layer, exposed through a different mask and then processed as for the first layer of resist. As an example, a two-layer film was fabricated in which the first layer (5-μm thick) possessed circular pores 5 μm in diameter with a 10μm spacing (edge-to-edge). The second layer (50-μm thick) possessed circular wells 75 μm in diameter with a 25-μm spacing (figure 2(e)). All of these multilayered films (n = 8) were released from the substrate without damage after a 24-h incubation in water. The resulting array of wells with porous bottoms has the potential for isolating and arraying single cells using gravity-driven flow through the porous well base for the subsequent analysis and tracking of cell behavior.

3.5 1002F films as re-usable stencils for patterned metal deposition

Stencils for metal sputtering are traditionally made of stainless steel, PDMS, or parylene. However these materials generally possess one or more of the following weaknesses: high cost, complex fabrication, or mechanical instability [4, 51, 53]. To determine whether micropatterned 1002F films might be employed as low-cost, re-usable stencils for materials deposition onto a variety of surfaces, 1002F films were fabricated with an array of 75-μm holes. The films were released and then placed onto the substrate (glass or PDMS) to be coated with a metal pattern (figure 3). A 20 nm-thick layer of Au:Pd mixture was then sputtered onto the photoresist-substrate assembly. The diameter of the metal dots patterned onto the substrate was 75.2 ± 3.3 μm for the glass substrate and 74.1 ± 4.2 μm for the PDMS substrate. Thus the 1002F stencil pattern was faithfully replicated onto the substrates. Furthermore the 1002F stencil was easily separated from the substrates after each use and could be re-used. The stencil pattern was reused up to 8 times (the greatest number tested) yielding a patterned spot diameter of 76.3 ± 1.9 μm. In these experiments, no mechanical disruption or tearing of films was observed.

3.6 1002F films to address a single cell within a monolayer of cells

Films (25 mm × 25 mm × 20 μm, ℓ × w × h) with a single through-hole, 10 μm in diameter, were fabricated and released. A fluid reservoir was attached on either side of the film and

H1299 cells were cultured to confluency on one side of the film. Media containing calcein AM dye was supplied to the compartment lacking the cells. Only the cell spanning the single pore should have access to the calcein AM-containing compartment. The nonfluorescent, membrane-permeant calcein AM is rapidly metabolized within cells to the fluorescent, membrane-impermeant dye calcein. Thus, living cells exposed to calcein AM become brightly fluorescent as the dye is metabolized and trapped within their cytosol. Fluorescence images of the cell-covered film demonstrated a single H1299 cell that was fluorescent (figure 4). This cell was also observed to span the 10-μm pore. All surrounding cells remained nonfluorescent and so did not have access to the fluid in the opposite compartment. The ability to easily micropattern photoresist films with discrete through-holes small enough for a single cell to span is an important advantage of 1002F films relative to PDMS and parylene films, and to commercially-available microporous membranes for cell culture. By growing cells atop a freestanding film with a single through-hole, we are able to show the delivery of an exogenous agent (here, the cytoplasmic dye Calcein AM) to a single cell within a contiguous monolayer. Contemporary methods of achieving this would rely on either micropipette injection of the single cell or on a single-cell microelectroporator. 1002F films should thus enable customizable study of the permeability of single cells to exogenous molecules (drugs, hormones, etc.) even when a cell is part of a contiguous monolayer.

4. Conclusion

The photoresist 1002F can be micropatterned with good replication of a master using photolithography and released without damage from the fabrication substrate in a matter of hours, all without the need for an underlying sacrificial layer. Freestanding films have previously been made using PDMS and parylene. PDMS films are mechanically fragile and the fabrication of through-holes is technically difficult. Parylene films have high autofluorescence and require complex, multi-step fabrication schemes. By contrast, 1002F photoresist films are mechanically resilient, have low autofluorescence, require only basic UV photolithography to micropattern, and can be made with through-holes with dimensions much smaller than those of PDMS (~35 μm limit) [4]. We have shown that freestanding photoresist films can be used as stencils for material deposition or as patterned supports for cell culture. Thus, freestanding photoresist films have potential in future chemical and biological applications and particularly as lab-on-a-foil devices.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

This work was funded with grants from the National Institutes of Health (T32GM7040-37 and EB012549). We wish to thank Joe Balowski, Wei Xu, and Frank Pai for fabrication assistance, Wallace Ambrose for assistance with SEM imaging, and Chris O'Conor and Farshid Guilak for assistance with tensile testing.

