LAYER-BY-LAYER ASSEMBLY ON POLYETHYLENE FILMS VIA “CLICK” CHEMISTRY

A Thesis

by

BRANDON SCOTT CHANCE

Submitted to the Office of Graduate Studies of
Texas A&M University
in partial fulfillment of the requirements for the degree of

MASTER OF SCIENCE

May 2007

Major Subject: Chemistry

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Approved by:

Chair of Committee,	David E. Bergbreiter
Committee Members,	Stephen A. Miller
	Jaime C. Grunlan
Head of Department,	David Russell

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ABSTRACT

Layer-by-Layer Assembly on Polyethylene Films
via “Click” Chemistry. (May 2007)
Brandon Scott Chance, B.S., Texas Lutheran University
Chair of Advisory Committee: Dr. David E. Bergbreiter

Layer-by-layer assembly has received much attention over the last fifteen years. This assembly process can be carried out using different methods including hydrogen-bonding, electrostatic, and to a lesser extent, covalent interactions. However, these assemblies are rarely seen on polyolefin substrates due to the lack of functionality on the surface.

“Click” chemistry has become very popular in recent years as a means to join modular compounds together. This thesis is the first published report to use “click” chemistry as a means for layer-by-layer assembly on a polymeric substrate. By designing polymers that contain alkyne or azide groups, it is possible to assemble them layer-by-layer on a polyethylene substrate.

Polymers based on *tert*-butyl acrylate were initially designed for use in organic solvents such as tetrahydrofuran. The copper catalyst that facilitated the 1,3-dipolar cycloaddition was air sensitive and expensive. To capture the true essence of “click” chemistry, a new system was designed based on *N*-isopropyl acrylamide (NIPAM)-based polymers. These polymers were water soluble and allowed for “click” chemistry to be performed in water and open to air in benign conditions.

With the development of a water soluble polymer system that could be modified to contain either azide groups or alkyne groups, layer-by-layer assembly was carried out in water. A polyethylene film was modified in a series of reactions to have an alkyne-functionalized surface. The poly(*N*-isopropyl acrylamide)-based polymers were layered in an alternating fashion to form multilayer assemblies. A series of control reactions were also performed, showing that these layers were interconnected via triazole linkages.

These assemblies were monitored by attenuated total reflectance spectroscopy. Once the layers were assembled, the polyvalent nature of the polymers allowed for further functionalization. Various surface functionalizations were established using fluorescence microscopy and contact angle analysis.

By using spectroscopic and chemical means, layer-by-layer assembly on polyethylene films was proven. Control reactions showed the necessity of components for triazole formation. Therefore, layer-by-layer assembly using “click” chemistry was achieved.

DEDICATION

To my wonderful wife, Amanda.

ACKNOWLEDGMENTS

I would like to start off by thanking my family. Mom, Dads, and Yvonne, thank you for all the advice both personal and professional you have given me throughout the years. Grandparents, thank you for helping mold me into the person I am today. Brothers and sister, thank you for helping me strive to be a good role model and for allowing a glimpse of what it was once like to be a child. To the rest of my family, thanks for simply being a part of my life and making things fun. Finally, I would like to say thank you to my wife, Amanda. You have stood by me for the last six years, through all the trials and tribulations that life has to offer, you were always there for me. For that I thank you and love you.

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Guys, we have lived together for five years and have a lifetime of memories. Thanks for being a shoulder to lean on and a friend to laugh with.

Dr. Bergbreiter, you were exactly what I needed to get through graduate school. I always like to compare you to an old football coach. You know exactly when to kick someone in the butt to get them motivated and when to let up. I really appreciate all the time you have spent teaching me and helping me grow both as a chemist and a person. For that, I will always be grateful.

Thank you to Sandy Manning, Julie Wilson, Joy Monroe, Jill Rutledge and the rest of the staff that is so vital to the graduate experience at Texas A&M. I would also like to thank the many great professors that I have had the pleasure of working with and learning from including Dr. Miller, Dr. Grunlan, Dr. Singleton, and Dr. Connell. I would also like to thank Dr. Cremer's group for allowing me to use their fluorescence microscopy facilities.

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TABLE OF CONTENTS

LIST OF FIGURES

FIGURE Page

FIGURE Page

LIST OF TABLES

TABLE Page

CHAPTER I

INTRODUCTION - MULTILAYER ASSEMBLY HISTORY AND "CLICK" CHEMISTRY

Multilayer assembly of organic compounds on surfaces has been explored for over seventy years. Surface modifications that employ such multilayer assembly techniques (terminology such as "layer-by-layer (LbL) assembly," "molecular self-assembly," and "multilayer assembly" are all interchangeable) can be performed on various insoluble substrates and have applications in chemosensing, biotechnology, and nanotechnology.[1,2] Most of this work involving layer-by-layer depositions or related covalent surface modification has involved inorganic solids. Surface modification and specifically layer-by-layer assembly on polymeric, carbon-based solid supports has received less attention.

Polymers that contain functional groups, such as poly(methyl methacrylate) and nylon, are organic materials that have received attention because of the functional groups inherently present on the surface can facilitate functionalization.[3,4] However, inert polymers such as polyolefins present a unique set of challenges due to the lack of functionality on their surfaces. Significant efforts have been made to develop procedures to functionalize these polymers' surfaces via various methods. Polyethylene (PE) has received much of this attention due to its availability, low cost, and many applications.

This thesis follows the style of *Macromolecules*.

Surface modification in general and LbL assembly in particular on a polymer surface, specifically polyethylene (PE), is important for several reasons. According to ExxonMobile, polyethylene is the most consumed polymer in the world. It acts as a diverse plastic than can be used as an alternative to glass, metal, or paper.[5] One of the drawbacks to chemically modifying polyethylene is its lack of functional groups. By functionalizing the surface and being able to assemble multiple layers of specific polymers, the surface functionality can be changed without changing the bulk properties of the polymer.

Combining layer-by-layer assembly and polyethylene functionalization is a specific area of multilayer assembly chemistry that has received little attention. This is because covalent layer-by-layer assembly on PE presents unique challenges. These challenges arise because the film must first be functonalized using harsh conditions such as plasma treatments or a Cr(IV) oxidant in sulfuric acid.[6] Once the surface is oxidized, it contains carboxylic acid functionality. The Bergbreiter group has used this chemistry to further functionalize polyethylene by various procedures including covalent layer-by-layer assembly on the surface.[7] These reactions have generally involved some sort of condensation reaction.[7,8] The work described here extends this chemistry using an alternative approach to covalent LbL, “click” chemistry.[9] The studies below both describe application of these Cu(I)-catalyzed cyclizations to a PE surface and show that such chemistry can be carried out in an environmentally benign solvent like water.

Layer-by-layer assembly on inorganic substrates such as gold and glass has been studied extensively over the last few years. Most of this LbL assembly has focused on the use of polyelectrolytes to form layers. Other chemistry besides electrostatic interactions can be used to effect layering. Hydrogen bonding and covalent LbL assembly have also been explored.

Hydrophilic/Hydrophobic Layer-by-Layer Assembly

Examples of LbL assembly based on hydrophilic/hydrophobic interactions have been around for nearly seventy years thanks to the work of Irving Langmuir and Katherine Blodgett.[10] In a simple, yet very nice experiment, Blodgett used a glass slide with stearic acid in a slightly alkaline solution to demonstrate the ability for a molecule to predictably orient itself based on hydrophilic/hydrophobic interactions (Figure 1-1).[11] The self-assembly that occurs in this experiment involves the lipid bilayers most people learn about in a high school biology class. Films built using these interactions have subsequently been described as Langmuir-Blodgett (LB) films.

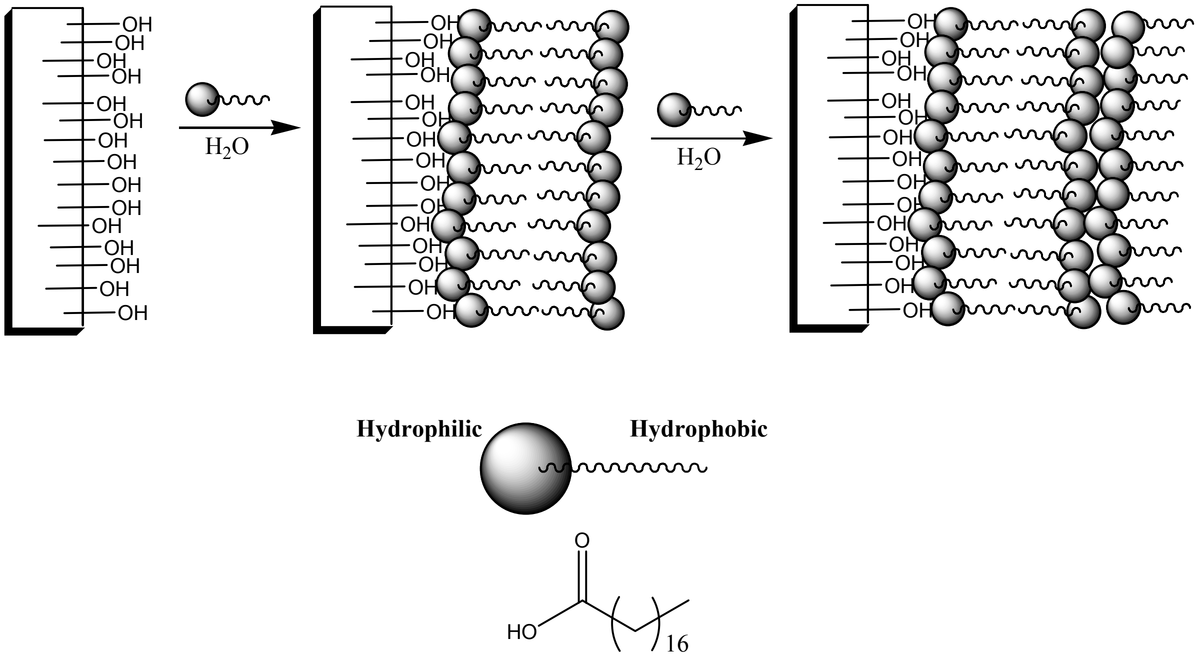


Figure 1-1. Example of Langmuir and Blodgett's LbL self-assembly of lipid bilayers using fatty acids.

Using wettability as an assay, Blodgett was able to show that layering did in fact occur. For instance, after the second oil deposit, where the hydrophilic acid groups were facing away from the glass surface, water coated the surface while mineral oil rolled off the surface. Once the third layer was added, hydrophobic carbon chains were facing away from the surface and water beaded up and rolled off while mineral oil adhered to the surface. Surface analysis techniques such as these are still used today in the form of contact angle analyses. Another unique aspect of this type of this layering is that the dipping solution contains a mixture of fatty acids on a water surface. The hydrophilic substrate or multi-layered hydrophobic substrate is dipped into the solution, and the fatty acid orientates itself onto the surface based on the order the layering occurred.

In the 1970s, Kuhn and Möbius published a series of studies detailing extensive experiments where multilayer assemblies were prepared using dyes such as cyanine substituted with paraffin (Figure 1-2).[12]

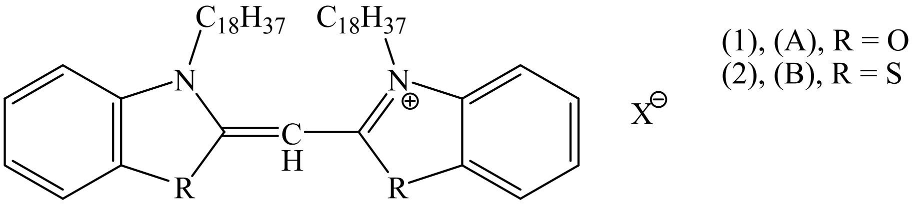


Figure 1-2. Paraffin-substituted cyanine dye analogues molecule.

By using dye-labeled fatty acids instead of simple fatty acids, Kuhn and Möbius were able to use UV spectroscopy to show that the bilayer assemblies formed have properties not shown by individual layers. For example, based on energy transfer between dyes, it was possible to show that interactions between layers can occur. In this experiment, a few layers of arachidic acid ($C_{19}H_{39}COOH$) were deposited on a glass slide with the hydrophilic acid groups ($-CO_2H$) facing away from the slide. Then, a layer of the dye (A) was spread over two thirds of the surface (zones 1 and 2) with pure arachidic acid spread over the final third of the surface. Next, zone 1 was covered by a single layer of arachidic acid and zones 2 and 3 were covered with 5 layers of arachidic acid. Finally, a layer of dye B was deposited over the whole surface. The product multilayer assembly is shown in Figure 1-3. In this experiment, dye A was chosen such that it absorbs ultraviolet light and fluoresces blue while dye B was chosen such that it absorbs blue light and fluoresces yellow. When the assembly shown in Figure 1-3 was irradiated with UV light, only dye A would be able to absorb the light. As a result, areas on the surface (zone 2) where dye A and B are separated by 150 Å exhibited only a blue fluorescence, indicative of dye A. However, in zone 1 where dye A and B are only 50 Å apart, a yellow color is observed because of energy transfer from dye A to dye B can occur. Finally, in zone 3 no color is observed because the only dye present, dye B, does not absorb UV radiation. Energy transfer experiments like this served as proof of concept experiment for subsequent work that has potential applications where functional multilayer modified surfaces are used as chemo- and biosensory nanoscale devices.[2]

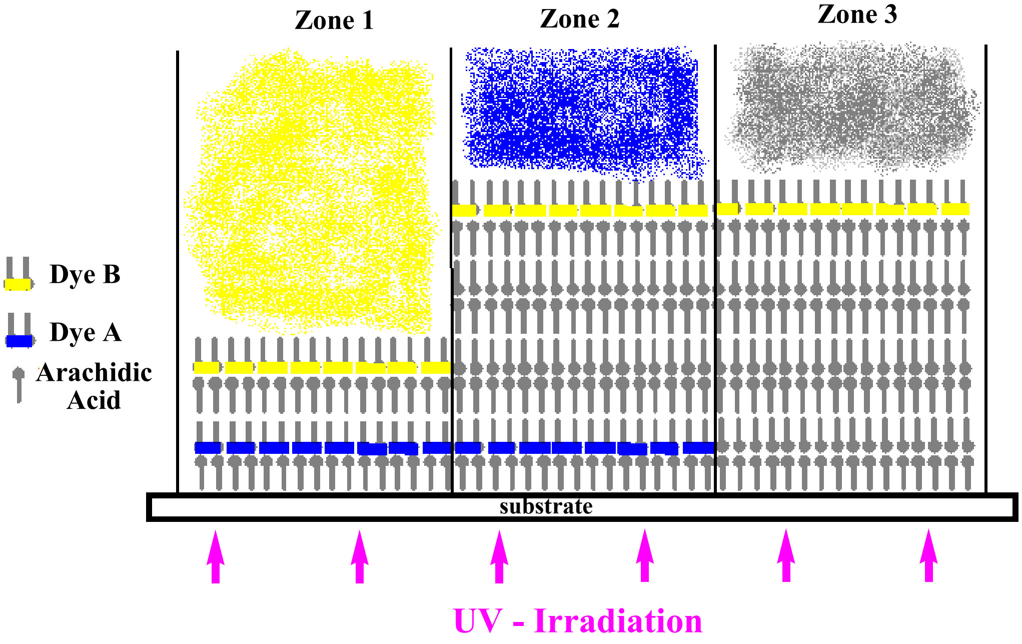


Figure 1-3. Layout and observations of an ultraviolet irradiation dye experiment involving dye-labeled fatty acids and LB layer-by-layer assembly on glass.[12]

Langmuir-Blodgett films are still being studied today. While such assemblies generally have only modest thermal and mechanical stability, today's LB films can be built using technologically advance equipment making them easier to prepare. A modern apparatus normally consists of a Langmuir trough with a dipping device used for lowering and raising the substrate.[13] There is normally a computerized, movable barrier used to keep a static surface pressure on the substrate and sensor to control this barrier. This method has been used to give near perfect layering over a multiple bilayers, but is nonetheless cumbersome. This has led to research directed toward the development of other methods of layer-by-layer assembly.

Electrostatic Layer-by-Layer Assembly

Electrostatic self-assembly was another breakthrough in layer-by-layer assembly. First described by Iler in 1966 using charged alumina and silica particles, there has been a renewed interest over the past fifteen years due to the boom in nanotechnology research.[14]

In 1997, *Science* published a review authored by Gero Decher that reinvigorated research in the layer-by-layer assembly field.[15] Decher first described his work in a series of electrostatic LbL assembly articles that initially appeared in 1991.[16] His *Science* article reviewed those earlier efforts and has spurred a renaissance of interest in electrostatic LbL assembly chemistry. Decher's goal was to devise procedures that could be used to construct future nanodevices. Decher's approach to this problem was based on his belief that there must be a fixed relationship between nanoscopic order and macroscopic orientation. To achieve this goal, one must know the location or orientation of every molecule in respect to the entire nanostructure. Decher claimed that high-quality multilayer thin films cannot be easily using covalently bound layers. He claims that the steric demands are too great for proper layering to occur. This reasoning drove Decher to develop a simple approach to layer-by-layer assembly that would be independent of both the topography and size of the substrate.

The simple solution to this problem was using a method that does not have steric constraints. Electrostatic interactions were chosen in place of covalent bonds. By taking a polyanion and polycation (Figure 1-4), Decher was able to design a scheme for the deposition of polymer thin films on a surface.

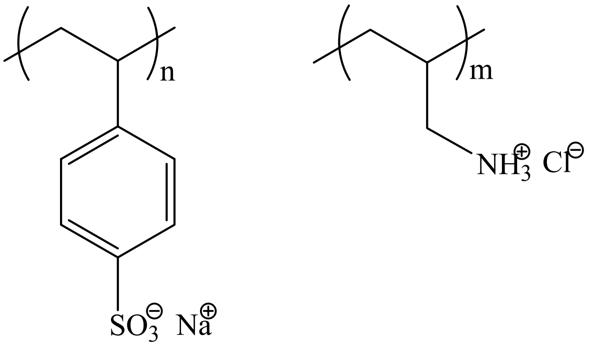


Figure 1-4. Polyelectrolytes – polyanionic sodium poly(styrene sulfonate) and polycationic poly(allylamine hydrochloride).

Until Decher's work, polyelectrolytes had seen little use in molecular self-assembly. By using a charged substrate, such as an anionic glass surface, he showed that a positively charged polymer like poly(allylamine hydrochloride), would adhere to the surface. The adsorption of this polyvalent polycation produced a charge reversal on the surface changing the surface charge from negative to positive. Polymer-bound ammonium salts that did not interact with anionic sites on the glass substrate were thus available to associate with a polyanion in a second step. When the single-layered substrate was dipped in a solution containing a polyanion like poly(styrene sulfonate). In a second step, the polyanion adhered to the polycation. Again, only some of the sulfonate groups of the polyanion bind to the ammonium groups. The remaining sulfonate groups create an overall negative charge on the surface setting the stage for another polycation adsorption event. The first two steps in this process are shown in Figure 1-5.

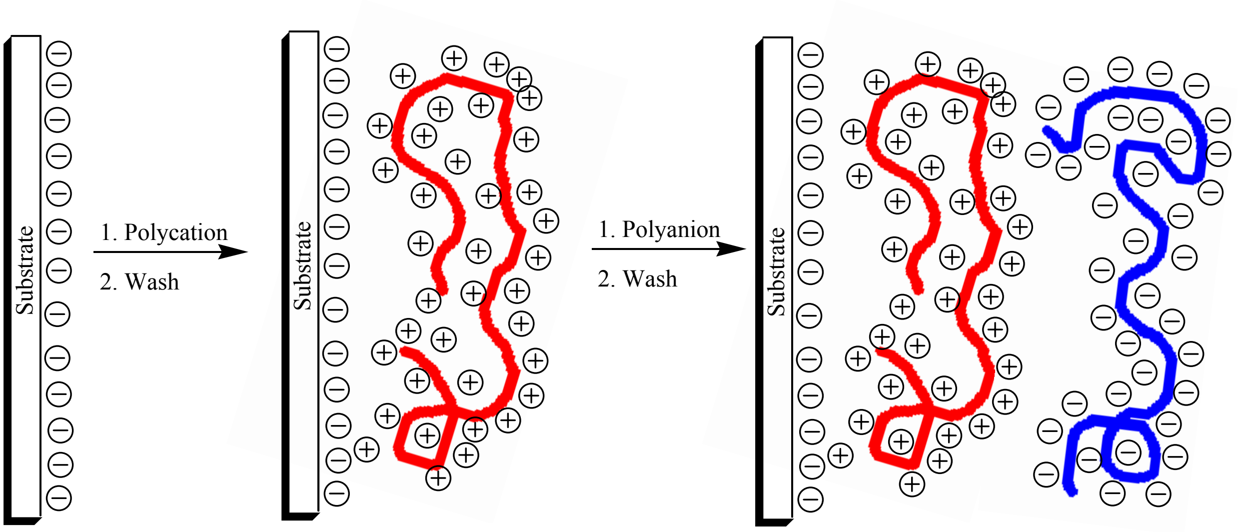


Figure 1-5. Polyelectrolyte electrostatic layer-by-layer assembly on an anionic substrate.

