Synthesis and Characterization of Polylactide-siloxane Block Copolymers as Magnetite Nanoparticle Dispersion Stabilizers

by
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Ragy T. Ragheb

Abstract

Polylactide-siloxane triblock copolymers with pendent carboxylic acid functional groups have been designed and synthesized for study as magnetite nanoparticle dispersion stabilizers. Magnetic nanoparticles are of interest in a variety of biomedical applications, including magnetic field-directed drug delivery and magnetic cell separations. Small magnetite nanoparticles are desirable due to their established biocompatibility and superparamagnetic (lack of magnetic hysteresis) behavior. For in-vivo applications it is important that the magnetic material be coated with biocompatible organic materials to afford dispersion characteristics or to further modify the surfaces of the complexes with biospecific moieties.

The synthesis of the triblock copolymers is comprised of three reactions. Difunctional, controlled molecular weight polymethylvinylsiloxane oligomers with either aminopropyl or hydroxybutyl endgroups were prepared in ring-opening redistribution reactions. These oligomers were utilized as macroinitiators for ring-opening L-lactide to provide triblock materials with polymethylvinylsiloxane central blocks and poly(L-lactide) endblocks. The molecular weights of the poly(L-lactide) endblocks were controlled by the mass of L-lactide relative to the moles of macroinitiator. The vinyl groups on the polysiloxane center block were further
functionalized with carboxylic acid groups by adding mercaptoacetic acid across the pendent double bonds in an ene-thiol free radical reaction. The carboxylic acid functional siloxane central block was designed to bind to the surfaces of magnetite nanoparticles, while the poly(L-lactide)s served as tailblocks to provide dispersion stabilization in solvents for the poly(L-lactide). The copolymers were complexed with magnetite nanoparticles by electrostatic adsorption of the carboxylates onto the iron oxide surfaces and these complexes were dispersible in dichloromethane. The poly(L-lactide) tailblocks extended into the dichloromethane and provided steric repulsion between the magnetite-polymer complexes.
This thesis is dedicated to my family for their unflagging love and support that I have been truly blessed with.
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“I can do all things through Him who strengthens me” – Phillippians 4:13
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## Abbreviations

<table>
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<th>Definition</th>
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<tr>
<td>D₃</td>
<td>1,1,3,3,5,5-hexamethylcyclotrisiloxane</td>
</tr>
<tr>
<td>D₃</td>
<td>1,3,5-trivinyl-1,3,5-trimethylcyclotrisiloxane</td>
</tr>
<tr>
<td>D₄</td>
<td>octamethylcyclotetrasiloxane</td>
</tr>
<tr>
<td>D₄</td>
<td>1,3,5,7-tetravinyl-1,3,5,7-tetramethylcyclotetrasiloxane</td>
</tr>
<tr>
<td>DSC</td>
<td>differential scanning calorimetry</td>
</tr>
<tr>
<td>NMR</td>
<td>nuclear magnetic resonance spectroscopy</td>
</tr>
<tr>
<td>GPC</td>
<td>gel permeation chromatography</td>
</tr>
<tr>
<td>Mₙ</td>
<td>number average molecular weight</td>
</tr>
<tr>
<td>VSM</td>
<td>vibrating sample magnetometry</td>
</tr>
<tr>
<td>LLA</td>
<td>L-lactide</td>
</tr>
<tr>
<td>PLA</td>
<td>Polylactic acid</td>
</tr>
<tr>
<td>PLLA-PMVS-PLLA</td>
<td>poly(L-lactide)-polymethylvinylsiloxane-poly(L-lactide) precursor</td>
</tr>
<tr>
<td>PLLA-P(COOH)-PLLA</td>
<td>Acid-functionalized poly(L-lactide)-polysiloxane-poly(L-lactide)</td>
</tr>
<tr>
<td>PLLA</td>
<td>poly(L-lactide)</td>
</tr>
<tr>
<td>PMVS</td>
<td>polymethylvinylsiloxane</td>
</tr>
<tr>
<td>TGA</td>
<td>thermogravimetric analysis</td>
</tr>
<tr>
<td>MAA</td>
<td>mercaptoacetic acid</td>
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CHAPTER 1