References

1. Webster A, Greenman J, Haswell SJ. J Chem Technol Biot. 2011; 86:10.
2. Becker H, Locascio LE. Talanta. 2002; 56:267. [PubMed: 18968500]
3. Desai SP, Taff BM, Voldman J. Langmuir. 2008; 24:575. [PubMed: 18081333]
4. Folch A, Jo BH, Hurtado O, Beebe DJ, Toner M. J Biomed Mater Res. 2000; 52:346. [PubMed: 10951374]
5. Chang TY, Yadav VG, De Leo S, Mohedas A, Rajalingam B, Chen CL, Selvarasah S, Dokmeci MR, Khademhosseini A. Langmuir. 2007; 23:11718. [PubMed: 17915896]

6. Madou, MJ. Fundamentals of Microfabrication: The Science of Miniaturization. Boca Raton; 2002.
7. Shaw JM, Gelorme JD, LaBianca NC, Conley WE, Holmes SJ. IBM J Res Dev. 1997; 41:81.
8. Deng T, Wu H, Brittain ST, Whitesides GM. Anal Chem. 2000; 72:3176. [PubMed: 10939384]
9. Wang Y, Phillips C, Xu W, Pai JH, Dhopeshwarkar R, Sims CE, Allbritton N. Lab Chip. 2010; 10:2917. [PubMed: 20838672]
10. Huh D, Matthews B, Mammoto A, Montoya-Zavala M, Hsin H, Ingber D. Science. 2010; 328:1662. [PubMed: 20576885]
11. Peeni BA, Conkey DB, Barber JP, Kelly RT, Lee ML, Woolley AT, Hawkins AR. Lab Chip. 2005; 5:501. [PubMed: 15856085]
12. Wang GJ, Lin YC, Hsu SH. Biomed Microdevices. 2010; 12:841. [PubMed: 20532635]
13. Geissler M, McLellan JM, Xia Y. Nano Lett. 2005; 5:31. [PubMed: 15792408]
14. Lommens P, Van Thourhout D, Smet PF, Poelman D, Hens Z. Nanotechnology. 2008; 19:245301. [PubMed: 21825806]
15. Hebert NE, Kuhr WG, Brazill SA. Anal Chem. 2003; 75:3301. [PubMed: 14570177]
16. Ogihara H, Fukasawa M, Saji T. ACS Appl Mat Int. 2011; 3:2108.
17. Cho J, Jang H, Yeom B, Kim H, Kim R, Kim S, Char K, Caruso F. Langmuir. 2006; 22:1356. [PubMed: 16430305]
18. Tao SL, Popat KC, Norman JJ, Desai TA. Langmuir. 2008; 24:2631. [PubMed: 18275232]
19. Chrisey LA, O'Ferrall CE, Spargo BJ, Dulcey CS, Calvert JM. Nucl Acid Res. 1996; 24:30400.
20. Erkan Y, Czolkos I, Jesorka A, Wilhelmsson LM, Orwar O. Langmuir. 2007; 23:5259. [PubMed: 17432889]
21. Sorribas H, Padeste C, Tiefenauer L. Biomaterials. 2002; 23:893. [PubMed: 11771708]
22. Lee CS, Lee SH, Park SS, Kim YK, Kim BG. Biosens Bioelectron. 2003; 18:437. [PubMed: 12604261]
23. Doh J, Irvine DJ. J Am Chem Soc. 2004; 126:9170. [PubMed: 15281792]
24. Petrou PS, Chatzichristidi M, Douvas AM, Argitis P, Misiakos K, Kakabakos SE. Biosens Bioelectron. 2007; 22:1994. [PubMed: 17027250]
25. Flavel BS, Gross AJ, Garrett DJ, Nock V, Downard AJ. ACS Appl Mat Int. 2010; 2:1184.
26. Psoma SD, van der Wal PD, Frey O, de Rooij NF, Turner AP. Biosens Bioelectron. 2010; 26:1582. [PubMed: 20732802]
27. Agirregabiria M, Blanco FJ, Berganzo J, Arroyo MT, Fullaondo A, Mayora K, Ruano-Lopez JM. Lab Chip. 2005; 5:545. [PubMed: 15856093]
28. Sun Y, Vernier PT, Behrend M, Marcu L, Gundersen MA. IEEE Trans Nanobioscience. 2005; 4:277. [PubMed: 16433293]
29. Agirregabiria M, Blanco FJ, Berganzo J, Fullaondo A, Zubiaga AM, Mayora K, Ruano-Lopez JM. Electrophoresis. 2006; 27:3627. [PubMed: 16977684]
30. Wang Y, Sims CE, Marc P, Bachman M, Li GP, Allbritton NL. Langmuir. 2006; 22:8257. [PubMed: 16952271]
31. Salazar GT, Wang Y, Young G, Bachman M, Sims CE, Li GP, Allbritton NL. Anal Chem. 2007; 79:682. [PubMed: 17222037]
32. Wang Y, Young G, Bachman M, Sims CE, Li, Allbritton NL. Anal Chem. 2007; 79:2359. [PubMed: 17288466]
33. Barbee KD, Hsiao AP, Heller MJ, Huang X. Lab Chip. 2009; 9:3268. [PubMed: 19865735]
34. Alan ML. J Non-Cryst Solids. 1985; 70:99.
35. Kim J, Song X, Kinoshita K, Madou M, White R. J Electrochem Soc. 1998; 145:2314.
36. Ranganathan S, McCreery R, Majji SM, Madou M. J Electrochem Soc. 2000; 147:277.
37. Ranganathan S, McCreery RL. Anal Chem. 2001; 73:893. [PubMed: 11289433]
38. Lorenz H, Despont M, Fahrni N, LaBianca N, Renaud P, Vettiger P. J Micromech Microeng. 1997; 7:121.
39. Feng R, Farris RJ. J Micromech Microeng. 2003; 13:80.
40. Khoo HS, Liu KK, Tseng FG. J Micromech Microeng. 2003; 13:822.