Once the polyelectrolyte interacts with the oppositely charged surface, the counter ions associated with it are released. This entropically drives the assembly process.[17] These structures can be designed and "tuned" using solution pH and various counterions.[17,18] However, there are drawbacks to this chemistry. For example, resulting nanostructures cannot always withstand acidic or basic solutions.[18]

Over the last decade there have been hundreds of articles published highlighting various electrostatic LbL assemblies.[17] These articles use inorganic/inorganic, inorganic/organic, organic/organic, biological/organic, and biological/biological bilayer assemblies. An example of inorganic/inorganic multilayer assembly is Sastry's work where he sequentially layered derivatized gold and silver colloidal particles on glass.[19] By derivatizing gold colloids with 4-aminothiophenol and derivatizing silver colloids with 4-carboxythiophenol he created a multilayer assembly by suitably changing the pH of the colloid-containing solution during the gold and silver colloid deposition steps.

In 2005, Cho assembled superhydrophobic organic/inorganic multilayer films electrostatically. In this case, subsequent crosslinking the layers using amidation produced a more stable product.[20] According to Cho, his nanocomposite materials have advantages over traditional inorganic/inorganic assemblies and polyelectrolyte assemblies that have low mechanical and chemical durability. Cho described a simple, 10-layer fabrication using poly(allylamine hydrochloride) (PAH), poly(acrylic acid) (PAA), ZrO_2, and hydrophilic silica nanoparticles followed by fluorination. By adding zirconium oxide particles to the layering procedure, the multilayer structure's hardness was increased, thus increasing the mechanical properties of the film. The product was then further stabilized by heat induced crosslinking to increase the chemical stability. He deposited 5 bilayers of PAH/PAA ($(PAH/PAA)_5$) on a silica wafer and subsequently added PAA-coated ZrO_2. This was followed by 1.5 bilayers of silica nanoparticles/PAH. After this deposition was complete, the wafer was heated to 215°C for 2 h to induce crosslinking via amide formation. The films were then fluorinated to promote hydrophobicity. When examining chemical stability, it was found that the crosslinked films retained their properties upon immersion in a water/dimethylformamide/zinc chloride solution and the non-crosslinked film did not. The crosslinked film was also harder than the non-crosslinked film, showing crosslinking not only inceased chemical stability, but also increased mechanical stability too (Table 1-1).

Table 1-1: Hardness Values of Various Nanocomposite Multilayer Films Determined by Nanoindentation

Composition	hardness (GPa)	thickness (nm)
$(PAH/PAA)_{60}$, non-crosslinked	0.75	642.8
$(PAH/PAA)_{60}$, crosslinked	1.36	576
(PAH/PAA-coated $ZrO_2)_{60}$, non-crosslinked	2.15	712.9

These results show that covalently bonded films can have greater durability in comparison to films made using only electrostatic interactions. The introduction of an inorganic component can further increase this durability.

All organic multilayer assemblies are the most commonly explored type of electrostatic multilayer assembly. Research by various groups has described many applications for the LbL assembly technique first published by Decher. One of these applications is the design of multilayer capsules for use in drug delivery. In the past, these capsules were formulated by absorbing polymers on a drug particle's surface or by the absorption of monomers and subsequent polymerization on a particle surface.[21] Instead of these methods, a novel approach is to use LbL assembly to manufacture the capsule. Because the process is completely stepwise, it should be possible to tune these capsules for various pore sizes and release conditions. In 2001, Sukhorukov described how this could be done. In this case he used fluoroscein dye as a model for a low molecular weight drug and followed its release.[22] Fluoroscein dissolves at a pH of 8 and Sukhorukov proved that assembling multiple polyelectrolyte layers around a fluoroscein particle retarded fluoroscein's dissolution. By using fluorescence spectroscopy, he determined the rate at which fluoroscein dissolved by following the rate of its appearance in the bulk solution. Upon deposition of 9, 13,15, and 18 layers of poly(styrenesulfonate) and poly(allylamine hydrochloride) the rate that fluorescence intensity increased was compared to the naked fluoroscein (Figure 1-6).

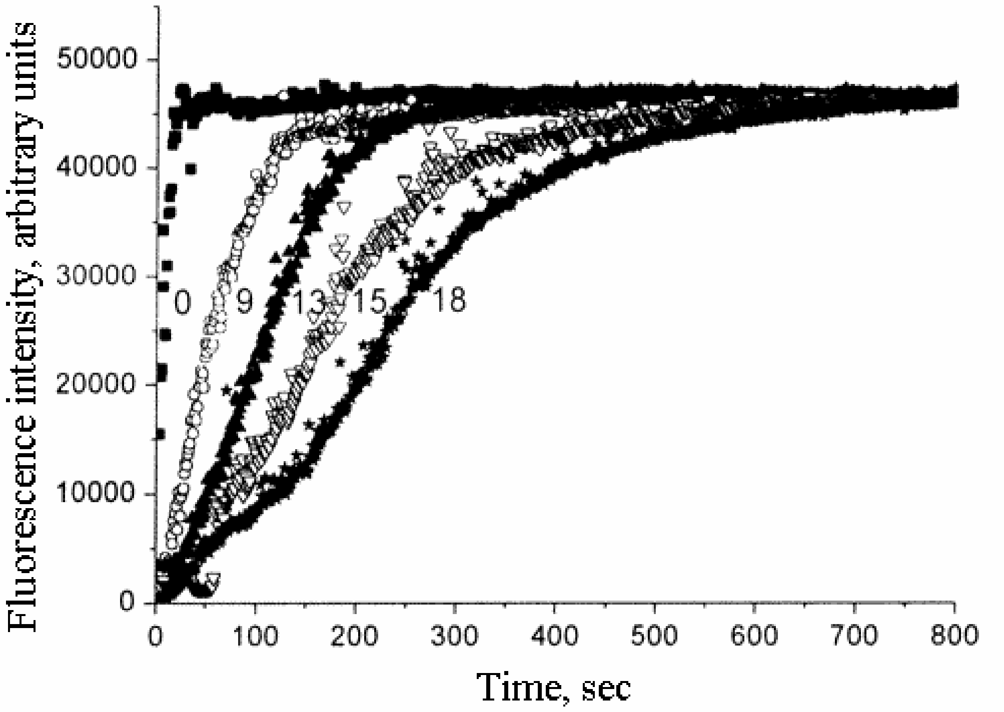


Figure 1-6. Fluorecence increase over time using variable shell thickness (9, 13, 15, and 18 layers), compared with naked (0) fluorescein particles.[22] Reprinted with permission from *J. Phys. Chem. B* **2001**, *105*, 2281-2284. Copyright (2001) American Chemical Society.

Dendrimers have also been a popular choice for researching drug delivery vehicles.[23] Caruso published an article in 2002 using dendrimers and LbL assembly to create drug delivery vehicles.[24] Once again, a fluorophore was used as model for possible uptake and release of a drug. Caruso layered poly(styrenesulfonate) and a fourth generation poly(amidoamine) dendrimer on a planar surface in order to determine the factors that were important for stable film formation. Once he determined that layer-by-layer assembly would occur on a flat surface, he then began using colloids (either polystyrene or melamine formaldehyde) as the substrate. Using UV and fluorescence spectroscopy, Caruso was able to show that the multilayer films could facilitate both uptake and the subsequent release of 4,5-carboxyfluorescein using a 10 layer system.

Caruso and Möhwald created protein/polyelectrolyte-based multilayer systems in 1999 using polystyrene particles as a substrate for colloidal LbL assembly.[25] Using fluorophore labeled proteins, they were able to successively manufacture spherical multilayer-assembled shells. This is an example of biological/organic multilayer assembly.

Biological/biological multilayer assemblies have potential applications in gene therapy and specialty thin film designs. For example, in 2006 Ji described an LbL assembly that could purportedly serve as a DNA delivery device.[26] Using the negatively charged phosphate backbone of DNA and poly-L-lysine (PLL) as the polycation, Ji was able to create films 10 bilayers (20 layers) thick. However, because the interaction between films is purely electrostatic, the DNA release occurred quickly and was uncontrollable. By using glutaraldehyde as a crosslinking agent, free amines on the PLL were crosslinked, strengthening the multilayer assembly and reducing the rate of DNA release. He varied the time that the multilayer systems are exposed to the crosslinking agent, and then measured the DNA release kinetics were measured (Figure 1-7).[26] His results showed that such assemblies have a tunable property for the release of DNA that could be useful in gene therapy treatments.

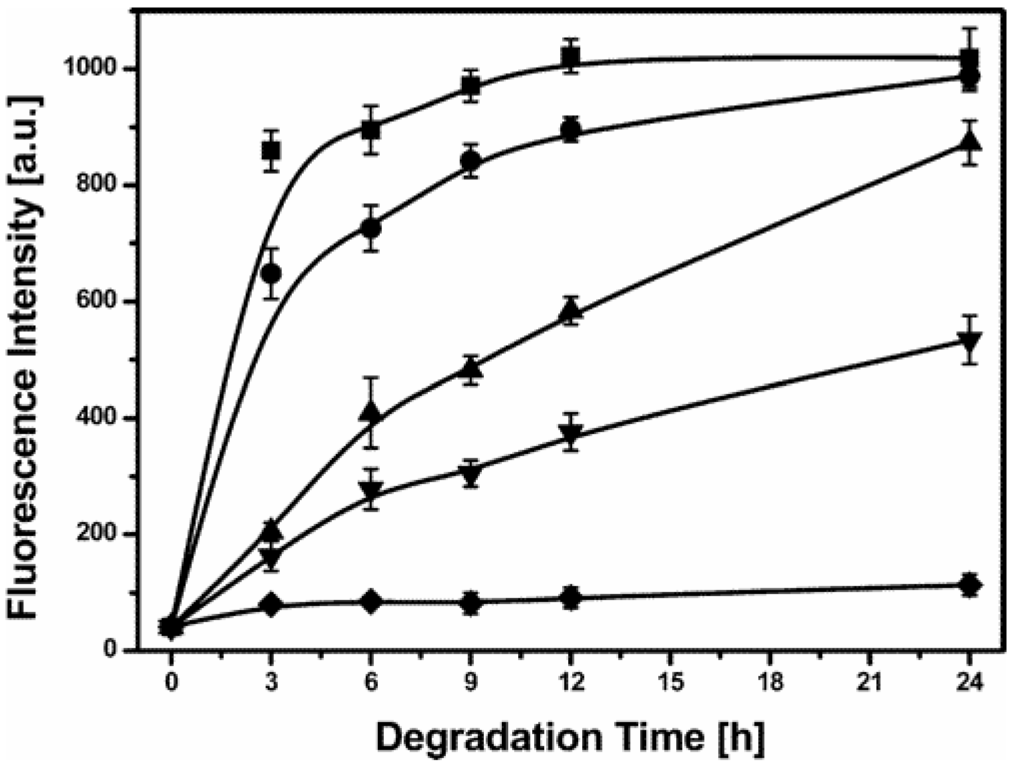


Figure 1-7. Fluorescence intensity of incubation solution, in which incubated PLL/DNA films with varying cross-linking time are exposed to a trypsin solution: (■) original film; (●) 10 min; (▲) 30 min; (▼) 60 min; and (♦) 180 min. Values are given as mean ± standard deviation (n=3).[26] Reprinted with permission from *Bioconjugate Chem.* **2006**, *17*, 77-83. Copyright (2006) American Chemical Society.

Covalent Layer-by-Layer Assembly

In theory, by building multiple layers via covalent bonds, one should be able to strengthen layer-to-layer adhesion, improving many of the chemical and mechanical properties of LbL assemblies. Original publications that discussed covalent LbL assembly used inorganic building blocks such as silanols. [27] Subsequent publications used polymers with various functional groups for multilayer assembly.[28-30]

This early work by Netzer and Sagiv published in 1983 demonstrated that one could make covalently linked bilayers using a silicon a substrate.[27] They functionalized this substrate using 15-hexadecenyltrichlorosilane (HTS), subsequent hydroboration and oxidation followed by readdition of the HTS to produce more grafting (Figure 1-8). Analysis by ATR-IR and contact angle measurements showed that hydrophobic terminal alkene was replaced by a hydrophilic terminal alcohol, as predicted.

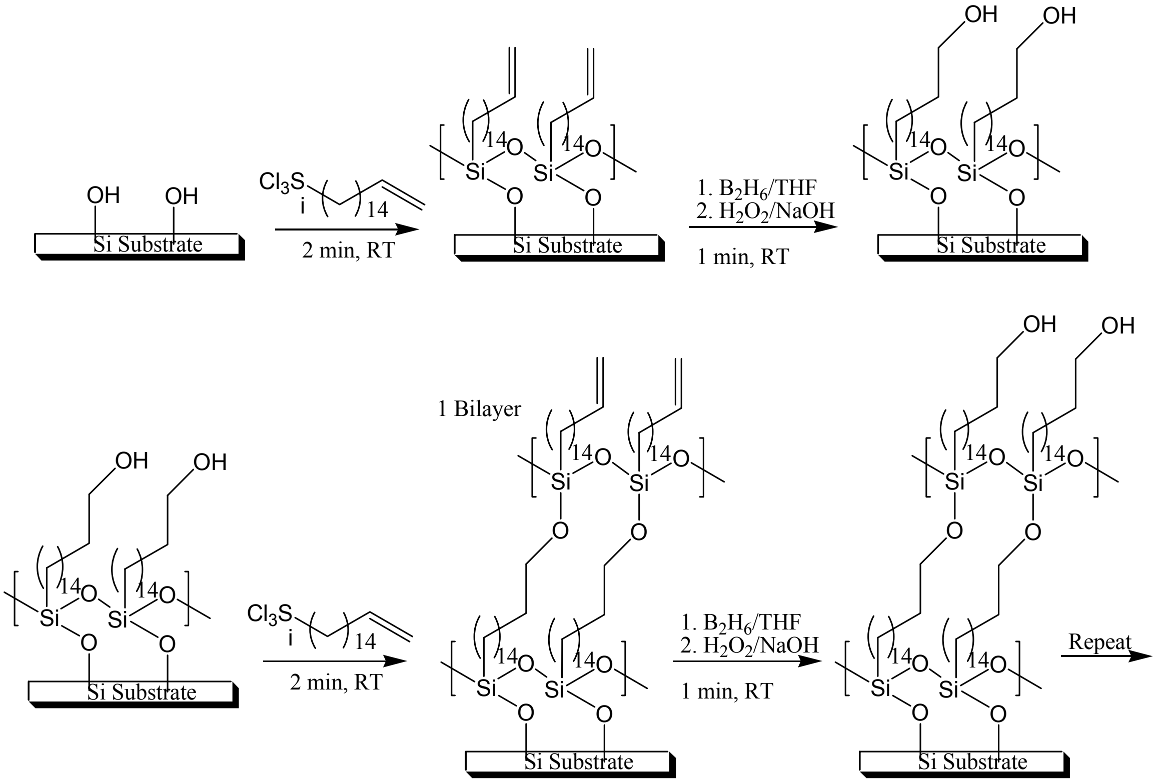


Figure 1-8. Multilayer formation of 15-hexadecenyltrichlorosilane using chemisorption and subsequent activation.

In 1996 Bergbreiter and Crooks published an article that used functionalized polymers to achieve layer-by-layer assembly on a gold substrate.[28] By using polyvalent polymers, they were able to create hyperbranched LbL films via condensation reactions. In their scheme, gold was first functionalized with mercaptoundecanioc acid to form a self-assembled monolayer (SAM) terminated with $–CO_2H$ groups. These acid groups were functionalized to from a mixed anhydride. Then an α,ω-diamino-terminated poly(*tert*-butyl acrylate) (H_2NR-PTBA-RNH_2) was added. The PTBA was thus coupled to the surface via amide bonds. Then *tert*-butyl esters bound to the surface were cleaved by acidolysis to form a poly(acrylic acid). This PAA layer could then be converted again to a mixed anhydride and allowed to react with more α,ω-diamino-terminated poly(*tert*-butyl acrylate) to yield a second layer (Figure 1-9). Repetition of the steps yielded multiple layers. The polymers are connected to each other via the terminal amino groups forming amide bonds with the PAA. Due to the polyvalent nature of the PAA, there are an abundance of $–CO_2H$ groups that can be used for subsequent functionalization. This also led to the layers to grow at a nonlinear rate allowing for increased layering and functionalization over traditional LbL.

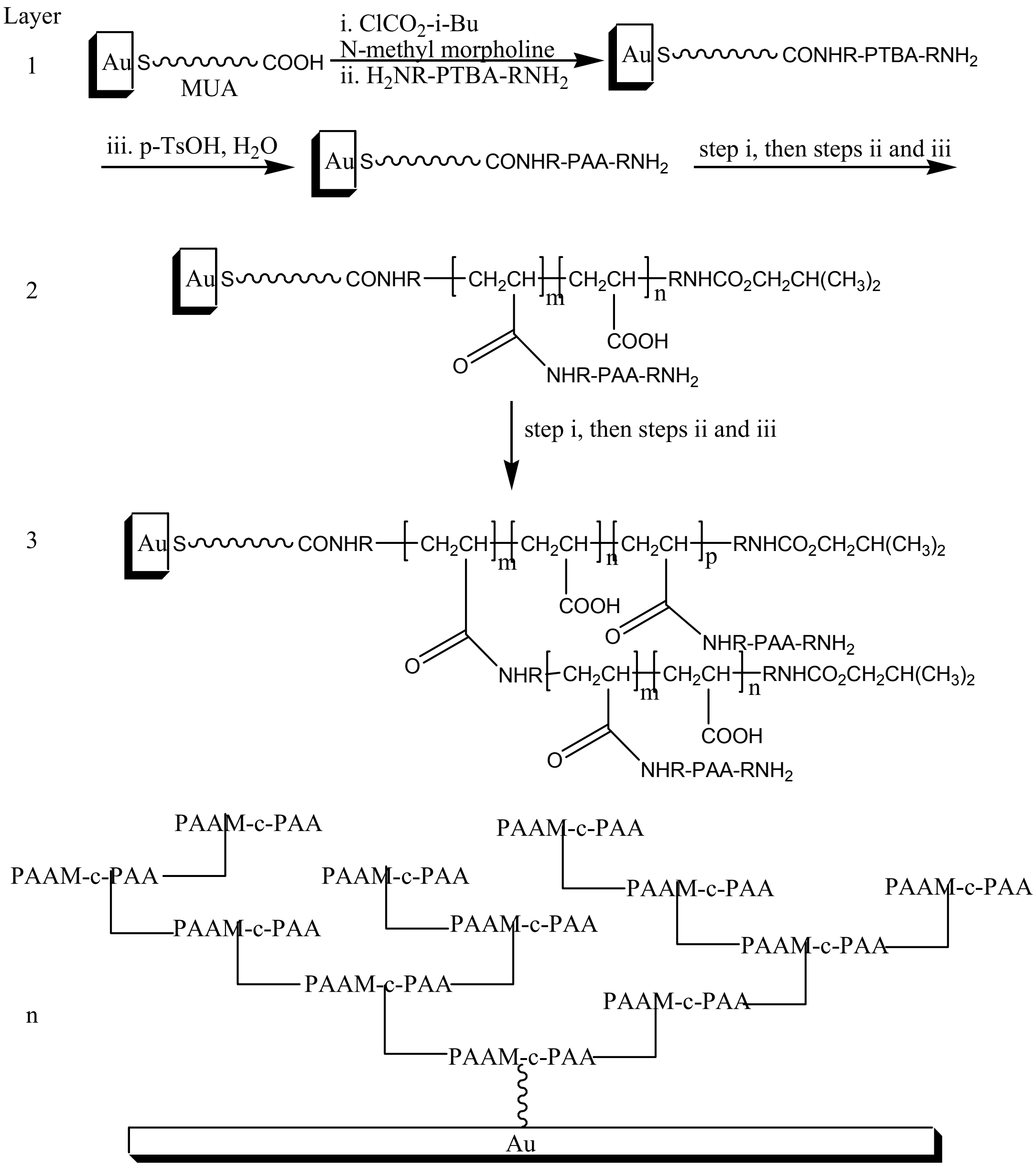


Figure 1-9. Hyperbranched polymer grafts prepared on a mercaptoundecanioc acid – modified gold substrate. H_2NR-PTBA-RNH_2 is an amine-terminated poly(*tert*-butyl acrylate) (R = $C(CN)(CH_3)(CH_2)_2CONH(CH_2)_2$), PAAM-c-PAA represents a random copolymer of poly(acrylic acid) and the poly(acrylamide) formed from poly(acrylic acid) carboxylic acid groups and the amines of the hydrolyzed PTBA derivative.

The grafting of PTBA groups on gold and later on PE using these procedures was monitored with ATR-IR spectroscopy and water contact angle goniometry. Control reactions omitting formation of the mixed anhydride were conducted and yielded very little layer growth. This suggests that covalent bond formation occurs and that the assemblies formed are not just ionic or H-bonded layer-by-layer assemblies on a gold surface. Other experiments showed that the high density of carboxylic acid groups in the PAA allowed for complexation of both iron and nickel.

