

In both cases, due to the lack of a shaking method, a moderate level of agglomeration was observed. AFM imaging reveals the presence of a pHEMA layer that uniformly covers the microparticles. Hence, complete conformational coating is not achieved due to a high degree of particle agglomeration.

In order to avoid particle agglomeration, changes in the piCVD procedure were introduced. Hydrogel coating of microparticles was performed in a stepwise manner to allow sample homogenization between piCVD cycles (as described in 2.2.3). Figure 2.19. compares SEM images of monodisperse microparticles coated using such procedure against uncoated particles. No agglomeration was observed, indicating that the introduction of homogenization steps in the piCVD process is a suitable solution to achieve conformational coating on microparticles.

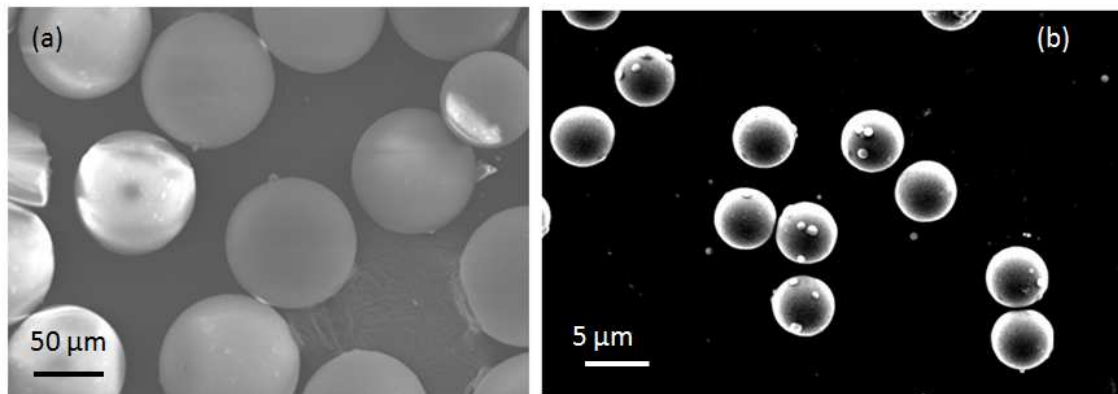


Figure 2.19. SEM images of silica spheres using a shaking method during the deposition. (a) 50  $\mu\text{m}$  silica microspheres and (b) 5  $\mu\text{m}$  silica microspheres coated with piCVD pHEMA. Images were obtained at 270X and 3000X magnification respectively.

## 2.4. Discussion

piCVD is a gentle method for preparing stable, reversibly swellable hydrogel films with nanoscale mesh size. The deposition of thin films of pHEMA has been verified by FTIR spectroscopy. In piCVD, the polymerization occurs primarily on the substrate surface and the cross-link density, and therefore the swelling properties of the film, can be controlled by changing the fractional saturation of the monomer vapor during the deposition.

It has been demonstrated that both bulk and graded co-polymers can be successfully deposited by piCVD. FTIR and ToF-SIMS analyses confirm that the reactive pentafluorophenyl ester group (PFM) remains intact after the photopolymerization, allowing for the formation of thin films capable of post-functionalization using amine-bearing moieties. The distribution of PFM within the film matrix has also been confirmed. In the graded co-polymer films, the PFM signals in both XPS and ToF-SIMS decrease from a maximum at the top surface, confirming the nanoconfinement of the reactive moiety on the near-surface region. Since the piCVD process involves real-time monitoring of film thickness, the compositional distribution can be chosen arbitrarily. For the graded co-polymer, the PFM is introduced into the feed gas exclusively during the final ~20 nm of film deposition, thereby confining the functionality only to the near-surface region only. In addition to reducing quantity of expensive functionalized monomer, there are two principal material properties benefiting from this near-surface confinement. First, the hydrogel properties of the bulk region of graded co-polymers are largely maintained. This is especially important when compared to the bulk co-polymers, which exhibit markedly limited swelling properties than the graded co-polymers. For the graded films, the underlying properties of the homopolymer can be chosen independently from the properties of the surface activity. Second, nearly all the PFM moieties in the graded co-

polymer are available for reaction. In the bulk co-polymer, much of the PFM is occluded within the polymer matrix, resulting in low conversion of this functionality due to steric hindrance. It should be noted that any vinyl co-monomer capable of being introduced into the reactor as a vapor can be used to form the graded functional film. Moreover, since the film thickness is monitored by *in situ* interferometry, it is possible to create a co-polymeric layer of controlled thickness, a feature not afforded by traditional solution methods. This interesting feature opens up new possibilities in the field of film coating that cannot be afforded by traditional wet methods.

