

# Synthesis and Characterization of Hydrogels Grown on Surfaces by ATRP

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## ABSTRACT

Biocompatible polymer networks with specific structure and orientation have tremendous potential in the biomedical field (e.g., recognition of specific proteins and other biomolecules for diagnostic and therapeutic applications). The control over the growth of these polymer networks on surfaces plays a vital role, since it acts as the interface between the device and the biological medium/environment. A surface initiated polymerization (SIP) technique, specifically atom transfer radical polymerization (ATRP), was applied for the controlled synthesis of hydrogel systems over Au and Si substrates. Patterning using microcontact printing (XY control) followed by ATRP (Z control), and optimization of the process variables for the synthesis of hydrogels (e.g., temperature responsive) on gold and silicon surfaces were completed. Characterization was done using atomic force microscopy (AFM) and fourier transform infrared imaging (FTIR).

## INTRODUCTION

Advancements in the field of nanoscale science and ensuing technologies have led to the development of various biomedical devices that have revolutionized the way health care is administered. Consequently there has also been a focus towards engineering the architectural design of materials on a molecular level from a variety of surfaces. The unlimited potential of these modified surfaces is clear, especially in the field of medical diagnostics and therapeutic approaches. Tethered polymer chains on solid surfaces are of theoretical interest and have potential applications in chemical separations, sensing, stabilization of colloidal suspensions, control of wetting and adhesion, corrosion resistance, and microelectronics.<sup>[1]</sup> Current research aims to use the intelligent polymer networks, based on hydrogel systems, for biomedical applications such as biosensing and targeted drug delivery.<sup>[2]</sup> The ability to control the molecular structure of surfaces makes it possible to pattern complex molecules relevant to biology, to fabricate microchannels appropriate for microfluidics, and to pattern and manipulate cells. These can be combined with SAMs for the commercial production of DNA arrays and

biosensors that require stringent control of surface properties.<sup>[3]</sup>

In this study, we have acquired spatial control over gold and silicon surfaces by using microcontact printing and atom transfer radical polymerization. Optimized reactions were carried over these surfaces using a wide variety of monomer units and crosslinkers. Reaction conditions were also varied in order to obtain better viability. The various polymer networks were characterized and analyzed using state of the art imaging techniques such as atomic force microscopy (AFM) and fourier transform infrared imaging (FTIR).

## EXPERIMENTAL METHODS

### Materials

All chemicals were purchased from Aldrich and used as received, unless noted otherwise. The monomers used for the ATRP reactions include N-isopropyl acrylamide (NIPAAm) and acrylic acid (AA) (Polyscience, used after vacuum distillation). The SAMs employed for gold patterning included 1-octadecanethiol (ODT) and 11-mercapto-1-undecanol (MUD). Other gold ATRP reagents used were 4-(chloromethyl) benzoyl chloride (CBC) or methyl-2-bromopropionate (MBP) as the initiator, copper (I) bromide as the catalyst and N,N,N',N' - pentamethyl diethyl triamine (PMDETA) or dipyriddy as the ligand. Reagents for contact printing (SAMs) over Si surfaces were purchased from Gelest Inc.; they were 2-(4-chloro sulfonyl phenyl)-ethyl trichloro silane (50% in toluene) (CTCS) and n-octadecyl trichloro silane (OTS). For polymerization from Si surfaces, p-toluene sulfonylchloride (TsCl) was used as the free initiator. The elastomer used in replica molding was poly(dimethylsiloxane) (PDMS), Sylgard 184 which was provided by Dow Corning. Surfaces over which experiments were carried out were gold wafers (Au, 500±25 µm, Platypus Technologies) and silicon wafers (Si, 500±25 µm, Virginia Semiconductor Inc.). SU-8 (MicroChem) was used for the preparation of Si master stamps. AFM soft contact mode tips (BS-SiNi) and non contact mode tips (BS-Tap) were purchased from Budget Sensors.