Introduction

For decades, polylactides have received enormous attention for biomedical applications due to their biocompatibility and biodegradability.\(^1\) Their degradation into naturally occurring metabolites, specifically lactic acid, are among several attractive characteristics.\(^2\) Biodegradation occurs through hydrolytic or enzymatic cleavage of the acyl-oxygen ester bonds. The biocompatibility and safety of polylactides has been well-established through extensive in vivo studies.\(^3\)

Properties such as morphologies and biodegradation rates of polylactides depend on the stereoisomers of the lactide monomers, molecular weights of the polymers, and functional endgroups.\(^4\) Poly(L-lactide) (PLLA) is a semicrystalline polymer with excellent mechanical properties. High molecular weight PLLA has a melt transition of approximately 180 °C and a glass transition temperature of approximately 67 °C.\(^5\) The homopolymer is commonly prepared by anionic or coordination-insertion ring-opening polymerization of L-lactide initiated by nucleophiles such as alcohols.\(^6\) The


coordination-insertion polymerization is often catalyzed by tin esters such as stannous octoate (Sn(Oct)₂).

Magnetic nanoparticles of magnetite can be stabilized by incorporating acid-functionalized poly(L-lactide)-siloxane copolymers to yield biocompatible and dispersible magnetite-polymer complexes (Figure 1.1). These complexes may then be incorporated into biocompatible microspheres and are of potential interest for biotechnological applications.

![Figure 1.1 Magnetite nanoparticles stabilized by polylactide-siloxane copolymers](image)

Potential applications for these magnetic materials include magnetic field-directed, targeted drug or gene delivery, magnetic cell separations (e.g., for bone marrow purification), enhanced MRI diagnostics, and magnetic hyperthermia therapy for treatment of tumors.⁷ Current technology utilizing magnetic microspheres is limited by

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the lack of control over microsphere size, shape, homogeneity, and magnetic susceptibility. The fundamental chemistry required for achieving precise, non-toxic polymer sheaths around such particles will be critical for biomedical applications. The chemical structure of the organic component is important since it isolates the magnetic nanoparticles from biological tissues. Advancements in preparing and understanding polymer-magnetic particle complexes may lead to the ability to localize high concentrations of drugs at a tumor site. These technologies could reduce the extreme side effects that occur with systemic cancer therapies.

This thesis describes the synthesis and characterization of poly(L-lactide-b-methylvinylsiloxane-b-L-lactide) triblock copolymers, and their derivatization with carboxylic acid groups for complexation to magnetite nanoparticles. The resultant magnetite-polymer complexes will be further incorporated into the formation of controlled-size microspheres for various biomedical applications.

CHAPTER 2
Literature Review

2.1 Overview

This chapter will discuss areas directly related to the research topic and is divided into five sections. The first section presents an overview of polysiloxane chemistry, including the physical properties and synthesis of cyclosiloxane monomers. The synthesis of vinyl substituted D₄ is discussed in detail. The second section is a review of the literature concerning the synthesis and properties of lactide monomers and polymers. Ring-opening polymerization of L-lactide and the characteristic initiators used for such reactions is discussed. The section concludes with a discussion of the biodegradation of polylactides. The third section briefly discusses the chemistry of the ene-thiol reaction, since this was an important chemical modification of the polymers in this research. The fourth section discusses copolymerizations of lactides and siloxanes. The final section gives an overview of magnetite and magnetic nanoparticle dispersions.

2.2 Polysiloxanes and Their Properties

2.2.1 Overview of Polysiloxanes

Polysiloxanes are versatile polymers with a silicon-oxygen backbone. Silicone and siloxane are terms that have been used interchangeably. Silicone represents compounds containing a silicon-oxygen bond, R₂SiO, and stems from the term ketone. However, it was found that silicon does not form double bonds with oxygen, rather it
forms Si-O-Si, leading to polymeric compounds. The term “silicone” is used primarily for technical products while “siloxane” is used for scientific nomenclature.