The mesh size of the resulting films, based on swelling properties, is small enough to allow for small molecule analytes to diffuse to the underlying substrate. This was confirmed by coating a sodium-sensing optode with a thin film of pHEMA; the optode retained its ability to detect its target analyte. The mild nature of piCVD, which utilizes no plasma or solvent, makes it ideal for coating the surfaces of optodes and other sensors designed for implantation. In addition, pHEMA deposited via piCVD may enhance the surface resistance to non-specific protein adhesion, which is especially useful for *in vivo* applications of sensors. Moreover, large and small particles can be coated as well, suggesting that piCVD has potential utility in the coating of particle sensors.

As mentioned before, the aims of this chapter were to study the viability of piCVD to deposit pHEMA and pHEMA-co-pPFM thin films with different spatial distribution of PFM groups within the polymer film. The incorporation of a functional molecule (amino-PEG) throughout the entire surface of the film was studied to ensure hydrogel surface reactivity, while maintaining important bulk properties, such as the water-swelling ability of the films. From this point of view, it seems a better option to keep the PFM on the surface to ensure its complete reaction.

However, current technological demands in the field of micro-electromechanical systems require micro-structuring or defined micro-patterning of functional molecules rather than uniform decoration of surfaces. The excellent results achieved so far encourage the further exploration of piCVD as a potential technique to engineer structured co-polymer surfaces to obtain bifunctional interfaces.

## **Chapter 3.**

### ***Biofunctional Polymer Surfaces***

Originally published as:

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**2010**, 31 (8), pp 735-739



### 3.1. Introduction

The previous chapter has shown the complete study of piCVD as a method for preparing ultrathin films of pHEMA and its PFM copolymer to obtain a tunable interface for sensing devices. However, the copolymers studied were randomly deposited; in this chapter micro-patterned bifunctional surfaces have been studied in order to create surfaces that spatially confine functionality.

Typical polymer patterning schemes, such as photolithography, direct printing and soft lithography, expose the underlying substrate in areas adjacent to the polymer (Nie & Kumacheva 2008; Siringhaus et al. 2000; Miller et al. 2002). In some applications, it is advantageous to cover the entire substrate with polymer. For example, the substrate may have no native chemical functionality and thus serve only as “wasted space”, or it may be chemically or biologically incompatible with the end-application. In these cases, the surface can be presented as two separate polymers. Schemes to create all-polymer patterned thin films generally focus on creating spatially regular variations in chemical identity or functionality. A number of techniques have been described for dual-patterned polymer surfaces, including specialized versions of imprint and soft lithography (Nie & Kumacheva 2008; Gates et al. 2005; Beh et al. 1999; Vaeth et al. 2000; Miller et al. 2002; Im et al. 2008), and plasma lithography (Goessl et al. 2001). Another common method is to use physical contact masks, such as transmission electron microscope (TEM) mesh grids. The use of TEM grids as physical masks has been described for surfaces patterning in SAMs (Harant et al. 2005), polymers (Malkov et al. 2008; Favia et al. 2003), and SAM/polymer systems (Slocik et al. 2006). These grids have features in the micrometer scale, enabling the creation of micropatterns. Such a processing scheme was described recently by Malkov et al., where ~50

$\mu\text{m}$  features were fabricated by plasma-polymerization of a polymer film on top of a polymer substrate to create alternating hydrophobic/hydrophilic patterns (Malkov et al. 2008). Favia et al. also used TEM grids along with plasma polymerization to form non-biofouling poly(ethylene oxide) patterns on cell adhesive poly(acrylic acid) thin films for patterned cell growth applications (Favia et al. 2003).