In 2002, Akashi's group used two different polymers to facilitate layer-by-layer assembly on quartz crystal.[29] Poly(acrylic acid) (PAA) and poly(vinylamine)-co-(*N*-vinylisobutyramide) were used to form a thermoresponsive hydrogel. Similar to the earlier work by Bergbreiter and Crook, the PAA had to first be activated to allow for amidation. Instead of ethyl chloroformate, 1-ethyl-3(3-(dimethylamino)propyl)carbodiimide (EDC) was used to activate the –CO_2H group. Film formation was analyzed using atomic force microscopy, a quartz crystal microbalance, reflection-absorption spectra, and contact angle analysis. In this example, the Akashi group was able to assemble multiple layers with less steps than previous reports because the PAA was pre-activated in a solution containing EDC prior to substrate immersion.[28]

Multilayer Assembly on Polyethylene

Polyolefins have rarely been used as a substrate for LbL assembly. In 2006, Bergbreiter and Grunlan published an article using poly(ethyleneimine) (PEI) and poly(methyl vinyl ether-*alt*-maleic anhydride) (Gantrez) as a way to effect multilayer assembly (Figure 1-10).[7] PE was first treated with chromic acid to oxidize the surface and ethyl chloroformate was used to activate the acids on the surface, forming mixed anhydrides. Amide bonds were formed with the addition of PEI. The PEI was treated with triethylamine and then Gantrez. Because of the polyvalent nature of each polymer the surface contains excess amines and excess anhydrides. This allows for LbL assembly to occur with the addition of each polymer and subsequently increases the concentration of functional groups. As more layers are assembled, more amines or anhydrides will be present.

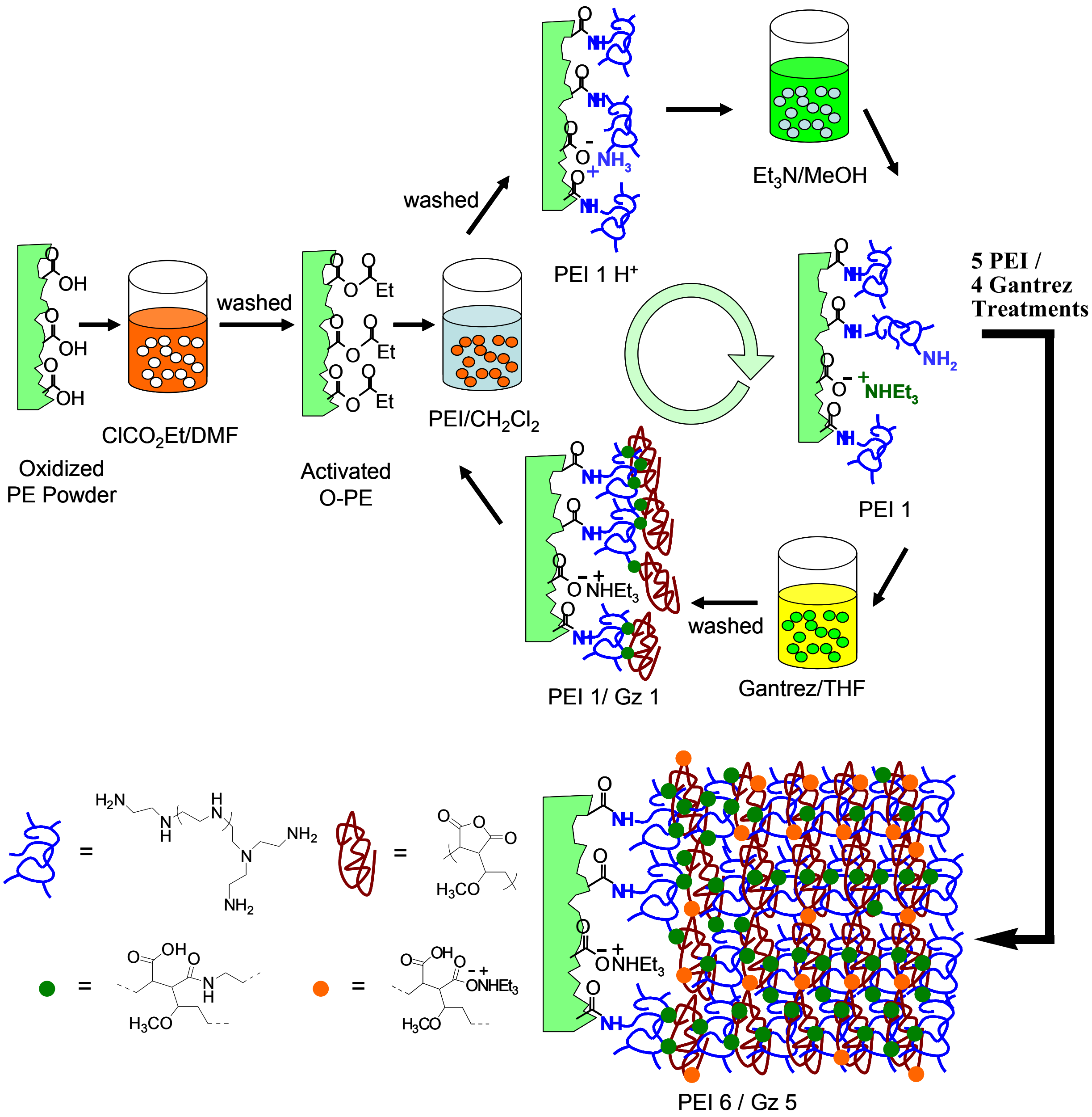


Figure 1-10. Procedure for covalent LbL assembly of PEI/Gantrez on oxidized PE particle surface.

“Click” Chemistry

All of the above methods, electrostatic self-assembly, assembly based on hydrophobicity, and covalent layer-by-layer assembly have received considerable attention. However, alternative chemistry to form covalent LbL assemblies remains of interest. In the work I’ve done, I have explored “click” chemistry as a means for layer-by-layer assembly. Prior to this report, only Sharpless, Hawker, and Caruso have described using “click” chemistry for surface modifications.[30,31]

The term “click” was first introduced as a description of a reaction by Sharpless in 2001. His stringent criteria were that a reaction can be classified as a “click” reaction only if: a reaction is modular; a reaction is wide in scope; a reaction gives high yields; a reaction generates easily removable byproducts; a reaction is regio- and stereospecific; a reaction must occur under simple reaction conditions and be insensitive to water and oxygen; a reaction must use a benign or easily removable solvent; and a reaction must use readily available starting materials.[9]

Perhaps the most well known and most facile of the click reactions is the Cu(I) catalyzed version of Huisgen’s 1,3-dipolar cycloaddition involving azides and alkynes (Figure 1-11).[32] The azide group is a stable functionality that can be carried along through various other reactions and is stable to dimerization, reduction, oxidation, and hydrolysis.

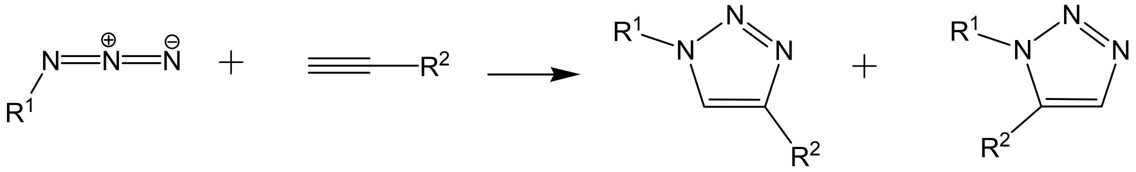


Figure 1-11. Example of Huisgen's 1,3-dipolar cycloaddition.

Huisgen's original method for triazole preparation called for high temperatures and long reaction times.[32] These reactions were not regioselective. With the development of Sharpless's method, a Cu(I) catalyst could be used, causing the reaction to proceed in water at room temperature in a matter of minutes giving only the 1,4 product (Figure 1-12). Reactions occur with many sorts of azides and alkynes. More electron deficient alkynes react faster.

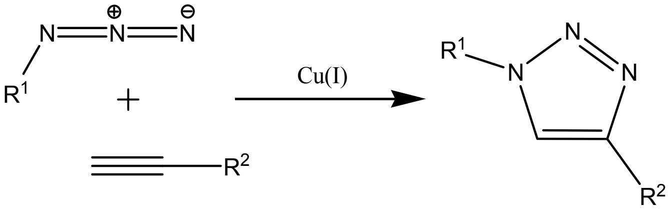


Figure 1-12. Example of "click" triazole formation.

"Click" Layer-by-Layer Assembly

Using linear polymers containing azides and alkynes as substrates in layer-by-layer assembly using "click" chemistry was recently reported by Caruso.[31] Caruso used poly(acrylic acid)(PAA) functionalized with either azides (PAA-Az) or alkynes (PAA-Alk) in sequential steps with copper sulfate/sodium ascorbate as the catalyst. Before functionalized PAA could be assembled on the surface, the surface had to be modified. The substrate (gold, silica, or quartz) was oxidized with piranha solution and a single monolayer of PEI was adhered to the surface using electrostatic interactions. The functionalized substrate was then dipped in a solution containing the PAA-Az copolymer and allowed to react for 20 min before being rinsed with water. This allowed for the PAA-Az to be adhered to the amine groups on the surface electrostatically. Next, the substrate was dipped into a PAA-Alk polymer solution and allowed to react for 20 min, forming the covalent triazole linkers. The same sequence was repeated with PAA-Az solution. By repeating these steps, a multilayer system was formed (Figure 1-13). However, while Caruso used covalent "click" chemistry, foundation of Caruso's assembly is adhered via electrostatic interactions. Thus, the resulting layer-by-layer assembly could suffer from the same chemical and mechanical durability issues that electrostatically assembled layers suffer from.

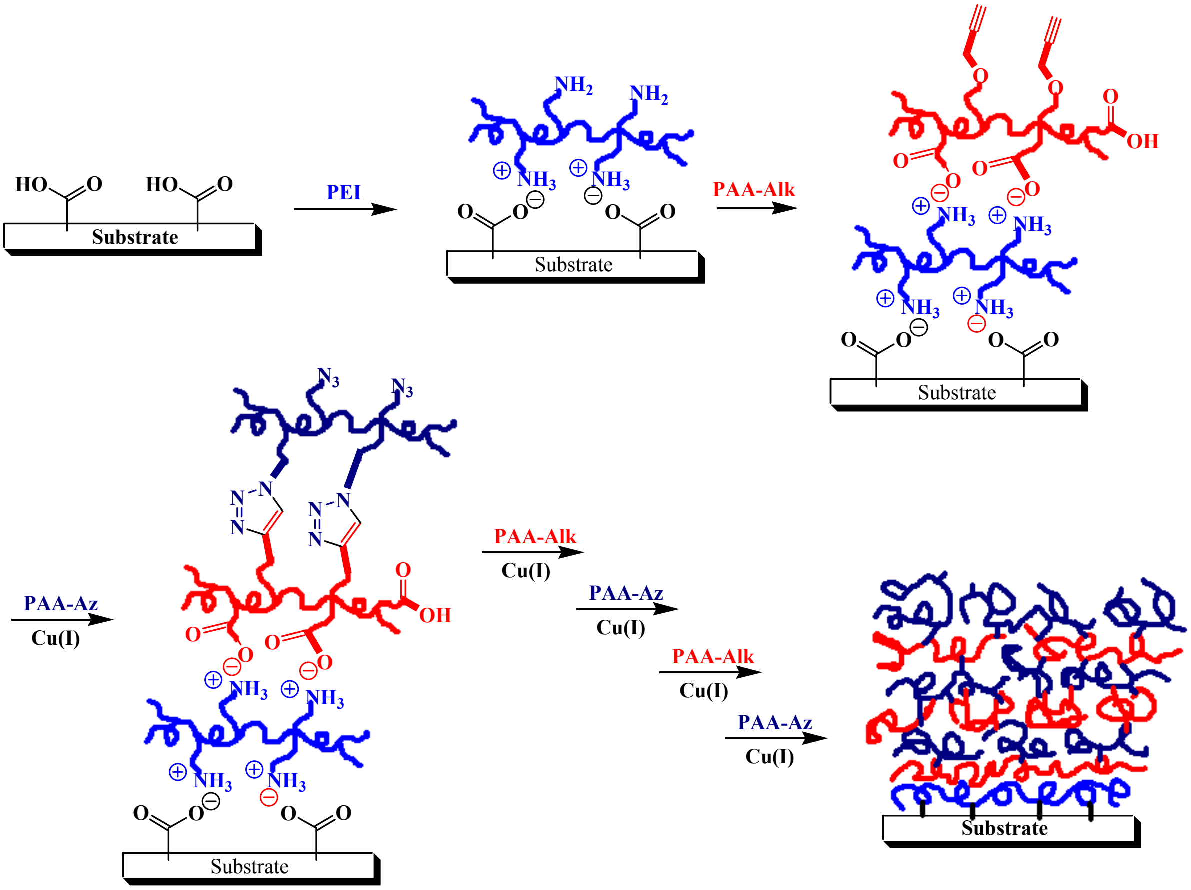


Figure 1-13. Representation of PAA click assembly on an oxidized substrate.

Non-covalent LbL assembly is an impressively simple technique. While the products can have low mechanical and chemical durability, it remains the most common route to multilayer assemblies. Covalent layer-by-layer assembly is an alternative. While many covalent assembly methods require long reaction times, multiple steps between layers, or reagents that must be prepared as needed, simple chemistry that uses commercial polymer anhydrides and polymeric amines or that uses “click” chemistry shows promise as an alternative route to functional surfaces. This thesis outlines a benchtop friendly method for a multilayer assembly using “click” chemistry on a polyethylene substrate. Each layer is covalently bound to the proceeding layer via a single “click” step using water as a solvent. Due to the polyvalent nature of the reagents, the product film is a mixture of azides, alkynes, and triazoles. These functionalities can act as “handles” to attach other groups.

CHAPTER II

SOLUTION PHASE MODEL REACTIONS AND POLYMER SYNTHESIS

To test the ideas to be used in “click” layer-by-layer assembly on a polyethylene surface, several steps are required. First, a synthesis of the necessary polymeric reagents had to be developed. Azide- and alkyne-modified poly(ethylene glycol) (PEG) and poly(*N*-isopropyl acrylamide)(PNIPAM) were prepared as examples of click macromolecular substrates for use in water. Polymers based on poly(*tert*-butyl acrylate)(PTBA) were also prepared for use in organic solvents. This chapter outlines the synthesis of these compounds.

Poly(ethylene glycol) (PEG) modified with a terminal azide goup was chosen to test the “click” reaction in an aqueous environment. PEG with reactive end groups is suitable because it is readily available and water soluble. Monomethyl-ether-PEG_{350} (**1**) was initially used as the starting material for a series of reactions. These reactions led to substrates that were used to form terminal triazoles. Methanesulfonyl chloride was first allowed to react with **1** to convert the alcohol into a good leaving group, forming the PEG_{350}-mesylate (**2**). An S_N2 reaction was then carried out using sodium azide to form **3**. The presence of the azide was established by the appearance of a signal corresponding to the $–CH_2-N_3$ at δ 3.4 ppm in the ^1H-NMR($CDCl_3$) spectrum. A peak at 2110 cm^{-1} in the infrared spectrum corresponding to the azide was also observed. To synthesize the 1,2,3-triazole, **3** was dissolved in water and an excess of propargyl alcohol was added. Copper(II) sulfate pentahydrate and sodium ascorbate were introduced and the reaction was allowed to proceed at room temperature for 24 h, forming **5**. This reaction scheme is shown in Figure 2-1. The formation of the triazole was established by the appearance of the aromatic C-H signal at δ 7.8 ppm in the ^{1}H-NMR($CDCl_3$) spectrum.

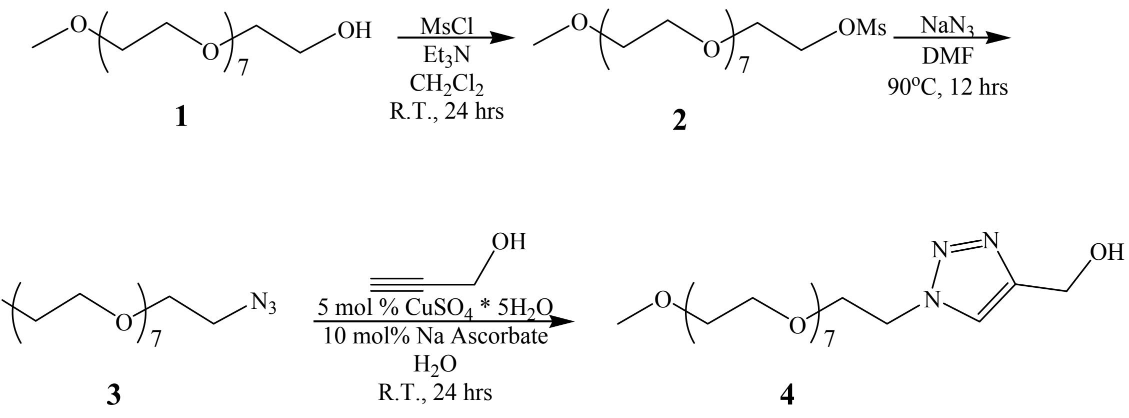


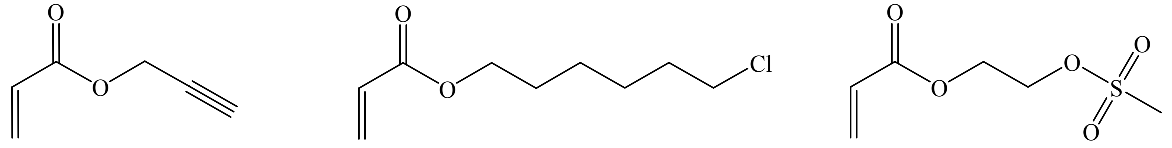
Figure 2-1. Reaction scheme to form a PEG_{350} 1,2,3-triazole.

Monomer Synthesis

While the PEG-azide could in principle be used for functionalizing a surface, this terminally functionalized polymer does not have the polyvalency needed for covalent layer-by-layer assembly. Other polyfunctional polymers had to be prepared for use in LbL assembly.

To take advantage of "click" chemistry for covalent LbL assembly, monomers were prepared that would function as building blocks. These monomers consisted of propargyl acrylate (**5**), 6-chlorohexyl acrylate (**6**), and 2-(methylsulfonyloxy)ethyl acrylate (**7**) (Figure 2-2).

Acryloyl chloride was added to a solution of propargyl alcohol and triethylamine in dichloromethane to form **5**. Monomers **6** and **7** were prepared in such a fashion to contain leaving groups that could later undergo substitution with sodium azide. Azide containing monomers were not synthesized due to safety concerns.[33] To form **6**, acryloyl chloride was added to a solution of dichloromethane containing 1-chlorohexanol and triethylamine. Monomer **7** was prepared using a different approach. The hydroxyl group on 2-hydroxyethyl acrylate was converted to the mesylate by adding methanesulfonyl chloride to a solution of dicloromethane containing 2-hydroxyethyl acrylate and triethylamine.



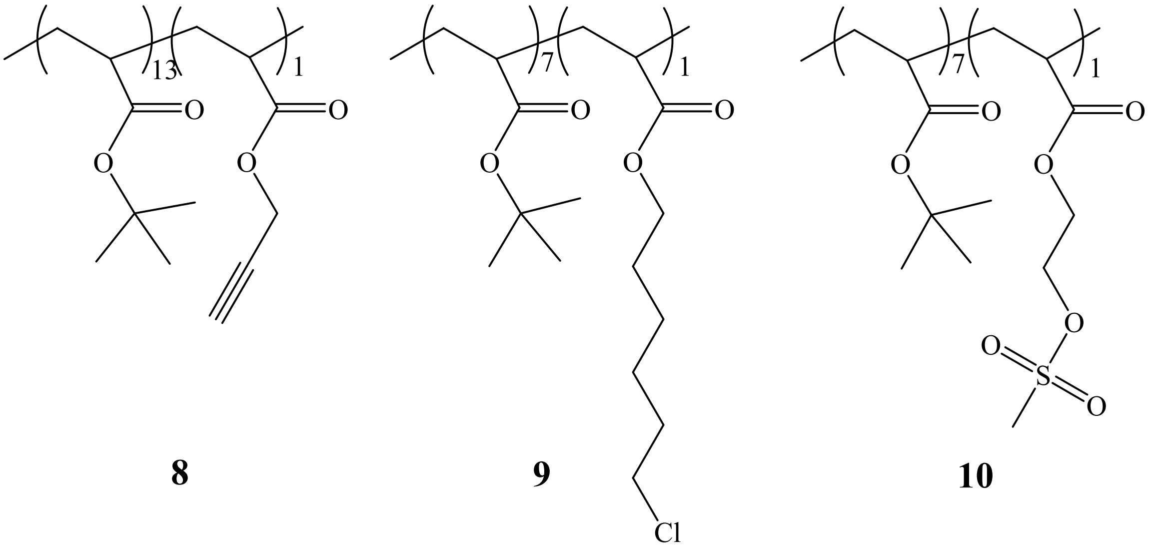
5 **6** **7**

Figure 2-2. Functionalized monomers for making alkyne- and azide-containing copolymers.

Polymer Synthesis

Copolymers containing the above monomers were then prepared. The major component of these copolymers consisted of *tert*-butyl acrylate (tBA) or *N*-isopropyl acrylamide (NIPAM).

