Photoinitiated Chemical Vapor Deposition: Mechanism and Applications

by

Salmaan Husain Baxamusa

B.S., Chemical Engineering
University of California, Berkeley, 2004

Submitted to the Department of Chemical Engineering in Partial Fulfillment of the Requirements for the Degree of

DOCTOR OF PHILOSOPHY IN CHEMICAL ENGINEERING
AT THE
MASSACHUSETTS INSTITUTE OF TECHNOLOGY

July 2009

© Massachusetts Institute of Technology. All rights reserved.

Signature of Author

Department of Chemical Engineering
July 14, 2009

Certified by

Karen K. Gleason
Professor of Chemical Engineering
Thesis Supervisor

Accepted by

William M. Deen
Professor of Chemical Engineering
Chairman, Committee for Graduate Students
Abstract

Photoinitiated chemical vapor deposition (piCVD) is developed as a simple, solventless, and rapid method for the deposition of swellable hydrogels and functional hydrogel copolymers. Mechanistic experiments show that piCVD is predominantly a surface reaction, allowing it to coat non-planar geometries such as particles. The process is gentle enough to coat delicate optical sensors without degrading their function. Chemically functional hydrogels can be synthesized by incorporating a comonomer, and this functionality can be nanoconfined to the near surface region. Random amphiphilic copolymer films deposited via piCVD represent a novel polymer film system, and these surfaces present molecular-scale compositional heterogeneities that interfere with protein adsorption events.

Also described is the mechanism by which thin films form on non-planar geometries via initiated chemical vapor deposition (iCVD). The conformality of these films in microtrenches is assessed and an analytical model is developed in order to quantify the sticking probability of the initiating radical. Mechanistic insight from these experiments is used to predict the conformality based on the fractional saturation of the monomer vapor.

Thesis Supervisor: Karen K. Gleason

Title: Associate Dean for Engineering Research and Professor of Chemical Engineering
To Andréa: wife, friend, advisor, scientist
ACKNOWLEDGEMENTS

While chemical vapor deposition occurs in a vacuum, good science and good learning does not. These acknowledgements cover only some of the many who have helped along the way and express only a fraction of my gratitude.

Professor Karen Gleason’s mentorship has been integral in my growth as a scientist and researcher. She has been alternatingly patient and enthusiastic, providing freedom when requested and direction when necessary. The guidance provided by Professors Bill Green and Klavs Jensen as members of my thesis committee has been invaluable. I also had the opportunity to assist Professor Green in teaching 10.34 in 2007, an experience which I count as a highlight in my graduate studies.

The culture in the Gleason research group has been one of collaboration and camaraderie. My colleagues have never hesitated to help me solve a problem or discuss an interesting issue. I worked particularly closely with Drs. Sreeram Vaddiraju, Shannan O'Shaughnessy, Tyler Martin, and Sung Gap Im, as well as with Wyatt Tenhaeff and Nathan Trujillo. I am especially thankful for the assistance of Kyle Stephens, an undergraduate researcher from Northeastern University, and Laura Montero, a graduate student from Universitat Ramon-Llull in Barcelona.

This work would not have been possible without the generosity of my funding agencies: the National Science Foundation Graduate Research Fellowship, the National Defense Science and Engineering Graduate Fellowship, and the Charles Stark Draper Laboratories. Working with and learning from Dr. Heather Clark and Matt Dubach at Draper was one of the great pleasures of my research.

My childhood friend Nathalie Snapp (nee deLeon) has been by my side for over fifteen years, and our graduate studies overlapped geographically as she studied chemistry at Harvard. We have always pushed each other to succeed, and I would be remiss if I didn’t mention her influence.

Finally, I thank my family. My father Yusuf Baxamusa, my mother Abida Baxamusa, and my sister Maria Kapadia (nee Baxamusa) have supported all of my endeavors, intellectual and otherwise. They instilled in me a love of success, a love of science, and a love of both self and others without which I would never have undertaken this task. My son Nuri has brought balance to my life and taught me that the joys of fatherhood are not so different from the joys of scientific inquiry.

Most importantly, I thank my lovely wife Andrée Schmidt. She is my best friend, my most trusted advisor, and a very talented scientist in her own right. Any contributions to science I have made or might hope to make are predicated on her unwavering faith in and unconditional love for me.
# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Title Page</td>
<td>1</td>
</tr>
<tr>
<td>Abstract</td>
<td>2</td>
</tr>
<tr>
<td>Dedication</td>
<td>3</td>
</tr>
<tr>
<td>Acknowledgements</td>
<td>4</td>
</tr>
<tr>
<td>Table of Contents</td>
<td>5</td>
</tr>
<tr>
<td>List of Figures</td>
<td>7</td>
</tr>
<tr>
<td>List of Tables</td>
<td>13</td>
</tr>
<tr>
<td>List of Notations</td>
<td>14</td>
</tr>
<tr>
<td>Chapter 1: Introduction</td>
<td>15</td>
</tr>
<tr>
<td>1.1 Background</td>
<td>16</td>
</tr>
<tr>
<td>1.2 Initiated Chemical Vapor Deposition</td>
<td>20</td>
</tr>
<tr>
<td>1.3 Photoinitiated Chemical Vapor Deposition</td>
<td>22</td>
</tr>
<tr>
<td>1.4 Scope of Thesis</td>
<td>24</td>
</tr>
<tr>
<td>1.5 References</td>
<td>25</td>
</tr>
<tr>
<td>Chapter 2: Thin Polymers with High Step Coverage in Microtrenches by</td>
<td>27</td>
</tr>
<tr>
<td>Initiated Chemical Vapor Deposition</td>
<td></td>
</tr>
<tr>
<td>2.1 Abstract</td>
<td>28</td>
</tr>
<tr>
<td>2.2 Introduction</td>
<td>29</td>
</tr>
<tr>
<td>2.3 Results and Discussion</td>
<td>31</td>
</tr>
<tr>
<td>2.4 Conclusions</td>
<td>41</td>
</tr>
<tr>
<td>2.5 Experimental</td>
<td>42</td>
</tr>
<tr>
<td>2.6 Acknowledgements</td>
<td>44</td>
</tr>
<tr>
<td>2.7 References</td>
<td>44</td>
</tr>
<tr>
<td>Chapter 3: Protection of Sensors for Biological Applications by</td>
<td>48</td>
</tr>
<tr>
<td>Photoinitiated Chemical Vapor Deposition (piCVD) of Hydrogel Thin Films</td>
<td></td>
</tr>
<tr>
<td>3.1 Abstract</td>
<td>49</td>
</tr>
<tr>
<td>3.2 Introduction</td>
<td>50</td>
</tr>
<tr>
<td>3.3 Experimental</td>
<td>52</td>
</tr>
<tr>
<td>3.4 Results and Discussion</td>
<td>55</td>
</tr>
<tr>
<td>3.5 Conclusions</td>
<td>65</td>
</tr>
<tr>
<td>3.6 Acknowledgements</td>
<td>67</td>
</tr>
<tr>
<td>3.7 References</td>
<td>67</td>
</tr>
</tbody>
</table>
Chapter 4: Thin Hydrogel Films with Nanoconfined Surface Reactivity by Photoinitiated Chemical Vapor Deposition

4.1 Abstract
4.2 Introduction
4.3 Experimental
4.4 Results and Discussion
4.5 Conclusions
4.6 Acknowledgements
4.7 References

Chapter 5: Random Copolymer Films with Molecular Scale Compositional Heterogeneities Interfere with Protein Adsorption

5.1 Abstract
5.2 Introduction
5.3 Experimental
5.4 Results and Discussion
5.5 Conclusions
5.6 Acknowledgements
5.7 References

Chapter 6: Conclusions and Future Work

6.1 Summary and Implications for Future Research
6.2 Ongoing and Incomplete Research
6.3 Avenues of Future Research
6.4 Concluding remarks
6.5 References

Appendix: Dual Patterned Surfaces by iCVD
LIST OF FIGURES

Figure 1-1 Page 18
Generic free radical polymerization mechanism. From top to bottom: an initiator decomposes into radicals; these radicals can then attack the carbon-carbon double bond of a vinyl monomer. These radicals then add additional monomer units to form a growing polymer chain. The chain can be terminated by any radical present in the reaction system, whether initiator, growing chain, or impurity, to form the final polymer chain.

Figure 1-2 Page 19
Comparison of deposition rate, functional group retention, and power input among two plasma CVD methods and iCVD. The size of the marker represents the power input. Data are from references 10 and 11.

Figure 1-3 Page 21
(a) Schematic of the iCVD reactor and typical operating parameters. (b) Depiction of the iCVD mechanism. The initiator passes through the hot zone around the filaments and thermally dissociates to form two initiating radicals. The monomer passes through the hot zone unaffected and adsorbs on the surface. The initiating radicals combine with surface-adsorbed monomer to form polymer.

Figure 2-1 Page 31
FTIR spectra of (a) iCVD pCHMA (b) PPCVD pCHMA and (c) spun-cast pCHMA standard. The close match between the iCVD polymer and the polymer standard indicate the retention of the cyclohexyl group upon deposition. The PPCVD polymer exhibits significant broadening in the 1150-1250 cm\(^{-1}\), indicating poor retention of the ester side group.

Figure 2-2 Page 33
Films deposited by (a) iCVD, (b) spin-on, and (c) PPCVD. The meniscus-like shape of the spin-on film clearly shows the effects of solvent surface tension, while the decreased film thickness at the external trench corners and increased thickness in the internal trench corners in the PPCVD film suggest a competition between etching and deposition. The iCVD film is continuous around the top, bottom, and sidewall of the trench.

Figure 2-3 Page 34
Scanning electron micrographs of iCVD deposited pCHMA in aspect ratio 3.4 trenches for mean free paths in the bulk vapor of (a) 93 µm, (b) 62 µm, (c) 46 µm and (d) 31 µm. The step coverage exhibits little dependence on the mean free path in the bulk vapor.
Figure 2-4
Step coverage and deposition rate as a function of mean free path of the vapor molecules in the bulk vapor. The step coverage is shown for three different trench aspect ratios L/w. The step coverage exhibits little or no dependence on the mean free path, although greater step coverage is observed for trenches with smaller aspect ratio. The deposition rate also exhibits weak dependence on mean free path. The error bar represents the uncertainty in the measurement of step coverage.

Figure 2-5
Scanning electron micrographs of iCVD deposited pCHMA in aspect ratio 3.4 trenches at (a) $P_m/P_m^{\text{sat}} = 0.11$, (b) $P_m/P_m^{\text{sat}} = 0.19$, (c) $P_m/P_m^{\text{sat}} = 0.36$ and (d) $P_m/P_m^{\text{sat}} = 0.72$. The step coverage decreases as $P_m/P_m^{\text{sat}}$ increases.

Figure 2-6
Step coverage and deposition rate as a function of fractional saturation of the monomer vapor, $P_m/P_m^{\text{sat}}$. The step coverage is shown for three different trench aspect ratios L/w. The step coverage decreases as $P_m/P_m^{\text{sat}}$ increases, and greater step coverage is observed for trenches with smaller aspect ratios. Operating at low $P_m/P_m^{\text{sat}}$ resulted in step coverage of 0.85 or greater for all aspect ratios. The error bar represents the uncertainty in the measurement of step coverage.

Figure 2-7
Data for the second experimental set plotted according to Eqn (2-3) for the four different fractional saturation conditions. The dashed line represents the linear best-fit line for the data and its slope is proportional to the sticking probability of the initiating radical. The sticking probability increases with the fractional saturation, reflecting its dependence on the surface concentration of monomer. The error represents one standard deviation in the uncertainty of the slope.

Figure 3-1
Proposed piCVD reaction mechanism. Ultraviolet light decomposes HEMA monomer into radical species either at the substrate or in the vapor phase. These radicals initiate polymerization by reacting with surface adsorbed monomer.
Figure 3-2
Page 57
FTIR spectra of (a) pHEMA standard and (b) piCVD-synthesized pHEMA. Note the close agreement between the standard and the piCVD polymer, indicating polymerization through the vinyl bond of the monomer and full retention of the hydroxyethyl side chain.

Figure 3-3
Page 59
Typical reversible swelling response of piCVD pHEMA in buffer solution for multiple swell/dry cycles. All thicknesses are normalized to the as-deposited thickness of 190 nm.

Figure 3-4
Page 60
Equilibrium swollen water content as a function of a) vapor residence time and b) fractional saturation of monomer during deposition. The swollen water content is the volume fraction of water in the film when swollen in aqueous phosphate buffer solution. Each measurement was performed three times on the same sample, and the error bars indicate one standard deviation of the measurements. For data points where error bars cannot be seen, the error is smaller than the size of the data marker.

Figure 3-5
Page 61
Average mesh size of swollen films as calculated by Eqn 3-1. The error bars indicate the uncertainty resulting from propagating the error of the corresponding swollen water content measurement in Figure 3b. For data points where error bars cannot be seen, the error is smaller than the size of the data marker.

Figure 3-6
Page 63
Surface nitrogen content after incubation in a 1 wt% protein solution for three hours at 37 °C. Because the as-prepared surfaces contain no nitrogen, any nitrogen signal after incubation must be due to the presence of adsorbed protein.

Figure 3-7
Page 64
Response curves of (a) uncoated optode and (b) optode coated with 100 nm piCVD pHEMA. The intensity is the fluorescence emission ratio of 570 nm/670 nm, exciting at 485 nm. The curves show the response of the optodes when submerged in pH 7.4 buffers containing I – 0 Na⁺, II – 140 mM Na⁺, III – 340 mM Na⁺, and IV - 140 mM Na⁺.

Figure 3-8
Page 65
SEM cross-section of a silica microsphere coated with piCVD pHEMA at a) 1600× magnification (scale bar = 10 μm) and b) 5500× magnification (scale bar = 2 μm). The arrows indicate the polymer layer.
Figure 3-9
SEM images of a) uncoated silica microspheres and b) silica microspheres coated with piCVD pHEMA. Both images were obtained at 1600x magnification and the scale bars represent 10 μm.

Figure 4-1
Schematic of the chemical composition (left) and physical structure of the homogeneous (top right) and graded (bottom right) copolymer films.

Figure 4-2
FTIR spectra of three copolymer compositions for a) homogeneous copolymers and b) graded copolymers, along with the spectra for pure pHEMA. The composition refers to gas phase molar composition during piCVD synthesis.

Figure 4-3
ToF-SIMS depth profile showing signal from m/z = 253.1, corresponding to a positively charged PFM fragment, as a function of film depth for both the homogeneous and graded copolymer (samples H3 and G3, respectively).

Figure 4-4
ToF-SIMS spectra of the homogeneous and graded copolymers. Characteristic peaks of the PFM comonomer are highlighted by the accompanying ionic structures.

Figure 4-5
Swollen water content as a function of the increasing PFM content for both the homogeneous and graded copolymer.

Figure 4-6
FTIR spectra of the copolymer synthesized by piCVD before and after the functionalization with H2N-PEG-NH2. a) homogeneous copolymer (sample H3); b) graded copolymer (sample G3).

Figure 5-1
(a) FTIR spectra of the copolymers, arranged upward in order of increasing PFA content. Peaks in the gray shaded regions correspond to the hydroxyethyl pendant group of HEMA and peaks in the red shaded area correspond to the fluoroalkyl side chain of PFA. (b) The carbonyl peak position shifts as a function of composition, indicating copolymerization.
(a) Dynamic swelling measurements of the copolymer films indicating slower water uptake with increasing hydrophobic content. Percentages indicate the mol fraction of PFA in the homopolymers. (b) The equilibrium water content measured after 60 minutes monotonically decreased with increasing hydrophobic content.

XPS measurements of the surface composition of the copolymer films as a function of the bulk film composition. The bulk films are 100 nm thick, while XPS probes only the outermost 5-10 nm.

Static and receding water contact angles as a function of composition. The large difference between the static and receding angles is a result of surface reconstruction. Error bars: standard deviation, n = 2. Where error bars cannot be seen, the uncertainty is smaller than the data marker.

Tapping mode AFM measurements show that the surface RMS roughness increases with increasing hydrophobic content. Height images of the surface at four different compositions are also shown. Scale bar = 300 nm.

(a) Representative time traces of the frequency shifts in the third harmonic of a QCM-D crystal sensor coated with the indicated polymer. The dashed line indicates the introduction of protein solution into the flow cell containing the sensor. Percentages indicate mol fraction of PFA in the film. (b) Frequency shifts (absolute magnitudes) of QCM-D crystal sensors coated with various copolymer compositions upon introduction of protein solution into the flow cell containing the chamber. Error bars: standard deviation (n=2). Proteins adsorbed to the copolymers less than they did for either of the homopolymers.

SEM images of trench cross-sections coated at (left) low P/P\text{sat} and (right) high P/P\text{sat}. The image on the right is courtesy Dr. Rama Sreenivasan.

FTIR spectrum confirming retention of structural relevant components of pDMAEM.
Figure A-1
Generic patterning scheme for iCVD polymers using a contact mask.

Figure A-2
Tilted-view SEM of intentionally flat patterned film. The polymer in the squares is PPFA and the surrounding matrix is PHEMA.

