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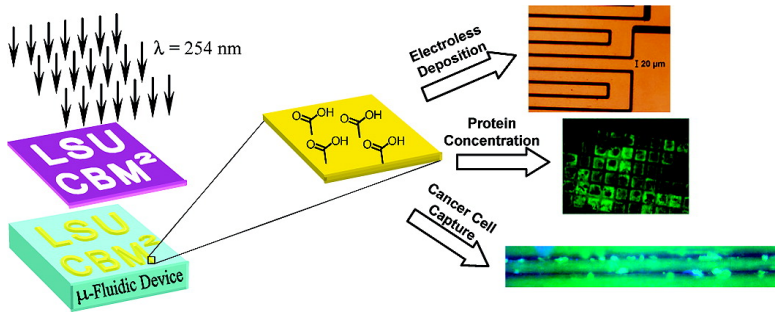
J. Am. Chem. Soc., **2005**, 127 (3), 842-843• DOI: 10.1021/ja0454135 • Publication Date (Web): 30 December 2004



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Published on Web 12/30/2004

Resist-Free Patterning of Surface Architectures in Polymer-Based Microanalytical Devices

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Received July 30, 2004; E-mail: tunnel@LSU.edu

Through use of carefully controlled photochemical reaction conditions and surface chemistry, we demonstrate the formation of micrometer- to millimeter-sized, chemically functionalized regions on the surfaces of polymer-based microfluidic analysis systems. Covalently attached, selective-capture elements, conducting metal films, and responsive-polymer bioanalyte concentrators can be readily patterned on the surface of both poly(methyl methacrylate), PMMA, and poly(carbonate), PC, microfluidic devices. These architectures are fabricated by chemical elaboration of carboxylic acid moieties resulting from direct, controlled UV exposure of the polymer device substrates in oxygen-rich environments. This direct-write photochemical patterning approach is significant for the advancement of polymer-based microfluidic devices because traditional photoresist techniques cannot be used (solvent incompatibility issues), and it is a simple, convenient process that is readily accessible to a variety of scientists and engineers.

Miniaturized chemical and biological analysis systems have moved to the forefront of the bioanalytical science arena because only small amounts of reagents are required to evaluate miniscule amounts of analytes, and the analyses can frequently be run in parallel.[1−4] Polymer-based microanalytical devices[5−10] offer distinct advantages over those made in silicon, glass, or quartz, in that polymer-based systems can be fabricated using simple, rapid methods (embossing/injection molding,[11,12] "soft lithography"[9,10]). However, it is clear that the current and potential applications of polymer-based systems will require development of a variety of surface chemistries[13,14] and patterning[15] thereof on the millimeter to nanometer scales. Modification of microdevice surfaces is of great importance because of the need for manipulation of fluid flow,[1] adsorption and preconcentration of materials,[16,17] single-cell growth studies,[18] construction of array and amplification devices,[19,20] and electrical communication within and outside of the device.

Carboxylic acid groups can be formed, without significant topographical changes, on the surfaces of PMMA and PC—substrates used extensively in embossing and injection molding fabrication of microanalytical devices[5−7]—by their UV irradiation in O_2 environments.[21] Specifically, this is achieved by exposure of the polymers, in air, to 254-nm light with a power density of 15 mW cm^{-2} for roughly 60 min or less (dose $\leq \sim$54 J cm^{-2}); these conditions maximize UV-induced carboxylic acid group production (from ester cleavage reactions) and minimize etching/ablation/depolymerization reactions that have been used to machine structures in polymers.[22−25] As previously shown by others, the use of high-fluence or more energetic light sources, or high-dose exposures at 254 nm, leads to machining of PMMA or PC, with concomitant formation of surface carboxyl groups, both resulting from a combination of oxidative and thermal decomposition routes.[22−24] Formation of monolayers of carboxylic acid groups on PMMA and PC using the conditions described here was confirmed by functional group-specific labeling, as shown in Figure 1[26] and imaging,[21] as well as X-ray photoelectron spectroscopy.[21] In comparison to their pristine counterparts, carboxylic acid-terminated (CT) devices exhibit substantially higher water wettabilities (PC: 50° vs 83°; PMMA: 52° vs 70°; 2 h exposure) and electroosmotic flow (PMMA: 4.5×10^{-4} vs 2×10^{-4} cm^2 V^{-1} s^{-1} at pH 7.0; PC: 5.4×10^{-4} vs 2.6×10^{-4} cm^2 V^{-1} s^{-1} at pH 6.0; 30 min exposure).[21]