41. Abgrall P, Lattes C, Conederal V, Dollat X, Colin S, Gue AM. J Micromech Microeng. 2006; 16:113.
42. Sidler K, Villanueva LG, Vazquez-Mena O, Savu V, Brugger J. Nanoscale. 2012; 4:773. [PubMed: 22170588]
43. Ghadarghadr S, Fucetola CP, Lee Cheong L, Moon E, Smith IH. Journal of Vacuum Science & Technology B: Microelectronics and Nanometer Structures. 2011; 29:06F401.
44. Du K, Liu Y, Wathuthanthri I, Choi C-H. Journal of Vacuum Science & Technology B: Microelectronics and Nanometer Structures. 2012; 30:06FF04.
45. Wang Y, Dhopeshwarkar R, Najdi R, Waterman ML, Sims CE, Allbritton N. Lab Chip. 2010; 10:1596. [PubMed: 20376386]
46. McPherson AL, Walker GM. AIP Adv. 2012; 2:012153.
47. Pai J-H, Wang Y, Salazar GTA, Sims CE, Bachman M, Li GP, Allbritton NL. Anal Chem. 2007; 79:8774. [PubMed: 17949059]
48. Gao J, Guan L. Chu J. 2010:754464.
49. Noh HS, Moon KS, Cannon A, Hesketh PJ, Wong CP. J Micromech Microeng. 2004; 14:625.
50. Lotters JC, Olthuis W, Veltink PH, Bergveld P. J Micromech Microeng. 1997; 7:145.
51. Wright D, Rajalingam B, Karp JM, Selvarasah S, Ling Y, Yeh J, Langer R, Dokmeci MR, Khademhosseini A. J Biomed Mater Res. 2008; 85A:530.
52. Fuard D, Tzvetkova-Chevolleau T, Decossas S, Tracqui P, Schiavone P. Microelectron Eng. 2008; 85:1289.
53. Yi SM, Jin SH, Lee JD, Chu CN. J Micromech Microeng. 2005; 15:263.