### Preparation of Si master stamps

Si wafers were cut to the necessary shape and size using a diamond scribe. The samples were then

washed with acetone and DI water and subsequently dried. The samples were preheated at 100 °C for 2 min. Spin coating of SU 8 was then done for 30 s at 2000 rpm. The thickness of the microstructure can be varied depending on the speed and the type of SU 8 used. The spin coated sample was then soft baked at 70 °C for 3 min and at 100 °C for 7 min. The hot sample was cooled at ambient conditions for 3 min. It was then exposed to UV light of intensity 17.5mW/cm<sup>2</sup> and wavelength of 365 nm for 15 s. The photomask used for photolithography was also washed initially with acetone, IPA and DI water. Post baking of the exposed sample was carried out for 1 min at 70 °C and for 3 min at 100 °C. The dried and photopatterned sample was then developed using SU developer for 4 min followed by IPA and DI water wash, each for 1 min. The washed sample was then dried using a nitrogen jet.

### Preparation of PDMS stamps

PDMS stamps were prepared using an 85% to 15% (volume %) ratio of Sylgard 184 PDMS base solution and the curing agent respectively on the Si master stamps. It is then cured for 1 hour at 100 °C. [4] A pattern of the microstructures as present in the photo mask is obtained.

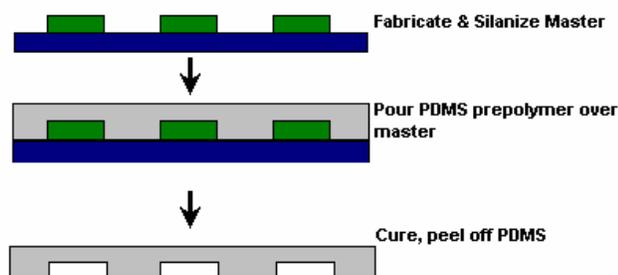


Figure 1. PDMS preparation

### Patterning and ATRP over gold surface

Au samples were cleaned with acetone, DI water and dried. A 4 mM solution of 1-Octadecane thiol (ODT, SAM 1, hydrophobic) in ethanol was prepared. The PDMS stamp was treated with the SAM solution, and then dried for 2 seconds. Microcontact printing ( $\mu$ CP) of this SAM was done for 30 seconds using a PDMS containing squares as the microstructures. The microcontact printed gold sample was then washed with ethanol and dried. PDMS stamp was also cleaned using ethanol.

The microcontact printed sample was then dipped in a 4 mM solution of 11-Mercapto-1-undecanol (MUD, SAM 2, hydrophilic) in ethanol for 24 hours. This SAM fills in the zones not occupied by SAM 1. An 8 mM solution of the initiator 4-Chloromethyl benzoyl chloride, CBC or Methyl-2-

bromopropionate, MBP in toluene was prepared. The gold sample which contained ODT and MUD was then immersed in this solution for 24 hours. At the end of 24 hours the sample was taken out, washed and rinsed with toluene and finally washed. The sample was finally dried for the ATRP reaction.

A solution made up of 1 mM copper (I) bromide catalyst, 3 mM of the ligand dipyriddy was prepared. A 100 mM solution of the monomer NIPAAm was mixed with the above solution using ethanol as solvent. The cleaned gold sample containing the thiols (SAM 1 as hydrophobic squares, hydrophilic SAM 2 between squares), and the initiator molecules (formed over SAM 2) is immersed in the monomeric solution. Nitrogen was bubbled through the solution for 45-60 minutes at a low flow rate. ATRP reaction of the sample was carried out at 60°C by keeping it in a temperature bath. At the end of the reaction the sample was rinsed with ethanol and then dried subsequently.

Various sets of samples were prepared using the above procedure but with different monomers, various crosslinkers, ratios of crosslinkers, ligands, reaction temperature and also over a wide variety of reaction time. Figure 2 shows a schematic representation of the ATRP process.