In the formation of polysiloxanes, the silicon can be combined with one, two, or three organic groups with the remaining bonds being to oxygen. The formula is as follows:

\[ R_nSiO_{(4-n)/2} \]

The “n” values range from 0 to 3 resulting in silica or a trifunctional, difunctional, or monofunctional siloxane unit. \( R_4Si \) denotes a silane since there is no bond to oxygen. Table 2.1 shows the representative nomenclature commonly utilized.\(^8\)

**Table 2.1** Structural Units of the Polyorganosiloxanes

<table>
<thead>
<tr>
<th>Structural formula</th>
<th>Composition</th>
<th>Functionality</th>
<th>Symbol</th>
</tr>
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<tbody>
<tr>
<td>( R_3Si-O- )</td>
<td>( R_3SiO_{1/2} )</td>
<td>Monofunctional</td>
<td>M</td>
</tr>
<tr>
<td>( -O-Si-O- )</td>
<td>( R_2SiO_{2/2} )</td>
<td>Difunctional</td>
<td>D</td>
</tr>
<tr>
<td>( -O-Si-O- )</td>
<td>( RSiO_{3/2} )</td>
<td>Trifunctional</td>
<td>T</td>
</tr>
<tr>
<td>( -O-Si-O- )</td>
<td>( SiO_{4/2} )</td>
<td>Tetrafunctional</td>
<td>Q</td>
</tr>
</tbody>
</table>

2.2.2 Preparation of cyclosiloxanes

Siloxane bonds can be formed by hydrolysis of chlorosilanes to produce silanols, which then can be condensed to form siloxanes. An example includes the reaction of trimethylchlorosilane with water to form an unstable silanol that condenses to form hexamethyldisiloxane:

\[
(CH_3)_3SiCl + H_2O \rightarrow (CH_3)_3SiOH + H_2O - HCl
\]

This resulting disiloxane can be utilized as an endcapping reagent for polymerization reactions to control the molecular weight of the siloxane polymer. Polymers that are prepared from hydrolysis, then condensation, yield linear and cyclic analogues (Figure 2.1).9 The cyclics, predominantly n = 4-6, can be separated by fractional distillation.

![Diagram of linear and cyclic analogues from hydrolysis](image)

**Figure 2.1** Linear and cyclic analogues from hydrolysis

The proportion of linear and cyclic siloxanes is strongly dependent on the reaction conditions. For the synthesis of cyclosiloxane monomers by hydrolysis and condensation, the intramolecular condensation should be optimized while simultaneously limiting the intermolecular condensation so that the degree of condensation is about 4.

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This ratio is favored in the presence of low concentrations of reactants. Slow addition of dimethyldichlorosilane to excess water favors production of cyclics.\textsuperscript{10} If a solvent such as methanol (miscible with water) is used in the reaction, this also favors the formation of cyclics. Solvent interactions during hydrolysis provide a means for controlling the resulting composition. Water-miscible solvents favor the production of cyclic compounds; however, polar solvents such as methanol may increase the amount of ring-opening reactions of the cyclics.\textsuperscript{11}

The tetramer, D\textsubscript{4}, is more thermodynamically stable than the trimer, D\textsubscript{3}, and D\textsubscript{4} is typically synthesized commercially by hydrolysis and condensation.\textsuperscript{12} The tetramers are generally used as monomers for equilibration reactions producing linear PDMS due to their cost-effectiveness. The more strained trimer, D\textsubscript{3}, is utilized for living polymerization. This monomer can be prepared with 1,3-dihydroxy-1,1,3,3-tetramethyldisiloxane and dichlorodimethylsilane in the presence of pyridine as a proton scavenger.\textsuperscript{13} Hexamethylocyclotrisiloxane can also be produced via condensation of dichlorodimethylsilane with a 10 mol % excess of zinc oxide.\textsuperscript{14}