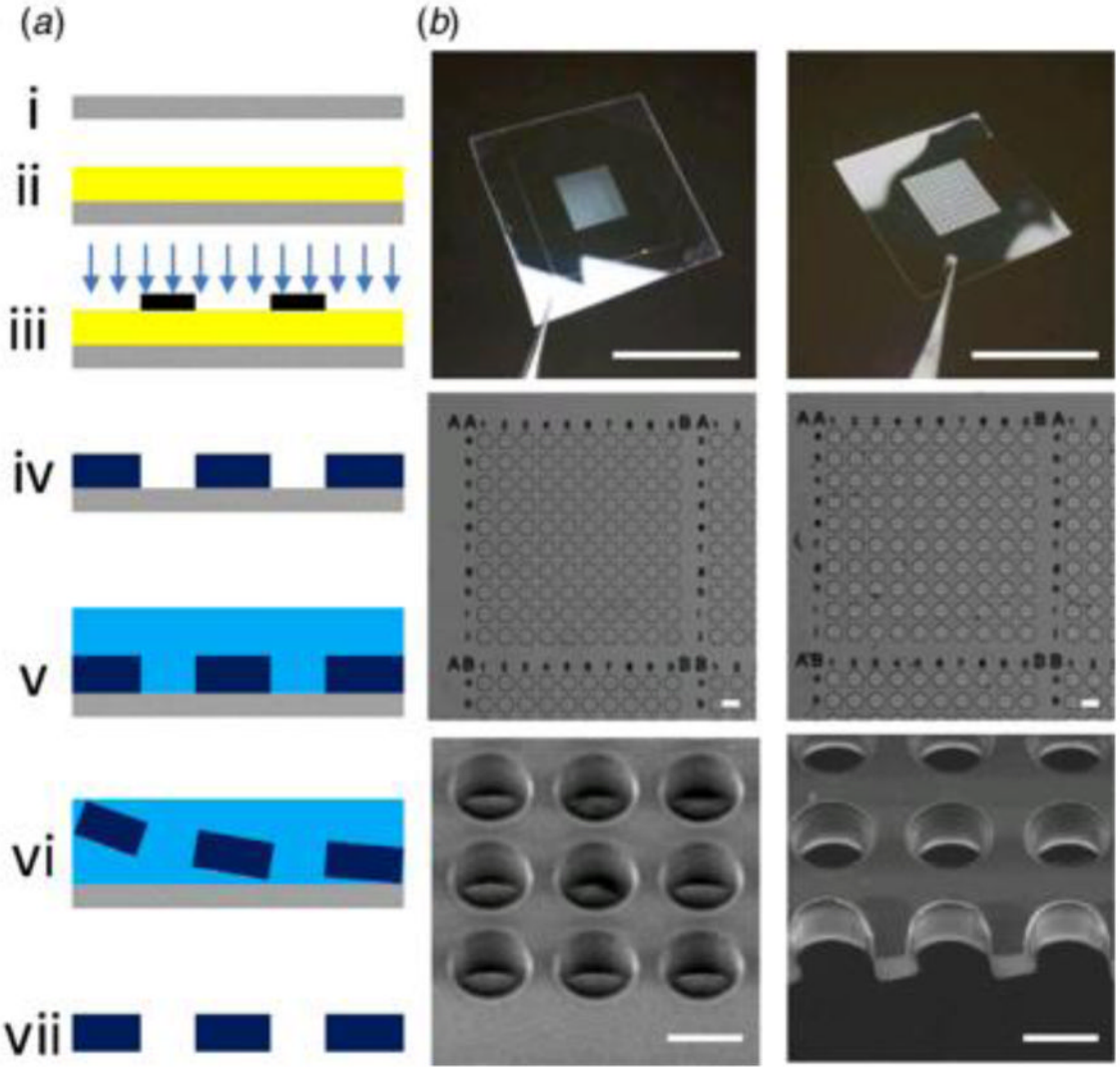

Figure 1.

Fabrication and release of photoresist thin films. (a) Schematic illustration of fabrication and release protocol: atop a clean glass substrate (i) a layer of negative photoresist monomer is spin-coated (ii). After exposure to UV light through a chrome mask (iii), the film is developed to remove unpolymerized monomer (iv). The patterned film is immersed in an aqueous solution (v) to reduce film adhesion to the glass substrate (vi). The intact film can be removed from the substrate and dried (vii). (b) Macroscopic (top row), brightfield optical (middle row) and SEM (bottom row) images of a 50 μm-thick film of 1002F photoresist (dimensions 25 mm × 25 mm) with an array of 10^4 circular wells (75 μm diameter) before (left column) and after (right column) release in deionized water. Scale bars: 25 mm (top row), 75 μm (middle and bottom rows).