Figure A-3
Tilted-view SEM of intentionally thickness-mismatched polymer films. The polymer in the squares is PPFA and the surrounding matrix is PHEMA. The expanded view shows the thickness difference at an edge.

Figure A-4
Fluorescent optical micrographs of squares of P(HEMA-co-PFM) in a matrix of PPFA (left) and the negative pattern (right). Prior to imaging, the films were functionalized with a fluorescein dye that reacts selectively with PFM.
LIST OF TABLES

Table 3-1
Experimental details of the samples prepared for this study. Page 53

Table 4-1
Experimental conditions for the copolymer synthesis. Page 78
**LIST OF NOTATIONS**

<table>
<thead>
<tr>
<th>Notation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABMP</td>
<td>azo bis methyl propane</td>
</tr>
<tr>
<td>AFM</td>
<td>atomic force microscopy</td>
</tr>
<tr>
<td>ALD</td>
<td>atomic layer deposition</td>
</tr>
<tr>
<td>BSA</td>
<td>bovine serum albumin</td>
</tr>
<tr>
<td>CHMA</td>
<td>cyclohexylmethacrylate</td>
</tr>
<tr>
<td>CVD</td>
<td>chemical vapor deposition</td>
</tr>
<tr>
<td>FTIR</td>
<td>Fourier transform infrared spectroscopy</td>
</tr>
<tr>
<td>HEMA</td>
<td>hydroxyethylmethacrylate</td>
</tr>
<tr>
<td>iCVD</td>
<td>initiated chemical vapor deposition</td>
</tr>
<tr>
<td>mtorr</td>
<td>millitorr</td>
</tr>
<tr>
<td>PECVD</td>
<td>plasma enhanced chemical vapor deposition</td>
</tr>
<tr>
<td>PEG-diamine</td>
<td>O,0-bis (2-aminoethyl) polyethylene glycol</td>
</tr>
<tr>
<td>PFA</td>
<td>perfluorodecylacrylate</td>
</tr>
<tr>
<td>PFM</td>
<td>pentafluorophenyl methacrylate</td>
</tr>
<tr>
<td>PHEMA</td>
<td>poly(hydroxyethyl methacrylate)</td>
</tr>
<tr>
<td>piCVD</td>
<td>photoinitiated chemical vapor deposition</td>
</tr>
<tr>
<td>piCVD</td>
<td>photoinitiated CVD</td>
</tr>
<tr>
<td>P$_M$/P$_M^{sat}$</td>
<td>fractional saturation of monomer vapor</td>
</tr>
<tr>
<td>PMMA</td>
<td>poly(methyl methacrylate)</td>
</tr>
<tr>
<td>PPCVD</td>
<td>pulsed plasma chemical vapor deposition</td>
</tr>
<tr>
<td>PPFA</td>
<td>poly(perfluorodecyl acrylate)</td>
</tr>
<tr>
<td>sccm</td>
<td>standard cubic centimeter per minute</td>
</tr>
<tr>
<td>SEM</td>
<td>scanning electron microscopy</td>
</tr>
<tr>
<td>TBPO</td>
<td>tert-butyl peroxide</td>
</tr>
<tr>
<td>ToF-SIMS</td>
<td>time-of-flight secondary ion mass spectroscopy</td>
</tr>
<tr>
<td>VASE</td>
<td>variable angle spectroscopic ellipsometry</td>
</tr>
<tr>
<td>XPS</td>
<td>X-ray photoelectron spectroscopy</td>
</tr>
</tbody>
</table>
Chapter 1

Introduction

Adapted from S.H. Baxamusa, S.G. Im, K.K. Gleason, Physical Chemistry Chemical Physics 2009, DOI: 10.1039/b900455f
1.1 Background

Chemical vapor deposition (CVD) is a mature technology for the preparation of inorganic thin films. CVD describes any process in which vapor phase precursors chemically react at a surface to generate a thin, solid film. It is widely used in the semiconductor industry and is found in virtually every integrated circuit fabrication plant in the world. Because it is a proven industrial manufacturing process, CVD is widely considered to be scalable from the bench to the plant and easily integrated into current processing methods for silicon wafers or microelectromechanical systems.¹,²

The principal features of CVD films stem from the semi-continuous, dry nature of the process. By altering the composition of the feed gas, film properties are easily and systematically tunable. The convective flow profiles of the gases can be engineered and the gaseous precursors easily diffuse into small features, resulting in coatings that are uniform over large areas while conformal on the nanoscale. The reduced pressure and continuous flow during CVD prevent impurities or unreacted precursors from entraining into the film.

While CVD is primarily used to deposit inorganic thin films, it is becoming an increasingly relevant technology for the preparation of polymer thin films. Polymer thin films can have a number of properties not afforded by metals and ceramics. Their low cost, mechanical flexibility, wide array of functionalities, and well-understood structure-composition-property relationships make polymers attractive for a number of applications in thin film technology.³,⁴ Polymer films can also be designed to be responsive so that their physical properties change in response to an external stimulus such as heat, moisture, or pH.⁵-⁷ Thus, the recent research in
polymer CVD can be understood as a desire to integrate the processing capability and scalability of CVD with the physical, chemical, and economic properties of polymers. Traditional polymer synthesis and deposition methods occur in the liquid phase, but the possibilities of vapor phase deposition of polymers are only now beginning to be realized.

The area of greatest potential impact for polymer CVD techniques may be in applications where the elimination of solvent is either advantageous or required. For example, residual entrained solvent in a thin film is a leading cause of failure in biocompatibility testing. In some polymerization systems, such as poly(furfuryl methacrylate), solution phase synthesis can promote undesired side reactions and yield low-quality polymers.\(^8\) Because of the surface tension inherent in liquid-phase systems, conformal coverage of thin films around micro- and nano-scale features can be difficult to achieve using traditional polymerization systems. As microfabrication techniques continue to shrink the size of achievable features, the need for conformal polymer deposition processes will become increasingly important. Factors governing conformality of polymer thin films are discussed in chapter 2.

Vapor deposition techniques are also advantageous when substrate damage, such as dissolution or swelling, occurs upon exposure to solvent and when the deposited film is not easily soluble, as is the case for many fluoropolymers,\(^9\) copolymers, and highly crosslinked polymers.

Recent research efforts in our group have focused on initiated chemical vapor deposition (iCVD) as an enabling technology for biocompatible and functional polymer thin films. iCVD borrows heavily from solution-phase polymerization. In a typical solution-phase
polymerization, monomer-initiator mixture is either heated or exposed to ultraviolet light. The thermal or radiative energy input is high enough to decompose the initiator into radicals, but low enough that the monomer and the resultant polymer are unaffected. In iCVD, the filament or the ultraviolet power density is kept similarly low. Initiating radicals react with the vinyl monomers via a free-radical mechanism to form a growing polymer chain. The chemistry shown in Figure 1-1 is representative of a generic free-radical polymerization.

Plasma enhanced CVD (PECVD) and pulsed-plasma CVD (PPCVD) are common polymer CVD techniques, but plasma deposited polymer films can have limited functional group retention due to collisions with highly energetic species and lower polymerization rate due to a

\[
\begin{align*}
I_2 & \rightarrow 2I^* \\
I^* + \text{vinyl} & \rightarrow I-R-R
\end{align*}
\]

\[
\begin{align*}
\text{polymer} + \text{impurity} & \rightarrow \text{final polymer}
\end{align*}
\]

Figure 1-1: Generic free radical polymerization mechanism. From top to bottom: an initiator decomposes into radicals; these radicals can then attack the carbon-carbon double bond of a vinyl monomer. These radicals then add additional monomer units to form a growing polymer chain. The chain can be terminated by any radical present in the reaction system, whether initiator, growing chain, or impurity, to form the final polymer chain.
competition between etching and deposition. Figure 1-2 compares the deposition rate, functional group retention, and power input for iCVD, PPCVD, and PECVD of poly(hydroxyethyl methacrylate) (PHEMA).\textsuperscript{10, 11} The power input in both plasma methods is non-selective. This results in non-selective chemistry in which unwanted side-reactions, such as the destruction of functional groups, occur in parallel with polymerization.\textsuperscript{12, 13} The power input in iCVD selectively activates the thermally or photolytically labile initiator, so high deposition rates are possible with complete retention of functional groups.

![Diagram](image)

**Figure 1-2:** Comparison of deposition rate, functional group retention, and power input among two plasma CVD methods and iCVD. The size of the marker represents the power input. Data are from references 10 and 11.
The vapor deposition of poly(para-xylylene) (commonly known by its trade name parylene) was developed over 60 years ago, and there has been much recent work in the CVD of substituted parylenes with functional moieties. The process involves the thermal decomposition of a [2,2]paracyclophane to form reactive intermediates which polymerize at the substrate surface. Unsubstituted parylene (Parylene-N) and chloro-substituted parylenes (Parylene-C and Parylene-D) have found widespread commercial use as an inert barrier, electrical insulator, and biocompatible coating. For most other functionalities, custom monomers representing derivatives of [2,2]paracyclophane must be synthesized. One goal of our research in iCVD is to use commercially available monomers in order to demonstrate the large-scale utility of these processes.

1.2 Initiated chemical vapor deposition

The typical iCVD reactor, shown schematically in Figure 1-3a along with typical reaction conditions, is a custom-built, pancake-shaped vacuum chamber with a viewport that enables real-time interferometric measurements of the film thickness. The monomer and initiator are metered into the reactor via mass flow controllers. Resistively heated filaments are suspended several centimeters above a deposition stage which is maintained at a constant temperature by backside contact with a recirculating water bath. The hot process gases that enter the reactor adsorb on the cooled substrate to form a polymer. The polymerization takes place almost entirely at the surface, as depicted in Figure 1-3b, because the vapor pressure of the growing polymer chain is too low for it to be present in the vapor phase at appreciable concentrations.
Figure 1-3: (a) Schematic of the iCVD reactor and typical operating parameters. (b) Depiction of the iCVD mechanism. The initiator passes through the hot zone around the filaments and thermally dissociates to form two initiating radicals. The monomer passes through the hot zone unaffected and adsorbs on the surface. The initiating radicals combine with surface-adsorbed monomer to form polymer.

The reactor pressure is a key parameter and is maintained by a throttling butterfly valve and an exhaust valve controller. It is important to note that the film thickness is controllable; because of the real-time interferometric measurements, the film growth can be terminated at the desired thickness. Typical iCVD growth rates are 10-100 nm/min and typical film thicknesses are 100-1000 nm.\textsuperscript{18,19}

The ability to replicate traditional free-radical polymerization chemistry in the vapor phase allows iCVD to produce nearly any free-radical polymer provided that its precursors have sufficient vapor pressures to flow into the reactor. Common iCVD reactions use a peroxide initiator such as tert-butyl peroxide and a methacrylate or acrylate monomer. Combining this
robust and well-known chemistry with the benefits afforded by vapor phase processing has led to rapid advancements in functional thin films that are conformal on a number of practical substrates. Quantitative models have been developed to predict deposition rate and molecular weight of iCVD homopolymers as a function of reaction conditions.\textsuperscript{20, 21} Additionally, quantitative understanding of iCVD copolymers have been developed.\textsuperscript{22} These models are critical to leveraging well-studied structure-property-composition relationships in polymers as well as the scale-up of iCVD reactors.

In this thesis, we studied iCVD on non-planar substrates and elucidated the mechanism governing the conformality of thin films inside of microtrenches. A simple analytical model was created in order to describe the step coverage within these trenches, and we used this model to estimate the sticking probability of initiating radicals. We found that these probabilities are dependent on the surface coverage of the adsorbed monomer during the deposition. This result has profound implications for the use of iCVD in conformal or non-conformal coatings for MEMS devices, membranes, and particles. It also served to elucidate the reaction mechanism and confirm the hypothesis that iCVD polymerization is primarily a surface reaction.

1.3 Photoinitiated chemical vapor deposition

In photoinitiated chemical vapor deposition (piCVD), ultraviolet light irradiates the substrate through the viewport. The radiation creates radicals which subsequently initiate the free-radical polymerization. A previous researcher in this group studied piCVD by introducing a separate photoinitiator, 2,2’-azobis(2-methylpropane) (ABMP) into the reactor and activating it
with radiation from a high-pressure mercury lamp.\textsuperscript{23} This reaction is exactly analogous to iCVD with the thermally labile initiator replaced with a photolytically labile initiator.

In this thesis, we studied the direct photoinitiation of methacrylate monomers in chapters 3-5. Specifically, PHEMA was deposited from its hydroxyethyl methacrylate (HEMA) monomer without the use of a separate photoinitiator. This resulted in a simplified experimental setup and analysis of the reaction. Because the specific wavelength of activation for the monomer coincided with the output radiation of a common germicidal lamp, the use of the high-pressure mercury lamp was eliminated. The power input for piCVD of this type was less than 80 $\mu$W/cm$^2$. The hydrogel swelling properties of PHEMA could be controlled by changing the fractional saturation of the monomer vapor. The hydrogel was also suitable for use as a water-permeable protective layer for optical sensors meant for use in biological experiments.

We also studied copolymers of PHEMA based on the piCVD platform. By controlled addition of pentafluorophenylmethacrylate (PFM) monomer into the feed gas, functional hydrogels were synthesized. The functionality could be incorporated throughout the depth of the film or nanoconfined only to the near-surface region. Taking advantage of the solventless nature of piCVD, we created copolymers of HEMA and perfluorodecylacrylate (PFA), two highly dissimilar monomers. Liquid phase copolymerization of these two monomers is difficult because the two monomers are generally not soluble in the same solvents. The properties of the thin films could be controlled by systematically varying the composition of the feed gas. The randomly amphiphilic nature of these copolymers were reflected in protein adsorption experiments. We found that the copolymer films adsorbed less protein than either of the pure homopolymers.
films (PHEMA or PPFA). These results indicated that presenting molecular-scale compositional heterogeneities can disrupt the interaction of proteins with a surface.

1.4 Scope of thesis

Chapter 2 analyzes the factors governing the conformality of iCVD thin films in micron-scale trenches. A simple analytical model for describing step coverage inside of these trenches is developed and is used to compute a sticking probability from experimental observations.

Chapter 3 presents photoinitiated chemical vapor deposition of hydrogel thin films. The structure and properties of these films are investigated, and the hydrogel is evaluated as a protective coating for optical sensors in biological environments.

Chapter 4 expands on the work presented in chapter 3 by introducing a chemically functional comonomer into the film. The comonomer is added in a graded fashion such that the functionality is confined only to the outermost (<20 nm) portion of the film. The graded copolymer is also compared to its homogeneous analogs.

Chapter 5 furthers the study of piCVD copolymers by copolymerizing HEMA with perfluorodecylacrylate (PFA) to produce randomly amphiphilic surfaces. The composition-dependent properties of these films are explored, and control over surface energy, surface composition, and swellability are demonstrated. The ability of these randomly amphiphilic surfaces to prevent protein adsorption are demonstrated by quartz crystal microbalance experiments.
Finally, chapter 6 places this work in perspective by suggesting possible research topics for future investigators, both within the context of the research presented in this thesis as well as iCVD in general.

1.5 References


Chapter 2

Thin Polymer Films with High Step Coverage in Microtrenches by Initiated Chemical Vapor Deposition

Originally published as S.H. Baxamusa, K.K. Gleason,

Chemical Vapor Deposition 2008, 14, 313-318.
2.1 Abstract

Initiated chemical vapor deposition (iCVD) is used to deposit thin films of poly(cyclohexylmethacrylate) (pCHMA) in microtrenches of depth 7 μm and widths 1-5 μm. By changing the fractional saturation of the monomer vapor, step coverage of 0.85 is achieved for the highest aspect ratio trench studied while maintaining a deposition rate of 15 nm/min. An analytical model for determining the sticking probability of the initiating radical (CH₃)₃CO⁻ is developed, and is experimentally shown to be a function of fractional saturation of monomer vapor. For the conditions studied, the sticking probability is between 1.1×10⁻²-5.0×10⁻². These results suggest that iCVD proceeds via reaction of a vapor phase initiating radical with a surface adsorbed monomer.
2.2 Introduction

The conformal deposition of thin films is important for many research areas, including microelectronics, microfluidics, and separations. In order to eliminate the effects of surface tension in small geometries, vapor phase processes are preferred. Considerable experimental and modeling work has been devoted to conformal inorganic coatings synthesized via chemical vapor deposition (CVD)\(^1\-^4\) or atomic layer deposition (ALD).\(^5\) Recent work has shown that ALD can coat the interior of nanoporous aerogels with copper.\(^6\)

However, there are thin film applications for which polymers are a more suitable material than inorganics. For example, polymer films have been used to reduce biofouling on membranes in contact with biological media\(^7\-^9\) or to impart a specific biological functionality at a surface.\(^10,\,11\) Polymers are also used in organic electronics as conductors\(^12,\,13\) or insulators.\(^14\) In these applications, a continuous, conformal polymer film on a non-planar geometry is often desirable. While ALD is a highly conformal deposition process, it is primarily used for inorganic materials such as metals, metal oxides, and metal nitrides.\(^15\) Micromachined inkjet technology has been used to coat trenches with photoresist polymer, but the resultant films show moderate step coverage and have only been demonstrated inside of trenches with very large openings (>150 \(\mu\)m) with mild aspect ratios.\(^16\)

Here, we show that very good step coverage is possible for polymer films grown inside microtrenches of width 1 – 5 \(\mu\)m and depth 7 \(\mu\)m via iCVD using a free-radical mechanism. In
iCVD, a vinyl monomer and a thermally labile initiator simultaneously flow into a reactor. Decomposition of the initiator at an array of heated filaments produces radicals which initiate a free-radical polymerization of the monomer through its vinyl bonds. This method has been used to deposit a variety of polymers such as hydrogels, alternating copolymers, functionalizable materials, antimicrobial films, insulating organosilicones, and sacrificial polymers for the production of air-gap structures. In this work, we have deposited pCHMA using tert-butyl peroxide (TBPO) as the initiator. pCHMA deposited via iCVD has been used previously as a sacrificial material in the production of air-gap structures. In addition, pCHMA is chemically similar to poly(methylmethacrylate) (pMMA), which has been used as a gate dielectric in thin-film transistors.