2.2.3 Ring-opening equilibria

Polysiloxanes are synthesized either through ring-opening equilibrations or living polymerizations. This section discusses equilibration reactions. Ring-opening equilibrium reactions of polysiloxanes can be conducted through either acid or base-

\textsuperscript{10} N. N. Sokolov, S. M. Akimova, \textit{J. Gen. Chem. (USSR)}, 26, 2276 (1956).
\textsuperscript{14} Ibid.
catalyzed polymerizations. Unstrained cyclosiloxane monomers such as D₄ are typically utilized. Larger rings such as D₅, D₆, and D₇ can also be employed and various ring substituents can be included. The siloxane bond can undergo substitution in the presence of a strong acid or base.¹⁵ Both cyclic and linear siloxane analogues experience bond cleavage and formation until a state of thermodynamic equilibrium is reached. This results in a gaussian molecular weight distribution of the linear polymers (i.e., \( \frac{M_w}{M_n} \sim 2 \)). D₄ has a heat of polymerization, \( \Delta H \), close to zero and the \( \Delta S \) is positive by 6.7 J/mol K.¹⁶ Thus, the driving force of the polymerization is primarily entropy. There is usually a decrease in entropy among most polymerizations since polymeric forms are usually more ordered than their disordered monomeric precursors.

2.2.3.1 Acid-catalyzed ring-opening equilibration

A wide variety of acid catalysts have been used for ring-opening polymerizations of siloxanes. Trifluoromethanesulfonic acid (triflic acid), sulfuric acid and acidic inorganic compounds such as clays, have been used most extensively.¹⁷ Mechanisms of polymerization have been proposed, but the acid-catalyzed equilibration is still not fully understood.¹⁸ It has been proposed that the oxygens in siloxanes become protonated with protonic acids such as sulfuric acid. Subsequently, the protonated species are attacked by nucleophiles at the partially positive silicon atoms and this leads

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¹⁸ Ibid.
to cleavage the Si-O bonds. Wilczek et al. have proposed a mechanism for ring-opening polymerization using triflic acid as the catalyst (Figure 2.2).

![Proposed mechanism for acid-catalyzed ring-opening polymerization of D₄](image)

**Figure 2.2** Proposed mechanism for acid-catalyzed ring-opening polymerization of D₄

### 2.2.3.2 Base-catalyzed ring-opening equilibration

Bases attack the silicon atoms of unstrained rings such as D₄, cleaving the silicon-oxygen bonds to produce silanolate reactive species which then dimerize. The reaction proceeds via three possible routes. The silanolate reactive species can react with other cyclics to propagate the polymer chain, backbite to form different cyclics, or react with other linear analogues. Siloxane dimers containing Si-C bonds are often used as endcapping reagents as a method of controlling molecular weight (Figure 2.3).

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19 Ibid.
20 Ibid.
As a result of higher ring strains and thus, lower activation energies (~16.5 ± 1.0 kcal/mol) for ring-opening, D₃ has higher reactivity than D₄ (which has lower ring strain and higher activation energy (~19.5 ± 1.0 kcal/mol)). The silicon atom will have a greater partial positive charge when there are more oxygens bonded to it. This results in higher susceptibility to nucleophilic attack.

Reactivities of different catalysts for the anionic ring-opening polymerization of D₄ were studied. Tetramethylammonium silanolate, tetrabutylammonium silanolate and potassium silanolate were compared. Potassium silanolate was found to be less reactive in polydimethylsiloxane equilibrations than the others. The potassium silanolate system

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required higher catalyst concentrations and/or longer reaction times and elevated temperatures to incorporate endcapping reagents effectively into the chains.

Cazacu, et al. used anionic ion-exchange resins as catalysts for equilibration of $D_4$ or 1,3,5,7-tetravinyl-1,3,5,7-tetramethylcyclotetrasiloxane ($D_4^{VI}$). The methylvinyl cyclic tetramer, $D_4^{VI}$ was found to be more reactive toward base than $D_4$ due to the vinyl groups being somewhat more electronegative than the methyl groups. One of the motivations for utilizing $D_4^{VI}$ was to synthesize polymers containing pendent vinyl groups that could be post-functionalized.