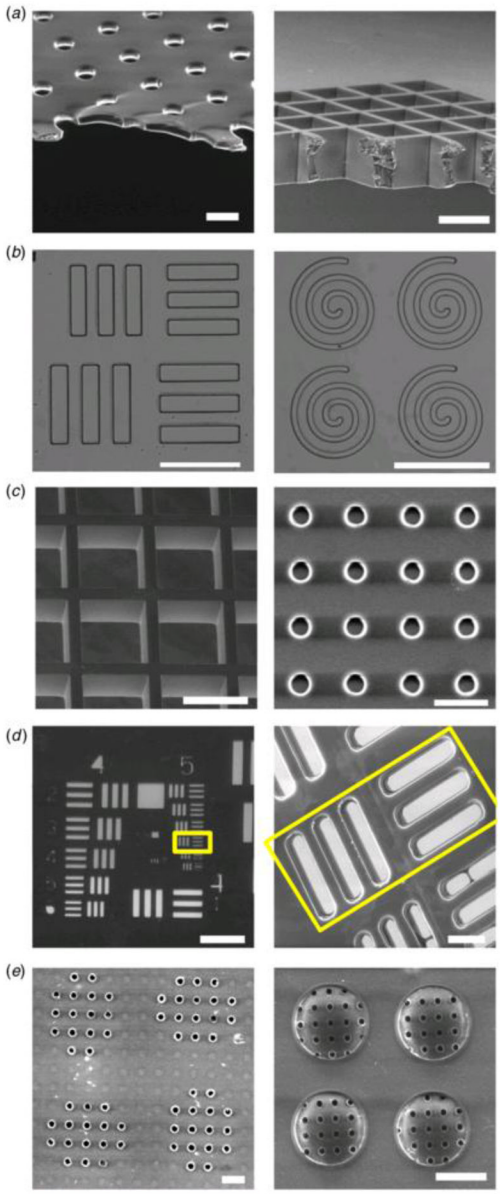

Figure 2.
Fabrication versatility of photoresist films. 1002F films can be fabricated with a variety of thicknesses (a), through-hole shapes (b), and through-holes sizes (c). The film in (d) demonstrates an aspect ratio of 6:1. Films with multiple layers each carrying a different pattern could be fabricated (e). Scale bars (left to right, top to bottom): 20, 200, 275, 625, 250, 15, 250, 25, 20, 50 μm.

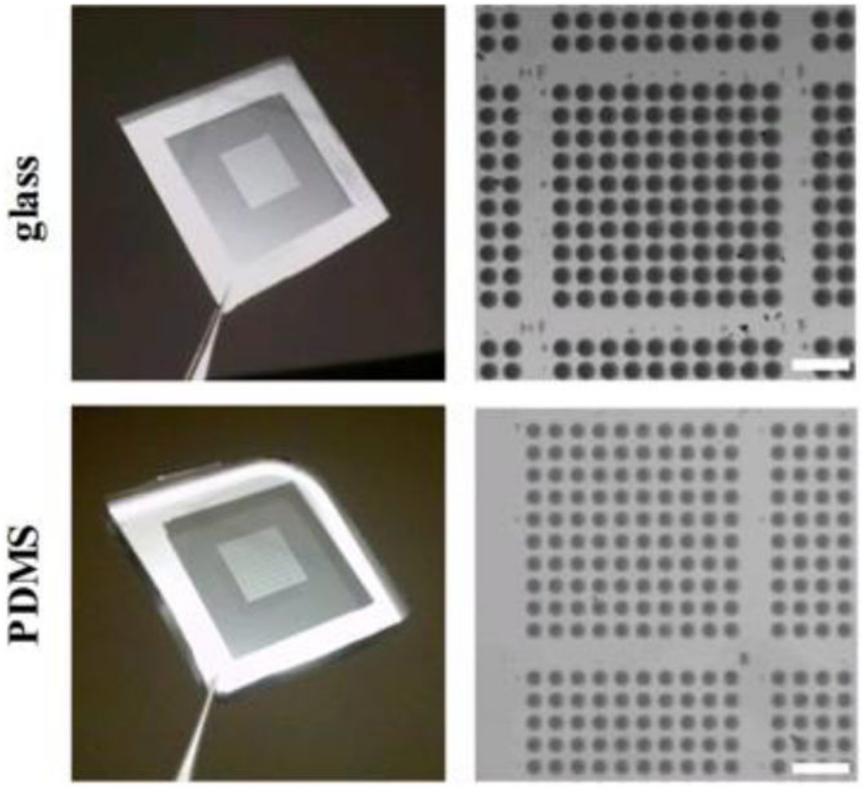

Figure 3.
Use of 1002F film as a stencil. Glass (top) and PDMS (bottom) were patterned with Au:Pd (20-nm thick layer) through a 1002F stencil. Macroscopic images of the sputtered substrates are shown in the left column (scale bars, 100 μm), while brightfield microscopic images are displayed in the right column. The macroscopic film is 25 × 25 cm.