Free radical polymerizations using azobisisobutyronitrile (AIBN) were performed with tBA and **5**, **6**, or **7** to form the copolymers in Figure 2-3. These polymers were prepared by adding AIBN, tBA, and the appropriate monomer to a solution of benzene and bubbling nitrogen through the solution for 45 min. The solution was then heated at 60 °C for 12 h to form **8**, **9**, or **10**. After removal of benzene under reduced pressure using a rotary evaporator the crude product polymer was dissolved in acetone and precipitated in a methanol/water mixture to remove excess monomer. These PTBA-based copolymers were chosen as models for performing various "click" reactions in an organic solvent. After polymer formation, *tert*-butyl groups can be cleaved by acidolysis to form a poly(acrylic acid)-based copolymer, which is water soluble.



8 **9** **10**

Figure 2-3. *Tert*-butyl acrylate copolymers.

To test whether **8** could be used for "click" chemistry; a low molecular weight alkyl azide was prepared. Methanesulfonyl chloride was added to a solution of dichloromethane containing octadecanol and triethylamine to form octadecyl methanesulfonate. The octadecyl methanesulfonate was then added to a solution of dimethylformamide (DMF) containing sodium azide and allowed to react for 12 h at 90 °C, to form octadecylazide.

Because PTBA is not water soluble, “click” reactions on **8** had to be performed in an organic solvent with a soluble copper catalyst. Tetrahydrofuran (THF) was chosen as the solvent and bromotris(triphenylphosphine) copper(I) ($(PPh_3)_3CuBr$) was selected as the soluble catalyst. An excess of octadecylazide was added to a THF solution containing **8**, the copper catalyst, and Hunig’s base. This reaction was degassed for 30 min. and allowed to react at 50 °C under N_2 for 12 h to form **11** (Figure 2-4).

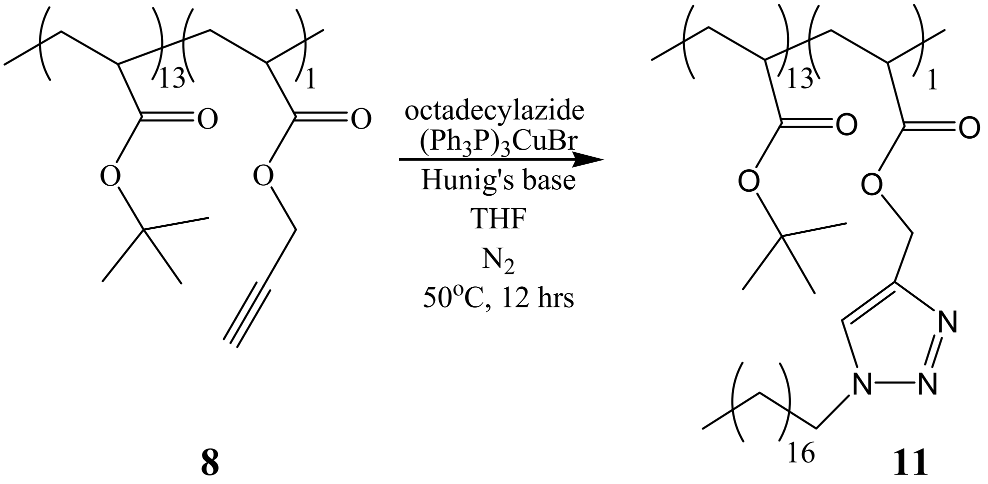


Figure 2-4. “Click” reaction on poly((*tert*-butyl acrylate)-co-(propargyl acrylate)).

The number average molecular weight (M_n) of **8** was 2.3 x 10^4 Da as determined by gel permeation chromatography (GPC). The M_n of **11** was 2.7 x 10^4 Da. This increase can be attributed to the formation of the octadecyl triazole. The disappearance of the –CH_2-alkyne signal at δ 4.6 ppm in the ^{1}H-NMR($CDCl_3$) spectrum and the appearance of an aromatic C-H signal at δ 7.8 ppm were also indicative of triazole formation. Triazole formation was chemically proven by using an alkyl iodide to form a triazolium salt. Iodomethane was added to **11** in acetone and allowed to react at 40°C for 3 days (Figure 2-5). Triazole conversion was confirmed by comparing the integral (1.68) of the -CH_2-alkene peak at δ 5.2 ppm in the ^{1}H-NMR($CDCl_3$) spectra of **11** to the integral (1.13) of the –CH_2-alkene peak of **12** at 4.38 ppm. The ratio corresponds to ~33% conversion.

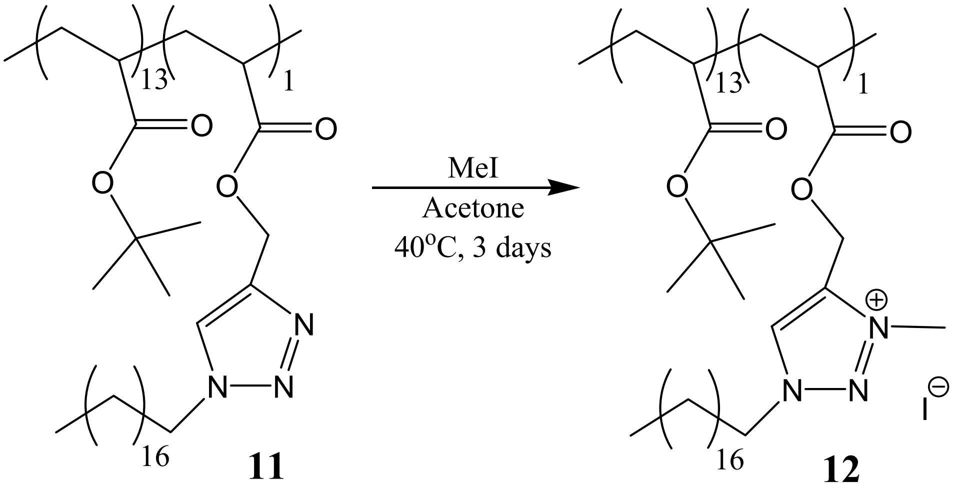
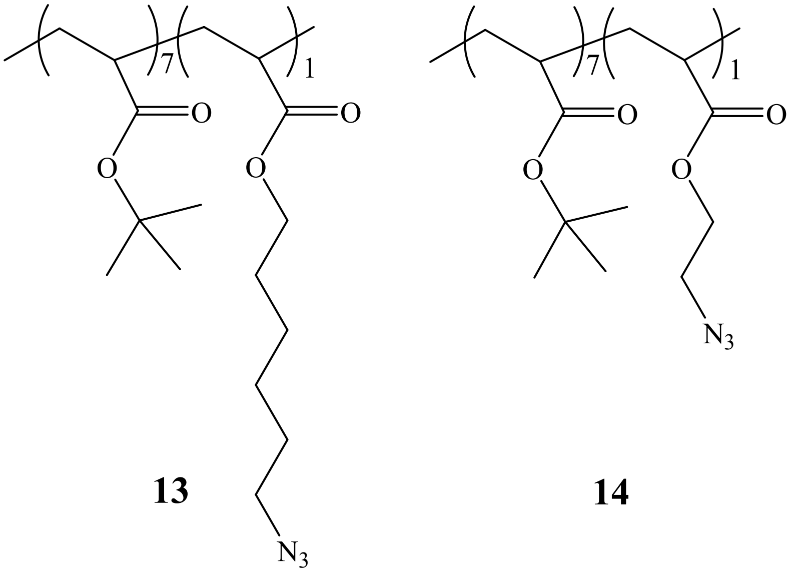


Figure 2-5. Formation of triazolium saltwith MeI and **11**.

Polymer **9** was converted to the azide by dissolution in DMF and the addition of sodium azide. The reaction was allowed to proceed at 90°C for 12 h to form poly((*tert*-butyl acrylate)-co-(6-azidohexyl acrylate)) (**13**). Polymer **10** was converted to poly((*tert*-butyl acrylate)-co-(2-azidoethyl acrylate)) (**14**) (Figure 2-6) using the same procedure.



13

14

Figure 2-6. Azide-containing poly(*tert* butyl acrylate)-copolymers.

Octyne and **13** were added to a solution of THF that contained $(PPh_3)_3CuBr$ and Hunig's base to form **15** (Figure 2-7). N_2 was bubbled through the reaction for 30 min. and the reaction was allowed to react at 50°C for 12 h. The ^{1}H-NMR($CDCl_3$) spectrum showed a signal at δ 4.3 ppm that corresponded to the $–CH_2$-N- of the triazole. Unfortunately, purification proved impossible. After removing the THF from the crude reaction mixture, **15** became insoluble in a variety of organic solvents for unknown reasons. Because of this, only crude ^{1}H-NMR($CDCl_3$) spectra were obtained.

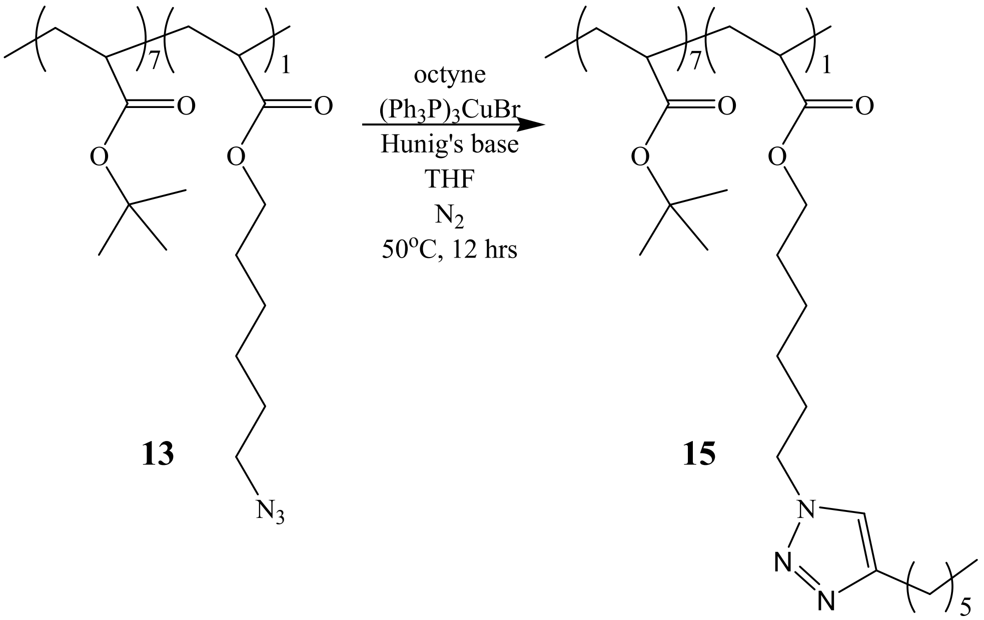


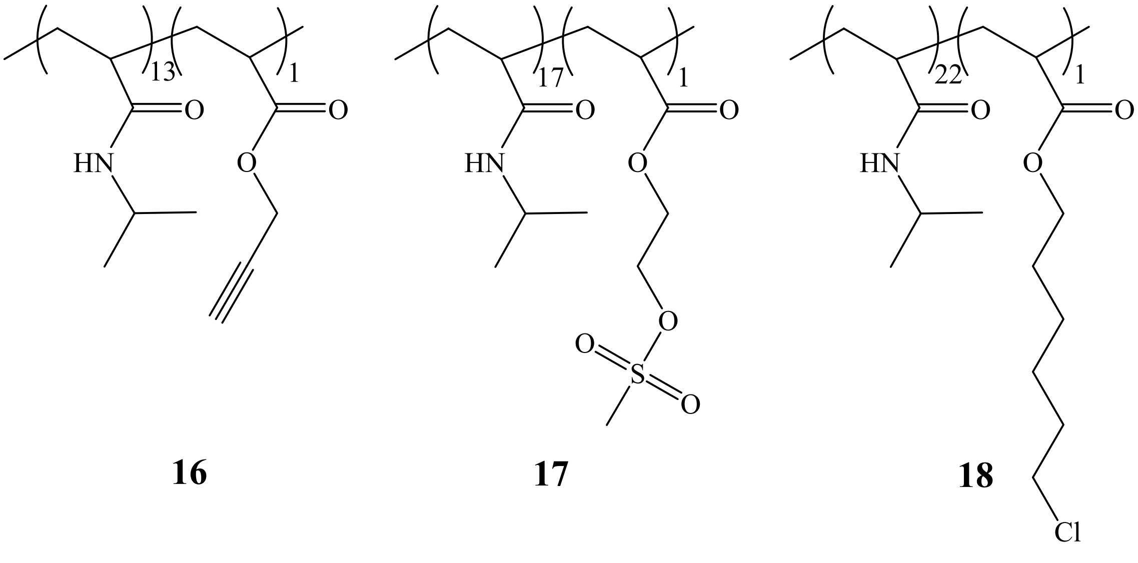
Figure 2-7. "Click" reaction of poly((*tert*-butylacrylate)-co-(6-azidohexyl acrylate).

PTBA-based polymers containing azides or alkynes were prepared and used in "click" reactions. However, these PTBA-based polymers were not water soluble and their formation required the use of an air sensitive catalyst. Also, purification proved difficult and in some cases, impossible.

To alleviate these problems, a new family of polymers was prepared that used *N*-isopropyl acrylamide (NIPAM) as the major component. By making poly(*N*-isopropyl acrylamide) copolymers (Figure 2-8), "click" reactions were insensitive to air and used water as the solvent. Also, purification was very easy, requiring only simple precipitations.

The first copolymer made was poly((*N*-isopropyl acrylamide)-co-(propargyl acrylate)) (**16**) (PNIPAM-Alk). NIPAM and AIBN were dissolved in benzene, 1,4-

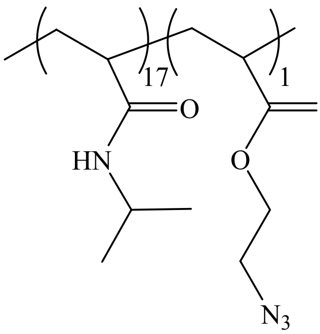
dioxane, or *tert*-butanol. Monomer **5** was then added and the solution was degassed under N_2 for 45 min. and allowed to react at 50°C for 12 h. However, when 1,4-dioxane or benzene was used as the solvent, the number average molecular weights of **16** were less than 1.3×10^4 Da as determine by GPC. Higher molecular weights were desired for use in LbL assembly. By changing the solvent to *tert*-butanol, molecular weights of 6.0×10^4 Da (GPC) were achieved. In an alternative procedure, poly((*N*-isopropyl acrylamide)-co-(2-(methylsulfonyloxy)ethyl acrylate)) (**17**) and poly((*N*-isopropyl acrylamide)-co-(6-chlorohexyl acrylate)) (**18**)were also prepared using AIBN and **6** or **7** in benzene. In these cases, a precipitate formed. These PNIPAM-based polymers were purified by dissolution in THF, acetone, or chloroform and precipitation into hexanes.



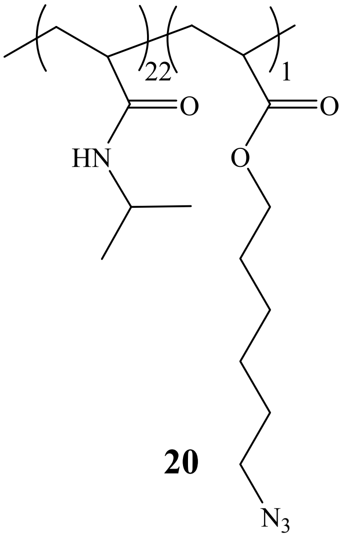
16 **17** **18**

Figure 2-8. Poly(*N*-isopropyl acrylamide)-based copolymers.

Polymers **17** and **18** were converted to the azide separately by dissolving each in DMF, adding sodium azide, and heating to 90°C overnight, forming **19** and **20** (Figure 2-9). These polymers had a M_n between 1.4 x 10^5 Da and 2.2 x 10^5 Da (GPC). Because PNIPAM is water soluble, a simple washing could not remove excess sodium azide, sodium chloride, or sodium mesylate. However, these impurities could be removed by taking advantage of the fact that **19** and **20** have a lower critical solution temperature of 30 and 29 °C respectively. To remove these impurities, aqueous solutions containing the polymer were centrifuged at 60°C twice. Because PNIPAM has an LCST, the polymer precipitated during centrifugation and could then be separated from the aqueous solution of salts. The final product polymer isolated from centrifugation was dried under vacuum.



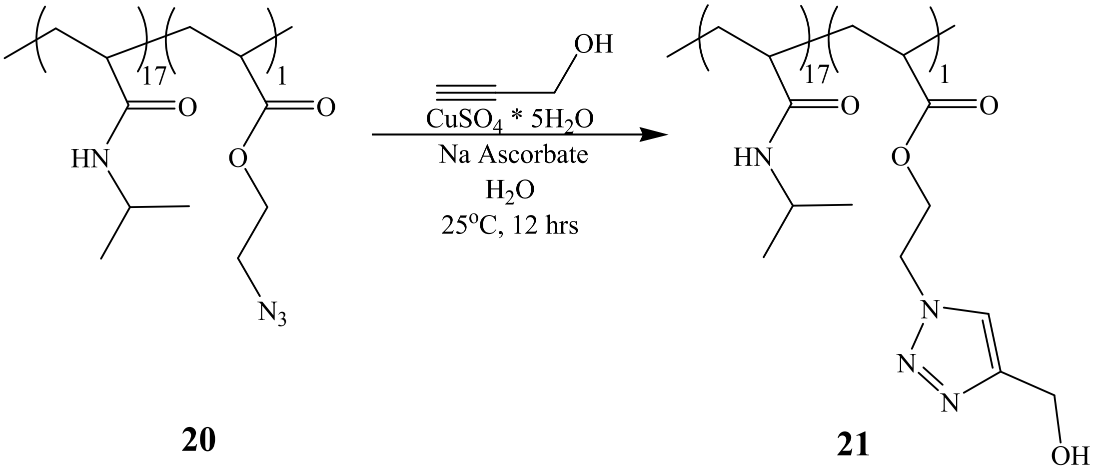
19



20

Figure 2-9. Poly(*N*-isopropyl acrylamide)-azide containing copolymers.

To show the versatility of the polymer and of "click" chemistry, both THF and water were used as solvents in "click" reactions with **19**. Copper sulfate pentahydrate, sodium ascorbate, and **19** were dissolved in water and propargyl alcohol was added to the solution. The reaction was allowed to proceed at 25 °C resulting in **21** (Figure 2-10). After 16 h, water was removed at reduced pressure using a rotary evaporator. The crude product was dissolved in THF and precipitated into hexanes. This resulted in the appearance of an aromatic –C-H triazole signal present at δ 7.4 ppm in the ^{1}H-NMR ($CDCl_3$) spectrum.

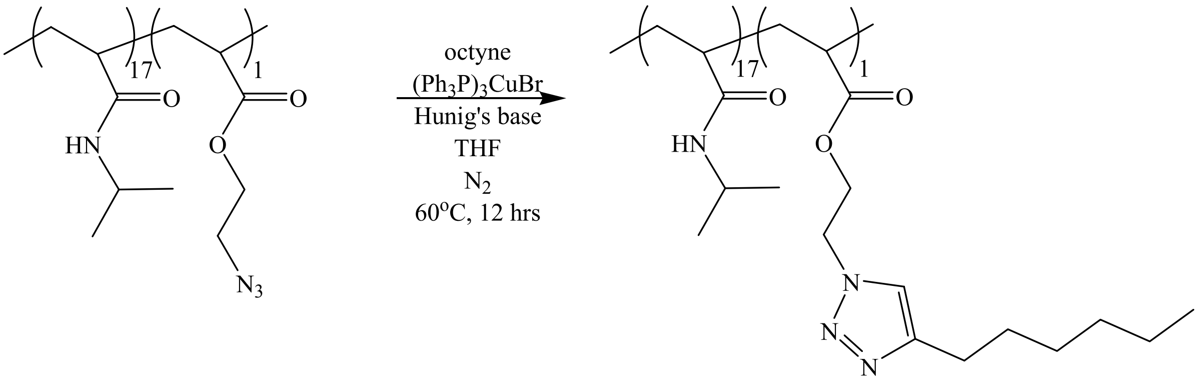


20

21

Figure 2-10. Poly((*N*-isopropyl acrylamide)-co-(2-azidoethyl acrylate)) "click" reaction in water.

Polymer **19** was also added to a solution of THF containing octyne, $(PPh_3)_3CuBr$, and Hunig's base. The solution was degassed with N_2 for 30 min. and heated at 60 °C for 12 h (Figure 2-11). The solution was concentrated and precipitated into hexanes, redissolved in THF, and precipitated again. This purification proved to be much easier than the column purification used on **11**. The formation of **22** was established by the appearance of a triazole aromatic –C-H signal at δ 7.5 ppm in the ^{1}H-NMR ($CDCl_3$) spectrum.



19 **22**

Figure 2-11. Poly((*N*-isopropyl acrylamide)-co-(2-azidoethyl acrylate)) "click" reaction in tetrahydrofuran.

Synthetic routes were developed for the production of polyfunctional copolymers that can be used in LbL assembly on a surface. Initially, copolymers soluble in organic media were explored as a possible means for LbL assembly. However, synthesis and purification of the PTBA-based copolymers proved difficult. To circumvent this problem, PNIPAM-based copolymers were prepared. These copolymers were easy to purify and were soluble in both aqueous and organic solutions. The water solubility of the PNIPAM-based copolymers, their LCST, and the air stability of the copper(II) sulfate pentahydrate catalyst make this system ideal for LbL assembly using "click" chemistry.