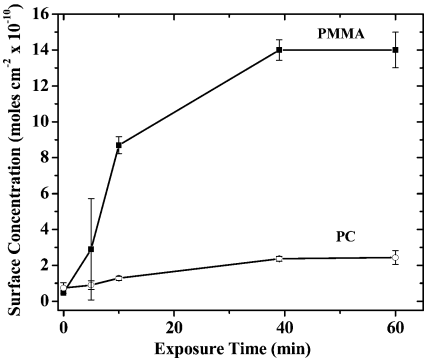

Figure 1. Effect of UV (λ = 254 nm, 15 mW cm^{-2}) exposure time on surface concentration[21] of carboxylic acid groups on poly(methyl methacrylate), PMMA, and poly(carbonate), PC, surfaces.

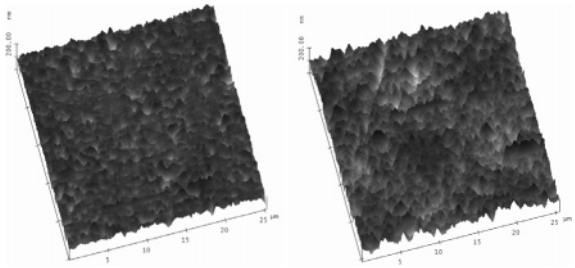

Figure 2. Tapping mode scanning force micrographs (25 μm × 25 μm) of PMMA sheets exposed to 254-nm light through a Ni mesh (7.6-μm-wide squares): 5 min (left) and 120 min (right). *Z*-range = 200 nm. The RMS surface roughness in the exposed areas increases from 13−15 nm (5 min exposure) to 23−25 nm (120 min exposure). Pristine PMMA sheets typically exhibit a surface RMS value of 13−16 nm.

A key characteristic of this work is the lack of significant physical damage to the polymer surfaces for short exposure times; however, longer exposure times of 60−120 min (dose of 54−108 J cm^{-2}) lead to measurable increases in surface roughness as shown in Figure 2. Serious damage to the polymer surfaces is observable by eye for exposures greater than 3 h.

Antibodies immobilized on the CT-terminated microanalytical devices can be used to capture whole mammalian cells. In Figure

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10.1021/ja0454135 CCC: $30.25

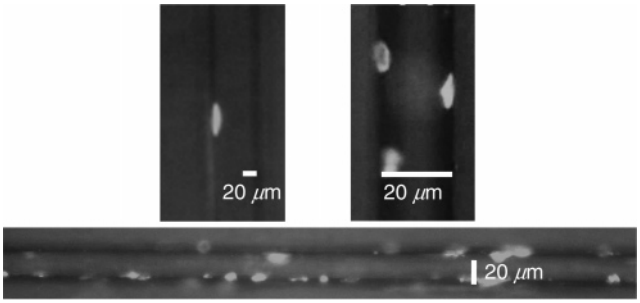

Figure 3. Fluorescently stained (4′-6-diamidino-2-phenylindole; λ_{ex} = 358 nm) EpCAM cells on (left) 50-μm- and (right, bottom) 20-μm-wide, 100-μm-deep CT-PMMA channels derivatized with anti-EpCAM antibodies resulting from pumping a 10^6 cells cm^{-3} solution through the 4-cm-long PMMA channels at 2 mm s^{-1} for 90 s. Image is 560-μm long in the bottom image.