Kantor, et al. investigated mechanisms of base catalyzed equilibrations of hexamethyldisiloxane (MM) and octamethylcyclotetrasiloxane ($D_4$) utilizing the base, tetramethylammonium hydroxide, as a catalyst. Data obtained from these investigations indicated that base-catalyzed equilibration of an M-D system involved the formation of relatively high molecular weight polymers at early reaction stages. These reactions subsequently undergo backbiting to result in lower molecular weight oligomers as shown in equations below.

\[
MD_xM + MM \rightarrow MD_{x-1}M + MDM \quad (1)
\]
\[
MD_xM + MDM \rightarrow MD_{x-3}M + MD_4M \quad (2)
\]

Number average molecular weights ($M_n$) as a function of time for a equilibration of a 1:1 molar mixture of MM and $D_4$ indicated there was an initial rapid increase in $M_n$, and a viscosity maximum was reached. After this point, the $M_n$ gradually decreased as the

27 Ibid.
mixture approached equilibrium. This data suggests predominant propagation steps occurring in the early stages of the reaction, leading to later reactions noted in equations above. Kantor, et al. suggested the following reaction schemes that contribute to an overall base catalyzed equilibration of MM and D₄:

\[ k_1 \quad -D_x^- + D_4 \rightarrow -D_x + 4^- \quad (3) \]
\[ k_2 \quad -D_x^- + MM \rightarrow MD_xM \quad (4) \]
\[ MD_xM + MM \rightarrow MD_{x-z}M + MD_zM \quad (5) \]
\[ MD_xM + MD_yM \rightarrow MD_{x+w}M + MD_{y-w}M \quad (6) \]

Equations 3 and 4 cause an increase in Mₙ while the backbiting reactions 5 and 6 produce no change in the number of molecules. Reactions 5 and 6 are responsible for the final equilibrium state.

### 2.2.4 Living Anionic Polymerization

D₃ is more reactive towards acids and bases than most other cyclosiloxanes due to its ring strain (50-63 kJ mol⁻¹ (12-15 kcal mol⁻¹)).²⁸ The polymerization of D₃ is exothermic as a result of the relief of this strain upon opening the ring. Organolithium reagents can be utilized as initiators at room temperature in the presence of a reaction promoter such as THF to produce lithium siloxanolates. The polymerization of D₃ can

result in the degree of polymerization increasing linearly with the percent conversion, thus signifying living polymerization reactions. There are no chain transfer or termination steps in the polymerization sequence. Polymerizations with D₃ can be taken to complete conversion of the monomer at room temperature without compromising the living nature of the reactions. It is known that the reactivity ratios between the vinyl substituted cyclic trimers (D₃⁻⁻⁻⁶⁰⁻⁻⁻³⁶⁻⁻⁻) and D₃ are quite different. The synthesis of this monomer by hydrolysis of methylvinylidichlorosilane produces only low yields of the target cyclic trimer molecule because the formation of larger unstrained rings is favored.

2.3 Polylactides and Their Properties

2.3.1 Introduction

For decades, polylactides have been of enormous interest in biomedical applications because of their biocompatibility and biodegradability. Specific desirable characteristics include: i) they decompose into naturally occurring metabolites, ii) a variety of useful properties can be obtained from tailoring a wide range of monomer derivatives, iii) degradation of these polymers only requires water, and iv) their safety is well documented in humans. These versatile polymers can be utilized for applications spanning medical and pharmaceutical fields. In the 1960s, American Cyanamid

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introduced polylactides as synthetic, degradable sutures composed of the polylactide derivative, poly(glycolic acid) (PGA). Ethicon developed similar materials containing both poly(lactic acid) (PLA) and PGA. Drug delivery applications were not developed until the early 1970s, when DuPont was awarded patents for polylactide/drug mixtures. These first drug delivery systems were used to deliver antimalarial drugs to mice and provided 14 weeks of protection. The utilization of polylactides for controlled release of small and large molecules has greatly advanced in the last 15 years. A more recent example of this technology includes Lupron (TAP Pharmaceutical Products, Inc.) for treating endometriosis and prostate cancer.