In this work, we aim to extend the use of physical masks to develop a process to fabricate all-polymer patterned surfaces with precise control over both the chemical and topographic features. This technique should allow the design of surfaces that not only present specific topographic reliefs, but also defined chemical spatial distribution. The patterning fabrication process proposed here is described schematically in Figure 3.1. This approach involves a four-step process that starts with the deposition of a first polymer film on a suitable substrate. Masked etching of the resulting film, followed by conformal blanket deposition of a second polymer film over the masked sample, delivers the micro-structured surface upon mask removal. The result is a dual-polymer surface micropatterned with respect to both chemical functionality and topography. The mask acts simultaneously as an etching mask for the first polymer and a lift-off mask for the second polymer, resulting in self-alignment of the patterns in a single lithographic step. The patterning scheme is independent of the polymers used and their deposition can proceed in either order.



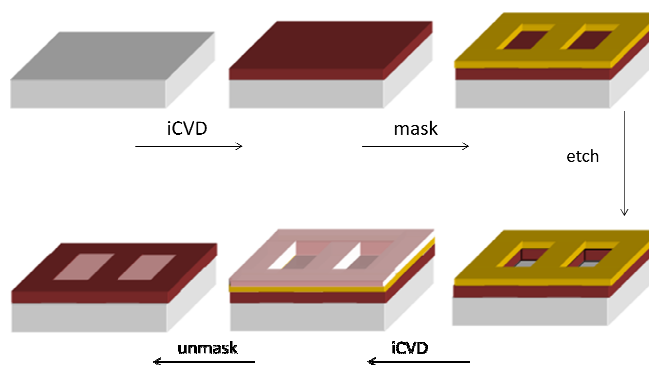


Figure 3.1. 3D Schematic representation of the patterning process (not to scale).

The polymer films are grown via initiated chemical vapor deposition (iCVD), a solvent-free method for the synthesis of conformal thin polymer films (Baxamusa et al. 2009; Tenhaeff & Gleason 2008). In iCVD, vapor-phase monomers and initiators flow into a custom-built vacuum reactor. Radical species are generated either by heated filaments or ultraviolet light; these radical species react with monomers adsorbed at a cooled substrate to initiate a polymerization. No solvent is used during iCVD, eliminating a number of material-compatibility issues. The patterning scheme presented here is completely generic and compatible with any polymer capable of being deposited by iCVD. iCVD has been used to deposit a wide variety of polymers and co-polymers, including click-functional, alternating, biocompatible, cross-linked, stimuli responsive and fluorinated polymers, which widens the scope of use of the resulting micro-structured surfaces (Baxamusa et al. 2009).

The thickness of the growing film is monitored in real-time using laser interferometry. This enables the surface to be patterned not only chemically, but also topographically. As compared to plasma polymerization, iCVD polymers have a higher retention of chemical structure, allowing for a greater degree of functional behavior, as well as greater conformality over non-planar geometries, which is critical for deposition inside the mask.

## 3.2. Experimental Section

### 3.2.1. Fabrication of Patterned Surfaces

Polymer films were deposited using iCVD. To run an initiated chemical vapor deposition iCVD, the reactor described in 2.2.1. was equipped with a filament array, which provided thermal energy for selective decomposition of molecules. The clearance between the filaments and the stage was 29 mm. The Nichrome filaments (80% Ni/20% Cr, AWG 26, Omega Engineering) were resistively heated to 280 °C, as measured by a thermocouple (Type K, AWG 36, Omega Engineering) directly attached to one of them. Similarly as in the piCVD experiments, the monomer's vapor was entered into the reactor through a MFC. The initiator TBPO was vaporized at room temperature and metered through a MFC. The monomer and initiator streams were joined before entering the reactor. In both cases, once the streams reached the chamber reactor, the polymerization took place all over the chamber.

In a typical deposition experiment, 1 – 3 sccm of monomers and 1 – 2 sccm of initiator flow were introduced into a custom vacuum chamber maintained at 100 – 500 mTorr. The monomers, perfluorodecylacrylate (PFA, Sigma Aldrich, 97%), HEMA (Sigma Aldrich, 99+%), and PFM (Monomer Polymer, 97%), and the initiator tert-butyl peroxide (TBPO, 98%, Sigma) were used as received without further purification. The temperature of the substrate was maintained between 25 – 45 °C by backside coolant circulation and the polymerization was either heat-initiated by thermal decomposition of initiator using tungsten filaments heated resistively to 300 – 350 °C or UV-initiated by radical formation upon UV irradiation of monomers. Typical deposition rates were in the range 10 – 100 nm·min<sup>-1</sup>.