Other polymer vapor deposition techniques utilize plasma or thermal decomposition of the monomer. The conformality of plasma deposited films can be affected by the presence of charged species and non-uniform electric fields. Polymers grown via thermal decomposition of the monomer, such as parylene, have been shown to conformally coat confined microgeometries. The CVD of parylene is thought to proceed by the chemisorption (i.e., reaction) of vapor phase monomers to reactive chain ends on the substrate surface. The monomers in iCVD, however, are not inherently reactive; they require the presence of an initiating radical to make the polymerization proceed. The presence of initiating radicals in the vapor phase therefore requires a separate analysis. Here, we investigate the effect of the mean free path and fractional saturation of the monomer vapor. These results are used to estimate the sticking probability of the initiating radicals and suggest a mechanism for film formation. Understanding both is critical for understanding the growth of conformal polymer thin films.
2.3 Results and Discussion

Two series of experiments were performed for this study. In the first series, the mean free path of molecules in the vapor phase was varied by adding a patch flow of inert N\textsubscript{2} and changing the deposition pressure accordingly. In the second series, the fractional saturation of the monomer vapor (the partial pressure of the monomer divided by its saturation pressure, \(P_{m}/P_{m}^{sat}\)) above the substrate was varied by changing the substrate temperature. All other process conditions for the two series were fixed. See the Experimental (section 2.5) for additional details.

2.3.1 Film characterization. Figure 2-1 compares a typical FTIR spectrum of iCVD pCHMA to pulsed plasma CVD (PPCVD) pCHMA and a polymer standard. None of the spectra show

![Figure 2-1: FTIR spectra of (a) iCVD pCHMA (b) PPCVD pCHMA and (c) spun-cast pCHMA standard. The close match between the iCVD polymer and the polymer standard indicate the retention of the cyclohexyl group upon deposition. The PPCVD polymer exhibits significant broadening in the 1150-1250 cm\textsuperscript{-1}, indicating poor retention of the ester side group.](image-url)
evidence of unsaturated carbon, either due to C=C stretching (1640-1660 cm\(^{-1}\)) or unsaturated C-H vibration (3000-3100 cm\(^{-1}\)). The iCVD deposited polymer shows excellent agreement with the standard, as both exhibit strong signals due to carbonyl stretching (1725 cm\(^{-1}\)), symmetric cyclohexyl CH\(_2\) vibration (2860 cm\(^{-1}\)), and antisymmetric cyclohexyl CH\(_2\) vibration (2937 cm\(^{-1}\)). The PPCVD pCHMA shows significant broadening in the region corresponding to C-C-O stretch (1150-1250 cm\(^{-1}\)), indicating poor retention of the ester side group. The spectra indicate that the iCVD film has undergone complete polymerization through the vinyl moiety of the monomer while retaining the cyclohexyl side group. This is typical of iCVD polymers, which have been shown to spectroscopically match their solution synthesized counterparts. All deposited films in both experimental series showed similar spectra.

2.3.2 Comparison to pulsed plasma CVD/solution processing. The scanning electron micrographs in Figure 2-2 compare trenches coated using iCVD, spin-on deposition, and PPCVD. The spin-coated film has little or no coverage of the sidewalls but a thick deposition layer at the trench bottom. The effects of solvent surface tension are clearly reflected in the meniscus-like shape of the film at the trench bottom. A vapor phase process such as plasma CVD eliminates the effects of surface tension. However, the PPCVD film exhibits regions of high and low thickness at the convex and concave corners of the trench, resulting in poor step coverage. This is likely due to a competition between etching and deposition due to the uneven distribution of charged species where the local electric field is non-uniform, such as around the trench corners. Because iCVD relies on neutral chemistry and there are no electric fields, no etching is observed.
Figure 2-2: Films deposited by (a) iCVD, (b) spin-on, and (c) PPCVD. The meniscus-like shape of the spin-on film clearly shows the effects of solvent surface tension, while the decreased film thickness at the external trench corners and increased thickness in the internal trench corners in the PPCVD film suggest a competition between etching and deposition. The iCVD film is continuous around the top, bottom, and sidewall of the trench.

2.3.3 Effect of mean free path. Figure 2-3 shows scanning electron micrographs of the polymer deposited in microtrenches for the first experimental series. The deposited films are smooth and continuous over the top, bottom, and sidewalls of the trench. Figure 2-4 shows the effect of mean free path on the deposition rate as well as the step coverage for trenches with three different aspect ratios. The mean free path was computed at the stage temperature and chamber pressure using standard kinetic theory. The step coverage was determined by dividing the film thickness at the bottom of the trench by the film thickness at the top of the trench. The trenches with the smallest aspect ratio were coated evenly across the bottom, sidewalls, and top and thus had nearly unity step coverage.
Figure 2-3: Scanning electron micrographs of iCVD deposited pCHMA in aspect ratio 3.4 trenches for mean free paths in the bulk vapor of (a) 93 μm, (b) 62 μm, (c) 46 μm and (d) 31 μm. The step coverage exhibits little dependence on the mean free path in the bulk vapor.

Figure 2-4: Step coverage and deposition rate as a function of mean free path of the vapor molecules in the bulk vapor. The step coverage is shown for three different trench aspect ratios L/w. The step coverage exhibits little or no dependence on the mean free path, although greater step coverage is observed for trenches with smaller aspect ratio. The deposition rate also exhibits weak dependence on mean free path. The error bar represents the uncertainty in the measurement of step coverage.

Neither the deposition rate nor the step coverage is a strong function of the mean free path of the vapor precursors, which indicates that homogeneous vapor phase collisions and
reactions are not significant components of the deposition mechanism. The weak dependence of step coverage on mean free path is consistent with the fact that the Knudsen number, the ratio of mean free path to a characteristic trench dimension, is \( Kn > 6 \) for all experiments. For \( Kn>1 \), collisions with the trench walls occur more frequently than collisions with other vapor phase molecules,\(^{35}\) so the mean free path of molecules in the bulk vapor above the substrate does not affect the step coverage inside the trench.

2.3.4 Effect of fractional saturation of monomer vapor. Figure 2-5 shows scanning electron micrographs of the polymer deposited in microtrenches for the second experimental series, in which the primary variable was substrate temperature. As in the first series, the deposited films are smooth and continuous over the top, bottom, and sidewalls of the trench. Figure 2-6 shows the dependence of deposition rate and step coverage on \( P_m/P_m^{sat} \). The partial pressure of the monomer was determined by multiplying the mole fraction of monomer in the feed gas by the chamber pressure, and the saturation pressure was evaluated using the Clapeyron equation at the substrate temperature. At the lowest fractional saturation studied, step coverage of 0.85 or greater was observed for all the trenches, and the lowest aspect ratio trench was coated evenly at all fractional saturations except \( P_m/P_m^{sat} = 0.72 \). Because the fractional saturation of monomer vapor determines the surface coverage of monomer, the strong dependence of step coverage on \( P_m/P_m^{sat} \) suggests that the process governing film formation depends on the interaction between reactive vapor species and adsorbed monomers.
Figure 2-5: Scanning electron micrographs of iCVD deposited pCHMA in aspect ratio 3.4 trenches at (a) \( \frac{P_M}{P_M^{\text{sat}}} = 0.11 \), (b) \( \frac{P_M}{P_M^{\text{sat}}} = 0.19 \), (c) \( \frac{P_M}{P_M^{\text{sat}}} = 0.36 \) and (d) \( \frac{P_M}{P_M^{\text{sat}}} = 0.72 \). The step coverage decreases as \( \frac{P_M}{P_M^{\text{sat}}} \) increases.

Figure 2-6: Step coverage and deposition rate as a function of fractional saturation of the monomer vapor, \( \frac{P_M}{P_M^{\text{sat}}} \). The step coverage is shown for three different trench aspect ratios \( L/w \). The step coverage decreases as \( \frac{P_M}{P_M^{\text{sat}}} \) increases, and greater step coverage is observed for trenches with smaller aspect ratios. Operating at low \( \frac{P_M}{P_M^{\text{sat}}} \) resulted in step coverage of 0.85 or greater for all aspect ratios. The error bar represents the uncertainty in the measurement of step coverage.
2.3.5 Determination of sticking probability. Sticking probabilities of reactive species are widely used in the analysis of chemical vapor deposition on non-planar substrates. In general, reactive species with low sticking probabilities encourage conformal deposition in trenches. The sticking probability of the reactive species in iCVD can be estimated using a simple analytical model.

A reactive species that travels to the bottom of a trench of depth $L$ will collide with the trench wall $n$ times. For each collision, the molecule has a sticking probability $\alpha$. A molecule that reacts at the top of the trench will have struck the wall zero times. Thus, the ratio of initiating radical flux at the bottom of the trench to flux at the top of the trench is:

$$S = \frac{(1-\alpha)^n}{(1-\alpha)^0} = (1-\alpha)^n \quad \text{Eqn (2-1)}$$

If the growth rate is proportional to the flux of the reactive species, then $S$ is the step coverage.

The number of collisions $n$ can be estimated as $n = (Z)(\tau)$, where $Z$ is the frequency of wall-molecule collisions and $\tau$ is the time required to diffuse to the bottom of the trench. When the Knudsen number is large, as in this case ($Kn > 6$ for all experiments), the collision frequency is approximately $Z \sim \frac{v_{\text{gas}}}{w}$, where $v_{\text{gas}}$ is the thermal velocity of the gas molecules and $w$ is the width of the trench. The diffusion time $\tau$ can be estimated as $\tau = \frac{L^2}{D}$, where $D$ is the diffusion coefficient. For Knudsen flow in trenches of width $w$, depth $L$, and infinite length, the diffusion coefficient is $D = 2.1(w)(v_{\text{gas}})^{3.6}$. Thus:

$$n = (Z)(\tau) = \left(\frac{v_{\text{gas}}}{w}\right)^2 \frac{L^2}{2.1(w)(v_{\text{gas}})^{3.6}} = \frac{1}{2.1} \left(\frac{L}{w}\right)^2 \quad \text{Eqn (2-2)}$$
Using the expression in (2-2) for \( n \), (2-1) can be linearized by taking the logarithm and assuming \( \Gamma \ll 1 \). This gives the relationship

\[
\ln(S) = -0.48 \left( \frac{L}{w} \right)^2 \quad \text{Eqn (2-3)}
\]

A plot of the logarithm of step coverage against the square of the aspect ratio should yield a straight line with slope \(-0.48(\Gamma)\). Figure 2-7 shows the data from the second experimental series plotted according to (2-3) and the corresponding sticking probabilities. All the sticking probabilities are much smaller than unity, which is expected for the level of step coverage seen
here. The sticking probability decreases as the monomer vapor approaches saturation, so deposition at low $P_m/P_{M^{sat}}$ results in better step coverage.

At the deposition conditions studied here, the flux of monomer to the surface is approximately $10^{23}$ m$^{-2}$ s$^{-1}$. In order to observe a growth rate of $\sim$50 nm/min, the sticking probability of the monomer would have to be $\sim10^{-6}$. However, the magnitude of the sticking probabilities as determined by the step coverage profiles is $1.1\times10^{-2}-5.0\times10^{-2}$. These results therefore suggest that the monomer is not the reactive species of interest.

The inverse relationship between the sticking probability of the reactive species and $P_m/P_{M^{sat}}$ is critical to elucidating its role in iCVD polymerization. The thermal decomposition of initiator results in the production of tert-butoxy radicals, which can then adsorb on the substrate surface. There, they may either desorb back into the vapor phase after some time $\tau_{surf}$ or react with a monomer to form a polymer chain after some time $\tau_{surf}$.

The surface lifetime of the initiating radical $\tau_{surf}$ can be computed as:

$$\tau_{surf} = N_s \sqrt{\frac{2\pi m k_b T}{P_r}}$$

where $N_s$ is the density of adsorption sites on the surface and $P_r$ is the partial pressure of the initiating radical. The density of adsorption sites is of the order of the monolayer surface concentration, which has been previously reported as $5\times10^{14}$ cm$^{-2}$. The partial pressure of the initiating radical cannot be known precisely, but if it is assumed that half of the peroxide bonds are broken, then the partial pressure can be estimated as 85 mtorr. For a substrate temperature of 30 °C, this corresponds to a surface lifetime $\tau_{surf} \approx 33 \mu$s.

The time required for a one propagation reaction is
\[ \tau_{nn} = (k_p [M])^{-1} \]  

Eqn (2-5)

where \( k_p \) is the propagation rate constant for the polymerization reaction and \([M]\) is the surface concentration of monomer. The propagation rate constants in iCVD have been found to closely match their liquid-phase counterparts when the surface concentration of monomer is assumed to be in equilibrium with the vapor concentration. Using a representative value of \([M]\) obtained from a BET isotherm of the closely related monomer butyl acrylate and a previously reported propagation rate constant for the free-radical polymerization of CHMA, the time for one propagation reaction is \( \tau_{nn} = 230 \mu s \).

As \( \tau_{nn} \) is an order of magnitude greater than \( \tau_{surf} \), a surface adsorbed initiating radical is more likely to desorb back into the vapor than it is to form a growing polymer chain. Thus, the sticking probability is not simply the probability that an initiating radical physisorbs to the surface; rather, it is the probability that a radical chemisorbs to the surface. Because the surface is populated with adsorbed monomer, this chemisorption is the irreversible reaction of the radical with a monomer to form a growing polymer chain. The inverse relationship between sticking probability and fractional saturation of monomer vapor is therefore a reflection of the increased monomer surface concentration at high \( P_M / P_{M}^{sat} \). A higher monomer surface concentration increases the number of sites at which a radical impinging from the vapor phase can react, which in turn increases the sticking probability.

2.4 Conclusions
The iCVD of pCHMA can coat trenches with aspect ratio of up to 5.5 with very good step coverage (>0.85) when operating in the Knudsen diffusion regime. The sticking probability of the rate-controlling deposition species was estimated from the observed step coverage profiles. As expected, lower sticking probabilities, and hence improved step coverage, were observed at increased substrate temperature. By increasing $P_m/P_{m}^{sat}$, the fractional saturation of the monomer vapor, the effect of increased surface concentration of monomer molecules was studied. The sticking probability was found to depend on the concentration of absorbed monomer at a fixed substrate temperature. The step coverage of films deposited in trenches is enhanced by operating at low $P_m/P_{m}^{sat}$, and excellent step coverage is obtained at $P_m/P_{m}^{sat} = 0.1$. While increased step coverage comes at the expense of growth rate, even the lowest observed deposition rate, 15 nm/min, is approximately one order of magnitude greater than a typical ALD coating process.\textsuperscript{41}

Combined with an analysis of the time scales of desorption and reaction, dependence of the sticking probability on surface coverage of the monomer strongly suggests that the rate limiting event is the chemisorption of an initiating radical, $(CH_3)_3CO\cdot$, on an adsorbed monomer site, the event which commences growth of a polymer chain. Those initiating radicals that do not react with monomers desorb back to the vapor phase. This mechanism is in contrast to the CVD of parylene wherein vapor phase monomer must strike an adsorbed radical.\textsuperscript{28} Despite the different mechanisms, the magnitudes of the iCVD sticking probabilities are comparable to those reported for parylene deposition, indicating that a similar level of conformality is possible.
The results presented here for the cyclohexylmethacrylate monomer are in principle general for vinyl monomers provided that the propagation reaction time is much longer than the adsorbed radical surface lifetime. At least two polymers previously grown via iCVD have propagation rate constants similar to that for pCHMA and so should demonstrate similar levels of step coverage.

2.5 Experimental

The reactor used for the iCVD of pCHMA has been described previously. The monomer CHMA (≥95%, Aldrich) and initiator TBPO (≥97%, Aldrich) were used as-received without additional purification. Vapors of both the monomer and the initiator were metered into a custom-built cylindrical vacuum chamber. An array of filaments, mounted 3 cm above the substrate, was resistively heated to decompose the TBPO. The temperature of the substrate was controlled via backside contact of the deposition stage with temperature-controlled water lines. The chamber pressure was maintained by a throttling butterfly valve.