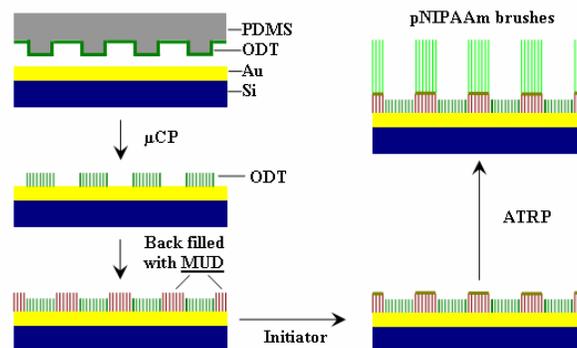


Figure 2. Scheme of  $\mu$ CP and ATRP over gold substrate.

### Patterning and ATRP over Si surface

In addition to the ATRP process that was carried out over gold surface,  $\mu$ CP and self assembly were carried out over Si samples also. The Si samples were cleaned using DI water followed by piranha cleaning for 20 minutes and finally dried.  $\mu$ CP of a 5 mM solution of n-Octadecyltrichlorosilane (OTS, SAM 1, hydrophobic) in toluene was done over the piranha cleaned Si sample. Rinsing was done using toluene.

A 2 wt% solution of 2-(4-chlorosulfonylphenyl)-ethyltrichlorosilane (CTCS, SAM 2, hydrophilic) was prepared using toluene as the solvent. The sample containing SAM 1 was immersed in the solution containing CTCS for 24 hours. After 24 hours the sample was washed with toluene, DI water and

finally dried. As with the gold samples CTCS SAMs occupied the regions not occupied by OTS SAMs because of hydrophobic-philic repulsions.

A similar monomeric solution as that used for gold samples was prepared with toluene taking the role of ethanol as the solvent. No CuBr was required as CTCS acted as a self catalyst. 1mM of p-Toluene sulfonylchloride (TsCl), a free initiator was also added to the monomeric solution. Nitrogen was passed just as described in the case of gold ATRP. Reaction was carried out at 60 °C. The sample was then washed with toluene and dried.

As in the case with gold, different samples were also prepared using Si as the substrate. Figure 3 shows a schematic representation of ATRP over Si substrates.

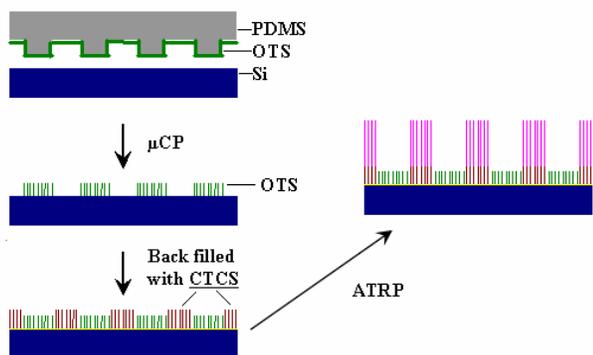


Figure 3. Scheme of  $\mu$ CP and ATRP over Si substrate

### Characterization

Characterization of the patterned polymeric brushes were performed using FTIR (Varian 7000), and AFM (Molecular Probes) was applied to investigate the fundamental characteristics of the surface initiated polymerization on both gold and silica substrates. The microstructures were measured for consistency using a Nikon Eclipse ME 600 Microscope. Non contact mode was preferred in the case of AFM analysis because the polymeric brushes were not rigid in the case of contact mode. Swelling studies were carried out in liquid cell setup.

## RESULTS AND DISCUSSION

### Clarity of Master Stamps and PDMS

The Si master stamps and the PDMS stamps were verified for clarity and corner definitions using the microscope and the contact mode of AFM.

From Figure 4 it is clear that the photolithography step of making master stamps is precise and a similar kind of microstructure is easy to produce using a suitable PDMS solution. The thickness of the master stamp was

confirmed using the contact mode of AFM as the microstructures unlike the polymer brushes were rigid.

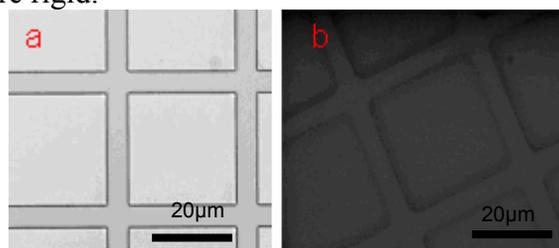


Figure 4. Nikon Microscope image of a) master stamp showing squares (pits) of 25  $\mu$ m and b) PDMS stamp of squares (elevated portions) 25  $\mu$ m width.