The exact deposition parameters were varied depending on the desired polymer. The deposition conditions for pHEMA and p(HEMA-co-PFM) have been described in 2.2.1. using piCVD technique. Otherwise, iCVD technique has been used to obtain the poly(perfluorodecylacrylate) (pPFA). The monomer, PFA and the initiator, TBPO were introduced into the reactor through a mass flow controller. A throttling butterfly valve (MKS, 653B) was used to control the pressure inside the chamber and the temperature was maintained at 30 °C through backside coolant circulation. The film growth was initiated using filaments heated resistively (Gupta & Gleason 2006; Baxamusa et al. 2008; Montero et al. 2009; Baxamusa et al. 2009). During both depositions, a laser interferometry (JDS Uniphase, 1508) allows monitoring the film thickness in real time.

A 2000 mesh TEM copper grid (Ted Pella, G2000) with 7.5 µm holes and 5 µm bars was used as the contact mask for patterning. In order to obtain intimate contact between the mask and the polymer film, a drop of liquid, usually water or acetone, was placed on top of the mask and gentle pressure was applied with either a cotton swap or a flat piece of silicon. As the liquid wicked into the film or evaporated, capillary forces produced excellent contact between the mask and the film.

The etching procedure was performed in a custom-built oxygen plasma chamber. For a plasma power of 60 W and oxygen pressure of ~100 mTorr, typical etch rates for methacrylate and acrylate polymers studied here were between 20 – 40 nm·min<sup>-1</sup>. In order to prevent displacement of the grids under vacuum, the plasma chamber was evacuated slowly by manually modulating a butterfly valve. Following the etching, the grid did not easily displace under normal handling procedures.

After the etching step-procedure, a second polymer layer was deposited using iCVD, as described above. Following this final deposition, the mask was carefully lifted off to reveal the dual-patterned polymer surface.

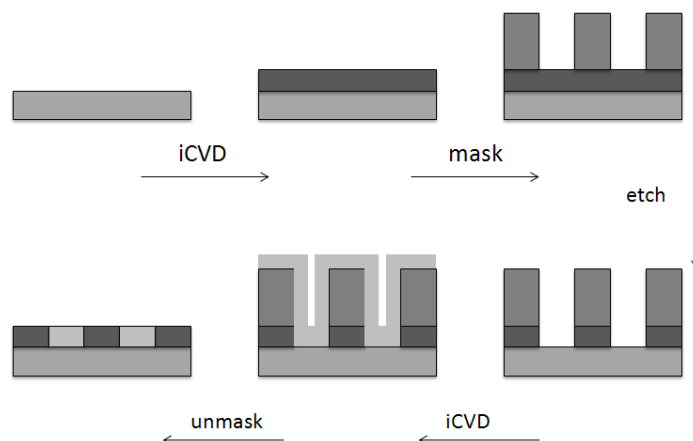


Figure 3.2. 2D Schematic representation of the patterning process (not to scale).

### 3.2.2. Structure Determination of Patterned Surfaces by AFM and SEM Analysis

#### ***Scanning Electron Microscopy (SEM)***

Micro-patterned surfaces were imaged by scanning electron microscopy (SEM, JEOL 6060) at 5 kV accelerating voltage. A tilt stage was used to obtain oblique-angle images. Micro-condensation experiments were carried out in an environmental SEM (ESEM) with a temperature-controlled stage maintained at 0 °C. Water vapor pressure inside the ESEM was maintained at 4.4 - 4.5 mtorr (96 - 98% relative humidity) in order to condense water droplets and images were obtained at 10 kV accelerating voltage.

#### ***Atomic Force Microscope (AFM)***

AFM images were acquired using an XE-100 Atomic Force Microscope (Park Scientific Instruments), with lateral resolution of 0.15 nm and vertical resolution of 0.05 nm, in non-

contact mode. The swelling behavior of the films was characterized using a wet cell (Park Scientific Instruments), operating in non-contact mode. XEP and XEI (Park Scientific Instruments) software packages were used for data acquisition and image processing respectively.