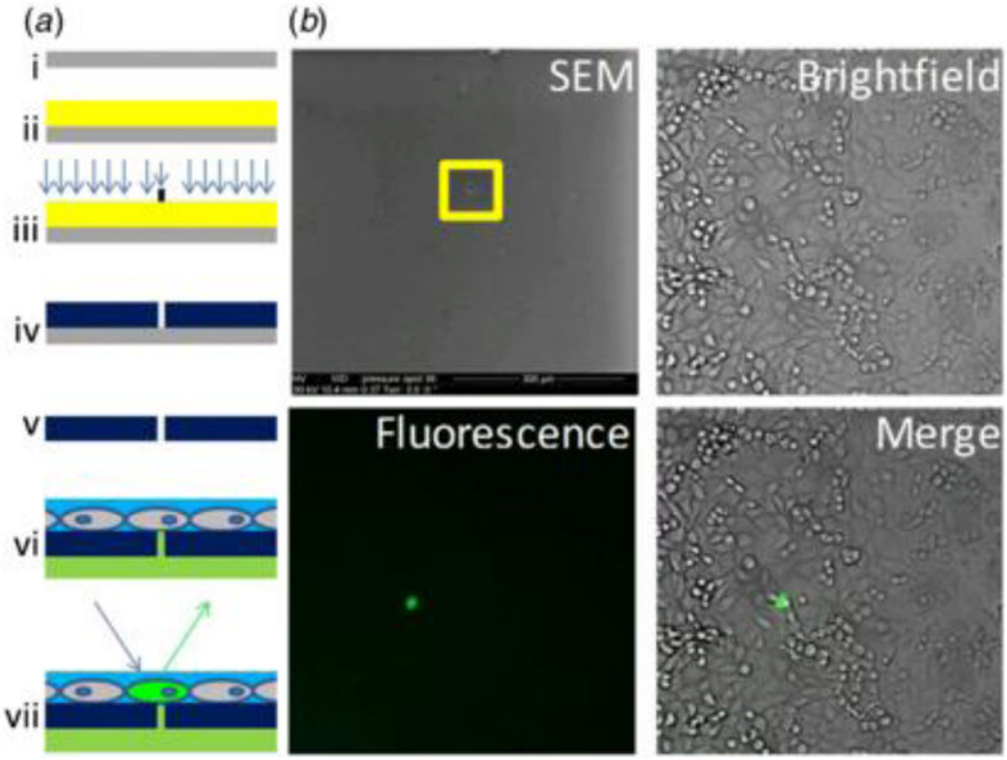

Figure 4.

1002F films for loading exogenous molecules into single cells in a monolayer. (a) Schematic illustration of fabrication, cell seeding, and cell staining: a film of 1002F photoresist with a single through-hole, 10 μm in diameter, is fabricated and released (i–v). H1299 cells were seeded onto the film and allowed to grow to confluency, at which time media containing 10 μM calcein AM dye was supplied to the lower compartment in order to load only the cell spanning the through-hole (vi). The film was then imaged at the site of the pore under brightfield and epifluorescence conditions(vii). (b) Images of the 1002F film with a single through-hole. SEM micrograph shows the location of the single through-hole; brightfield micrograph shows a confluent layer of H1299 cells; fluorescence micrograph shows a single cell spanning the through-hole that has been loaded with the calcein dye; brightfield and fluorescence images have been merged to illustrate the single fluorescent cell in the monolayer.

Table 1

Removal of 1002F films by immersion in water

Time (h)	Undamaged (%)[a]	Damaged (%)[a]	Non-removable (%)[a]
1	7 ± 12*	20 ± 34	73 ± 31
2	40 ± 17	60 ± 17	0 ± 0
4	87 ± 12	13 ± 12	0 ± 0
8	93 ± 12	6 ± 12	0 ± 0
12	100 ± 0	0 ± 0	0 ± 0

[a]Average ± standard deviation (n = 3 independent trials with 20 films/trial)