Two series of experiments were conducted for this study. In the first series, the stage temperature was fixed at 50 °C with a nitrogen patch flow of 0, 2, 4 or 8 sccm and chamber pressure 300, 450, 600, or 900 mtorr, respectively. The chamber pressure was varied to keep the partial pressures of the monomer and initiator constant. The addition of the patch flow decreased the mean free path of the vapors in the deposition chamber while all other deposition parameters remained constant. In the second series, the stage temperature was 30, 40, 50, or 60 °C while the patch flow was eliminated and the pressure fixed at 300 mtorr. Varying the substrate temperature changed only $P_m/P_{stat}$, the fractional saturation of the
monomer vapor. For all experiments, the flowrates of CHMA and TBPO were 2.6 sccm and 1.3 sccm, respectively, and the filament temperature was 300 °C. This temperature is sufficient to break the thermally labile peroxide bond in the TBPO but is insufficient to decompose CHMA.

Laser interferometry was used during all depositions to track the thickness of the growing films. The cycle thickness was determined by dividing the film thickness on a flat substrate, as measured by variable-angle spectroscopic ellipsometry (VASE), by the number of cycles. The VASE measurements were performed on a J.A. Woollam M-2000 spectroscopic ellipsometer, and data were gathered at an incident angle of 70° and 225 wavelengths. The interferometric measurements were also used to terminate film growth between 300-350 nm.

The reactor was reconfigured for PPCVD by attaching a radio frequency power supply (ENI Power Systems, Model HF-650) to the filament array, creating a top electrode. The bottom electrode was the reactor stage, which was grounded. An antenna tuner (Heathkit, SA-2060A) was used to minimize the reflected power. The plasma power was 60 W and was pulsed for 30 ms/70 ms on/off cycles.

For the spin-coated sample, poly(methylmethacrylate) (PMMA) cast onto a substrate using a four-inch spin-coater (Laurell Technologies, WS-400B-6NPP/lite). Approximately 1 mL of PMMA dissolved in anisole (Microchem) was cast onto a wafer spinning first at 500 rpm for 5 seconds and then at 1500 rpm for 45 seconds. Any remaining anisole was evaporated by heating the substrate to 180 °C on a hot plate for 30 minutes. This method produces high-quality films on flat substrates and is commonly used for the preparation of photoresists.
All films were deposited on silicon substrates patterned with trenches generously supplied by Analog Devices. The wafers had trenches of three nominal widths: 1 μm, 2 μm, and 5 μm. Each trench had a nominal depth of 7 μm. The substrates were used as-received.

Scanning electron microscopy (JEOL JSM-6060) was used to characterize the film growth in trenches. Each sample was sputter-coated with ~10 nm of gold (Denton Desk II) prior to microscopy. Step coverage was determined by measuring the image of the film thickness at the bottom and top of the trench and dividing these two measurements.

The chemical structure of the film was determined by Fourier Transform Infrared Spectroscopy (Nicolet Nexus 870ESP). Spectra were gathered in transmission mode using a liquid N₂ cooled MCT detector at 4 cm⁻¹ resolution averaged over 64 scans. A pCHMA standard (Aldrich) was cast onto a flat silicon wafer from a solution of tetrahydrofuran. All other samples were as-deposited ICVD or PPCVD films.

2.6 Acknowledgements

The authors thank the National Defense Science and Engineering Graduate Fellowship and Draper Laboratories UIRaD for financial support and Dr. Ed Gleason of Analog Devices for supplying the substrates.

2.7 References


45
Chapter 3

Protection of Sensors for Biological Applications by Photoinitiated Chemical Vapor Deposition (piCVD) of Hydrogel Thin Films

3.1 Abstract

We report photoinitiated chemical vapor deposition (piCVD), a gentle synthetic method for the preparation of ultra thin films (~100 nm) of the hydrogel poly(hydroxyethyl methacrylate) (pHEMA). piCVD occurs near room temperature and requires only mild vacuum conditions. The deposited films swell rapidly and reversibly in buffer solution and the swelling properties can be controlled via the deposition conditions. Analysis of the swelling data indicates that the mesh size of the hydrogel creates a selectively permeable coating. The mesh is large enough to allow small molecule analytes to permeate the film but small enough to prevent the transport of large biomolecules such as proteins. X-ray photoelectron spectroscopy (XPS) shows that the films decrease non-specific adhesion of the protein albumin by nearly eight-fold over bare silicon. A dry process, piCVD is suitable for coating particles with diameters as small as 5 μm. The absence of solvents and plasmas in piCVD allows films to be direct synthesized on optode sensors without degradation of sensitivity or response time.
3.2 Introduction

The modification of surfaces to enhance their compatibility with biological media, both in vivo and in vitro, is of great interest for applications ranging from biomedical implants\textsuperscript{1-3} to tissue engineering.\textsuperscript{4,6} Surface modification is also critical for sensing applications\textsuperscript{7-10} with particular focus on the potential of an in vivo glucose sensor to assist in the treatment of diabetic individuals.\textsuperscript{11} However, any sensor that is to come into contact with biological media, including in vivo implants, must be compatible with the physiological environment. Chief among compatibility concerns is the ability of a surface to resist non-specific protein adhesion, to prevent both biofouling on the device surface as well as inflammation and thrombosis.\textsuperscript{12}

Biologically-relevant sensing devices represent a unique challenge in this regard, since any surface modification that reduces non-specific protein adhesion must still allow for the passage of the analytes of interest.\textsuperscript{11} Additionally, the surface modification process must not degrade the functionality of the device.\textsuperscript{9} Attaching long polymer brushes is a common method of enhancing the biocompatibility of surfaces,\textsuperscript{13-15} but these methods require chemical modification of the surface that can degrade the sensor function. Thin polymer films that are not covalently attached are another common modification,\textsuperscript{16} but the solvents used in their preparation can degrade the device, particularly enzymatic biosensors.\textsuperscript{9,11} The hydrogel poly(hydroxyethylmethacrylate) (pHEMA) has been deposited without a solvent via a plasma
process, but never directly on a sensor presumably because the energetic species present in the glow discharge can damage the device.

Thus, for sensors for biological applications or physiological implantation, a solvent- and plasma-free method for the synthesis of stable, swellable, crosslinked hydrogel thin films is necessary. Here, we present the photoinitiated chemical vapor deposition (piCVD) of ultra thin pHEMA films with tunable crosslink density. pHEMA has been used extensively in biological and biomedical applications and its biocompatibility, including resistance to protein adhesion, has been investigated. When synthesized as a crosslinked network, pHEMA films have small mesh sizes that prevent the permeation of large biomolecules. In this work, the polymerization is initiated by exposing monomer vapors under moderate vacuum to low power density ultraviolet light. This method is similar to iCVD, a dry process that has been used to synthesize a variety of polymers as thin films. No solvent or plasma is used, the polymerization occurs near room temperature (20-40 °C), and the hydrogel can be synthesized on virtually any surface. The films synthesized in this work are crosslinked during the deposition, and the crosslink density allows for the passage of water and small molecule analytes while preventing the transport of macromolecules such as proteins. The films are stable in aqueous media and more resistant to non-specific protein adhesion than bare silicon. Additionally, the piCVD synthesis is gentle enough to coat a delicate optode sensor without degrading its response to its target analyte, sodium. Because sensors for the detection of physiologically significant analytes are often fabricated in particulate form, we also demonstrate here that microparticles can be easily and conformally coated.
3.3 Experimental

3.3.1 Film synthesis. The 200 mm reactor used to deposit the thin films is a modification of a previously described vacuum chamber used for iCVD.\textsuperscript{29} The reactor was previously outfitted with an array of filaments which could be heated to initiate the polymerization. In this work, the filaments were not used; instead, a low-power ultraviolet lamp (Model UVG-54, UVP) was mounted 9.0 cm above the reactor. The lamp emits ultraviolet light at 254 nm wavelength. A quartz viewport allowed the light to enter the chamber. The viewport was 2.5 cm thick, and the substrate stage was located 3.3 cm into the reactor. Thus, the total distance from the substrate to light source was 14.8 cm. The light intensity at this distance was measured as 50 $\mu$W/cm\textsuperscript{2}. A laser interferometer allowed for real time tracking of the deposited film thickness and termination of growth at the desired film thickness.

HEMA monomer (99+\%, Aldrich) was used as-received without any additional purification. The liquid monomer was vaporized in a stainless-steel jar and its vapor was metered into the reactor through a mass-flow controller (Model 1152, MKS). No separate photoinitiator was used. The chamber pressure was maintained by a throttling butterfly valve (Model 653B, MKS) and the substrate temperature ($T_S$) was controlled via backside contact of the deposition stage with temperature-controlled water lines. Two experimental series were conducted for this study: one investigating the effect of mean free path of the vapor (experimental series A) and the other investigating the effect of substrate temperature (experimental series B). The experimental conditions are summarized in Table 3-1. All films in experimental series A and B were approximately 200 nm thick and deposited on flat silicon wafers. Deposition rates varied between 1 - 40 nm/min depending on the synthesis conditions.
<table>
<thead>
<tr>
<th>Experimental Condition</th>
<th>( T_s (^\circ C) )</th>
<th>Pressure (mtorr)</th>
<th>HEMA Flowrate (std cm³/min)</th>
<th>( \frac{P_m}{P_m^{\text{sat}}} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>A1</td>
<td>30</td>
<td>100</td>
<td>2.5</td>
<td>0.42</td>
</tr>
<tr>
<td>A2</td>
<td>30</td>
<td>100</td>
<td>2.0</td>
<td>0.42</td>
</tr>
<tr>
<td>A3</td>
<td>30</td>
<td>100</td>
<td>1.5</td>
<td>0.42</td>
</tr>
<tr>
<td>A4</td>
<td>30</td>
<td>100</td>
<td>1.0</td>
<td>0.42</td>
</tr>
<tr>
<td>B1</td>
<td>20</td>
<td>100</td>
<td>2.0</td>
<td>0.94</td>
</tr>
<tr>
<td>B2</td>
<td>25</td>
<td>100</td>
<td>2.0</td>
<td>0.63</td>
</tr>
<tr>
<td>B3</td>
<td>30</td>
<td>100</td>
<td>2.0</td>
<td>0.42</td>
</tr>
<tr>
<td>B4</td>
<td>40</td>
<td>100</td>
<td>2.0</td>
<td>0.20</td>
</tr>
</tbody>
</table>

\( \frac{P_m}{P_m^{\text{sat}}} \) is the partial pressure of the monomer divided by its saturation pressure evaluated at the stage temperature.

Table 3-1. Experimental details of the samples prepared for this study.

Additionally, experimental condition B2 was also used to deposit films on large silica microspheres of diameter 50-100 \( \mu \text{m} \) (Polysciences) and small, monodisperse spheres of nominal diameter 5.0 \( \mu \text{m} \) (Bangslab). The large microspheres were placed in a petri dish in the vacuum chamber, manually agitated after every 100 nm of deposition to prevent particle agglomeration, and coated with approximately one micron of polymer. The small particles were diluted in tetrahydrofuran, dispersed onto a silicon wafer, dried overnight, and then placed in the reactor for deposition. Experimental condition B2 was also used to deposit 100 nm of film onto an flat optode sensor, whose preparation has been described elsewhere.\text{superscript}30 The
as-prepared optode was coated without further modification. The responses of the coated and uncoated optodes were characterized via fluorometry as described previously.\textsuperscript{30, 31}

3.3.2 Chemical characterization. The chemical structure of the piCVD film was determined by Fourier Transform Infrared (FTIR) Spectroscopy (Nicolet Nexus 870ESP). The piCVD films were analyzed as-deposited on the silicon wafers. To compare piCVD-synthesized pHEMA with conventional solution-synthesized pHEMA, a pHEMA standard (Aldrich) was spun-cast onto a silicon wafer from a 1.0 wt\% tetrahydrofuran solution. Spectra were gathered in transmission mode using a liquid N\textsubscript{2} cooled MCT detector at 4 cm\textsuperscript{-1} resolution averaged over 64 scans.

3.3.3 Swelling characterization. The film swelling capacity was determined via spectroscopic ellipsometeric (M-2000, J.A. Woollam) measurements of thickness. The wafer was cut into 2.5 cm x 8 cm strips prior to measuring thickness. Dry film thicknesses were determined by spectroscopic ellipsometry at an incident angle of 75°. The data were fit to a Cauchy-Urbach isotropic model (WVASE 32, J.A. Woollam).

The films were then mounted in a liquid cell (J.A. Woollam) and the cell was injected with pH 7.4 phosphate buffer solution (Cellgro, Mediatech). Ellipsometric data were then collected 1, 3, 5, 10, and 30 minutes following injection of the buffer solution and fit to a Cauchy-Urbach isotropic model with an ambient water layer in order to determine the swollen thickness. In all cases, the film reached its equilibrium film thickness (within 1 nm) after 5 minutes. The water content of the swollen film was determined by dividing the increase in film thickness by the total thickness of the swollen film. This method of determining equilibrium swollen water content has been previously shown to closely match the more complex effective medium approximation,\textsuperscript{32} where the swollen polymer is modeled as a composite layer of dry polymer
and water. To test the stability of the polymer films and reversibility of the swelling response, the films were rinsed in deionized water, dried in a vacuum oven overnight, and the dry and swollen thicknesses were obtained again.

3.3.4 Interaction with proteins. X-ray photoelectron spectroscopy (XPS) was used to quantify the degree of non-specific protein adhesion on the p(HEMA) films. A 1 wt% protein solution was prepared by dissolving 200 mg of bovine serum albumin (BSA, Fraction V, Sigma Aldrich) in 19.8 mL phosphate buffer solution. Three pieces of sample B2 and three pieces of a bare silicon wafer were incubated in the protein solution for three hours at 37 °C. Samples were then rinsed with approximately 5 mL buffer solution to remove any non-bound protein and dried gently under nitrogen. The surface nitrogen content of each sample was then quantified by XPS (Kratos AXIS Ultra) survey scans.

3.3.5 Particle characterization. After coating with pHEMA, the large microspheres were freeze-fractured and the particle cross-section was imaged via scanning electron microscopy (SEM, JEOL-5910). For the small microspheres, both uncoated and coated particles were imaged (JEOL-6320FV) and their diameters measured via built-in image processing in the SEM software (JEOL Orion).

3.4 Results and Discussion

3.4.1 Deposition mechanism and chemical structure. In iCVD, a thermally labile initiator flows into the reactor along with a vinyl monomer. It is thought that iCVD proceeds by the reaction of vapor phase radicals, generated at hot filaments above the substrate, with surface adsorbed monomer.\(^3\) In the piCVD process described here, HEMA is the only species
introduced into the reactor; therefore, the polymerization must be initiated by the UV irradiation of HEMA monomer. Indeed, at UV wavelengths below 267 nm, carbonyl species are known to decompose into radicals,\textsuperscript{34} which in turn can initiate a free-radical polymerization.

Further research, beyond the scope of this current report, is required in order to determine whether this decomposition occurs in the vapor phase, at the surface, or in both locations because the ultraviolet light both passes through the vapor and is incident on the substrate. Surface radicals can react with the vinyl monomers present at the surface to create polymer. Vapor phase radicals can either adsorb to the surface and subsequently react with adsorbed monomers, or directly strike adsorbed monomers and react by an Eley-Rideal mechanism\textsuperscript{35} to form a growing polymer chain. These three potential initiation events are shown schematically in Figure 3-1. Because the polymer growth at the surface can be measured by laser interferometry, the thickness of the film can be precisely controlled.

![Figure 3-1: Proposed picVD reaction mechanism. Ultraviolet light decomposes HEMA monomer into radical species either at the substrate or in the vapor phase. These radicals initiate polymerization by reacting with surface adsorbed monomer.](image)

\footnotesize{\textsuperscript{34} H = HEMA, R$^\text{'}$ = Radical}
Despite the fact that the monomer itself decomposes into radical species, the piCVD polymer film retains the vast majority of the pendant hydroxyl and carbonyl groups present in the monomer. Figure 3-2 compares a typical FTIR spectrum of piCVD pHEMA to a polymer standard. The absence of peaks due to unsaturated carbon at 1640-1660 cm\(^{-1}\) or 3000-3100 cm\(^{-1}\) indicates that the monomer has polymerized through its vinyl moiety to form a polymer. Both the piCVD and standard polymer exhibit a broad peak at 3200-3600 cm\(^{-1}\), corresponding to the hydroxyl group, and a sharp peak at 1725-1730 cm\(^{-1}\), corresponding to carbonyl stretching. The spectra therefore demonstrate that the piCVD of HEMA monomer proceeds through a free-radical mechanism while retaining the side-group functionality.

3.4.2 Swelling properties and film structure. To function as a protective overlayer for biosensor, a thin film must allow for the passage of small analytes from the medium to the

Figure 3-2. FTIR spectra of (a) pHEMA standard and (b) piCVD-synthesized pHEMA. Note the close agreement between the standard and the piCVD polymer, indicating polymerization through the vinyl bond of the monomer and full retention of the hydroxyethyl side chain.
sensor. It is therefore critical that the film swell when in contact with a biological medium while remaining adhered to the sensor substrate. All the films synthesized in this study exhibited a rapid, reversible swelling response while maintaining adhesion to the substrate. As characterized by in situ spectroscopic ellipsometry, the films reached their equilibrium swollen water content within 5 min of submersion in pH 7.4 buffer solution. Upon rinsing in deionized water and drying under vacuum, the films returned to their original thickness. When submerged again, the films rapidly returned to their swollen state. Figure 3-3 shows a typical response to several of these swell/dry cycles. Despite the fact that the piCVD films are simply physisorbed to the silicon substrate and not covalently bound, the original thickness is recovered after each swell/dry cycle. This suggests that that polymer does not leach out of the film when submerged in buffer solution, an important property for any material with potential for biological or physiological use. It also indicates that the crosslinking within the film is not due exclusively to physical entanglements; purely physical crosslinking would result in the loss of film in the swelling and washing steps.