Figure 5 shows the AFM image of such a master stamp. The thickness as found using the cross section image is found to be 1.5 $\mu$ m which is as calculated with respect to SU 8 used and the speed of spin coating process.

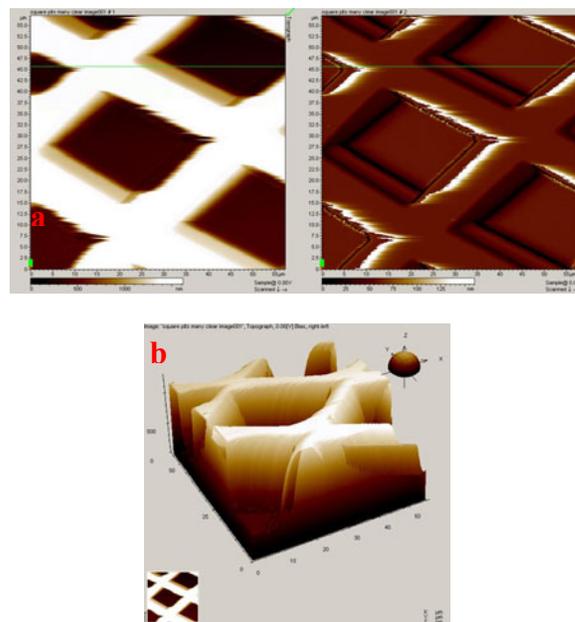


Figure 5. Contact mode AFM image of master stamps a) raw 2-D image showing topography and deflection buffers and b) 3-D image of the master stamp of thickness 1.4  $\mu$ m.

### ATRP over Gold

The effect of hydrophobic and hydrophilic SAMs on forming ATRP brushes over gold was observed using the microscope. FTIR was used to verify the presence of any polymer over the surface at the end of the reaction and AFM was used to determine the thickness of the polymer brushes.

When examined using the microscope a slight presence of polymer film over the square regions is

observed. As expected the monomer solutions went to the square regions which contains hydrophilic SAMs whereas regions between squares contained the hydrophobic SAMs.

The non contact mode AFM analysis was also carried out and Figure 6 shows the flattened image of a gold sample in which ATRP was carried out for 24 hours using N-isopropyl acrylamide. A clear pattern was observed and the horizontal cross section cut along the green line showed a change in thickness of the polymer brush over the scan area in the flattened profile. Raw data is being processed to get the real height of the polymer brush along the cross section.

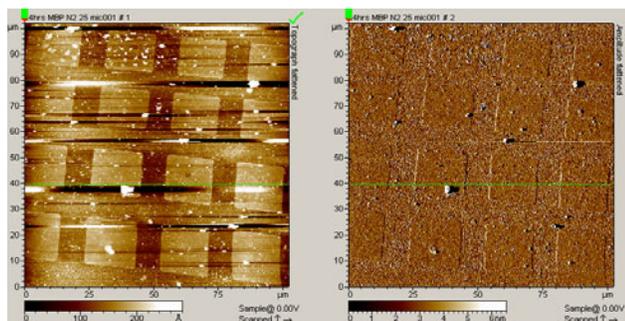


Figure 6. Non contact mode AFM image showing the flattened topography and deflection (2-D) buffers of an ATRP sample carried for 24 hours over gold surface.

### ATRP over Silicon

AFM, FTIR and microscopic analysis were carried over Si samples too. The patterns obtained by  $\mu$ CP over Si substrates were analyzed using the Nikon Eclipse Microscope.

The hydrophobic and hydrophilic SAM layers over Si substrate were viewed and it was observed that the SAM layers were non uniform throughout the sample. ATRP was still carried over these samples and the resultant polymerized square was viewed using the microscope. We observed that there was a presence of liquid film over the polymer brushes.