The AFM consists of a cantilever with a sharp tip at its end that is used to scan the specimen surface. The cantilever is typically silicon or silicon nitride with a tip radius of curvature on the order of nanometers. When the tip is brought into proximity of a sample surface, forces between the tip and the sample lead to a deflection of the cantilever according to Hooke's law. Depending on the situation, forces that are measured in AFM include mechanical contact forces, van der Waals forces, capillary forces, chemical bonding, electrostatic forces, magnetic forces, Casimir forces and solvation forces among others. Typically, the deflection is measured using a laser spot reflected from the top surface of the cantilever into an array of photodiodes.

### **3.2.3. Surface Functionalization of the Patterned Structures**

Fluorescent functionalization of p(HEMA-co-PFM) was performed by incubating the sample in a 10 mM solution of fluorescein-5-thiosemicarbazide (FTSC) in ethanol for 3 min. This amine-bearing fluorescent dye reacts rapidly with the pentafluorophenyl ester functional group of PFM to form an amide bond to the polymer surface (O'Shaughnessy et al. 2007). After incubation, films were rinsed extensively with ethanol and dried under a stream of N<sub>2</sub>. The fluorescent films were imaged on a Zeiss Axiovert 200 inverted microscope equipped with a FITC filter set. The excitation and emission peaks for FTSC are 492 nm and 516 nm, respectively.

### 3.3. Results

#### 3.3.1. Fabrication of Ordered Surfaces via Patterning Processes

The multistep deposition procedure described in 3.2.1. was used to fabricate a micro-patterned mesh-like surface from HEMA and PFA via piCVD and iCVD, respectively. Briefly, a pHEMA film was first deposited on the surface of a silicon wafer via piCVD. Subsequently, a TEM grid was placed on the hydrogel surface and the sample was etched to generate micro-patterned cavities to deposit the second polymer, pPFA via iCVD. Finally, the mask was carefully removed to obtain the desired patterned surface, which was confirmed by scanning electronic microscopy (SEM).

The SEM images in Figure 3.3. show top-down and oblique-angle views of a typical patterned surface resulting from this process. The polymer in the square features is the hydrophobic pPFA and the polymer in the surrounding matrix is the hydrophilic pHEMA. Careful examination of the features confirmed fidelity to the TEM grid, since both the dimensions and the patterns were maintained: the squares are  $7.5\ \mu\text{m}$  across with a  $12.5\ \mu\text{m}$  pitch.

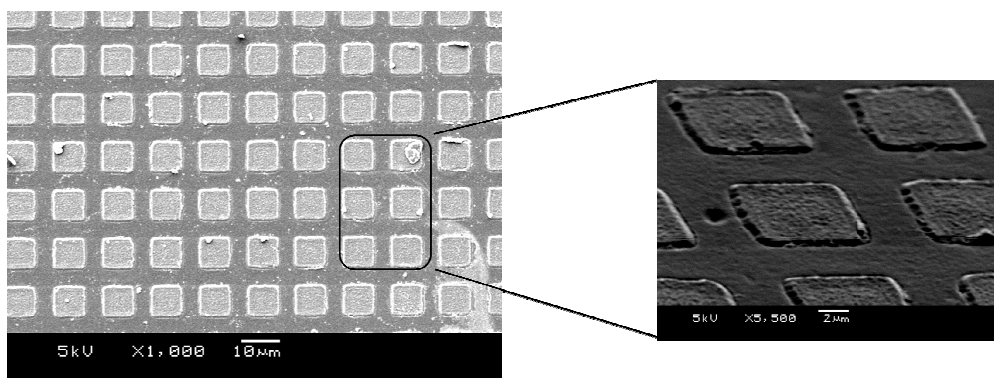


Figure 3.3. Top-down and oblique-angle SEM of typical patterned surface.

The surface is generated using this technique with pPFA in the squares and pHEMA in the surrounding matrix. (Left scale bar =  $10\ \mu\text{m}$  and right scale bar =  $2\ \mu\text{m}$ ).