After decades of research and development, the literature describing the synthesis and characterization of these biomedical polymers is vast. This chapter includes four sections. The first will discuss and compare the preparation and characterization of different lactide monomer derivatives. The second section will discuss the mechanisms and conditions by which lactides are polymerized via ring-opening polymerizations. The third section will discuss studies that have been conducted utilizing a variety of catalysts for ring-opening polymerization of lactides. Finally, the biocompatibility and biodegradation of polylactides will be discussed.

### 2.3.2 Lactide Monomers

Lactic acid is one of the simplest chiral molecules and exists as the two stereoisomers, D- and L-lactic acid (Figure 2.4).
The L isomer differs from the D form in its effect on polarized light. For L-lactic acid, the plane is rotated in a counter-clockwise (laevo) direction, whereas the D form rotates the plane in a clockwise (dextro) direction. Lactic acid can be produced by a petrochemical route as a mixture of L and D isomers. In contrast, fermentation-derived lactic acid is almost exclusively the L-lactic acid enantiomer. The ability to produce the L-isomer in high purity is important for the process and can lead to stereoregular polymers. By controlling factors such as time and temperature along with catalyst type and concentration, it is possible to prevent racemization of D- and L-lactic acid units in the final polymers.\(^{35}\)

Lactide, the cyclic dimer of lactic acid is prepared by heating lactic acids under controlled conditions. Giling et al. synthesized both lactide and glycolide monomers in the same manner.\(^{36}\) Glycolide was synthesized by heating 1000 g of glycolic acid under nitrogen, adding 1 g of Sb\(_2\)O\(_3\), and raising the temperature to 120 °C. Once the water was removed, the temperature was increased to 180 °C and the pressure was lowered from 760 to 5 mm Hg over 4 to 6 hours. This resulted in a low molecular weight molten dark


yellow glycolic acid. Glycolide was subsequently sublimed and distilled. White crystalline pure glycolide was obtained once washed to remove the yellow color and recrystallized from ethyl acetate. The authors synthesized lactide in a similar fashion.\textsuperscript{37}

L-lactic acid can also be controllably racemized to D-lactic acid. Hence, three forms of the lactide monomer are possible. One can tailor the molecular architecture of the polylactides through polymerization of the lactide cyclic monomers. Compositional control of the lactide mixture further dictates the vast array of properties that can be created in the final polymer. The L,L and D,D isomers of the 6-membered lactide monomers are optically active; the meso form is optically inactive (Figure 2.5).

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{lactide_isomers.png}
\caption{Three stereoisomers of lactide}
\end{figure}

\subsection{Ring Opening Polymerization}

\subsubsection{Overview of Lactide Polymerization}

The stereochemical composition of the lactide monomer stream can determine the stereochemical composition of the resulting polymer. The melting points of the polymers and their rates and extents of crystallization depend on the isomer composition and

\textsuperscript{37} Ibid.
sequence in the polymers.\textsuperscript{38} PLA, prepared from L-lactide, has an equilibrium melting point of 207 °C and a glass transition temperature of about 60 °C.\textsuperscript{39} A higher melting stereocomplex comprised of a 1:1 mixture of poly(L-lactide) and poly(D-lactide) is also known.\textsuperscript{40} The maximum “practical” obtainable melting point of sterochemically pure poly(lactide) (either L or D) is around 180 °C with an enthalpy of melting of 40-50 J/g.\textsuperscript{41} Introducing stereochemical defects into the poly(L-lactide) (e.g., by incorporating controlled amounts of meso-lactide or D-lactide) reduces the melting point, rate of crystallization, and extent of crystallization with minimal effect on the glass transition temperature.\textsuperscript{42} PLA resins containing more than 93% of L-lactic acid are semi-crystalline while PLA with 50-93% L-lactic acid is amorphous.\textsuperscript{43} The presence of either meso- or D-lactide units in PLLA leads to imperfections in the crystalline structure, thus reducing the percent of crystallinity. The glass transition temperature of PLA ranges from 50 °C to 80 °C while the melting temperature ranges from 130 °C to 180 °C.\textsuperscript{44} The optimum temperature range for crystallization of poly(L-lactide) is 105-115 °C.\textsuperscript{45} Crystallization under these conditions is relatively slow with a half-time of about 2.5 min.\textsuperscript{46} The crystallization half-time increases approximately 40% for every 1% of meso-lactide incorporated into the polymer. Nucleating agents have been shown to effectively increase the nucleation density, and subsequently increase the crystallization process.\textsuperscript{37}