The presence of a liquid film prevented us from getting better AFM images as the non contact mode interaction between the film and the AFM tip resulted in ripples over the solvent fluid. This resulted in noisy AFM images and therefore the thickness of the polymer network was not recognized. Therefore the samples were vacuum dried for 2 hours and then analyzed using the non contact mode of AFM (Figure 7).

The cross section (not shown) cut along the green line showed that the thickness of the polymer brush over the square regions was in the range of 950-1020 nm (which can be also interpreted using the 3-D image) over a period of 48 hours. Recent results showed that the inconsistency in polymer

thickness throughout the sample is greatly reduced when ATRP was carried out under inert  $N_2$  atmosphere.

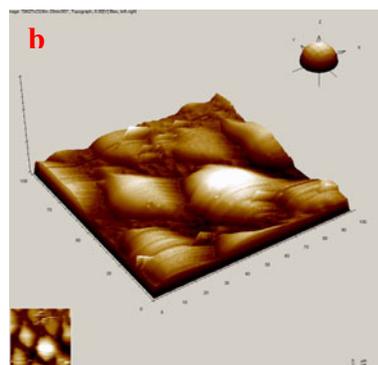
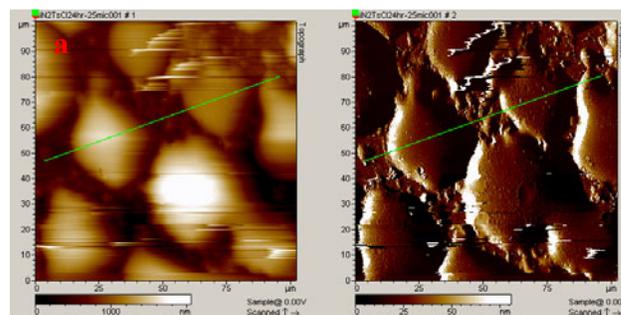


Figure 7. Non contact mode AFM image showing a) raw 2-D image showing topography and deflection buffers and b) 3-D image of polymer brush over squares.

An FTIR analysis was also carried over a 55 hour ATRP reacted sample using N-isopropyl acrylamide (NIPAAm) as the monomer.

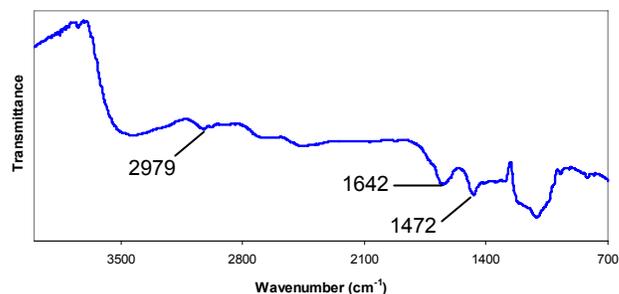


Figure 8. FTIR absorbance profile of a Si sample over which ATRP was carried out for 55 hours using NIPAAm.

The absorbance profile (Figure 8) shows the presence of N-isopropyl acrylamide in the polymeric form over the square regions (which were focused). Characteristics of the monomer such as CH and CO bond stretching and NH bending is clearly revealed in the 1450 – 1650 wave number regions of the absorbance plot.

## CONCLUSIONS

To conclude we have successfully demonstrated a route for forming patterned polymeric chains on Au surfaces by using a method which uses both soft lithography ( $\mu$ CP) and a SIP method (ATRP) as the viable techniques. We have also showed that by using an inert atmosphere, better micropatterns can be achieved over Si surfaces. We have produced clear and precise micropatterns over Si master stamps using photolithography which were reproduced successfully as PDMS stamps. Results show that the thickness of polymer networks over surfaces can be controlled by varying the reaction conditions. We have also used crosslinkers to produce intelligent polymer networks such as temperature responsive hydrogels. Characterization and analysis using AFM and FTIR can be used to further improve the system and can be employed to study the response behavior of hydrogel networks when stimulated environmentally. Finally, outcomes of this study clearly show the effect of  $\mu$ CP and ATRP as simple and powerful techniques for precise patterning and growth of polymers over surfaces. These systems can be used as biosensors and as drug delivery carriers.

## REFERENCES

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