In order to control the swellability of these films, it is important to understand whether the polymerization is initiated in the vapor phase or on the substrate surface. Figure 4a shows the swellability as a function of vapor residence time in the reactor (experimental series A). The residence time was determined by dividing the chamber volume (5467 mL) by the vapor flowrate. Changing the residence time alters UV exposure time for gaseous monomer molecules as they pass through the reactor. The relative independence of film swellability on irradiation time suggests that the polymerization is not a vapor phase process and that irradiation chemistry at the surface is the dominant initiation mechanism for film deposition.
To test this hypothesis, the surface concentration of monomer was systematically varied while holding residence time fixed (experimental series B). This was accomplished by varying the ratio of the partial pressure of the monomer to its saturation pressure at the stage temperature, $P_{M}/P_{M}^{sat}$. This ratio will be referred to as the fractional saturation of the monomer and has previously been shown to control the concentration of monomer at the substrate. The saturation pressure is evaluated using the Clapeyron equation. Figure 4b displays a strong dependence of swellability on $P_{M}/P_{M}^{sat}$, consistent with a polymerization mechanism which is primarily a surface process. Changing $P_{M}/P_{M}^{sat}$, and therefore the surface concentration of monomer during synthesis, allows for the control of the swelling properties.

The moderate degree of swelling and the reversibility of the swelling response suggest that the films are highly crosslinked. The origin of the crosslinking is unclear since no separate crosslinker was introduced into the reactor. However, if the pendant carbonyl group can be decomposed into radicals under UV irradiation as suggested earlier, then each pendant group

![Graph showing reversible swelling response of piCVD pHEMA](image)

*Figure 3-3. Typical reversible swelling response of piCVD pHEMA in buffer solution for multiple swell/dry cycles. All thicknesses are normalized to the as-deposited thickness of 190 nm.*
on the polymer chain can potentially act as a crosslinker. Furthermore, HEMA monomer may undergo transesterification or etherification to produce dimethacrylates, which are commonly used as crosslinking agents.\textsuperscript{38, 39} Finally, physical crosslinking via chain entanglement is also a possibility, although purely physical crosslinking is unlikely given the stability of the film over several swell/dry cycles.

Understanding the degree of crosslinking, regardless of the nature of the crosslinks themselves, is critical to understanding how these films can potentially be used as a protective overlayer for sensors in a biological environment. Non-specific protein adhesion can potentially damage the device, so the film must be crosslinked enough to prevent transport of proteins from the medium to the device surface. At the same time, the analyte must be able to permeate the film.
The crosslinking is intimately related to the swollen water content of the film; for highly
crosslinked networks, the swollen water content and the average molecular weight between
crosslinks satisfy the following equation:

\[
\frac{1}{\bar{M}_c} = \frac{2}{\bar{M}_h} \cdot \frac{\bar{v}}{V_1} \left[ \ln \left( 1 + \frac{V_2}{V_1} + \chi \left( \frac{V_2}{V_1} \right)^2 \right) \right] \left[ 1 - \frac{M_r}{2\bar{M}_c} \left( \frac{V_2}{V_1} \right)^{2/3} \right]^{\gamma-3} \]

where \( \bar{M}_c \) is the average molecular weight between crosslinks, \( \bar{v} \) is the specific volume of
pHEMA (0.87 cm\(^3\)/g), \( V_1 \) is the molar volume of water (18 cm\(^3\)/mol), \( M_r \) is the molecular weight
of the HEMA repeat unit (130 g/mol), \( V_{2,s} \) is the ratio of the thickness of the dry polymer to the
thickness of the swollen polymer (measured via ellipsometry), and \( \chi \) is the Flory-Huggins
interaction parameter (varies with water content\(^{41} \)).

![Graph](image)

Figure 3-5. Average mesh size of swollen films as calculated by Eqn 3-1. The error bars indicate the uncertainty resulting from propagating the error of the corresponding swollen water content measurement in Figure 3b. For data points where error bars cannot be seen, the error is smaller than the size of the data marker.
This theory is developed for linear polymer chains of number-average molecular weight $\bar{M}_n$ that undergo crosslinking by the introduction of a crosslinking agent. Measuring $\bar{M}_n$ for the piCVD films is difficult because the crosslinking occurs in situ and without a separate chemical species. Here, $\bar{M}_n$ is assumed to be large enough that the term in which it appears can be neglected. This is a common assumption and one that provides an upper bound on $\bar{M}_c$. The molecular weight between crosslinks can in turn be used to compute the average mesh size in the swollen film.\textsuperscript{23,42} It should be noted that the crosslink density as calculated by (1) is an effective value that does not distinguish between physical entanglements and chemical crosslinking. The most likely source of uncertainty in this calculation is in the measurement of the swollen water content and therefore $v_{2,1}$. Figure 3-5 shows the average mesh size for films B1-B4 as computed by (3-1), including the propagated uncertainty in $v_{2,1}$. Each of these mesh sizes is larger than the hydrodynamic radii of physiologically relevant analytes. For example, sugars such as glucose and sucrose and metal cations such as $\text{Na}^+$ and $\text{Mg}^{2+}$ all have hydrodynamic radii of less than 0.5 nm\textsuperscript{43-45} and should easily permeate the mesh. However, these mesh sizes are too small to allow for the permeation of large biomolecules such as proteins. For example, albumin is a $3.8 \text{ nm} \times 15.0 \text{ nm}$ ellipsoid molecule and fibrinogen is a $9 \text{ nm} \times 45 \text{ nm}$ ellipsoid.\textsuperscript{46} An example of sodium ions successfully penetrating the mesh will be discussed later.

3.4.3 Protein adhesion. While the films are capable of protecting device surfaces from contact with proteins, the films themselves should also resist non-specific protein adhesion. XPS characterization of the piCVD films following incubation in a protein solution (BSA, 1 wt%)
provided a convenient proxy for measuring the degree of protein adhesion. As the p(HEMA) film does not contain any nitrogen, any nitrogen detected by the highly surface-sensitive XPS must be due to surface-bound proteins. Figure 3-6 compares the nitrogen content of a p(HEMA) surface incubated in a solution of bovine serum albumin (BSA) with a control silicon surface. The p(HEMA) film exhibits an eight-fold decrease in surface nitrogen signal over bare silicon, corresponding to a reduction of surface-bound proteins.

3.4.4 Sensor and particle coating. To demonstrate the gentle nature of the piCVD process, a sodium-sensing optode was coated with 100 nm of pHEMA. The optode is a chromoionophore and ionophore in a polymer matrix cast as a film (<10 μm thickness) on a 1 cm diameter glass coverslip. The responses of both an uncoated optode and a coated optode to varying levels of sodium ion concentration are shown in Figure 3-7a and 3-7b, respectively. It is evident that the piCVD process does not damage the optode functionality.

![Surface nitrogen content after incubation in a 1 wt% protein solution for three hours at 37°C. Because the as-prepared surfaces contain no nitrogen, any nitrogen signal after incubation must be due to the presence of adsorbed protein.](image)

Figure 3-6. Surface nitrogen content after incubation in a 1 wt% protein solution for three hours at 37°C. Because the as-prepared surfaces contain no nitrogen, any nitrogen signal after incubation must be due to the presence of adsorbed protein.
Figure 3-7. Response curves of (a) uncoated optode and (b) optode coated with 100 nm piCVD pHEMA. The intensity is the fluorescence emission ratio of 570 nm/670 nm, exciting at 485 nm. The curves show the response of the optodes when submerged in pH 7.4 buffers containing I - 0 Na⁺, II - 140 mM Na⁺, III - 340 mM Na⁺, and IV - 140 mM Na⁺.

The coated optode also shows little or no degradation in response time when compared to the uncoated optode. The response of the device is governed by the diffusion of sodium ion through optode matrix, which is several microns thick. The nanoscale thickness of the overlaying pHEMA film does not add significantly to the distance that the ion must diffuse. Additionally, the fact that the sodium ion diffuses through the film is consistent with the calculated mesh size. Small molecule analytes, such as ions, have no difficulty diffusing through a film with a mesh size on the order of several nanometers.

Because piCVD is a dry process, the geometries that can be coated with pHEMA are not limited to planar surfaces. Indeed, many sensors of physiologically relevant analytes are being miniaturized as microparticles to take advantage of high surface areas and reductions in response time. As a dry process, piCVD can conformally coat microgeometries while
avoiding the effects of solvent tension, which tends to result in particle agglomeration. Figure 3-8 shows a cross section of a ~50 μm microsphere coated with approximately 1 μm of pHEMA. The coating is continuous and conformal around the outside of the particle. Figure 3-9 compares SEM images of uncoated and coated monodisperse microparticles. The uncoated microspheres have an average diameter of 5.06 ± 0.04 μm and the coated microspheres have an average diameter of 5.39 ± 0.04 μm, indicating that the particles were coated with approximately 165 nm of hydrogel.

3.5 Conclusions

We have demonstrated that piCVD is a gentle method for preparing stable, reversibly-swellable, hydrogel films with nanoscale mesh size. The deposition of thin films of p(HEMA) has
Figure 3-9. SEM images of a) uncoated silica microspheres and b) silica microspheres coated with piCVD pHEMA. Both images were obtained at 1600× magnification and the scale bars represent 10 μm.

been verified by FTIR spectroscopy. The homopolymer deposited in this work enhances the surface resistance to non-specific protein adhesion, as investigated by XPS. Future work may focus on the incorporation of comonomers that enhance biocompatibility. For example, it is thought that an amphiphilic surface can enhance the biocompatibility of blood-contacting surfaces, and HEMA copolymerized with 2-methoxyethylacrylate has been shown to reduce platelet adhesion. Moreover, active surfaces may be possible by the addition of a click-functional comonomer such as pentafluorophenylmethacrylate. An advantage of this process is the ease of forming copolymers, including copolymers of p(HEMA), and controlling film composition via the synthetic conditions. Future work will also focus on understanding the long-term stability of these films in physiological environments.

In piCVD, the polymerization occurs primarily on the substrate surface and the crosslink density, and therefore the swelling properties of the film, can be controlled by changing the fractional saturation of the monomer vapor during the deposition. The mesh size of the film,
based on swelling properties, is small enough to allow for small molecule analytes to the underlying substrate. This was confirmed by coating a sodium-sensing optode with a thin film of p(HEMA); the optode retained its ability to detect its target analyte. The mild nature of piCVD, which utilizes no plasma or solvent, make it ideal for coating the surfaces of optodes and other sensors designed for implantation. Particles as small as 5 μm can be coated as well, suggesting that piCVD has potential utility in the coating of particle sensors.

3.6 Acknowledgements

The authors thank the National Defense Science and Engineering Graduate Fellowship, Draper Laboratories UIRaD, and the Generalitat de Catalunya Research Consolidated Group grant (SGR.2005) for financial support.

3.7 References
Chapter 4

Thin Hydrogel Films withNanoconfined Surface Reactivity by Photoinitiated Chemical Vapor Deposition

Originally published as L.M. Montero, S.H. Baxamusa, S. Borros, K.K. Gleason, Chemistry of Materials 2009, 21, 399-403
4.1 Abstract

Several property requirements have led to the modification of hydrogels by incorporating functional groups. The current work seeks to achieve graded functional group incorporation into hydrogel thin films using the one-step technique of photoinitiated CVD (piCVD). The functional group pentafluorophenylmethacrylate (PFM) is copolymerized with hydroxyethyl methacrylate (HEMA). Because PFM reacts easily with amine groups, the incorporation of PFM results in a platform for subsequent functionalization. The graded copolymer confines the PFM to the near surface region (~20 nm) allowing the control of the hydrogel film properties independently of the surface reactivity. While homogeneous incorporation of PFM in the hydrogel matrix inhibits swelling, the swollen water content of pure pHEMA is nearly preserved in the graded copolymer. FTIR spectroscopy shows that the absorption peaks corresponding to the fluorinated phenyl ring in the graded copolymer disappear after functionalization with O,O-bis (2-aminoethyl) polyethylene (PEG-diamine), suggesting a nearly complete conversion of the PFM bonds.
4.2 Introduction

Hydrogels are polymer networks that have the capability of absorbing large amounts of water without dissolving.\textsuperscript{1, 2} Some hydrogels are able to achieve similar water content to human tissue and exhibit excellent biocompatibility, and as a result, have gained strong acceptance in bioengineering.\textsuperscript{3, 4} Hydrogels have been modified by many available chemistries and techniques to incorporate functional groups.\textsuperscript{5-11} Kawaguchi et al. investigated active esters in quaterpolymer microspheres that were allowed to undergo hydrolysis or aminolysis.\textsuperscript{12} Functionalized dextrans were studied by Maire and co-workers for bearing coboxylate, benzylamide and sulfate groups, which exhibit binding capacity.\textsuperscript{13} Such functionalized hydrogels have been used for varied applications such as targeted cell adhesion,\textsuperscript{14-16} selective functional protein binding,\textsuperscript{11, 17, 18} and drug delivery carriers.\textsuperscript{5}

Because of the limited ability of large molecules such as proteins or other biologically-relevant ligands to diffuse into polymers, functional groups at the surface react most readily. Unreacted functional groups within a hydrogel matrix are problematic because they can negatively impact bulk properties and generate undesired reactions, particularly over long time scales.\textsuperscript{19} Thus, some groups have centered their attention on changing only the near-surface properties of hydrogel films. Burnham et al. presented a method for creating a surface-patterned streptavidin-conjugated polyacrylamide hydrogel that can be used to generate biofunctionalized templates.\textsuperscript{20} The penetration depth of the streptavidin was 4 μm, which was
approximately one quarter of the thickness of the film, and fewer than 2% of the binding sites were successfully utilized. Zhu et. al. grafted carboxyl groups onto polycaprolactone membranes surface under UV light to create surfaces functionalizable via carbodiimidization chemistry.\textsuperscript{21} Hu and co-workers presented a procedure to covalently link polymers to the surface of poly(dimethylsiloxane) by ultraviolet graft polymerization.\textsuperscript{22} Each of these processes requires two steps: one to create the bulk material and a second to introduce the desired functionality onto the surface.

The current work seeks to achieve both homogenous and graded functional group incorporation into hydrogel thin films using the one-step technique of photoinitiated CVD (piCVD). Previously, piCVD was demonstrated as a means of systematically controlling the crosslink density of hydrogels deposited from hydroxyethylmethacrylate (HEMA) and the resultant the degree of swelling.\textsuperscript{23} Here, the functional comonomer pentafluorophenylmethacrylate (PFM) is copolymerized with HEMA. The solubility contrast of the hydrophilic HEMA monomer and the hydrophobic PFM monomer makes this copolymer difficult to achieve via solution phase techniques. Previous work demonstrated that the PFM group can be successful incorporated into films by plasma enhanced CVD\textsuperscript{24} and initiated CVD.\textsuperscript{25} Because the ester group of PFM reacts easily with amine groups,\textsuperscript{17} the incorporation of PFM results in a platform for subsequent functionalization with a multitude of amine containing compounds.

While pentafluorophenylesters have been widely used to create functional surfaces, the piCVD technique is, to our knowledge, the first one-step process to create surface functional groups without requiring any modification of the substrate surface. Chilkoti and coworkers
reported MAPS, a multi-step solvent-based procedure to modify polymer surfaces with functional pentafluorophenyl esters at the surface.\textsuperscript{26, 27} However, this process requires the underlying polymer layer to undergo an overnight carboxylation step involving a number of corrosive or toxic reagents. Such reagents may not be compatible with biologically-relevant substrates, such as sensors or tissue scaffolds, or may be of potential concern for materials destined for physiological implantation.

Polymer CVD techniques are compatible with any substrate not affected by reduced pressure, and can coat fragile substrates such as sensors\textsuperscript{23} and complex geometries such as particles\textsuperscript{23, 28} or trenches.\textsuperscript{29} Paracyclophanes functionalized with pentafluorophenyl esters have been deposited previously by CVD.\textsuperscript{30, 31} However, the nanoconfinement of these functional groups to the near-surface area via a graded copolymerization has not yet been demonstrated.

Because piCVD is a vapor phase process involving the continuous flow of reactant gases, the introduction and distribution of functional groups can be controlled simply by varying the composition of the incoming feed gas. As the growth rate of films is monitored in situ by interferometry, we are also able to demonstrate nanoscale control over the incorporation of the functional groups throughout the depth of the film.

Hydrogels with homogeneous incorporation of functional groups, here termed homogeneous copolymers, are synthesized by maintaining constant flow rates of both HEMA and PFM throughout the course of the deposition. The strategy for achieving graded layers in which PFM is confined to the near surface region (\textasciitilde20 nm) is to flow the PFM monomer into the CVD reactor only during the final period of growth. The continuity in growth with the first pure HEMA layer creates a gradient in functional group incorporation without the need for physically
stacking chemically dissimilar layers. Because the pure HEMA layer does not need to be chemically modified in order to incorporate the functional groups, no lengthy carboxylation step is required, and the total deposition time for the entire structure is approximately 15 minutes.