\textsuperscript{39} Ibid.
\textsuperscript{40} H. Tsuji, Y. Ikada, \textit{Macromolecules}, 26, 6918 (1993).
\textsuperscript{42} Ibid.
\textsuperscript{43} Ibid.
\textsuperscript{44} Ibid.
\textsuperscript{45} Ibid.
\textsuperscript{46} Ibid.
2.3.3.2 Reaction Mechanisms of Ring-Opening Polymerization

Low molecular-weight poly(lactic acid)s can be synthesized directly from the different isomers of lactic acid. For higher molecular-weight polymers, ring-opening polymerization of the 6-membered lactide rings is favored to produce polylactides. From the various stereoisomers of the cyclic dimer, a variety of polymers can be synthesized. These include poly(L-lactide), poly(D-lactide), polymers from the meso-lactide, and copolymer mixtures. This section will focus on the ring-opening mechanism of lactides to produce high-molecular weight polylactides. The polymerization of lactides can be induced by four different classes of initiators and reaction mechanisms: 1) cationic polymerizations, 2) anionic polymerizations, 3) coordination-insertion mechanisms, and 4) enzymatic polymerizations. Focus will be given to the three non-enzymatic polymerization methods.

Anionic polymerization of lactides can be initiated by alkali metal alkoxides. However, phenoxides and carboxylates are also active at higher temperatures. Initiation and propagation consist of a nucleophilic attack of the anion onto the carbonyl group of the lactide, followed by the cleavage of the acyl carbon-oxygen bond (Figure 2.7). Chain growth proceeds via an alkoxide reactive species. This reaction can involve side reactions, such as abstraction of the methine proton from a monomer or chain. This can result in racemization as a result of the planarity of the delocalized anion during deprotonation and reprotonation. The deprotonated anionic species from these side

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reactions can initiate new chains and thus deprotonation of the monomer may also lead to chain transfer, thus leading to low to moderate molecular weights.

Figure 2.6 Anionic polymerization of lactides

Extensive studies from two research groups have shown that extremely strong acids can initiate cationic polymerization of lactides. However, this is not the most widely used method since it only yields low to moderate molecular weights slowly below 50 °C. The mechanism (Figure 2.6) involves the protonation or alkylation of the carbonyl O-atom, resulting in electrophilic activation of the O-CH bond. This bond is then cleaved by nucleophilic attack of another monomer. This step is propagated until a monofunctional nucleophile, such as water, terminates the chain. Nucleophilic

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substitution at the chiral carbon results in optically pure poly(L-lactide) prepared at temperatures equal to or less than 50 °C.50

Figure 2.7 Cationic polymerizations of lactides

At higher temperatures, cationic polymerization results in racemization, which changes the physical and mechanical properties of the resulting polylactide.