CHAPTER III

POLYETHYLENE SURFACE MODIFICATION

Layer-by-layer assembly on a polyethylene surface has been effected by the Bergbreiter group using a variety of strategies.[7] These include covalent assembly and hybrid procedures that use both covalent modification and ionic LbL assembly.[7,28] However, LbL assembly using "click" chemistry on a polyethylene substrate has not been reported. With the development of the water soluble, PNIPAM-based azide and alkyne containing polyfunctional polymers described in chapter II, I was able to show that LbL assembly can be achieved on a functionalized polyethylene substrate. Polyethylene films are inert polymers with no surface functionality. Thus, polyethylene films had to be subjected to a series of reactions to introduce alkynes that could be used to initially bind an azide containing polymer via triazole formation. A series of alternating reactions of azide and alkyne containing polymers was then carried out. The LbL assembly process was followed by attenuated total reflectance infrared (ATR-IR) spectroscopy. X-ray photoelectron spectroscopy (XPS), contact angle goniometry, and fluorescence microscopy were also used for surface analysis. Control reactions omitting various components needed for triazole formation were also performed. This chapter describes the initial surface functionalization, the LbL assembly process, and the control reactions on a polyethylene substrate. The results of various surface analyses will also be discussed.

Polyethylene films were functionalized using a series of reactions beginning with surface oxidation. This oxidation was carried out by immersion of a polyethylene film in a sulfuric acid solution containing chromium(III) oxide.[34] This reaction was allowed to proceed for 5 min. at 90 °C. Carboxylic acid groups were introduced onto the surface and their presence verified by the appearance of a corresponding carbonyl stretch at ~1708 cm^{-1} in the ATR-IR spectra. The oxidized polyethylene film (PE_{ox}) was then immersed in a solution of dichloromethane containing ethyl chloroformate and *N*-methyl morpholine—a process that introduces mixed anhydrides to the surface. This reaction was allowed to proceed at room temperature for 45 min. Mixed anhydride formation was evident by the appearance of a new peak in the ATR-IR spectrum at ~1825 cm^{-1}. After three washings with dichloromethane, the mixed anhydride polyethylene film (PE_{MA}) was immersed in a solution of propargyl alcohol and triethylamine to introduce the alkyne functionality. The PE_{MA} was stirred in this solution for 4 h at room temperature. The appearance of an ester stretch at ~1740 cm^{-1} in the ATR-IR spectrum indicated the formation of propargyl ester groups on the surface. An alkyne peak was not seen. The entire reaction scheme introduction of a surface alkyne group is depicted in Figure 3-1.

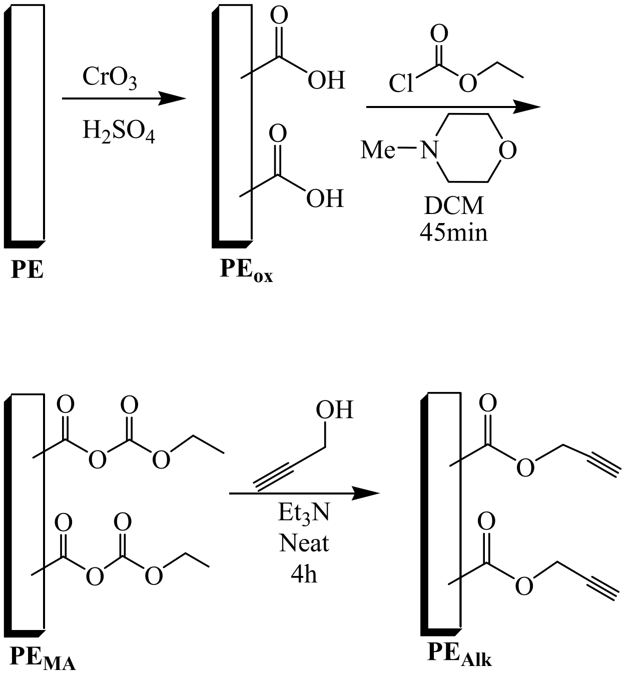
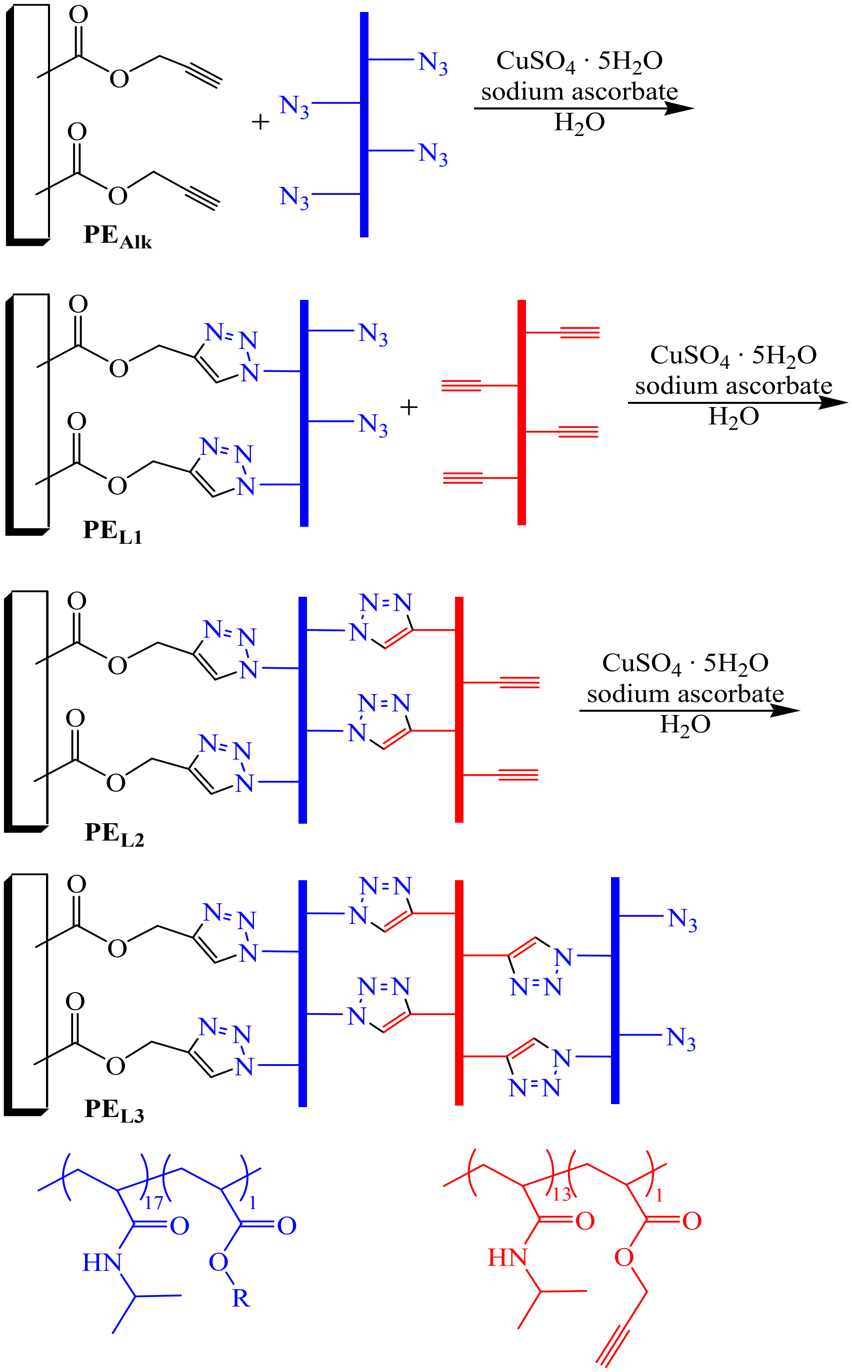


Figure 3-1. Alkyne functionalization of a polyethylene film.

Nomenclature

Once a polyethylene surface was functionalized with alkynes, copolymers with azide (**19** or **20**) functionality were introduced. The LbL assembly was carried out with PNIPAM polymers. Thus, the “click” reactions could be carried out in water using copper(II) sulfate pentahydrate and sodium ascorbate. The use of water and PNIPAM macromolecular reagents has several advantages. First of all, the need for organic solvents is eliminated. Second, an expensive organic-soluble copper catalyst is no longer needed. Also, by using water and the copper(II) sulfate catalyst, the reaction is no longer sensitive to air and takes place at room temperature. After a surface was treated with the azide functionalized copolymer, the product polyvalent azide surface was washed with water. Then copolymers with alkyne functionality (**16**) were allowed to react with the resulting azide-rich surface. After this reaction was complete (1 h at 25 °C), the alkyne-rich surface was washed with water. Each step where a functionalized copolymer is introduced, it is considered introducing a “layer”. In the multilayer assembly process, the polyethylene film products are designated as PE_{Lx} with “x” representing the layer number. Since all of the films used for LbL assembly start as PE_{Alk}, the first layer introduced is always an azide functionalized copolymer. This film is designated as a PE_{L1} film. Subsequent reaction of an alkyne functionalized copolymer with this PE_{L1} surface indroduces layer 2, and the product is designated PE_{L2}. This pattern continues all the way to a twelfth layer. An odd numbered layer is the product of an azide functionalized copolymer and has an excess of azides on the surface. An even numbered layer is the product of an alkyne functionalized copolymer and has an excess of alkynes on the surface (Figure 3-2).



19 R = $C_2H_4N_3$
20 R = $C_6H_{12}N_3$

16

Figure 3-2. Example of layer-by-layer assembly on a polyethylene film and the nomenclature used for each film.

Layer-by-Layer Assembly

All of the PE_{Lx} films were assembled with **16** acting as the PNIPAM-based alkyne. Two different PNIPAM-based azide copolymer reagents were used. One contained a two carbon linker (**19**) and the other contained a six carbon linker (**20**). LbL assembly reactions on PE_{Alk} were initially performed using **19** and **16**. PE_{Alk} immersion solutions were prepared using 100 mg of **19**, 5 mg of copper(II) sulfate pentahydrate, and 10 mg of sodium ascorbate in 12 mL of water. The PE_{Alk} film was stirred for 1 h, washed twice with water, once with acetone or ethanol, and dried by flowing N_2 across the surface. The resulting PE_{L1} was them stirred in an aqueous solution of **16**, copper(II) sulfate pentahydrate, and sodium ascorbate. After 1 h, the film was washed with water and acetone or ethanol to yield PE_{L2}. This procedure was repeated using a fresh solution of **19**, copper(II) sulfate pentahydrate, sodium ascorbate resulting in the azide-rich PE_{L3}. Next, a fresh solution containing **16**, copper(II) sulfate pentahydrate, and sodium ascorbate was stirred with the PE_{L3} film resulting in PE_{L4}. These procedures were repeated in an alternating fashion until a PE_{L12} system was prepared (Figure 3-3). Layer growth was monitored by the growth of the peaks at ~1545 cm^{-1} and ~1645 cm^{-1} corresponding to mono-substituted amides in the ATR-IR spectra. A spectra showing PE_{Alk}, PE_{L2}, PE_{L4}, PE_{L6}, PE_{L8}, PE_{L10}, and PE_{L12} is shown in Figure 3-4.

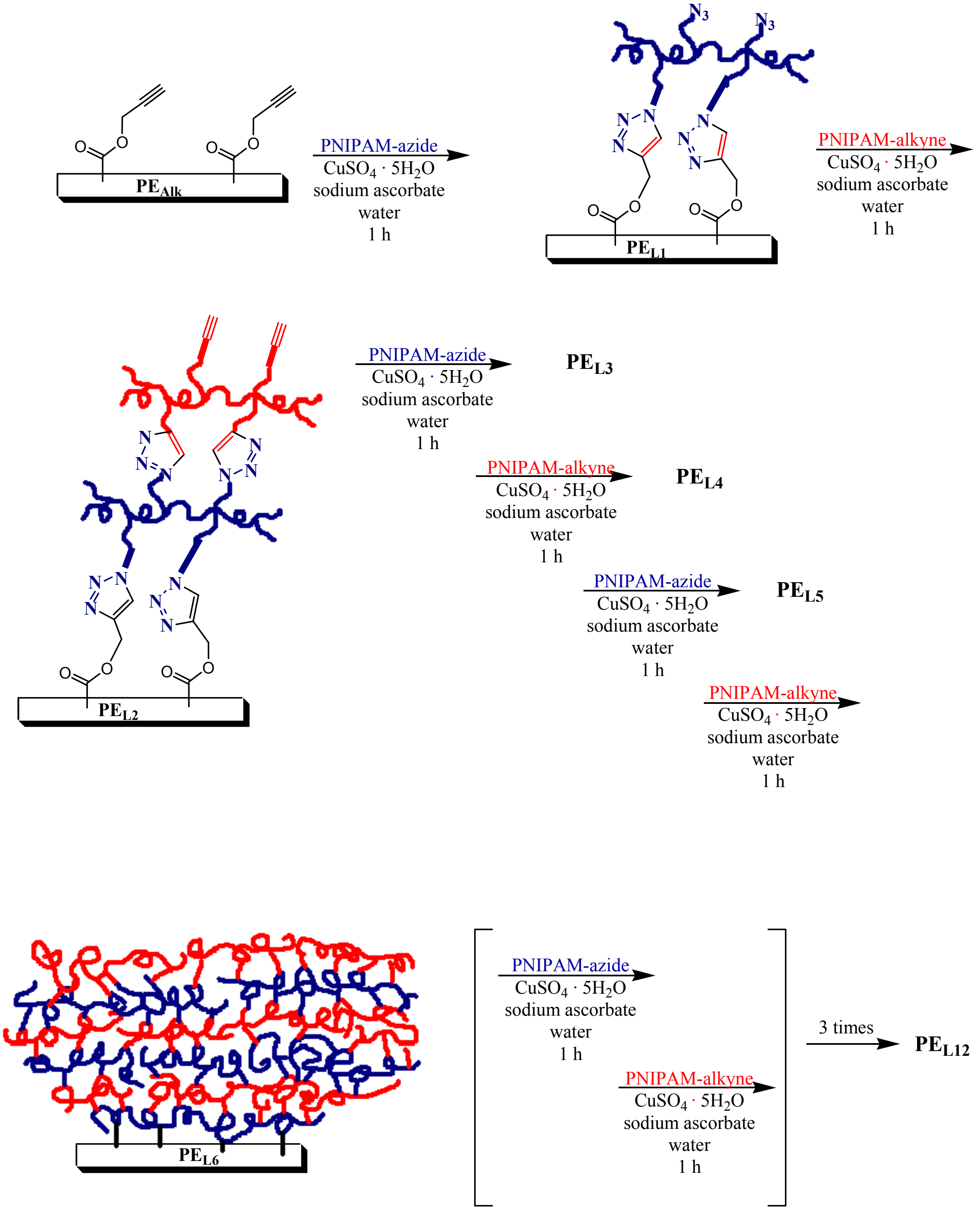


Figure 3-3. Representation of polyethylene layer-by-layer assembly using PNIPAM-based copolymers.

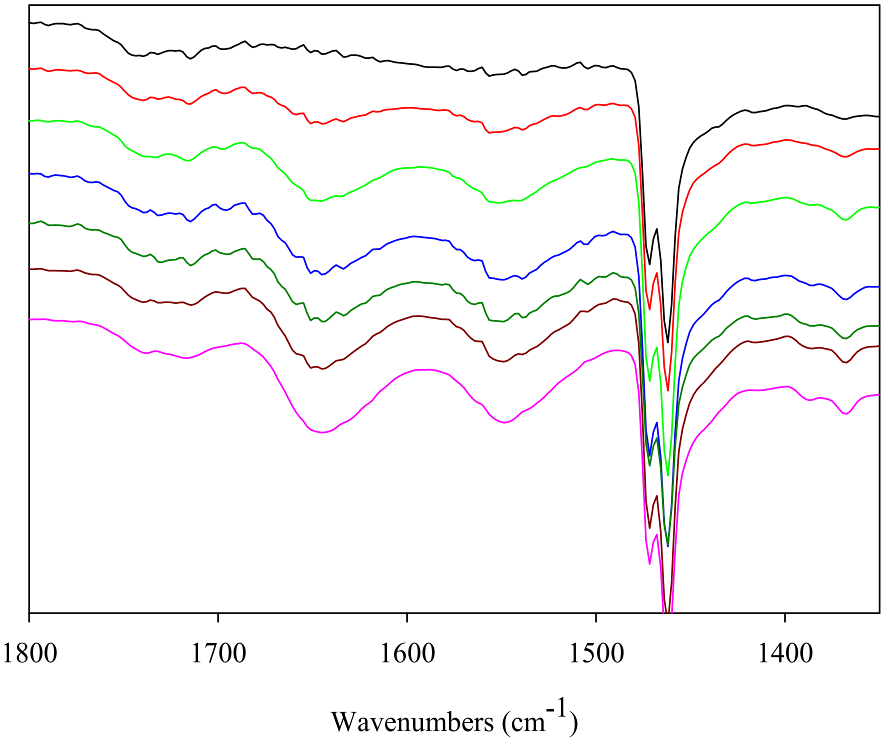


Figure 3-4. ATR-IR spectra showing layer growth using **16** and **19** (PE_{Alk} —; PE_{L2} —; PE_{L4} —; PE_{L6} —; PE_{L8} —; PE_{L10} —; PE_{L12} —).

A series of control reactions were carried out to show that the PNIPAM was not simply absorbing to the surface (e.g. via H-bonding or some other non-covalent process) and that covalent LbL assembly was taking place. Two PE_{Alk} films were immersed in a solution containing **19**, copper(II) sulfate pentahydrate, and sodium ascorbate. These films were allowed to react for 1 h to form PE_{L1}. They were washed three times with water and once with acetone. The film was then immersed in a solution containing **16**, copper(II) sulfate pentahydrate, and sodium ascorbate to form PE_{L2}. Once again, the films were subjected to a solution containing **19**, copper(II) sulfate pentahydrate, and sodium ascorbate to form PE_{L3}. At this point, one of the two PE_{L3} films was stirred in a solution containing only **16** for 1 h. The PE_{L4} film was then washed with water and subjected to a solution containing **19** for 1 h. The resulting PE_{L5} was subjected to alternating solutions of **16** and **19** until the product was PE_{L12}. The ATR-IR spectra showed very little growth after the initial third layer due to the lack of a copper catalyst. A second PE_{L3} film was immersed in a THF solution containing lithium aluminum hydride to reduce the azide groups on the surface. This PE_{L3} film was then stirred in an aqueous solution containing **16**, copper(II) sulfate pentahydrate, and sodium ascorbate for 1 h resulting in PE_{L4}. The film was then washed with water and subjected to a solution **19**, copper(II) sulfate, and sodium pentahydrate, resulting in PE_{L5}. The procedure was repeated with a solution containing **16** and the copper(II) system (PE_{L6}) and again with a solution containing **19** and the copper(II) system (PE_{L7}). These immersions were repeated to form a 12 layer system (PE_{L12}). Due to the lack of azide groups for **16** to bind to in the initial step that formed PE_{L4}, there was no way for subsequent layering reaction to affix to the surface. This led to very little growth observed in the ATR-IR spectrum.

These control reaction schemes are shown in Figure 3-5 and the ATR-IR spectrum comparing a PE_{L12} film to the two control reactions are shown in Figure 3-6.

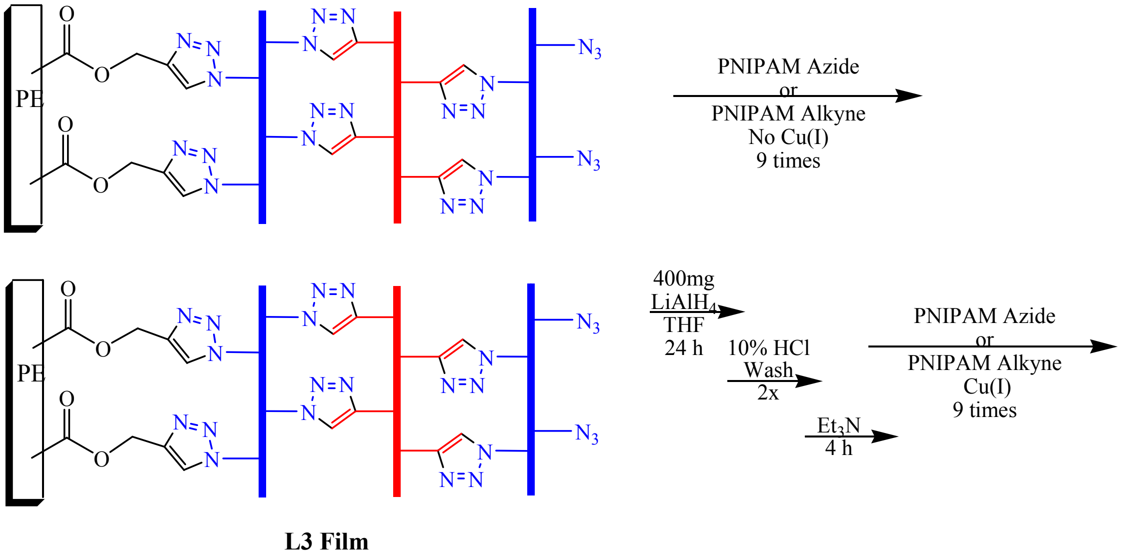


Figure 3-5. Control reactions on PE$_{L3}$ film.