We directly compare the homogeneous copolymer, the graded copolymer, and the pure HEMA films, providing insight into the importance of functional group distribution on reactivity and properties. Graded functional layers via piCVD offer several potential benefits. First is the ability to independently control bulk film properties, like swellability and modulus, and surface reactivity. Here, we show that the swellability of a hydrogel can be maintained by incorporating the functional comonomer only within the near-surface region. Second is the elimination of functional groups in the bulk of the film which have limited ability to react yet can degrade bulk film properties. In this study, the reactivity of the both the homogeneous and the graded films with PEG-diamine is monitored by Fourier Transform infrared (FTIR) spectroscopy. Finally, the graded films enable reduced usage of the expensive functional monomer.

Figure 4-1: Schematic of the chemical composition (left) and physical structure of the homogeneous (top right) and graded (bottom right) copolymer films.
4.3 Experimental

4.3.1 Hydrogel Preparation. The piCVD process and reactor have been described in detail previously. All samples were deposited on silicon wafers (Waferworld) maintained at 30 °C through backside coolant circulation. PFM (95%, Monomer Polymer) and HEMA (99%+, Sigma Aldrich) monomers were utilized without further purification. HEMA was heated to 80 °C in a temperature-controlled crucible and its vapors were metered into the reactor through a mass flow controller (MKS, 1152). The flow rate of PFM, which was heated to 60 °C in a separate crucible, was also metered with a mass flow controller. No separate photoinitiator was used. A throttling butterfly valve (MKS, 653B) was used to control the pressure inside the chamber. The film growth was initiated by exposing the substrate to 50 μW/cm² ultraviolet light of 254 nm wavelength. Film growth was observed in situ through interferometry and used to obtain the desired film thickness.

Two types of films were deposited in this work: homogeneous copolymers and graded copolymers. For the homogeneous copolymers, both monomers, HEMA and PFM, were introduced into the reactor simultaneously during the polymerization. The HEMA flow rate was held constant for all the homogeneous copolymer depositions, while the PFM flow rate was systematically varied between samples. The reactor pressure was varied for each deposition to maintain the HEMA partial pressure at 100 mTorr. Film growth was terminated at approximately 115 nm. For the graded copolymer, HEMA was initially introduced into the reactor and the polymerization proceeded until approximately 90 nm of film was deposited. Then, PFM was introduced into the feed gas while remaining constant the HEMA flow and the copolymer was deposited for an additional 25 nm of film deposition. The flow rates and
pressures for both the homogeneous and graded copolymers are summarized in Table 4-1. It should be noted that while the copolymer composition is controlled by changing the feed gas composition, these values are not equal. This is because piCVD is a surface reaction, and the monomers will be present on the substrate as adsorbed species as a function of their individual volatilities. In this paper, we report the composition of the feed gas unless otherwise noted.

<table>
<thead>
<tr>
<th>Samples</th>
<th>HEMA flowrate (sccm)</th>
<th>PFM flowrate (sccm)</th>
<th>$P_{total}$ (mTorr)</th>
<th>Molar composition (% PFM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>H0 and G0</td>
<td>2.0</td>
<td>0.0</td>
<td>100</td>
<td>0%</td>
</tr>
<tr>
<td>H1 and G1</td>
<td>2.0</td>
<td>1.0</td>
<td>150</td>
<td>33%</td>
</tr>
<tr>
<td>H2 and G2</td>
<td>2.0</td>
<td>3.0</td>
<td>250</td>
<td>60%</td>
</tr>
<tr>
<td>H3 and G3</td>
<td>2.0</td>
<td>5.0</td>
<td>350</td>
<td>71%</td>
</tr>
</tbody>
</table>

For the homogeneous films (series H) all the indicated flowrates were used throughout the deposition. For the graded films (series G), no PFM is used at the start of the deposition.

Table 4-1: Experimental conditions for the copolymer synthesis.

4.3.2 Film Characterization. FTIR spectroscopy was carried out on a Nicolet Nexus 870 in normal transmission mode equipped with a MCT detector and KBr beamsplitter. Spectra were acquired over the range of 400 to 4000 cm\(^{-1}\) with a 4 cm\(^{-1}\) resolution for 256 scans. To allow for accurate comparison, all spectra were thickness normalized and baseline corrected; no other processing was performed.

The TOF-SIMS analysis reported here were performed on a ToF-SIMS type ION-TOF IV instrument, equipped with Bi polyatomic primary ion source, a Cs/electron impact dual source column (DSC), and a low-energy electron flood gun (for charge compensation of insulating
samples). The incidence angle of both the Bi and Cs ion sources was 45°. Sputter etching of the surface was accomplished with a beam of 500eV Cs+ ions (with a target current of 30 nA) rastered over a 400 mm x 400 mm area. A pulsed beam of 25 keV Bi3++ ions, scanned over a 100 mm x 100 mm region centered within the sputtered area, was used to generate secondary ions for analysis in negative ion mode. A high current beam of low energy (<20 eV) electrons was employed for charge compensation. Mass resolution (m/Dm) was higher than 5000 and full spectra from 1 to 800 amu were acquired for all depths profiles. The signals are plotted once they are completely stabilized; the initial period is due to a transient effect until a sputtering steady state is reached. The surface oxidation also contributes to this effect modifying the ionization at the first film nm.

Dry and swollen film thicknesses were measured via spectroscopic ellipsometry (M-2000, J.A. Woollam). All data were collected at a 75° incident angle for 220 wavelengths between 313 nm and 718 nm and fit to a Cauchy-Urbach isotropic model to obtain the thickness. First, the dry film thickness was determined. Then, the samples were then mounted in a liquid cell and immersed in pH 7.4 buffer. Data were collected 1, 3, 5, 7, and 10 minutes; for all films, the equilibrium swollen thickness was reached after 5 minutes. The swollen water content was determined by dividing the increase in film thickness by the total thickness of the swollen film. The procedure was repeated to test the stability of the polymer films and reversibility of the swelling response. The measurements were obtained again after having rinsed the films in deionized water and dried them overnight in a vacuum oven.

4.3.3 Sample Modification. Functionalization of the samples was performed with a 0.05 M solution of O,O-bis (2-aminoethyl) polyethyleneglycol (PEG-diamine) (Sigma Aldrich) in ethanol
(100%, VWR). The hydrogels were immersed in the solution and maintained at 30°C for 1h. The sample then was rinsed with ethanol to remove any unreacted ligand and dried with room temperature nitrogen and analyzed by FTIR.

4.4 Results and Discussions

4.4.1 FTIR Characterization. Figure 4-2 compares the FTIR spectra of three homogeneous copolymers of varying compositions to three graded copolymers of the same near-surface composition. A pHEMA film synthesized with piCVD is shown for reference. The labeled mole percentages of HEMA and PFM represent the gas phase composition. In most cases, the film composition will be different, reflecting the differences in the volatility of the two monomers and their reactivity ratios. The spectrum of the pure HEMA contains three main vibrational

![Figure 4-2: FTIR spectra of three copolymer compositions for a) homogeneous copolymers and b) graded copolymers, along with the spectra for pure pHEMA. The composition refers to gas phase molar composition during piCVD synthesis.](image)
modes. The most intense of these peaks is centered at \(1725\ \text{cm}^{-1}\) and signifies the C=O stretching. The C-H bending appears in its normal range of 1500-1350 cm\(^{-1}\). The peak centered at \(1260\ \text{cm}^{-1}\) signifies the stretching vibrational mode of C-O. The presence of PFM is indicated by three main absorption bands. The narrow, weak peak that appears at \(1774\ \text{cm}^{-1}\) can be associated with the retention of the carbonyl group from the active ester. The fluorinated phenyl ring is expressed at \(1522\ \text{cm}^{-1}\) as a sharp peak with a high intensity. The C-F vibrations are also present at \(1000\ \text{cm}^{-1}\). The PFM peaks in the FTIR spectra for the homogeneous copolymer are clearly expressed for all the ratios. There is a lower signal from the PFM peaks in the graded copolymer than in the homogeneous copolymer because it is only present near the surface of the film, as opposed to the homogeneous copolymer that has PFM incorporated throughout the hydrogel matrix.

### 4.4.2 Depth Profiles

Depth profiles of positive ion ToF-SIMS spectra confirmed the film structure of the homogeneous and graded copolymers. Figure 4-3 shows the intensity at m/z = 253.1 as a function of film depth for both the homogeneous and graded copolymer (samples H3 and G3, respectively).

![Figure 4-3: ToF-SIMS depth profile showing signal from m/z = 253.1, corresponding to a positively charged PFM fragment, as a function of film depth for both the homogeneous and graded copolymer (samples H3 and G3, respectively).](image-url)
253.1, which corresponds to the charged PFM monomer fragment,\textsuperscript{35} as a function of film depth for both the homogeneous and graded copolymers. The copolymer shows a relatively constant PFM content throughout the film depth. The graded copolymer shows PFM present in the first 20 nm of film, confirming that the functionality in the graded copolymer is nanoconfined to the near surface region. This is consistent with the fact that PFM was introduced only in the final stages of the deposition. The surface PFM content (at zero depth) is comparable to that in the homogeneous copolymer, indicating that both have a similar density of functional groups at the surface. However, the functionality in the graded copolymer is nanoconfined to the near-surface region. Positive ion ToF-SIMS spectra confirming retention of the PFM structure are shown as Figure 4-4.

4.4.3 Degree of Swelling and Water Content. The ability to swell defines the nature and function of a hydrogel. Consequently, retaining its swelling properties while incorporating surface-active components is extremely important. Figure 4-5 displays the swollen water

![Figure 4-4: ToF-SIMS spectra of the homogeneous and graded copolymers. Characteristic peaks of the PFM comonomer are highlighted by the accompanying ionic structures.](image)
content for the homogeneous and graded copolymers for different degrees of PFM incorporation. It can be seen that with an increasing PFM content, the swollen water content decreases from 20% (pure pHEMA) to 3% (71% PFM). The homogeneous copolymer does not retain the swelling properties of the HEMA due to the hydrophobicity of PFM. However, for the graded copolymers, the swollen water content of pure pHEMA is mainly preserved even with increasing PFM content. These results suggest that physical swelling properties of a hydrogel can largely be maintained even after incorporating an ultrathin copolymeric layer. This decouples the underlying physical properties of the hydrogel from the chemical properties of the surface activity, allowing these two properties to be chosen independently.

4.4.4 Hydrogel Functionalization. The pentafluorophenyl ester moiety functionalizing the polymer surface easily reacts with amine groups. During the reaction, the pentafluorophenyl group is replaced by an amide bond. This reactivity allows the functionalization of the hydrogel by any nucleophilic agent in a single-step reaction. Figure 4-6a shows the spectra of

![Swollen water content as a function of the increasing PFM content for both the homogeneous and graded copolymers.](image)
the homogeneous copolymer and Figure 4-6b shows the spectra of the graded copolymer before and after functionalization with PEG-diamine for one hour.

After functionalization, a peak is expected to appear at 1107 cm\(^{-1}\), a strong and a wide peak attributed to the C-O vibration of the PEG. In both the functionalized homogeneous and graded copolymers, PEG functionalization is confirmed by the presence of this peak in the FTIR spectra. There is far more PFM in the homogeneous copolymer so, as expected, there is far more PEG attached to the homogeneous copolymer. However, the absorption peaks corresponding to the fluorinated phenyl ring only disappear completely in the case of the graded copolymer. This suggests that the functionalized homogeneous copolymer contains a significant fraction of unreacted PFM that can be susceptible to undesired subsequent reactions with nucleophiles. Unlike the homogeneous copolymers, the graded copolymer provides a nearly complete conversion of the PFM bonds. This phenomenon can be explained due to the inability of the reactive amines to diffuse through the film. This could be especially important if the films are

![Figure 4-6: FTIR spectra of the copolymer synthesized by piCVD before and after the functionalization](image)

Figure 4-6: FTIR spectra of the copolymer synthesized by piCVD before and after the functionalization

84
functionalized with large macromolecules, such as proteins. From this perspective, it is desirable to nanoconfine the PFM on the surface as in the graded copolymers to ensure its complete reaction.

4.5 Conclusions

This work has demonstrated that both homogeneous and graded copolymers 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 with primary amines. The distribution of PFM within the film depth has also been confirmed. In the graded copolymer 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 to the near-surface region. Because the piCVD process involves real-time tracking of film thickness, the compositional distribution can, in principle, be chosen arbitrarily.

For the graded polymer, the PFM is introduced into the feed gas only during the final ~20 nm of film deposition, thereby confining the functionality only to the near-surface region. In addition to reducing quantity of expensive functionalized monomer, there are two primary materials property benefits to this near-surface confinement. First, the hydrogel properties of the bulk region of graded copolymers are largely maintained. This is especially important when compared to the homogenous copolymers, which exhibit markedly worse swelling properties than the graded copolymers. 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 copolymer are available for reaction. In the homogeneous copolymer, 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 comonomer capable of being introduced into the reactor as a vapor can be used to form the graded functional film. Moreover, because the film thickness is monitored by in situ interferometry, it is in principle possible to create a copolymeric layer of controlled thickness, a feature not afforded by traditional solution methods. Future work will focus on engineering the thickness of the copolymeric layer based on the size of the ligand used in subsequent functionalizations.

4.6 Acknowledgements

The authors thank the Generalitat de Catalunya for the Research Consolidated Group grant: SGR-2005 to Grup d’Enginyeria de Materials (GEMAT), the Draper Laboratoires UiRAD, and the National Defense Science and Engineering Graduate Fellowship for providing funds to support this research. The authors are grateful for the assistance of Dr Raúl Perez from the Nanotechnology Platform from the Parc Científic de Barcelona, Universitat de Barcelona for performing the ToF-SIMS experiments.

4.7 References


35 L. Francesch, Universitat Ramon Llull, 2008.
Chapter 5

Random Copolymer Films with Molecular Scale Compositional Heterogeneities that Interfere with Protein Adsorption

To be submitted for publication
5.1 Abstract

We present surfaces with compositional heterogeneities on smooth surfaces at a molecular length scale with the goal of disrupting surface-protein interactions. These surfaces are synthesized by utilizing photoinitiated chemical vapor deposition (piCVD) to deposit thin films of random copolymers consisting of highly hydrophilic and highly hydrophobic comonomers. Swellability, wettability, and surface roughness could be systematically controlled by tuning the copolymer composition. The surface composition was dynamic and the surface reconstructed based on the hydration state of the film. Proteins adsorbed to the copolymer films less readily than either of the respective homopolymers, indicating a synergistic effect resulting from the random copolymer presenting molecular-scale compositional heterogeneity. These results provide direct evidence that protein adsorption can be disrupted by such surfaces.
5.2 Introduction

There has been considerable research effort in materials that resist biofouling when placed in contact with biological or physiological fluids. Biofouling can be broadly described as any process in which biopolymers (such as proteins) or whole organisms (ranging from single-cell bacteria to tubeworms) attach to a surface. This is usually associated with degraded or impeded performance of an engineering system such as biomedical implants, water filtration membranes, or the hull of an ocean-going vessel.\textsuperscript{1-3}

It is thought that surfaces with compositional heterogeneities on the length scale of the foulant of interest may discourage thermodynamically favorable interactions between the foulant and the surface, which in turn would limit adsorption events. These heterogeneities are usually presented by amphiphilic films incorporating components with very different surface energies. For example, hyperbranched fluoropolymers (HBFP) crosslinked with polyethelyeneglycol (PEG) phase segregates when cast as a thin film; the HBFP-rich phase presents a low surface energy domain and the PEG-rich phase presents a high surface energy domain. This phase segregation could produce domains smaller than one micron and tended to reduce the irreversible adsorption of zoospores as compared to bare glass. However, protein adsorption increased with increasing HBFP content on the surface, suggesting that the length scale of the compositional heterogeneity was small enough to disrupt microorganisms but too large to sufficiently disrupt protein-surface interactions.\textsuperscript{4, 5} Comblike block copolymers with
grafted amphiphilic side chains and patterned hydrophilic/hydrophobic stripes on the microscale displayed resistance to the adsorption of zoospores and diatoms, but their protein resistance was not examined.6,7

Proteins are an important foulant class, since adsorbed proteins can subsequently recruit cells or microorganisms to the surface, so surfaces that resist protein adhesion can potentially block other foulants as well.8,9 Preparing surfaces with compositional heterogeneities designed to resist protein adsorption requires that the heterogeneities occur over very small length scales. While a typical protein has areal dimensions of 10-1000 nm², only a small portion of the protein initiates contact with a surface. By varying the interfacial pressure during protein adsorption experiments, Macritchie calculated this area to be between 1-2 nm² for a variety of proteins, independent of the size of the protein.10 Thus, it is believed that a set of residues form an “anchor” with which the protein initiates contact with the surface. Once the initial point of contact is made, the cooperative effects of proximity to the surface make additional points of contact more likely after the initial adsorption event occurs.11 Surfaces with molecular-scale compositional heterogeneities could potentially disrupt the initial adsorption event and therefore enhance resistance to protein adsorption.