Integrity of the chemical nature of the films and consequently their physicochemical properties was confirmed by the micro-condensation experiments shown in Figure 3.4. As water condenses on the surfaces, droplets preferentially form on the hydrophilic regions made of pHEMA. This behaviour confirms that the polymeric materials retained their physicochemical properties after iCVD and piCVD deposition.

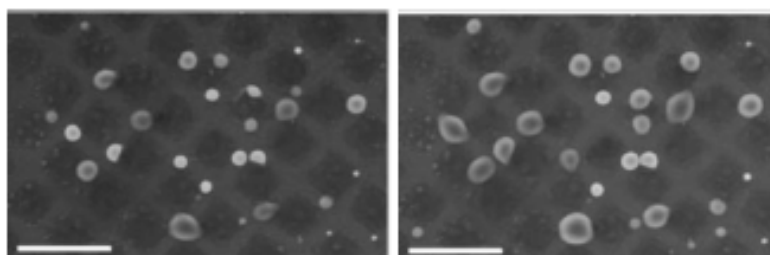


Figure 3.4. Dynamic microcondensation experiment.

The image shows water preferentially condensing and droplets growing on the hydrophilic region outside of the squares (scale bar = 20  $\mu\text{m}$ ).

In order to demonstrate that the observed domains contained distinct polymers with minimal cross-contamination, surfaces having structured domains of inert pPFA and chemically reactive p(HEMA-co-PFM) were fabricated. After incubation of the resulting samples in a solution of a suitable fluorescent dye known to react with the PFM groups, the patterns were observed under a fluorescent optical microscope. The images in Figure 3.5. show that fluorescence was confined to the matrix or to the squares, depending on whether the reactive polymer was deposited as the first or second layer, respectively. No fluorescence was observed on the inert polymer, which confirms the specificity of the process.

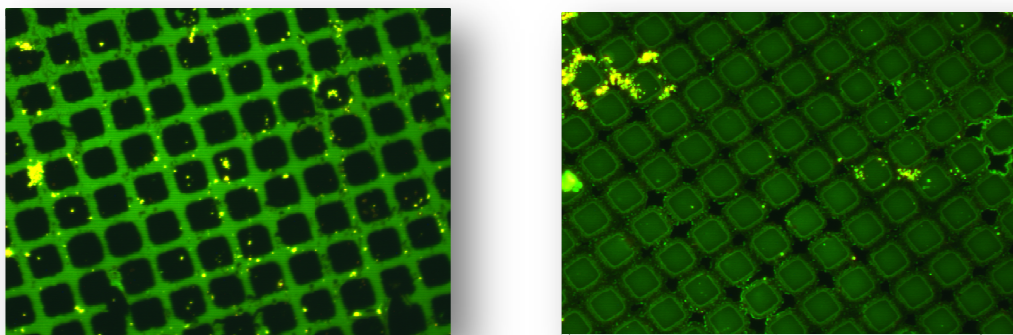


Figure 3.5. Spatially-selective fluorescent functionalization of patterned films.  
Right: p(HEMA-co-PFM) in the grid and pPFA in the squares. Right: inverse pattern.

This technique is not only capable of introducing 2D features on a surface, but it can also be used to design protrusions or depressions on the surface to incorporate tridimensional reliefs. Since the thickness of the growing polymer film is monitored in real-time, the second polymer layer can be height-matched to the first polymer layer, or it can be made intentionally taller or shorter. However, thickness monitoring, cannot occur inside of the vias defined by the mask, because the interferometry laser spot size is too large ( $>10^5 \mu\text{m}^2$ ), when compared to the lateral features of the contact mask ( $\sim 50 \mu\text{m}^2$ ).

### 3.3.2. Thickness Evaluation of Film Micro-geometries

In order to control the thickness of the second polymer film, it is important that the thickness of the film measured outside the vias matches the thickness of the film inside the vias. Conformal deposition on non-planar geometries is a key feature of iCVD not always observed in plasma polymerization (Baxamusa & Gleason 2008a). For the masks used in this study, the vias are  $7.5 \mu\text{m}$  squares that are between  $15 - 30 \mu\text{m}$  deep. The step coverage of iCVD polymer films within micro-geometries of similar dimensions has been studied previously and it has