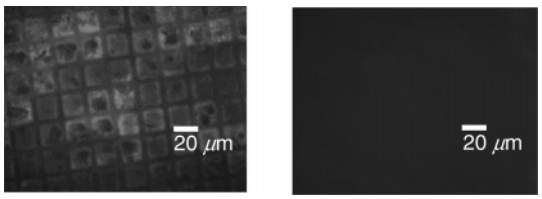

Figure 4. Fluorescence micrographs (λ_{ex} = 488 nm) of 18 μm × 18 μm pNIPAAm patterns (Ni mesh mask) on PMMA exposed to 1.0 mg/mL fluorescein-labeled goat anti-rabbit IgG antibody (150 000−160 000 Da) in pH 7.4, 0.01 M PBS, for 2 h at 40 °C (left) and 0.5 °C (right).

3 are surface-captured, MCF-7 cells that overexpress EpCAM, a cell-surface protein that has been identified as a marker for breast cancers. Capture was achieved by hydrodynamically pumping, at 2 mm s^{-1} for 90 s, a suspension of MCF-7 cells through hot-embossed, CT-PMMA microfluidic channels[27] whose surfaces were derivatized with anti-EpCAM antibodies.[21] Fluidic modeling and experimental studies demonstrate that there was an optimum flow velocity for maximum cell capture.[28] In experiments performed at 2 mm/s^{-1}, cell density was a function of the smallest channel cross section dimension; narrow (20 μm) channels had a higher capture efficiency (higher density) for the MCF-7 cells than the wider microchannels. Deep, high-aspect-ratio channels reduced the probability of captured cells clogging a narrow channel and reduced the pressure required to drive the cells through the device. In the case of the 50-μm-wide, 100-μm-deep channels, only occasionally would one observe MCF-7 cell capture (one cell was found attached to the surface of the 4-cm-long channel; Figure 3, left), but numerous cells were routinely observed on the surface of the 20-μm-wide, 100-μm-deep channels; Figure 3, right and bottom.

Capture of proteins from aqueous solution in an array format can be achieved through immobilization of thermally responsive polymers on the microdevice surfaces. Patterns of carboxylic acids are readily formed by substrate irradiation through a simple contact mask such as a Ni mesh. Exposure of protein solutions to thermally responsive poly(*N*-isopropylacrylamide), pNIPAAm,[17,29−31] films on PMMA surfaces leads to deposition of the proteins only in the pNIPAAm-modified regions at temperatures (T_{soln}) above the lower critical solution temperature of the pNIPAAM (T_{LCST}, 32 °C); Figure 4. Patterns of pNIPAAm on PMMA were obtained by free-radical polymerization of NIPAAm monomer from 2,2′-azobis(2-methylpropionamidine)-derivatized, patterned carboxylic acid regions.[21,31] pNIPAAm-modified PMMA surfaces are able to act as protein capture devices when $T_{soln} > T_{LCST}$ (hydrophobic, fouling surface), but do not interact with solution-phase proteins below T_{LCST} (hydrophilic, nonfouling); Figure 4. Additionally, XPS studies of pNIPAAm surfaces exposed to solutions of poly-L-methionine (30 000−50 000 Da) at $T_{soln} < T_{LCST}$ confirm that protein is virtually undetectable, as is the case for protein-covered surfaces (formed at $T_{soln} > T_{LCST}$) that have subsequently been placed in aqueous buffers with $T_{soln} <$ LCST so as to desorb the protein.[21]

The work described here lays the foundation for the laterally selective modification of PMMA- and PC-based microfluidic analysis devices, an area that is of great importance to the analytical and biological sciences arenas.[5−7] Using the chemistry developed here, we are currently exploring the use of electrolessly deposited metal interconnects/electrodes, integrated oligonucleotide and protein arrays for the early detection of disease biomarkers, as well as environmentally responsive control of flow in nanofluidic polymer-based devices.

Acknowledgment. This work was supported by grants from the National Science Foundation (CHE-0108961, EPS-0346411, DBI-0138048, ENG-0139656 (REU Program), DGE-0237765, and DMR-0116757) and the National Institutes of Health (R24CA842625, R21CA099246, and R01HG001499). We thank Dr. R. Truax for cell culture and isolation work.

Supporting Information Available: Experimental details (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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JA0454135