This phenomenon was observed when curvature-driven phase-segregation of mixed self-assembled monolayers (SAMs) on metal nanoparticles was reported to produce domains as small as 0.5 nm. These particles showed excellent resistance to protein adsorption.12,13 On flat surfaces, however, it was found that phase segregation of mixed SAMs led to domains tens of nanometers across, which allowed proteins to adsorb preferentially on the hydrophobic
domains. For coating a generic substrate of an arbitrary geometry, polymer coatings are a promising alternative to SAMs.

To the best of our knowledge, polymer films with molecular level heterogeneities in surface composition and their interaction with proteins has not been previously reported. Such studies are difficult for two reasons. First, the preparation of such films requires the random copolymerization of hydrophilic and hydrophobic monomers. Monomer pairs of highly contrasting solubility typically lack a common solvent, making synthesis very difficult and limiting the achievable hydrophilic contrast between comonomers. Second, when such polymers can be synthesized, they are very difficult to cast as the smooth, thin films required both for application and for characterization of protein interaction. The copolymerization of hydrophilic acrylates and methacrylates with perfluorinated alkyl acrylates and methacrylates have been reported, but efforts to cast them as a thin film resulted in extremely rough and non-uniform surfaces.

In this work, we synthesized thin films with the goal of presenting smooth surfaces with compositional heterogeneities on the length scale of the individual monomer molecule. To deposit the films studied in this work, we utilized photoinitiated chemical vapor deposition (piCVD). piCVD is a solvent-free, single-step technique for the preparation of smooth, thin polymer films that are both conformal over nanoscale geometries and uniform over large areas (dozens of square centimeters). In piCVD, monomer vapors are metered into a vacuum chamber where they adsorb and, upon exposure to ultraviolet light, polymerize on a cooled substrate via a free-radical mechanism. We have previously reported the use of piCVD for the
No solvent is required, and the polymer is both synthesized and cast as a thin film in a single step.

We copolymerized the hydrophilic hydroxyethylmethacrylate (HEMA) with the hydrophobic perfluorodecylacrylate (PFA) to create a randomly amphiphilic thin polymer film. Surfaces of pure poly(HEMA) (PHEMA) and polyPFA (PPFA) have water contact angles of 17° and 130°, respectively, reflecting their very different surface energies. HEMA is hydrophilic due to its pendant hydroxyl, and PHEMA polymer is commonly used in applications where high water content is important, such as in contact lenses, wound dressings, and other physiological systems. In contrast, the fluorinated alkyl side chain of PFA is highly hydrophobic and has a lower surface energy than poly(tetrafluoroethylene) (PTFE, commonly known by its trade name Teflon).  

By adjusting the relative flowrates of the HEMA and PFA comonomers, films over a wide compositional range could be synthesized. The water contact angle, swellability, and surface roughness could be systematically controlled by varying the composition. X-ray photoelectron spectroscopy (XPS) and contact angle measurements demonstrate that the copolymer films are capable of undergoing significant surface reconstruction in their hydrated states. Quartz crystal microbalance experiments showed that copolymer films adsorbed less protein than either of the corresponding homopolymers films, supporting the hypothesis that molecular-level heterogeneities can interfere with protein adsorption. To the best of our knowledge, this is the...
first demonstration of protein adsorption resistance using randomly amphiphilic copolymer films synthesized and deposited as a film in a single step.

5.3 Experimental

*Film deposition.* The piCVD process and reactor have been described in detail previously. PFA (97%, Sigma Aldrich) and HEMA (99%+, Sigma Aldrich) monomers were utilized without further purification. HEMA and PFA were heated in separate crucibles to 80 °C and 85 °C, respectively. No separate photoinitiator was used. Vapors of each monomer were metered through mass flow controllers (MKS, 1152). Various copolymer compositions were obtained by adjusting the relative flowrates of the two monomers. Typical flowrates were between 0-3 sccm for HEMA and approximately 0-1 sccm for PFA.

The vapors met and mixed at a common manifold prior to entering the reactor. A throttling butterfly valve (MKS, 653B) was used to control the pressure inside the chamber at 100 mtorr. Film growth was initiated by exposing the substrate to single-wavelength (254 nm) ultraviolet light of 50 μW cm⁻² (UVP, UVG-54). The film was deposited on a silicon wafer (Waferworld) maintained at 35 °C by backside contact with a temperature-controlled stage. Film growth was monitored *in situ* through interferometry and growth was terminated at approximately 100 nm. Typical film growth rate was approximately 10 nm min⁻¹.

Pure PPFA homopolymers for control experiments were deposited using a previously described method.
Film characterization. FTIR spectroscopy was carried out on a Nicolet Nexus 870 in normal transmission mode equipped with a MCT detector and KBr beamsplitter. Spectra were acquired over the range of 400 to 4000 cm\(^{-1}\) with a 4 cm\(^{-1}\) resolution for 256 scans. The data were baseline corrected and each spectrum was normalized based on the intensity of the carbonyl absorption.

The swelling characteristics of the films were measured via dynamic spectroscopic ellipsometry (M-2000, J.A. Woollam). Spectra of the dry films were obtained for several minutes prior to injecting pH 7.4 phosphate buffer saline (PBS) into the liquid cell. Spectra were periodically collected over the course of one hour. All data were collected at a 75° incident angle for 220 wavelengths between 313 nm and 718 nm and fit to a Cauchy-Urbach isotropic model with an ambient water layer using commercial modeling software (WVASE32, J.A. Woollam). This model fit the refractive index (as a function of wavelength) and the film thickness to the experimental data. The water content of the swollen film was determined by dividing the increase in thickness by the total swollen thickness.

The composition of the film was determined by measuring the refractive index at a wavelength 633 nm, as determined by ellipsometry, and linearly interpolating based on the measured refractive indices of the pure PHEMA and PPFA homopolymers. The surface roughness and morphology was measured with atomic force microscopy (AFM, Dimension 3000, Digital Instruments) in tapping mode. Surface composition was measured by X-Ray Photoelectron Spectroscopy (XPS, SSX-100, Surface Science Instruments) survey scans. The XPS was equipped with a monochromatized Al K\(\alpha\) source.
Contact angle was measured using a goniometer equipped with an automated dispenser (Model 500, Rame-Hart). A 20 µL droplet of water was placed on the surface and the static angle was measured immediately. In order to probe the effects of surface reconstruction, the receding angle was measured by allowing this droplet to dry in ambient environment. The contact angle was monitored as the droplet volume decreased. In all cases, the water contact angle initially decreased as the droplet volume decreased. The ultimate receding contact angle was measured when no further change in the angle was observed as droplet volume decreased, indicating an equilibration in surface reconstruction. In general, this procedure took approximately 30 minutes.

Protein adsorption onto the polymer films was measured by quartz crystal microbalance with dissipation monitoring (QCM-D, Model E4, Q-sense). Gold-coated QCM-D sensors with a fundamental frequency of 5 MHz (QSX-301, Q-sense) were cleaned in a piranha bath (70/30 v/v concentrated sulfuric acid and hydrogen peroxide) and rinsed with ethanol prior to use as a deposition substrate. Duplicate samples of QCM-D sensors with deposited polymers were placed in a flow cell and the films were allowed to hydrate for 2.5 hours in flowing PBS (100 µL min⁻¹). Bovine serum albumin (BSA, 10 mg mL⁻¹ in PBS) was then introduced into the cell at a rate of 100 µL min⁻¹ for 2 hours. The frequency of the harmonics and dissipation at these frequencies were monitored as the protein adsorbed to the polymer film. The temperatures of the crystals were maintained at 37 °C throughout the experiment. Additional details of the QCM-D technique have been previously described.³⁰,³¹
5.4 Results and Discussions

The copolymerization is achieved by simultaneously flowing both monomers into the reactor. By adjusting the relative flowrates of the two monomers, the composition can be systematically altered. This compositional change is evident in the FTIR spectra of the copolymers, shown in Figure 5-1a. As the mole fraction of PFA in the copolymer increases, peaks corresponding to symmetric and asymmetric stretches of the pendant fluoroalkyl chain evolve at 1205 cm\(^{-1}\) and 1239 cm\(^{-1}\), respectively. A peak appearing at 1152 cm\(^{-1}\) corresponds to the CF\(_2\)-CF\(_3\) stretching frequency at the end of the pendant group. A corresponding decrease in intensity of CH\(_2\) wags and deformations centered at 1025 cm\(^{-1}\), 1077 cm\(^{-1}\), 1157 cm\(^{-1}\), and 1273 cm\(^{-1}\) confirms the decreasing mole fraction of HEMA in the copolymers. The broad hydroxyl peak centered around 3500 cm\(^{-1}\) (not shown) was also observed to decrease in intensity.\(^{32}\)

![Figure 5-1: (a) FTIR spectra of the copolymers, arranged upward in order of increasing PFA content. Peaks in the gray shaded regions correspond to the hydroxyethyl pendant group of HEMA and peaks in the red shaded area correspond to the fluoroalkyl side chain of PFA. (b) The carbonyl peak position shifts as a function of composition, indicating copolymerization.](image-url)
The FTIR spectra also confirm that the polymers were true copolymers, not physical blends of homopolymers. A systematically shifted single carbonyl peak centered around 1730 cm\(^{-1}\) in the deposited films is observed, indicating a random copolymer with a single effective carbonyl bonding environment. Figure 5-1b shows that the carbonyl peak position shifts from 1727 cm\(^{-1}\) for PHEMA homopolymer to 1731 cm\(^{-1}\) for the copolymer with the greatest PFA content. The location of the carbonyl stretch for PPFA homopolymer is 1741 cm\(^{-1}\), consistent with the direction of the observed frequency shift.\(^{25}\) Had the polymers been co-deposited, rather than copolymerized, a split carbonyl peak would be observed because there would be two distinct carbonyl bonding environments.\(^{33}\)

The copolymer compositions were quantified by measuring the refractive index of the films using spectroscopic ellipsometry. The bulk composition of the film can be determined quantitatively by assuming that the refractive index of the copolymer is a weighted linear average of the corresponding pure homopolymers. All bulk compositions in this study were measured by spectroscopic ellipsometry.

The film composition was reflected in the swelling properties of the films. While PHEMA is a hydrogel, the hydrophobic PPFA has water-repellent properties similar to PTFE. Copolymerizing hydrophilic and hydrophobic comonomers resulted in both slower water uptake and lower equilibrium water content, as shown in Figure 5-2a. All the copolymer films examined exhibited some degree of swelling behavior, but the equilibrium water content monotonically decreased with increasing hydrophobic content as seen in Figure 5-2b.
Although the films are only 100 nm thick, the bulk composition of the film does not reflect the surface composition of the film. In air or vacuum, the hydrophobic fluorinated alkyl chains of PFA will preferentially orient outward at the surface while the hydrophilic hydroxyl moiety of HEMA will preferentially orient inward. The surface composition in vacuum was quantified by XPS survey scans, which have a sampling depth of approximately 5 nm. As shown in Figure 5-3, the surface was always enriched in PFA as compared to the bulk for all film compositions except the pure homopolymers. In vacuum, the surface was over 50% PFA at bulk PFA concentrations below 20%. As XPS probes only the near-surface depth of the film, this result confirms the preferential outward orientation of the hydrophobic side chains and the inward orientation of the hydrophilic side chains in vacuum.

![Figure 5-2: (a) Dynamic swelling measurements of the copolymer films indicating slower water uptake with increasing hydrophobic content. Percentages indicate the mol fraction of PFA in the homopolymers. (b) The equilibrium water content measured after 60 minutes monotonically decreased with increasing hydrophobic content.](image-url)
Figure 5-3: XPS measurements of the surface composition of the copolymer films as a function of the bulk film composition. The bulk films are 100 nm thick, while XPS probes only the outermost 5-10 nm.

However, the orientation of the side chains at the surface is dynamic; the hydroxyl moiety can be made to orient outward if the film is exposed to water. This can be observed when measuring the water contact angle of the films. Static and ultimate receding water contact angles on the copolymer films are shown in Figure 5-4. The static contact angle increases rapidly with increasing hydrophobic content and saturates near the value for the PPFA homopolymer. The receding contact angle was measured by monitoring the evaporation of a 20 µL water droplet on the film surface. Because this evaporation occurred over the course of approximately 30 minutes, the receding angle reflects the surface composition in a reconstructed hydrated state. The large difference between the static and the receding angles suggests surface reconstruction at the film-water interface, so that hydrated films display a different surface than dry films. This can have important implications for the adsorption of proteins, since in practical applications such adsorption is likely to occur on a hydrated film.
AFM height imaging of the films showed only nanoscale roughness. Figure 5-5 shows that the RMS roughness of the PHEMA homopolymer film was 0.6 nm, and the roughness increased with PFA content and reached a plateau of approximately 5 nm. This trend is at least partially a consequence of the respective glass transition temperatures ($T_g$) of the PHEMA and PPFA (approximately 80 °C and -20 °C, respectively). As more PFA is incorporated into the copolymer, the film is increasingly amorphous, resulting in greater mobility of polymer chains and therefore greater surface roughness. The increase in chain mobility is also consistent with the observed difference between the static and receding water contact angles in Figure 5-5, which plateaus at approximately 75° when the composition exceeds 35% PFA. The surface roughness plateaus at the same composition, suggesting that chain mobility is an important process when the film is taken from a dry to a hydrated state.
Figure 5-5: Tapping mode AFM measurements show that the surface RMS roughness increases with increasing hydrophobic content. Height images of the surface at four different compositions are also shown. Scale bar = 300 nm.

Three representative QCM-D time traces in Figure 5-6a each show a negative shift in the third harmonic frequency of the crystal (14.9 MHz) when the polymer-coated sensor was exposed to a protein solution. These shifts occurred rapidly (within 15 minutes) upon introduction of protein into the sensor flow chamber. Similar negative shifts were observed for the fifth (24.8 MHz) and seventh (34.7 MHz) harmonics (not shown). A decrease in the harmonic frequency of a QCM-D sensor indicates a mass increase at the surface.30, 31, 34 Because the films were allowed to fully hydrate prior to protein exposure, this mass increase can be associated with the rapid adsorption of proteins to the polymer films. Hydrophobic surfaces are known to foul easily due to the hydrophobic effect,35 and Figure 5-6a shows that proteins adsorb readily to the highly hydrophobic PPFA homopolymer. The magnitude of the frequency shift is less for the PHEMA homopolymer as it is for PPFA, consistent with previous observations that hydrophilic surfaces tend to be more protein resistant than hydrophobic surfaces.36
The magnitude of the frequency shifts at the third, fifth, and seventh harmonic frequencies is shown as a function of composition in Figure 5-6b. At intermediate copolymer compositions, the frequency shift, and therefore the adsorbed protein mass, is less than the shift observed for either of the homopolymers. A representative time trace for a copolymer is shown in Figure 5-6a. Less protein adsorbs to the copolymer surfaces than for either of the homopolymers, with a minimum observed when the hydrophobic content is 40%.

If the interaction area between the surface and the protein were much larger than the length scale of the compositional heterogeneity, then the surface would appear uniform to the protein. Alternatively, if the interaction area were much smaller, then the surface would present itself to the protein as a set of disparate domains. In both cases, it would be expected [Image 18x9 to 594x783]

Figure 5-6: (a) Representative time traces of the frequency shifts in the third harmonic of a QCM-D crystal sensor coated with the indicated polymer. The dashed line indicates the introduction of protein solution into the flow cell containing the sensor. Percentages indicate mol fraction of PFA in the film. (b) Frequency shifts (absolute magnitudes) of QCM-D crystal sensors coated with various copolymer compositions upon introduction of protein solution into the flow cell containing the chamber. Error bars: standard deviation (n=2). Proteins adsorbed to the copolymers less than they did for either of the homopolymers.
that the degree of protein adhesion for the copolymers would fall between those observed for the homopolymers. Indeed, the material properties studied for these copolymers were intermediate to the material properties of the pure homopolymers. The observation that the copolymers show a greater resistance to protein adsorption than either of the homopolymers supports the hypothesis that nanoscale compositional heterogeneities discourage thermodynamically favorable interactions between the protein and the surface. In this sense, the proteins themselves can be thought of as probes that query the surface at extremely small length scales, much smaller than the length scales achievable by AFM, ellipsometry, XPS, and contact angle.

Detailed modeling of the mass of the adsorbed films was difficult to obtain for all the samples studied. This is due in part to inherent signal drift over the time scale of the experiment as well as the slow but continued hydration of the films over long periods. However, for a number of films accurate determination of film thickness was obtainable using commercial modeling software to fit the observed frequency and dissipation shifts to a Maxwell-Voight model (Q-sense, QTools). Assuming a protein adlayer density of 1.3 g cm\(^{-3}\), the areal mass density of adsorbed protein was calculated. In general, a one hertz frequency shift in the third harmonic corresponded to approximately 25 ng cm\(^{-2}\) of adsorbed protein. Thus, the lowest observed adsorbed protein density for the copolymer film was \(\sim 25\) ng cm\(^{-2}\), compared to \(\sim 150\) ng cm\(^{-2}\) for the PHEMA homopolymer and \(\sim 500\) ng cm\(^{-2}\) for the PPFA homopolymer.
5.5 Conclusions

We used piCVD to copolymerize hydrophilic and hydrophobic monomers rapidly via a free-radical mechanism to produce a thin film. The individual monomers and their respective homopolymers have highly contrasting properties, and the copolymerization was enabled by eliminating the use of solvent. The surface composition of the copolymers was dynamic and significant surface reconstruction was observed when the films were taken from a dry to wet state. By controlling the flow rates of the monomers in the feed gas, systematic variation in the composition of the copolymer was achieved, enabling us to tune the material properties of the copolymers between those of the homopolymers.