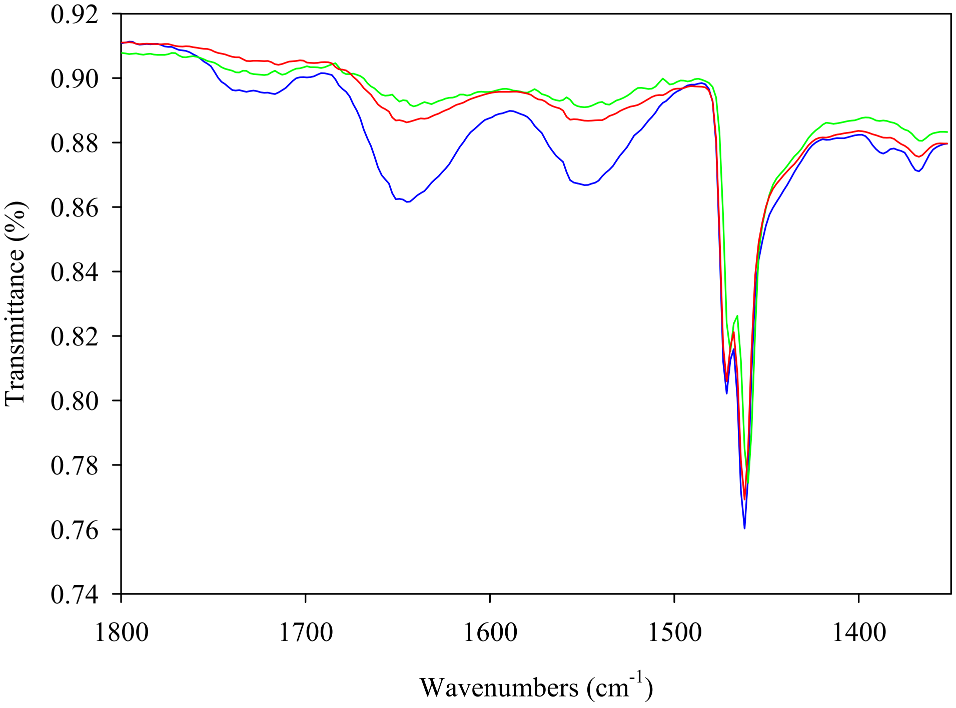


Figure 3-6. ATR-IR spectra of PE$_{L12}$ film and PE$_{L3}$ films with Cu omitted or chemical azide reduction (— PE$_{L12}$; — PE$_{L12}$ without copper after layer 3; — PE$_{L12}$, azide reduction after layer 3).

The small amount of growth in both control reactions led me to believe that a very small amount of physical absorption took place. However, the difference in the two control systems and the system assembled with both azides and copper present demonstrate that covalent linkers between layers were created via triazoles. The scatter plot in Figure 3-7 shows the PNIPAM growth over a period of twelve layers. Figure 3-7 plots the intensity of the mono-substituted amide peak at ~1645 cm^{-1} in the ATR-IR spectra for the control reactions and the LbL assembly that contains the copper catalyst and the azide functionality.

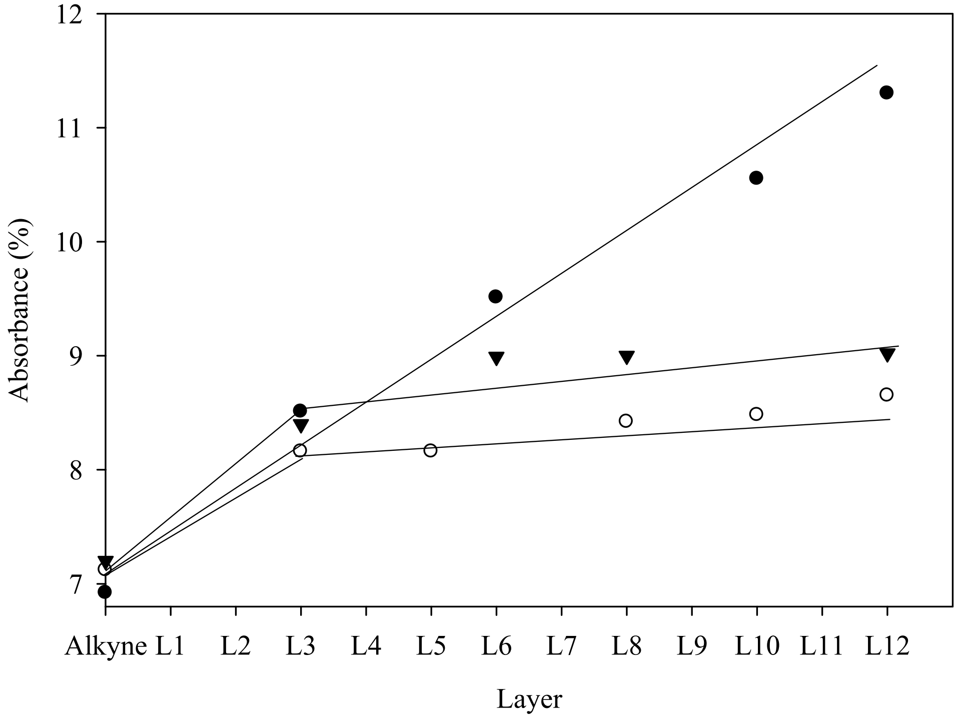


Figure 3-7. Scatter plot showing normal layer growth with C_2 linker versus control reactions. This plot uses the intensity of the mono-substituted amide peak found at ~1645 cm^{-1} in the ATR-IR spectra (● PE_{L12} built with C_2 linker; ○ PE_{L12} assembled without Cu; ▼ PE_{L12} assembled after azide reduction).

Although it was apparent that LbL assembly was taking place using **19**, there were some drawbacks. First of all, the PE_{L12} multilayer system that was created using a C_2-linker had an amide stretch only 30% as tall as the parent polyethylene film stretch (~1460 cm^{-1}) according to the ATR-IR spectra. Also, the characteristic azide stretching signals at ~2100 cm^{-1} were not visible in the ATR-IR spectrum. The desire for greater layering ability and the appearance of azide peaks in the ATR-IR spectras led to multilayer system synthesis using a different polymer system.

PNIPAM-bases polymers that contained six carbons between the azide and ester group had already been developed (**20**). By having a C_6 linker between the ester and the azide, I hoped that layering would increase due to a lack of steric interactions with the isopropyl groups of the PNIPAM. Also, by stationing the azide further from the polymer backbone, it should become visible in the ATR-IR spectrum. A PE_{Alk} film was immersed in a solution containing 100 mg of **20**, 5 mg of copper(II) sulfate pentahydrate, and 10 mg of sodium ascorbate and allowed to react for 1 h to form PE_{L1}. The PE_{L1} film was washed with water and ethanol and placed in a solution that contained **16**, copper(II) sulfate, and sodium ascorbate to form PE_{L2}. After 1 h, the film was washed and immersed in a fresh solution of the copper catalyst system and **20** to form PE_{L3}. This process was continued with solutions containing the catalyst system and **16** or solutions containing **20** until PE_{L11} was synthesized. As suspected, the longer linker caused an increase in mono-substituted amide peaks in the ATR-IR. When compared to the parent polyethylene peak, the amide peaks on PE_{L11} were 50% of the parent peak height. This was a 20% increase over the LbL assemblies built using **19**. PE$_{\mathrm{Alk},}$ PE$_{\mathrm{L2}}$, PE$_{\mathrm{L4}}$, PE$_{\mathrm{L6}}$, PE$_{\mathrm{L8}}$, PE$_{\mathrm{L10}}$, and PE$_{\mathrm{L11}}$, are seen in Figure 3-8.

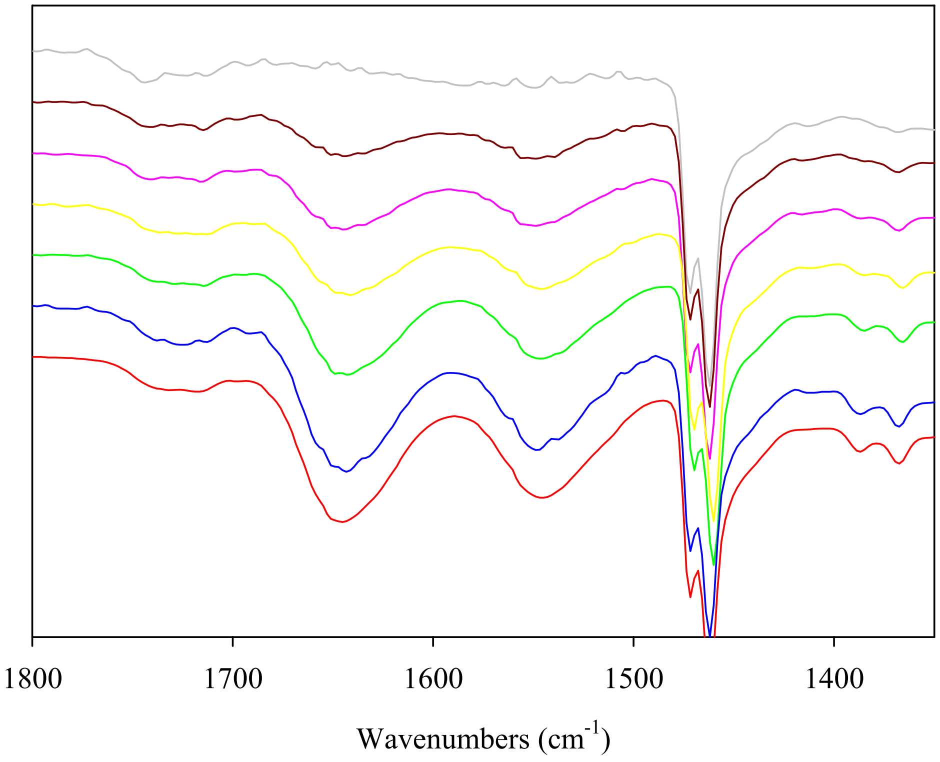


Figure 3-8. ATR-IR spectra showing layer growth using **16** and **20** (PE$_{\mathrm{Alk}}$ —; PE$_{\mathrm{L2}}$ —; PE$_{\mathrm{L4}}$ —; PE$_{\mathrm{L6}}$ —; PE$_{\mathrm{L8}}$ —; PE$_{\mathrm{L10}}$ —; PE$_{\mathrm{L11}}$ —).

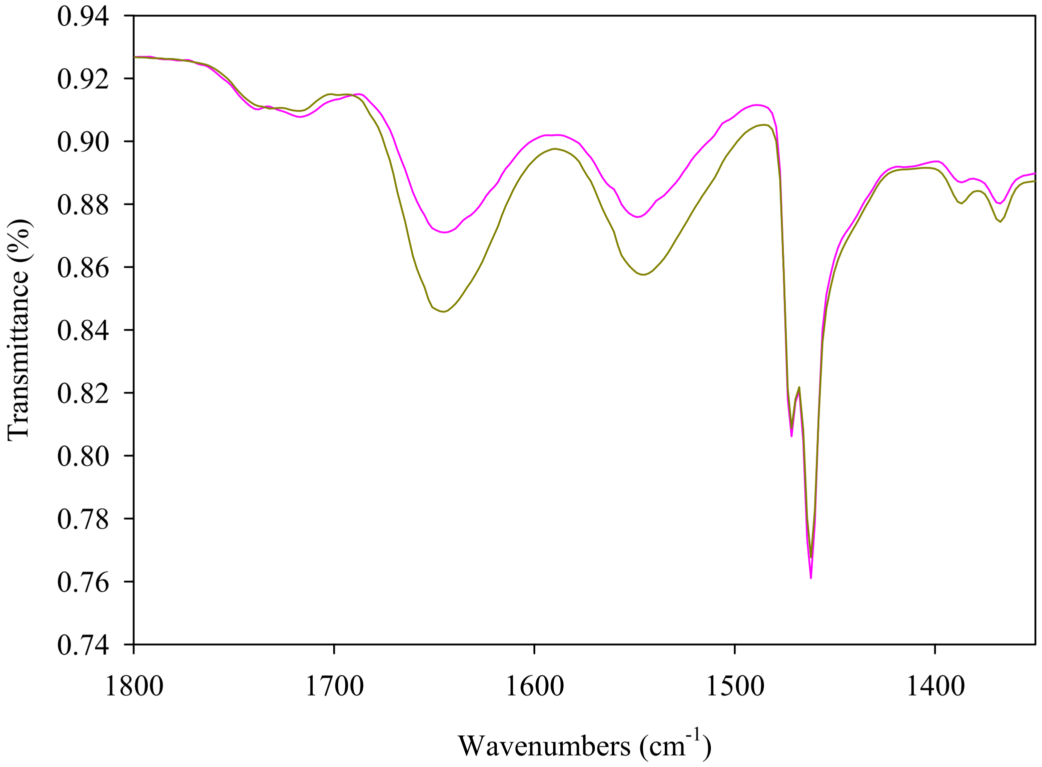


Figure 3-9. ATR-IR spectra comparing LbL assembly using **19** (C_2 linker; —) versus **20** (C_6 linker; —) as the azide component.

An ATR-IR spectrum comparing a PE_{L12} film layered using **19** (C_2 linker) and a PE_{L11} film layered using **20** (C_6 linker) is shown in Figure 3-9. A scatter plot showing the rate of PNIPAM growth using **19** (C_2 linker) versus **20** (C_6 linker) is shown in Figure 3-10. The mono-substituted amide peak at 1645 cm^{-1} in the ATR-IR spectra is slightly more intense than the mono-substituted amide peak at 1550 cm^{-1}, accounting for the variance in ratio seen in Figure 3-10.

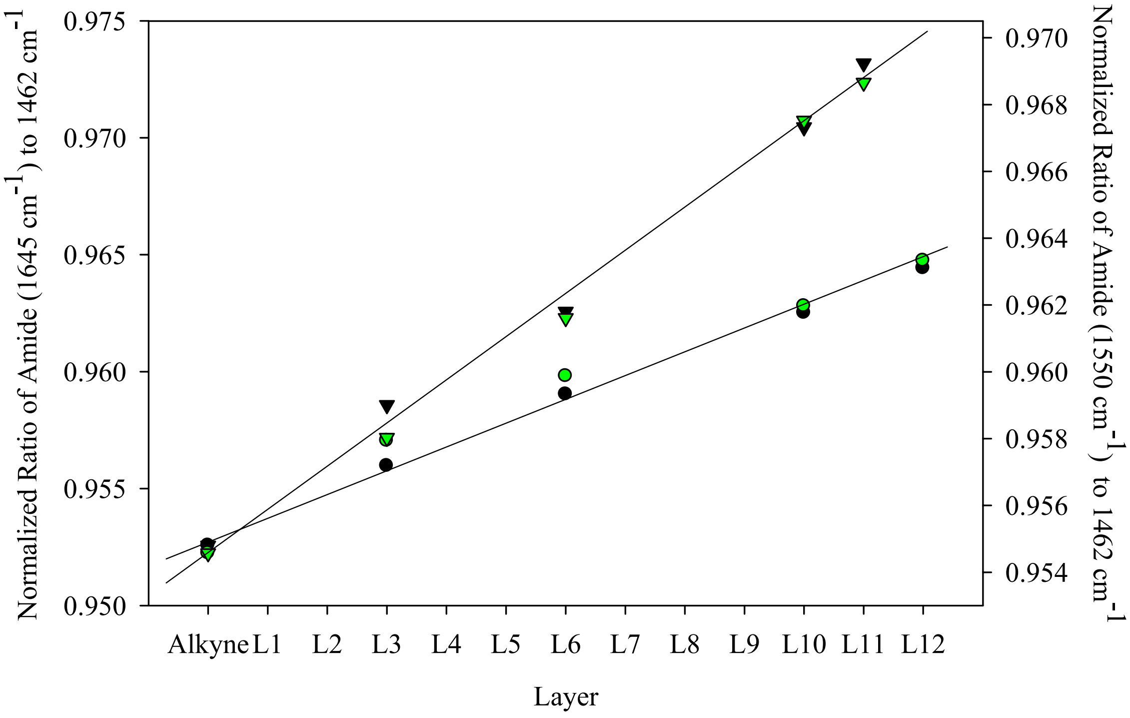


Figure 3-10. Layer growth on PE film using **19** (C_2 linker; ● 1645 cm^{-1} ratio; ● 1550 cm^{-1} ratio) versus **20** (C_6 linker; ▼ 1645 cm^{-1} ratio; ▼ 1550 cm^{-1} ratio) as the azide component in "click" LbL assembly. ATR-IR spectra were normalized and the ratio taken between the amide peak at 1645 cm^{-1} and the polyethylene peak at 1462 cm^{-1} and the ratio between the amide peak at 1550 cm^{-1} and the polyethylene peak at 1462 cm^{-1}.

The ATR-IR spectrum also confirmed the presence of azide groups. This spectrum is interesting because it shows that the azide groups are visible with odd-numbered layers and invisible with even-numbered layers (Figure 3-11). Therefore, when **16** is the upper-most layer (even numbered PE_{Lx}), it covers unreacted azide groups, rendering them invisible in an ATR-IR spectrum.

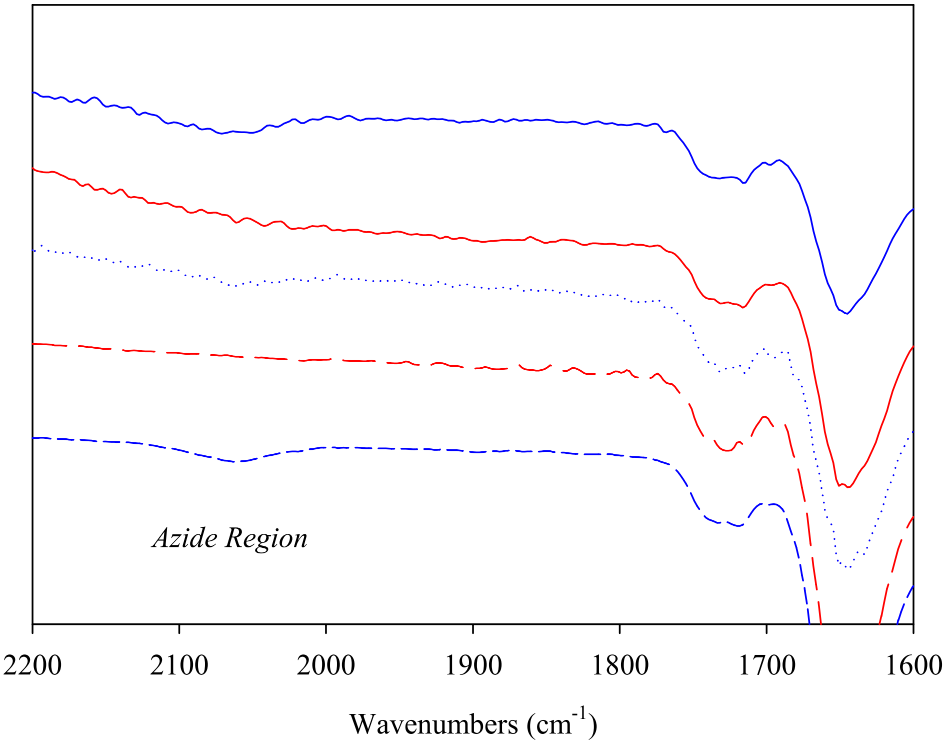


Figure 3-11. Azide region of ATR-IR spectra corresponding to PE film layered with **16** and **20** (PE_{L7} —; PE_{L8} —; PE_{L9} ⋯; PE_{L10} – –; PE_{L11} - - - -).

Other Surface Experiments and Instrumental Data

Other surface analyses were also performed using XPS, fluorescence microscopy, and water contact angle. These experiments were used to show the ability for an azide- or alkyne-rich surface to be modified. The presence of triazoles throughout the multilayer system was verified.

To show the presence of triazoles throughout the multilayer assembly, a PE_{L7} film prepared using **19** was subjected to methyl iodide in chloroform for 3 days (Figure 3-12).

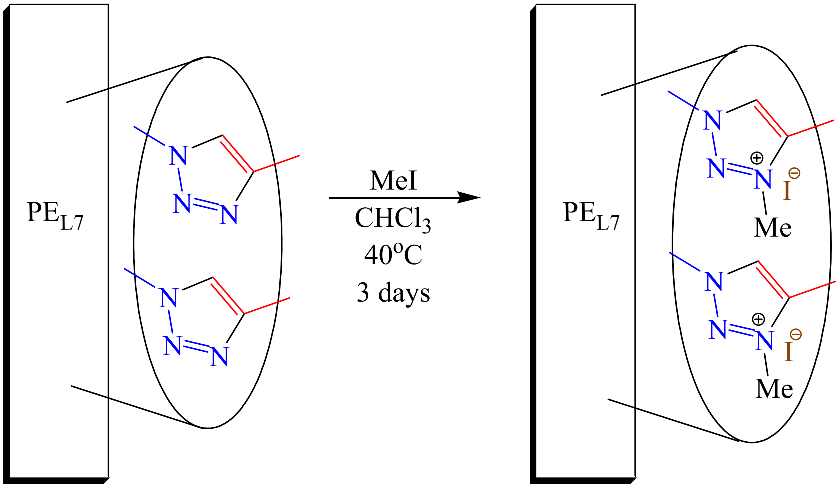


Figure 3-12. Methylation of PE_{L7} film surface.