Most significant was the observation that less protein adsorbs to the surface of the copolymer than for either of the two homopolymers. The degree of protein adsorption is the only property of the copolymer film that was not between the properties of the homopolymers. This phenomenon provides direct evidence supporting the hypothesis that surfaces presenting molecular-scale compositional heterogeneities, such as these copolymers, interfere with protein adsorption. Because these heterogeneities occurred over the length scale of the individual monomers, they were not directly observable using analytical techniques such as AFM, ellipsometry, XPS, and contact angle, each of which average properties over an area of at least one square micron. Thus, the proteins can be thought of surface nanoprobes that reveal the effects of a random copolymer consisting of hydrophobic and hydrophilic monomeric units.

The molecular level heterogeneities are enabled by relying on random copolymerization rather than phase segregation. These results suggest that solventless processes are an
important route to creating topographically smooth surfaces presenting hydrophilic and hydrophilic moieties on the molecular length scale relevant to understanding and controlling protein adsorption.

5.6 Acknowledgements

The authors thank that National Science Foundation Graduate Research Fellowship Program and Draper Laboratories UI-RAD for financial support. The authors also thank Jonathan Shu at the Cornell Center for Materials Research for performing XPS measurements.

5.7 References


Chapter 6

Conclusions and Future Work
6.1 Summary and Implications for Future Research

In this thesis, we began in Chapter 2 by investigating the conformality of thin films deposited on non-planar geometries using iCVD. The conformality was found to depend on the fractional saturation of the monomer vapor during deposition. An analytical model was developed and the experimental data was fitted to the model in order to compute the sticking probability. Better step coverage was observed when the sticking probability was low, and the sticking probability was found to increase with the fractional saturation of monomer vapor. Thus, in order to create conformal films over an arbitrary geometry, it is suggested that future researchers operate at low fractional saturation of the monomer vapor. Alternatively, in applications where a non-conformal film may be desired, such as a membrane filtration system,
operating at high fractional saturation of monomer vapor is recommended. This recommendation was tested by Dr. Rama Sreenivasan, a postdoctoral researcher in Professor Gleason’s research group, and he indeed observed highly non-conformal coverage (Figure 6-1).

The system studied in Chapter 2 used a CHMA and TBPO as a model system in which there is a single monomer that is much less volatile than the initiator. In that case, the conformality was governed by the sticking probability of the initiating radical and the interpretation of the changes in sticking coefficient was straightforward. More complex iCVD systems are possible, however, and it is unclear previously unaccounted phenomena might affect the conformality of thin films in micron-scale features.

For example, copolymer films are common by iCVD, and it would be useful to understand how the addition of a second monomer affects the resultant conformality. It is speculated here that as long as all the monomers far less volatile than the initiator, then the sticking probability of the initiating radical should still be the primary determinant of conformality. An interesting experiment might be to map the conformality not to the fractional saturation of the monomer vapor, but rather to the surface coverage of monomer adlayer. If the sticking probability of the initiating radical were the primary determinant of conformality, then the sticking probability should be a function solely of the total equilibrium surface concentration of adsorbed monomer. In other words, for a copolymer film, the observed conformality should be independent of the composition of the adlayer. This hypothesis can be probed by utilizing QCM to measure the mass of the adlayers for both pure monomer and mixed-monomer vapors.
The analysis in Chapter 2 was consistent with a model in which the initiator “sticks” only when it directly strikes a vinyl monomer with the appropriate orientation and reacts irreversibly, that this event occurs with a constant probability, and that these reactions are directly proportional to polymerization rate. There are a number of situations where this model may be violated:

- The model assumes that the time for a single propagation reaction is much slower than the surface lifetime of the initiating radical. This assumption can be violated when the propagation reaction is very fast or when the surface lifetime of the radical is very long. The latter is possible if a less volatile initiator such as tert-butyl peroxybenzoate is used. In this case, an analytical solution may not be appropriate. However, either of the two violations noted above would be expected to result in poorer conformality in trenches.

- The model also assumes that an initiator that directly strikes an adsorbed monomer will react with a constant probability. However, for copolymerization systems with mixed adlayers, it is easy to imagine the possibility that one monomer is more reactive than the other (that is, the initiating radical has a different sticking probability depending on which adsorbed monomer it strikes). This may be particularly true if a di- or tri-vinyl monomer is utilized. However, given the relative involatility of di- or tri-vinyl species, this should not greatly affect conformality.

- Most importantly, the analytical model assumed that film growth rate is linearly proportional to the collision rate of initiating radicals. This is true when the ratio of monomer to initiator is high. However, when this ratio is very low, the polymerization rate saturates and is independent of the composition of the feed gas. In this case, conformality
should also be independent of sticking probability since initiator consumption within the features should not change the polymerization rate. This phenomenon may account for the observation by Dr. Gozde Ince that homopolymers of EGDA monomer are conformal at all investigated conditions. If the growth rate is independent of the local initiator concentration, either for the reason stated above or an as-yet unknown reason, then the film should expected to conformal regardless of the sticking probability.

Additional work in understanding the conformality of thin films deposited by iCVD would also include the investigation of thin film deposition in nanoscale and very-high aspect ratio trenches. While iCVD polymers have been deposited in membranes with 80:1 aspect ratios, a systematic understanding of the conformality in such features has not performed. A complementary study could include a simple simulation to understand the conformality as a function of collision frequency and sticking probability.

Upon gaining an understanding of the factors governing conformality in the iCVD system, we then described the development of piCVD and described its use in the synthesis of three material systems: swellable hydrogels, functional surfaces with vertically-graded chemical architecture, and surfaces with controlled protein adhesion properties. These materials were all based on HEMA and desired functionality was added through the use of a comonomer.

The homopolymer hydrogels described in Chapter 3 were stable and reversibly swellable, spectroscopically matched conventionally-polymerized PHEMA, and displayed tunable swellability based on processing conditions. These hydrogels were successfully deposited on microparticles and optode sensors; the latter were not damaged during the piCVD process,
demonstrating its gentle nature. The hydrogels were also shown to reduce the degree of non-specific protein adhesion as compared to bare silicon.

The single-step synthesis of vertically-graded functional hydrogels was described in Chapter 4. By altering the feed gas composition during deposition, the functionality could be confined only to the near-surface region. The vertical grading was confirmed by ToF-SIMS depth profiling. The vertically-graded copolymers retained the swelling properties of the underlying hydrogel whereas homogeneous copolymers showed degraded swelling properties. Most importantly, when the functional groups were confined to the near-surface region, all of the functional groups could be converted upon reaction. An extension of this study would be to study the effects of grading depth (the depth to which to functional group is nanoconfined) and ligand size on functional group conversion. It seems likely that larger ligands would not penetrate as far into the film. Systematically increasing the ligand size or changing the depth of nanoconfinement would presumably result in lower conversion throughout the depth of the film. Elemental markers on the ligand in conjunction with ToF-SIMS depth profiling would shed light on the degree of functionalization as a function of depth. This work could be potentially useful for creating design rules for the application of such films to engineering systems.

The properties of amphiphilic, random copolymers of HEMA and PFA polymerized by piCVD were studied in Chapter 5. The swellability, wettability, and surface roughness could be systematically controlled by tuning the copolymer composition. The surface composition was dynamic and the surface reconstructed based on the hydration state of the film. As measured by QCM-D, proteins adsorbed to the copolymer films less readily than either of the respective
homopolymers, indicating a synergistic effect resulting from the random copolymer presenting molecular-scale compositional heterogeneity.

As with any copolymer system, there are a number of additional studies that could yield interesting results. One of the hypothesized properties of this copolymer is that the random copolymerization does not allow the system to phase segregate. Indeed, no evidence of phase segregation was observed by AFM. However, scanning tunneling microscopy (STM) may be useful in observing domains, if they exist, on the nanoscale. If such phase segregation exists, it may be driven by either temperature or solvation. To that end, differential scanning calorimetry could be used to find the glass transition temperature and then AFM or STM performed above the transition temperature may be used to observe whether phase segregation occurs. Another option would be to perform AFM under aqueous conditions.

The fouling behavior of these films could be further explored by testing against a wider variety of foulants, including other proteins (such as lysozyme or fibrinogen) or microorganisms such as *Ulva* (algae spores). Additionally, AFM tips functionalized with a foulant can be used to generate force-distance interaction curves between the surface and the foulant. For example, functionalizing a tip with a bovine serum albumin molecule and repeatedly tapping the tip onto the film while recording the force would yield interaction curves of an individual protein molecule with the surface. Such information would elucidate the thermodynamic driving forces, both enthalpic and entropic, for protein adsorption.
6.2 Ongoing and Incomplete Research

Patterned thin films were an area of ongoing research at the time of completion of this thesis. Significant progress was made and the results to date are detailed in the appendix.

6.3 Avenues of Further Research

There is never enough time to pursue all the avenues of inquiry that pique a scientist’s interest. The sign of a successful researcher is that he or she is able not only to conceive of interesting experiments but also to identify which of those hold the greatest promise for scientific success, engineering application, or commercial development. My hope is that the two ideas I present below pique the reader’s interest as they did mine. But, I also leave to the reader the task of judging the merits of the following ideas and whether they should be pursued.

6.3.1 Shape memory polymers. Shape memory polymers display a remarkable ability to regain a programmed initial shape after undergoing deformation. Return to the initial shape is triggered by an external stimulus, usually heat, and is routinely observed even after deformations as large as 200%. A shape-memory polymer is typically a copolymer or interpenetrating network consisting of a deformable component and a crystallizable component. The deformable component is typically a soft polymer such as butyl acrylate. The crystallizable component locks the shape of the polymer upon deformation. This locking mechanism need not be crystallization per se; it can interact via many different interactions, including hydrogen
bonding. The network points formed between the two components program the original shape.

Above a certain transition temperature (usually termed the melting temperature), the polymer can be easily deformed. Upon cooling below the melting temperature, the crystallizable component locks the shape of the polymer. At this point, the load can be removed and the polymer will retain its deformed shape. Heating past the melting point provides sufficient thermal energy to reverse the crystallization, allowing the polymer to regain its originally programmed shape.\(^3\)

Currently, shape memory polymers are synthesized in the liquid phase, but dry processing such as iCVD opens the possibility of creating conformal coatings with shape memory. These coatings could be potentially useful for actuating in reversible sensors or microfluidics, among other applications. The key challenge for inquiry along these lines would be the identification of a shape-memory polymer whose precursors are iCVD compatible.

Commonly-used soft monomers for the soft component are alkyl acrylates such as n-butyl acrylate,\(^4\) tert-butyl acrylate,\(^5\) or methyl methacrylate.\(^6\) These and similar monomers have been deposited by iCVD. The more difficult challenge is identifying an appropriate crystallizable component. These tend to be large molecules with a high degree of intermolecular interactions, both of which are correlated with low vapor pressures. In order to achieve flow into an iCVD reactor, 1-10 torr of backing pressure is required.

Di(ethyleneglycol) dimethacrylate (DEGDMA) has been used in shape memory polymers previously.\(^5\) Its volatility is considered borderline ($P^{\text{vap}}(113 \, ^\circ\text{C}) = 1 \, \text{torr}$) for traditional iCVD
vapor delivery systems. A novel delivery system incorporating a bubbler may make this monomer iCVD compatible. The closely related di(ethyleneglycol) divinyl ether (DEGDVE) has been used as an iCVD crosslinker. DEGDMA and DEGDVE have analogous ethyleneglycol chains in the middle of the molecule. Thus, DEGDVE could potentially be used as a crystallizable component for iCVD shape memory polymers. Copolymers of DEGDVE with n-butyl acrylate may exhibit shape memory properties.

6.3.2 Zwitterionic polymers. Zwitterionic surfaces show excellent resistance to non-specific protein adhesion and can be used as stimulus transducers for self-assembling systems. One can imagine a number of applications of zwitterionic polymers for which a solution-based coating method would not result in the desired degree of conformality or substrate compatibility. As with shape memory polymers, the biggest obstacle to synthesizing iCVD zwitterionic copolymers is the low volatility of precursor materials.

I will present one material system for the production of zwitterionic polymers via iCVD. Zhang et al. reported the synthesis of a zwitterionic monomer by the reaction between a methacrylate with a tertiary amine-terminated side chain with a propiolactone. The resultant ring-opening reaction produced a carboxybetaine side chain with both a quartenary amine cation and a carboxylate anion. Carboxybetaines, as well as sulfobetaines and phosphobetaines, have been shown to resist non-specific protein adhesion.

The methacrylate described above, dimethylaminoethylmethacrylate (DMAEM) can be easily polymerized by iCVD. The basic reactor conditions are:

- DMAEM flow: 1-3 sccms, source temperature: 75 °C.
The structure of iCVD poly(dimethylaminoethylmethacrylate) (PDMAEM) was confirmed by FTIR (Figure 6-2). In principle, this polymer film should be reactive with β-propiolactone or β-butyrolactone to form zwitterionic carboxybetaine side groups, although the permeability of the functionalizing agent, solvent choice (if any), and concentration of the functionalizing agent would require investigation. Another possible functionalizing agent is 1,3-propanesultone, which would react to form a sulfobetaine.

Another potential route to zwitterionic films is to conjugate an amino acid with a functionalizable film. While amino acids are zwitterions, they can exist in a neutral state by
shifting a proton. Such a shift occurs upon vaporization. Thus, neutral gas phase amino acids with a suitable side group (such as the amine on lysine) can potentially react with the film and then revert to their zwitterionic state.

Potentially interesting properties of zwitterionic polymer films would be pH-dependent behavior (such as swelling) and fouling resistance. They could be used in switching and actuating, biological coatings, and fuel cell applications.

6.4 Concluding remarks

The goal of this thesis was to gain mechanistic understanding of iCVD and to develop novel deposition strategies and materials for potential future applications. It is hoped that the work described here has not only met these goals, but also contributed both academically and practically to the field of surface modification. Wolfgang Pauli once observed “God created the solids, the Devil their surfaces.” If Pauli’s witticism is taken as axiomatic, then perhaps surface science and engineering is divinely inspired.

6.5 References


Appendix

_Dual Patterned Surfaces by iCVD_
A number of methods are available for patterning iCVD films, including electron beam lithography,\textsuperscript{1} capillary force lithography,\textsuperscript{2} and colloidal lithography.\textsuperscript{3} This appendix describes a generic method for producing surfaces with patterns of two different iCVD polymers. In most patterning processes, the polymer film appears in a spatially regular pattern and the substrate is exposed in other areas. This process can be used to create a surface with no exposed substrate.

Figure A-1 shows a schematic for this method. A blanket iCVD polymer is first deposited on a surface. Then, a mask is placed in intimate contact with this polymer film. A commercially available copper TEM grid (P/N, Ted Pella, Inc.) is a good choice, although the smallest available feature is only 7.5 microns. Then, the substrate is placed in oxygen plasma and the exposed polymer is anisotropically etched. Typical etch rates observed for iCVD polymers are 20-40
Figure A-2: Tilted-view SEM of intentionally flat patterned film. The polymer in the squares is PPFA and the surrounding matrix is PHEMA.

nm/min at a plasma power of 60 watts.

If the mask is not in intimate contact with the film, then the etchant will undercut the mask and the resultant film will lack pattern fidelity. To achieve intimate contact, the mask was placed on the substrate and a single drop of liquid was placed on top of the mask. As the liquid wicked into the films and evaporated, capillary forces produced excellent contact between the mask and the film. For this reason, the liquid used should be a relatively good solvent for the polymer. However, a strong solvent is not recommended as this will dissolve the film. After the etching step, another iCVD film is deposited without removing the grid. The TEM grid can then be carefully removed to reveal the dual patterned surface.

By monitoring both depositions by interferometry, and by operating at conditions that give good step coverage, the relative thicknesses of the patterned domains can be controlled. For example, in Figure A-2, both domains were deposited at approximately the same thickness.
The domains appear distinct even while the overall film appears flat. On the other hand, Figure A-3 shows a film where one domain was intentionally made thinner than the other. Figure A-4 shows that a fluorescein dye can be selectively conjugated to domains with complementary functionality, confirming that the patterning produces domains containing distinct polymers with little intermixing.

Figure A-3: Tilted-view SEM of intentionally thickness-mismatched polymer films. The polymer in the squares is PPFA and the surrounding matrix is PHEMA. The expanded view shows the thickness difference at an edge.

Figure A-4: Fluorescent optical micrographs of squares of P(HEMA-co-PFM) in a matrix of PPFA (left) and the negative pattern (right). Prior to imaging, the films were functionalized with a fluorescein dye that reacts selectively with PFM.
References