After 3 days, the PE_{L7} film was analyzed with X-ray photoelectron spectroscopy (XPS). The resulting elemental analysis and the theoretical elemental analysis for a single bilayer (10 Å) deep section of the film is shown in Table 3-1.

Table 3-1: Theoretical and Actual Carbon, Oxygen, and Nitrogen Content on PE_{L7} Film

Element	Theoretical (%)	Actual (%)
Carbon	73.8	70.85
Oxygen	13.2	15.36
Nitrogen	12.7	13.45
Iodine	0.4	0.1

Copper and iodide made up the final 0.34% of the XPS elemental analysis. Since methyl iodide boils at 42 °C and the film was stored under vacuum, the only methyl iodide on the film should be bound to triazoles. Therefore, the presence of methyl iodide (0.1%) on the film is indicative of triazole formation. Based on the theoretical number of triazoles that should be present in a single bilayer, about 25% formed triazolium salts.

Fluorescence microscopy experiments were also performed to demonstrate the accessibility of azides throughout the multilayer system. In this case, a PE_{L3} and PE_{L12} film were immersed in a 10:1 water:THF solution containing a dansyl label with an alkyne handle (**23**) (Figure 3-13).

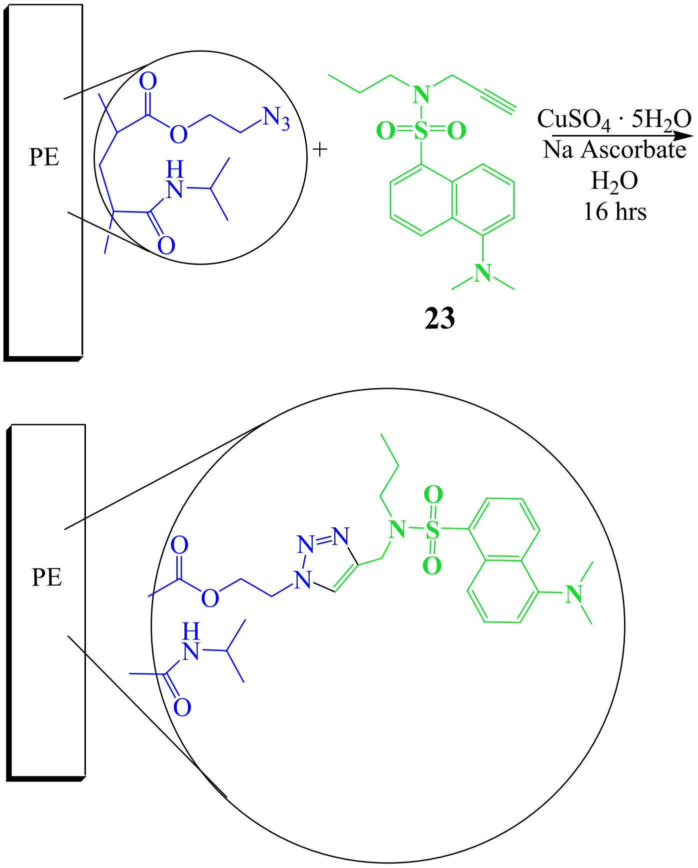
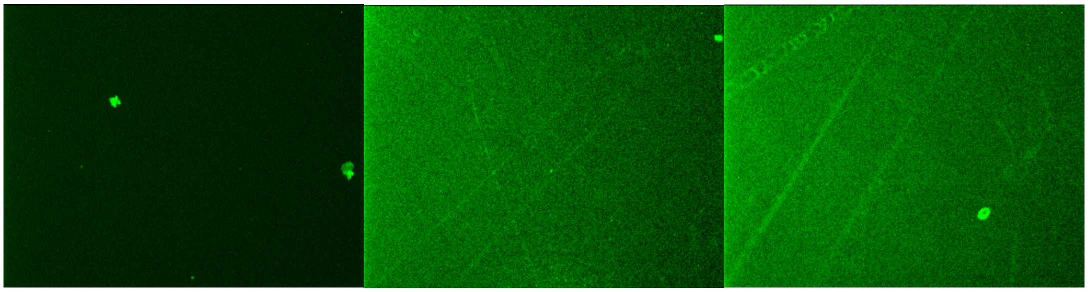


Figure 3-13. Dansyl labeling of PE_{Lx} film.

Fluorescence microscopy images were then taken of PE_{ox}, dansyl-labeled PE_{L3}, and dansyl-labeled PE_{L12} films and the intensity measured. This is shown in Figure 3-14. The PE_{L3} film is capped with azides and the PE_{L12} film is capped with alkynes. The intensity of the dansyl-labeled PE_{L3} and the dansyl-labeled PE_{L12} films were roughly equivalent (405 and 410). These similar intensities indicate that the same amount of azides were accessible in each film. In the case of the PE_{L12} film, there are handles available for the dansyl label to affix to due to the presence of unreacted azides throughout the system. The PE_{L3} film has very azide groups present within the system, but has an abundance of azide groups present on the surface. This demonstrates the polyvalent nature of the PNIPAM polymers used in LbL assembly.

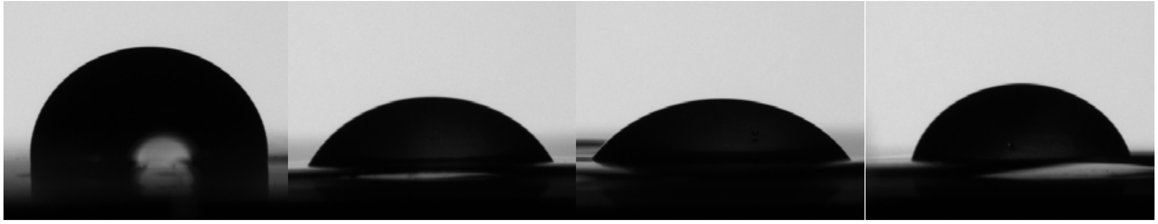


PE_{ox} dansyl-labeled PE_{L3} dansyl-labeled PE_{L12}

Figure 3-14. Fluorescence microscopy images (3 mm^2) of PE_{ox} and PE_{Lx} film subjected to dansyl labeling.

A series of experiments were also performed to measure surface force energy by contact angle analysis. By measuring water contact angles on a surface, hydrophobicity and hydrophilicity changes can be determined. As a surface is functionalized, its contact angle will change based on the groups present on that surface. Polyethylene films are hydrophobic (non-wettable) by nature and have an obtuse contact angle. As functional groups like carboxylic acids or water soluble polymers are introduced, the contact angle should decrease because a hydrophilic (wettable) surface is being formed.

A series of experiments were performed using a contact angle goniometer and the results are shown in Figure 3-15. First, contact angle measurements were taken using a drop of distilled water a PE film surface. The PE film had an advancing contact angle (θ_a) of 94°. The same experiment was then performed using PE_{ox} and the θ_a was 65°, showing that the addition of carboxylic acid groups led to a wettable surface. Next, a PE_{L12} film made with **16** and **20** was examined. It had a θ_a of 53°, showing PE_{L12} was even more hydrophilic than the oxidized film. Finally, a PE_{L12} film was stirred in a 3:1 THF:water solution containing octadecyl azide, copper(II) sulfate pentahydrate, and sodium ascorbate. This capped the surface with hydrophopic octadecyl chains. The θ_a only increased from 53° to 74°. This was consistent with functionality at the surface with a hydrophobic reagent. However, the relatively low contact angle (74°) suggests that coverage of the surface by octadecyl groups is low. This is to be expected due to the low azide functionality compared to PNIPAM on the surface.



PE $\theta_a = 94^\circ$

PE_{ox} $\theta_a = 65^\circ$

PE_{L12} $\theta_a = 53^\circ$

$PE_{L12} – C_{18}H_{37}N_3$ $\theta_a = 74^\circ$

Figure 3-15. Images and θ_a of water droplet on polyethylene and functionalized polyethylene.

CHAPTER IV

EXPERIMENTAL SECTION

General

tert-Butyl acrylate was filtered through basic alumina before use. *N*-Isopropyl acrylamide was recrystallized from a 9:1 hexane:benzene mixture. All other reagents were purchased from commercial sources and used as received. Benzene, THF, and DMF were dried over 3 Å molecular sieves. Dichloromethane, ethanol, ethyl acetate, and acetone were used as received. t*ert*-Butyl alcohol and 1,4-dioxane were used from new, sealed bottles and no further drying was performed. Distilled water was used for all washings and reactions.

NMR spectra were obtained using a Mercury 300 MHz or Unity 300 MHz spectrometer. GPC measurements were carries out on a Viscotek Model 270 detector equipped with a I-MBMMW-3078 mixed bed column using THF as a solvent and a Model VE 3580 RI detector. Molecular weights were determined relative to polystyrene standards. A Bruker Tensor 27 series FT-IR spectrometer with a Pike MIRacle accessory with an angle of 45° using a ZnSe crystal was used. X-ray photoelectron spectroscopy (XPS) was carried out using a Kratos Axis Ultra XPS using a monochromatic Al Kα source (400 W) in a UHV environment (ca. 5×10^{-9} torr). Surface composition was determined by normalized integration of the resulting peaks using Kratos software Fluorescence microscopy images were taken using a Nikon Eclipse model E800 Advanced Research Microscope with a UV-2E/C DAPI filter at a magnification of 10x.

Contact angle measurements were carried out using a KSV Instruments CAM200 Optical Goniometer equipped with a 30 fps Firewire camera. All films were dried under vacuum for 4 h prior to analysis.

Synthesis

MeO-PEG$_{350}$-OMs (2). Triethylamine (0.43 g, 4.29 mmol) was added to a solution of poly(ethylene glycol) monomethyl ether (**1**) M_w = 350 g/mol (1 g, 2.86 mmol) in 20 mL of CH_2Cl_2. This solution was cooled to 0 °C and methanesulfonyl chloride (0.49 g, 4.29 mmol) was slowly added to the reaction mixture. The reaction mixture was allowed to stir for 24 h. The organic phase was washed with 3 M HCl (3 x 30 mL), saturated $NaHCO_3$ (2 x 50 mL), brine (2 x 50 mL), and dried over sodium sulfate. The solvent was removed under reduced pressure and the product oil was dried under vacuum yielding 0.915 g (75%): ^{1}H NMR ($CDCl_3$) δ 3.09 (3H, s), 3.38 (3H, s), 3.55-3.78 (26H, PEG), 4.38 (2H, t, J = 4.5 Hz).

MeO-PEG$_{350}$-N$_3$ (3). Sodium azide (0.1 g, 1.5 mmol) was added to a solution of **2** (0.5 g, 1.17 mmol) in 15 mL of DMF. The solution was stirred under N_2 for 12 h at 90 °C. The solvent was removed under reduced pressure to yield 0.36 g (81%)of product: ^{1}H NMR ($CDCl_3$) δ 3.38 (3H, s), 3.55-3.72 (28H, PEG-CH_2-N_3); IR (KCl plate, cm^{-1}) 2110 (azide stretch).

MeO-PEG$_{350}$-triazole (4). Propargyl alcohol (0.08 g, 1.42 mmol) was added to a solution of **3** (0.3 g, 0.71 mmol) in 3 mL of distilled water. Sodium ascorbate (0.014 g, 0.071 mmol) and copper(II) sulfate pentahydrate (0.009 g, 0.035 mmol) were dissolved in 2 mL of distilled water. The copper solution was added to the solution containing **3**

and stirred for 24 h. The aqueous solution was extracted twice with CH_2Cl_2. The organic layer was then dried over sodium sulfate and the solvent was removed under reduced pressure to yield 0.25g (80%) of the PEG-triazole product; ^{1}H NMR ($CDCl_3$) δ 3.38 (3H, s), 3.49-3.69 (26H, PEG), 3.84 (2H, t, *J* = 4.6 Hz), 4.25 (1H, s), 4.53 (2H, t, *J* = 4.7 Hz), 7.82 (1H, s).

Propargyl acrylate (5). Acryloyl chloride (4.05 g, 45 mmol) was added dropwise to a cold solution (0 °C) of propargyl alcohol (3 g, 53.3 mmol) and triethylamine (5.45 g, 54 mmol) in 100 mL of CH_2Cl_2. The solution was allowed to stir for 24 h at 25 °C. The solution was then washed with water (2 x 50 mL), 0.1 M HCl (3 x 50 mL), $NaHCO_3$ (2 x 50 mL), and brine (2 x 50 mL). The organic phase was dried over magnesium sulfate and the solvent removed under reduced pressure. The recovered product weighed 4.1 g (83%): ^{1}H NMR ($CDCl_3$) δ 2.5 (1H, t, *J* = 2.5 Hz), 4.75 (2H, d, *J* = 2.9), 5.88 (1H, dd, *J* = 10 and 1.4 Hz), 6.14 (1H, dd, *J* = 17.3 and 10.7 Hz), 6.45 (1H, dd, *J* = 17.1 and 1.2 Hz); ^{13}C NMR ($CDCl_3$) δ 52.1, 75.4, 78.0, 128.0, 132.3, 165.6.

6-Chlorohexyl acrylate (6). 1-Chlorohexanol (3 g, 21.9 mmol) was added dropwise to a cold solution (0 °C) of acryloyl chloride (2.6 g, 28.5 mmol) and triethylamine (2.23 g, 22 mmol) in 50 mL of CH_2Cl_2. The solution was allowed to stir for 24 h at 25 °C. The solution was then washed with 0.1 M NaOH (2 x 50 mL), 0.1 M HCl (3 x 50 mL), 0.1 M $NaHCO_3$ (2 x 50 mL), and brine (2 x 50 mL). The organic phase was dried over magnesium sulfate and the solvent removed under reduced pressure. The remaining liquid monomer weighed 3.72g (89%): ^{1}H NMR ($CDCl_3$) δ 1.43 (4H, m), 1.73 (4H, m), 3.52 (2H, t, *J* = 6.2), 4.15 (2H, t, *J* = 6.0), 5.8 (1H, dd, *J* = 9.9 and 1.6 Hz), 6.10 (1H, dd, *J* = 10.4 and 17.6 Hz), 6.38 (1H, dd, *J* = 17.1 and 1.4 Hz); ^{13}C NMR ($CDCl_3$) δ 25.6, 26.5, 28.5, 32.5, 45.2, 64.7, 128.8, 130.8, 165.5.

2-(Methylsulfonyloxy)ethyl acrylate (7). 2-Hydroxyethyl acrylate (2 g, 17 mmol) and triethylamine (2.61 g, 26 mmol) in 75 mL of CH_2Cl_2 were cooled to 0 °C. Methanesulfonyl chloride (2.95 g, 26 mmol) in 20 mL of CH_2Cl_2 was added dropwise. The reaction was allowed to warm to 25 °C for 7 h. The organic phase was washed with water (2 x 50 mL), 0.1 M HCl (3 x 50 mL), $NaHCO_3$ (2 x 50 mL), and brine (2 x 50 mL). The organic phase was dried over sodium sulfate and the solvent was removed under reduced pressure. 1.7 g (51%) of product remained: ^{1}H NMR ($CDCl_3$) δ 3.05 (3H, s), 4.38 (4H, br), 5.84 (1H, d, *J* = 7.8), 6.08 (1H, dd, *J* = 16.8 and 16.9), 6.39 (1H, d, *J* = 16.8): ^{13}C NMR ($CDCl_3$) δ 37.7, 62.1, 67.6, 128.0, 132.0, 165.9.

Poly((*tert*-butyl acrylate)-co-(propargyl acrylate)) (8). *tert*-Butyl acrylate (3 g, 23.4 mmol), propargyl acrylate (0.28 g, 2.5 mmol), and 2,2'-azo-bis(isobutyronitrile) (AIBN) (14 mg, 0.085 mmol) were dissolved in 75 mL of benzene. The solution was degassed by bubbling N_2 for 30 min. The reaction mixture was then heated for 12 h at 60 °C while under a nitrogen atmosphere. Benzene was removed under reduced pressure. The remaining polymer was dissolved in 25 mL of acetone and precipitated into 250 mL of 50:50 methanol:water. After filtration, the pure polymer was dried under vacuum giving 1.15 g (35%) of the polymer: ^{1}H NMR ($CDCl_3$) δ 1.15-2.00 (bm), 2.00-2.72 (bm), 4.65 (bs); $M_n = 2.3 \times 10^4$ Da (GPC). PDI = 1.76.

Poly((*tert*-butyl acrylate)-co-(6-chlorohexyl acrylate)) (9). *tert*-Butyl acrylate (3 g, 23.4 mmol), 6-chlorohexyl acrylate (0.5 g, 2.6 mmol), and 2,2'-azo-bis(isobutyronitrile)

(AIBN) (14 mg, 0.085 mmol) were dissolved in 75 mL of benzene. The solution was degassed with bubbling N_2 for 30 min. The reaction mixture was then heated for 12 h at 60 °C while under a nitrogen atmosphere. Benzene was removed under reduced pressure. The remaining polymer was dissolved in 25 mL of acetone and precipitated into 250 mL of 50:50 methanol:water. After filtration, the pure polymer was dried under vacuum; giving 2.42 g (69%): ^{1}H NMR ($CDCl_3$) δ 1.15–1.72 (bm), 1.81 (bm), 2.22 (bs), 3.55 (bt), 4.03 (bs).

Poly((*tert*-butyl acrylate)-co-(2-(methylsulfonyloxy)ethyl acrylate)) (10). *tert*-Butyl acrylate (2 g, 15.6 mmol), 2-(methylsulfonyloxy)ethyl acrylate (0.32 g, 1.56 mmol), and 2,2'-azo-bis(isobutyronitrile) (AIBN) (10 mg, 0.06 mmol) were dissolved in 75 mL of benzene. The solution was degassed with bubbling N_2 for 30 min. The reaction mixture was then heated for 12 h at 60 °C while under a nitrogen atmosphere. Benzene was removed under reduced pressure. The remaining polymer was dissolved in 25 mL of acetone and precipitated into 250 mL of 50:50 methanol:water. After filtration, the pure polymer was dried under vacuum; giving 1.81 g (78%): ^{1}H NMR ($CDCl_3$) δ 1.16–1.78 (bm), 1.88 (bm), 2.27 (bs), 3.13 (bs), 4.28-4.55 (bm).

"Click" Reaction on poly((*tert*-butyl acrylate)-co-(propargyl acrylate)) (11). Octadecyl azide (0.29 g, 1 mmol), Hunig's base (0.17 g, 1 mmol), tris(triphenylphosphine)copper bromide (46 mg, 0.05 mmol), and **8** (0.5g, 0.5 mmol) were dissolved in 50 mL of THF. The reaction was degassed with N_2 for 30 min. and allowed to proceed for 12 h at 50 °C under a nitrogen atmosphere. The product was extracted with 200 mL of ethyl acetate and washed with brine (3 x 100 mL). The organic phase was removed under reduced pressure and the remaining oil purified by silica gel column chromatography (3:1 hexane:ethyl acetate). Solvent was removed under reduced pressure and the product was dried under vacuum to give 0.51 g (78%): ^{1}H NMR ($CDCl_3$) δ 0.88 (t, *J* = 6.3 Hz), 1.1-1.62 (bm), 1.86 (bm), 2.22 (bs), 4.36 (bs), 5.32 (bs), 7.8 (bs); $M_n = 2.7 \times 10^4$ Da (GPC); PDI = 1.73.

Methylation of 11 (12). Methyl iodide (0.47 g, 3.7 mmol) and **11** (0.4 g, 0.37 mmol of functionalized polymer) in acetone were allowed to react for 3 d at 40 °C. The solvent and MeI were removed under reduced pressure. Based on spectral data, the reaction was only 40% complete: ^{1}H NMR ($CDCl_3$) δ 0.88 (t, *J* = 6.3 Hz), 1.1-1.62 (bm), 1.86 (bm), 2.22 (bs), 4.37 (bs), 4.50 (bs), 4.67 (bs), 5.21 (bs), 5.46 (bs), 5.8 (bs).

Poly((*tert*-butyl acrylate)-co-(6-azidohexyl acrylate)) (13). Sodium azide (1.17 g, 18 mmol) and **9** (2.24 g, 1.5 mmol of functionalized polymer) were dissolved in 200 mL of DMF and heated to 90 °C for 12 h. The DMF was removed under reduced pressure. Ethyl acetate (100 mL) was added and the organic phase was washed with water (3 x 100 mL). The ethyl acetate was removed under reduced pressure and the polymer was dried under vacuum. 1.86 g (83%) of polymer was recovered: ^{1}H NMR ($CDCl_3$) δ 1.15-1.71 (bm), 1.82 (bm), 2.22 (bs), 3.28 (t, *J* = 4.8 Hz), 4.02 (bs).

Poly((*tert*-butyl acrylate)-co-(2-azidoethyl acrylate)) (14). Sodium azide (0.36 g, 5 mmol) and **10** (0.4 g, 0.36 mmol of functionalized polymer) were dissolved in 200 mL of DMF and heated to 90 °C for 12 h. The DMF was removed under reduced pressure. Ethyl acetate (100 mL) was added and the organic phase was washed with water (3 x 100 mL). The ethyl acetate was removed under reduced pressure and the polymer was dried under vacuum to yield 0.25 g (66%) of product: ^{1}H NMR ($CDCl_3$) δ 1.17-1.98 (bm), 2.23 (bs), 3.51 (bs), 4.22 (bs).

"Click" reaction of poly((*tert*-butylacrylate)-co-(6-azidohexyl acrylate) (15). Octyne (0.1 g, 0.46 mmol), Hunig's base (0.114g, 0.92 mmol), tris(triphenylphosphine)copper bromide (42 mg, 0.046 mmol), and **13** (0.5g, 0.46 mmol) were dissolved in 50 mL of THF. The reaction was degassed with N_2 for 30 min and allowed to proceed for 12 h at 50 °C under a nitrogen atmosphere. The THF was removed under reduced pressure. While the original crude product was soluble in THF, the product after solvent removal was insoluble in THF, ethyl acetate, dichloromethane, ethyl ether, DMF, acetone, and methanol. A crude ^{1}H NMR was obtained showing the formation of the -CH_2-N of the triazole at 4.3 ppm and the gradual disappearance of the –CH_2-N_3 at 3.3 ppm.

Poly((*N*-isopropyl acrylamide)-co-(propargyl acrylate)) (16) (PNIPAM-Alk). *N*-Isopropyl acrylamide (5 g, 44 mmol), propargyl acrylate (0.48 g, 4.3 mmol) and AIBN (7.5 mg, 0.046 mmol) were dissolved in 250 mL of *tert*-butanol. The reaction mixture was degassed for 45 min. with N_2 and the reaction was allowed to proceed for 12 h at 70 °C under a nitrogen atmosphere. The solvent was removed under reduced pressure and the crude polymer was dissolved in 50 mL of chloroform. The chloroform solution was precipitated into hexanes (500 mL). This precipitation was performed twice. The polymer was then dried under vacuum: ^{1}H NMR ($CDCl_3$) δ 0.71-2.61 (bm), 4.01 (bs), 4.66 (bs), 5.93-7.17 (bm); $M_n = 6.1 \times 10^4$ Da (GPC); PDI = 2.31.

Poly((*N*-isopropyl acrylamide)-co-(2-(methylsulfonyloxy)ethyl acrylate)) (17)

N-Isopropyl acrylamide (5 g, 44 mmol), 2-(methylsulfonyloxy)ethyl acrylate (0.854 g, 4.5 mmol) and AIBN (27 mg, 0.16 mmol) were dissolved in 250 mL of benzene. The reaction mixture was degassed for 45 min. with N_2 and the reaction was allowed to proceed for 12 h at 70 °C under a nitrogen atmosphere. After 12 h, a precipitate formed at the bottom of the flask. The benzene was simply decanted and the residue dissolved in 75 mL of THF. The solution was then precipitated into 600 mL of hexanes (2 times), filtered, and dried under vacuum. The pure polymer weighed 4.5 g (83%): ^{1}H NMR ($CDCl_3$) δ 0.70-2.62 (bm), 3.17 (bs), 3.76 (bs), 4.00 (bs), 4.45 (bs), 5.66-7.20 (bm).

Poly((*N*-isopropyl acrylamide)-co-(6-chlorohexyl acrylate)) (18). *N*-isopropyl acrylamide (5 g, 44 mmol), 6-chlorohexyl acrylate (0.854 g, 2.9 mmol) and AIBN (15 mg, 0.092 mmol) were dissolved in 250 mL of benzene. The reaction mixture was degassed for 45 min. with N_2 and the reaction was allowed to proceed for 12 h at 70 °C under a nitrogen atmosphere. After 12 h, a precipitate had formed at the bottom of the flask. The benzene was simply decanted and the residue dissolved in 70 mL of $CHCl_3$. The solution was then precipitated into 700 mL of hexanes (2 times), filtered, and dried under vacuum. The pure polymer product weighed 4.5 g (81%): ^{1}H NMR ($CDCl_3$) δ 0.78–2.51 (bm), 3.53 (bt), 4.01 (bs), 5.78-7.04 (bm).

Poly((*N*-isopropyl acrylamide)-co-(2-azidoethyl acrylate)) (19). Sodium azide (0.123 g, 1.7 mmol) and **17** (2 g, 0.95 mmol of functionalized polymer) were dissolved in 100 mL of DMF and heated to 90 °C for 12 h. DMF was removed under reduced pressure and the crude polymer was dissolved in 100 mL water. The polymer product had an LCST of 30 °C. Because of this, the aqueous solution was the centrifuged (1500 rpm, 20 min.) at 60 °C, causing the polymer product to precipitate. The polymer was again dissolved in 100 mL of water, and the centrifugation procedure was repeated. The polymer was filtered and dried under vacuum to yield 1.75 g (90%): ^{1}H NMR ($CDCl_3$) δ 0.66-2.77 (bm), 3.55 (bs), 4.03 (bs), 4.28 (bs), 5.8-7.25 (bm). $M_n = 1.4 \times 10^5$ Da (GPC); PDI = 2.01.

Poly((*N*-isopropyl acrylamide)-co-(6-azidohexyl acrylate)) (20). Sodium azide (0.5 g, 7.0 mmol) and **18** (4.5 g, 1.7 mmol of functionalized polymer) were dissolved in 200 mL of DMF and heated to 90 °C for 12 h. DMF was removed under reduced pressure and the crude polymer was dissolved in 150 mL water. The polymer product had an LCST of 30 °C. Because of this, the aqueous solution was the centrifuged (1500 rpm, 20 min.) at 60 °C, causing the polymer product to precipitate. The polymer was again dissolved in 100 mL of water, and the centrifugation procedure was repeated. The polymer was filtered and dried under vacuum to yield 3.38 g (75%): ^{1}H NMR (D_2O) δ 0.77-2.42 (bm), 3.38 (bs), 3.94 (bs), 4.17 (bs); $M_n = 2.2 \times 10^5$ Da (GPC); PDI = 2.13.

Aqueous "click" reaction of poly((*N*-isopropyl acylamide)-co-(2-azidoethyl acrylate)) (21). Propargy alcohol (0.154 g, 2.75 mmol), **19** (1 g, 0.48 mmol of functionalized polymer), copper(II) sulfate pentahydrate (18 mg, 0.072 mmol), and sodium ascorbate (30 mg, 0.15 mmol) were dissolved in 150 mL of water. The reaction was stirred at 25 °C for 24 h. Approximately 75 mL of the water was removed by reduced pressure. The polymer product had an LCST of about 30 °C. Because of this, the aqueous solution was the centrifuged (1500 rpm, 20 min.) at 60 °C, causing the polymer product to precipitate. The polymer was again dissolved in 100 mL of water, and the centrifugation procedure was repeated. The polymer was filtered and dried under vacuum to yield 0.65 g (64%): ^{1}H NMR ($CDCl_3$) δ 0.55-2.91 (bm), 4.02 (bs), 4.19-5.0 (bm), 5.93-7.19 (bm), 7.38 (s).

Organic "click" reaction of poly((*N*-isopropyl acylamide)-co-(2-azidoethyl acrylate)) (22). Tris(triphenylphosphine)copper bromide (22 mg, 0.023 mmol), **19** (0.5 g, 0.24 mmol), were dissolved in a THF (75 mL) solution that contained octyne (53 mg, 0.48 mmol), and Hunig's base (62 mg, 0.48 mmol). The reaction mixture was degassed with N_2 for 30 min. and heated at 60 °C for 12 hours while under a nitrogen atmosphere. After 12 h, 60 mL of the solvent was removed under reduced pressure. The remaining THF was precipitated into 150 mL of hexanes. The solid product was filtered, redissolved in 15 mL of THF and precipitated into 150 mL of hexanes. The off-white solid was filtered and dried to yielding 0.44g (84%): ^{1}H NMR ($CDCl_3$) δ 0.59-2.57 (bm), 2.71 (bt), 4.02 (bs), 4.23-4.76 (bm), 5.83-7.25 (bm), 7.51 (bs).

Dansyl-alkyne (23). A mixture of *N*-propyl-5-dimethylaminonaphthalene-1-sulfonamide (0.87 g, 3.0 mmol) and cesium carbonate (1.17 g, 3.6 mmol) in 10 mL of dry DMF was placed in a flame-dried flask. The solution was allowed to stir at room temperature for 1 h. An 80% (by weight) toluene solution of propargyl bromide (4.45 g, 30 mmol) was then added and the solution was heated at 80 °C for 48 h. The solution was then allowed to cool and solvent was removed under vacuum. The crude product was then purified by silica gel column chromatography (3:1, hexanes:ethyl acetate) to yield 0.874g (88.6%) of product: ^{1}H NMR ($CDCl_3$) δ 0.78 (3H, t, J = 7.3 Hz), 1.54 (2H, m, J = 7.6 Hz), 2.08 (1H, t, J = 2.4 Hz), 2.82 (6H, s), 3.32 (2H, t, J = 7.6 Hz), 4.15 (2H, d, *J* = 2.4 Hz), 7.13 (1H, d, *J* = 8.1 Hz), 7.49 (2H, m, *J* = 7.3 Hz), 8.20 (1H, d, *J* = 7.0 Hz), 8.31 (1H, d, *J* = 8.3 Hz), 8.50 (1H, d, *J* = 8.5); ^{13}C NMR ($CDCl_3$) δ 10.79, 20.47, 35.38, 45.17, 47.86, 73.19, 77.12, 114.94, 119.41, 122.89, 127.79, 129.38, 129.78, 129.98, 130.26, 134.49, 151.44.

Surface Modification of Polyethylene Films

Oxidation of Polyethylene. (PE_{ox})[34] The polyethylene film was provided by Soltex (Fortiflex J60-110-157, density 0.961 g/mL). The films were cut into 1.5 × 3 cm pieces. These pieces were extracted using CH_2Cl_2 in a jacketed Soxhlet apparatus for 15 h and dried under vacuum for 15 min. The films were stirred in a mixture of $CrO_3/H_2O/H_2SO_4$ (1:2:1) for 5 min at 90 ° C to form an oxidized film. After 10 min., the films were washed with water and then acetone and allowed to air dry. The oxidized films were extracted using CH_2Cl_2 in a jacketed Soxhlet apparatus for 15 h and finally dried under vacuum for 15 min. ATR-IR spectroscopy was used to confirm oxidation of the surface with a new carbonyl peak appearing at 1708 cm^{-1}.

Polyethylene film activation (PE_{MA}). PE_{ox} was immersed in a solution of dichloromethane (12 mL) that contained *N*-methyl morpholine (1.08 g, 10.7 mmol). Ethyl chloroformate (0.88 g, 8.15 mmol) was added dropwise and the reaction was allowed to proceed for 45 min. The films were then removed and washed with dicloromethane (3 x 10 mL). The film was then dried under a stream of nitrogen for 2 min. The ATR-IR spectrum confirmed that mixed anhydride activation was successful with a new carbonyl peak appearing at 1825 cm^{-1}.

Alkyne-functionalized polyethylene (PE_{Alk}). PE_{MA} was immersed in a solution of propargyl alcohol (6.98 g, 125 mmol) and triethylamine (1.37 g, 13.6 mmol). The film was stirred for 4 h before being washed with water (3 x 10 mL) and ethanol (1 x 10 mL). The film was dried under a stream of nitrogen for 2 min. The ATR-IR spectrum confirmed the ester formation with the disappearance of the anhydride peak at 1825 cm^{-1} and the appearance of an ester peak at 1740 cm^{-1}. No alkyne stretch was observed.

General procedure for layer-by-layer assembly on PE_{Alk} (PE_{Lx}). Aqueous solutions (12 mL) were prepared containing various PNIPAM copolymers (100 mg, **16, 19,** or **20**). Copper(II) sulfate pentahydrate (5 mg, 0.02 mmol) and sodium ascorbate (10 mg, 0.05 mmol) were added to the solution and the appropriate PE film was immediately immersed for 1 h at 25 °C. The films were then washed with water (3 x 10 mL) and ethanol (1 x 10 mL) and dried with streaming nitrogen for 2 min. ATR-IR spectroscopy was used to monitor layering.

Procedure for LbL assembly using 16 and 19 (PE_{Lx}). PE_{Alk} was immersed in an aqueous solution of **19** and the copper catalyst system. The reaction was allowed to proceed for 1 h and the film was removed, washed with water (3 x 10 mL) and ethanol (1 x 10 mL), and dried with streaming nitrogen for 2 min. (PE_{L1}). ATR-IR spectroscopy confirmed PNIPAM was attached to the surface by the appearance of peaks at 1545 cm^{-1} and 1645 cm^{-1} that correspond to mono-substituted amides. The PE_{L1} film was then immersed in an aqueous solution containing **16** and the copper catalyst system. This reaction proceeded for 1 h and the film was removed, washed, and dried as described above (PE_{L2}). The ATR-IR spectra showed an increase in the intensity of the mono-substituted amide peaks. The PE_{L2} film was again immersed in an aqueous solution containing **19** and the copper catalyst system and allowed to react for 1 h. The film was removed, washed, and dried (PE_{L3}). The ATR-IR spectra showed an increase in the intensity of the mono-substituted amide peaks. The PE_{L3} film was then immersed in an aqueous solution containing **16** and the copper catalyst system. This reaction proceeded for 1 h and the film was removed, washed, and dried (PE_{L4}). The ATR-IR spectra showed an increase in the intensity of the mono-substituted amide peaks. These alternating reactions were continued ($PE_{L5,}$ PE_{L6}, PE_{L7}, PE_{L8}, PE_{L9}, PE_{L10}, PE_{L11}, and PE_{L12}) until the desired layer was reached. In some cases, the covalent LbL assembly was halted at PE_{L3} or PE_{L7} so that other modifications could be performed.

Omission of Copper Catalyst. The covalent assembly process on a PE_{L3} film was continued using aqueous solutions (100 mg polymer, 12 mL of water) that contained only polymer and no copper(II) sulfate pentahydrate or sodium ascorbate. PE_{L3} was immersed in an aqueous solution containing only **16** and allowed to stir for 1 h. The film was removed, washed, and dried (PE_{L4}). ATR-IR spectroscopy showed no increase in intensity of the mono-substituted amide peaks (1545 cm^{-1} and 1645 cm^{-1}). The reaction was repeated with an aqueous solution of only **19**. Once again, there was very little growth evident. These alternating reactions werer repeated until PE_{L12} was formed. There was very little change in the intensity of the mono-substituted amide peaks over the course of the LbL assembly. This proved the necessity of the copper catalyst system. These results can be seen in Figure 3-5 and 3-6.

Azide reduction on PE_{L3}. A PE_{L3} film placed in a solution of dry THF (30 mL) and $LiAlH_4$ (400 mg, 10 mmol). The reaction was allowed to proceed under a nitrogen atmosphere for 24 h. The film was washed with 10% HCl (2 x 10 mL) and stirred in triethylamine (13.88 g, 0.137 mol) for 4 h. The ATR-IR spectra showed a decrease in the intensity of the mono-substituted amide peaks. This was expected because $LiAlH_4$ will reduce amide groups. It was assumed that all of the azide groups were also reduced.[35] The film was then immersed in an aqueous solution containing **16** and the copper catalyst system and allowed to react for 1 h. The film was removed, washed, and dried (PE_{L4}). The ATR-IR spectra showed very little increase in the mono-substituted amide region. The PE_{L4} film was immersed in an aqueous solution containing **19** and the copper catalyst system and allowed to react for 1 h. The film was removed, washed, and dried (PE_{L5}). This series of alternating reactions was repeated until the PE_{L12} was formed. The film was then sonicated in water for 10 minutes. ATR-IR spectroscopy showed very little increase in the intensity of the mono-substituted amide peaks. This reaction series showed that azides were necessary for LbL assembly. These results can be seen in Figure 3-5 and 3-6.

Procedure for LbL assembly using 16 and 20 (PE_{Lx}). PE_{Alk} was immersed in an aqueous solution of **20** and the copper catalyst system. The reaction was allowed to proceed for 1 h and the film was removed, washed, and dried (PE_{L1}). ATR-IR spectroscopy confirmed PNIPAM was attached to the surface based on the appearance of peaks at 1545 cm^{-1} and 1645 cm^{-1} that correspond to mono-substituted amides. A peak at 2075 cm^{-1} was also seen and is indicative of the presence of azides on the surface. The PE_{L1} film was then immersed in an aqueous solution containing **16** and the copper catalyst system. This reaction proceeded for 1 h and the film was removed, washed, and dried (PE_{L2}). The ATR-IR spectra showed an increase in the intensity of the mono-substituted amide peaks and the disappearance of the azide peak. The PE_{L2} film was again immersed in an aqueous solution containing **20** and the copper catalyst system and allowed to react for 1 h. The film was removed, washed, and dried (PE_{L3}). ATR-IR again showed an increase in the intensity of the mono-substituted amide peaks and the reemergence of the azide peak. The PE_{L3} film was then immersed in an aqueous solution containing **16** and the copper catalyst system. This reaction proceeded for 1 h and the film was removed, washed, and dried (PE_{L4}). ATR-IR spectroscopy showed an increase in the intensity of the mono-substituted amide peaks and disappearance of the azide peak. These alternating reactions were continued (PE_{L5}, PE_{L6}, PE_{L7}, PE_{L8}, PE_{L9}, PE_{L10}, and PE_{L11}) until the desired layer was reached. In this case, the use of polymer **20** instead of polymer **19** showed a dramatic increase in the intensity of the mono-substituted amide peaks on the ATR-IR spectra. It is believed that lack of steric interference from the isopropyl groups caused the increase in layering.

Methylation of PE_{L7} surface. A PE_{L7} was stirred in a solution of methyl iodide (100 mg, 0.71 mmol) in chloroform (35 mL) for 3 days at 40 °C. The film was washed with chloroform (3 x 10 mL) and dried under vacuum for 2 days. XPS showed the presence of iodide on the surface with about 25% methylation based on the number of theoretical triazoles per bilayer (Table 3-1).

Dansyl labeling of PE_{L3} and PE_{L12}. A dansyl alkyne (**23**) solution was made in THF (0.6 mg/mL). 1 mL of this solution was added to 10 mL of water. A PE_{L3} film and a PE_{L12} film (made using **16** and **19**) were immersed in the solution. Copper(II) sulfate (5 mg, 0.02 mmol) and sodium ascorbate (10 mg, 0.05 mmol) were added and the reaction was allowed to proceed at 25 °C for 1 h. The films were then washed with 0.1 M HCl (2 x 10 mL), 0.1 M NaOH (2 x 10 mL), water (2 x 10 mL), and ethanol (1 x 10 mL). The films were dried under a stream of nitrogen for 2 min. Fluorescent microscopy images were taken and the PE_{L3} film had an intensity of 305 arbitrary units (a.u.) and the PE_{L12} film had an intensity of 310 a.u.

Octadecyl azide capping. A PE_{L12} film (made with **16** and **20**) was immersed in a solution (12 mL) made up of 3:1 THF:water. Octadecyl azide (30 mg, 0.1 mmol), copper(II) sulfate pentahydrate (5 mg, 0.02 mmol) and sodium ascorbate (10 mg, 0.05 mmol) were added and the reaction mixture with the film stirred for 1 h. The film was then removed, washed with THF (2 x 10 mL), water (2 x 10 mL) and ethanol (1 x 10 mL), and dried under a stream of nitrogen for 2 min. It was then dried in a vacuum for 4 h. Presence of octadecyl groups were confirmed by comparative contact angle measurements (see text – Figure 3-14).

CHAPTER V

CONCLUSION

Poly(*N*-isopropyl acrylamide) copolymers functionalized with azides and alkynes formed a multilayer assembly on a polyethylene substrate. Covalent layer-by-layer assembly was achieved by using “click” chemistry to form triazoles that covalently couple the first layer of polymer to the polyethylene surface and then link each layer to one another covalently. Unlike previous examples that used electrostatic interactions for substrate binding, this new method for covalent assembly is solely based on the formation of triazole linkages. This method has the advantage of be carried out in water under ambient conditions and is not air-sensitive. It is thus a “Greener” method of polyethylene grafting than other procedures that use organic solvents. The success of this PNIPAM-based covalent layer-by-layer assembly process was established by several analytical procedures. Attenuated total reflectance infrared spectroscopy both showed that the grafting occurred and showed that increasing the number of carbons between the azide group and the polymer backbone increased the amount of grafting. Control reactions showed that the presence of azide groups and a copper catalyst were required for successful layer-by-layer assembly. Thus, the polymeric reagents were not simply physically absorbing on the substrate via hydrophobic or hydrogen bond-based interactions. Methylation of the triazole linkers yielded a triazolium salt that was analyzed by X-ray photoelectron spectroscopy. This XPS data showed that ca. 25% of the triazoles on the surface could be converted to triazolium iodide salts. Fluorescence microscopy of surfaces labeled with an alkyne containing a dansyl fluorophore showed both that the covalent assemblies can be derivatized after formation and that the assembly is macroscopically uniform. Water contact angle analysis further established that the physical properties of the polyethylene surface could be changed using “click” chemistry. Layer-by-layer assembly using “click” chemistry is a new approach for modifying surfaces. This first report of layer-by-layer assembly on a polyolefin substrate using “click” chemistry should be a general route into functional thin film grafts that could be used in future applications.

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