Polymerization can also occur via a coordination-insertion mechanism. Catalysts for such reactions are typically metal alkoxides or esters having a covalent metal-oxygen bond and the character of weak Lewis acids.51 The most commonly used tin initiator is

stannous(II) ethylhexanoate (SnOct2). The initiating species is a tin alkoxide, formed prior to the polymerization.52 Lactide coordinates with the metal via the carbonyl O-atom, enhancing the electrophilicity of the carbonyl group so that insertion of the lactone into the metal-oxygen bond occurs (Figure 2.8). High molecular weight polymers, good reaction rates, and low levels of racemization are observed with tin-catalyzed polymerization of lactide. Tin initiators are capable of producing stereoregular polymers53 of narrow molecular weight distribution and controllable molecular weight with well defined endgroups.54 Typical conditions for polymerization are 180-210 °C with tin octoate concentrations ranging from 100-1,000 ppm, and less than 24 hours to reach approximately near quantitative conversions. These polymerizations are first order

![Figure 2.8 Coordination-insertion chain growth mechanism of lactide to PLA; R = growing polymer chain](image-url)

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in both catalyst and lactide. Frequently, initiators containing hydroxyl groups such as 1-octanol are utilized to control both molecular weight and endgroup structure.\textsuperscript{55}

Aluminum alkoxides, and tin alkoxides, are also commonly used initiators for the polymerization of lactides. A major difference between the tin and the aluminum-based initiators is that tin initiators are good transesterification catalysts, whereas aluminum initiators are not. Extensive experimental investigations of polylactide polymerizations utilizing different aluminum initiators have been performed by a number of groups.\textsuperscript{56} Tin initiators have the advantage of being more hydrolytically stable than those of aluminum and can be easier to handle and use in polymerizations. After several years of research on tin alkoxides, controlled polymerizations of advanced structures are possible.\textsuperscript{57} Under mild reaction conditions, the undesirable transesterification reactions are less pronounced and structures like triblocks, macrocyclics, multiblocks, resorbable networks and star-shaped structures can be prepared.\textsuperscript{58}

The reaction mechanisms with SnOct\textsubscript{2} are not fully understood. Stannous octoate was believed to initiate polymerization of lactide monomers by a cationic polymerization mechanism as presented by Nijenhuis, et al., but little experimental evidence was provided.\textsuperscript{59} On the other hand, it has been shown that both anionic and cationic polymerizations of L-lactide involve strong racemization above 50 °C, whereas SnOct\textsubscript{2}

\textsuperscript{58} Ibid.
can yield optically pure poly(L-lactide) even at 180 °C when the reaction time is short.\textsuperscript{60} This evidence supports the coordination-insertion mechanism. SnOct\textsubscript{2} does not contain alkoxide (or hydroxide) groups, and it was also previously demonstrated that lactones do not insert into Sn-carboxylate bonds under normal polymerization conditions, whether or not Sn(II) or Sn(IV) carboxylates are involved.\textsuperscript{61}

Authors have reported that addition of alcohols (including diols) accelerates the polymerization and allows control over structure and molecular weights.\textsuperscript{62} Proton NMR spectroscopy was used for detailed studies at room temperature to reveal that SnOct\textsubscript{2}, combined with an alcohol, establishes a rapid complexation equilibrium and that this interaction is stronger than the interaction between SnOct\textsubscript{2} and lactide. This suggests that the interaction of SnOct\textsubscript{2} with the alcohol (when added as a co-initiator) proceeds by a chain growth step. On the basis of these results, chain growth via reaction between coordinated alcohol (or chain end) and a lactone was hypothetically formulated.

Zhang, et al. postulated that the reaction of SnOct\textsubscript{2} with alcohols yields a tin alkoxide (OctSnOR) that initiates the polymerization of lactide and lactones via the classical coordination-insertion mechanism.\textsuperscript{63} The initiation was suggested to occur by monomer insertion into the metal alkoxide active center. MALDI-TOF mass spectroscopy was used to confirm this mechanism as initiated with Sn(Oct)\textsubscript{2}, with either water or an alcohol as the co-initiator.\textsuperscript{64} Bu[O(O)C(CH\textsubscript{2})\textsubscript{3}]\textsubscript{n}OSnOct, and

[O(O)C(CH₂)₅]ₙOSn cyclics confirm an “active chain end” mechanism occurred, with Sn(Oct)₂ reacting with covalent metal carboxylates to produce alkoxide initiators for the polymerization. Another slightly different proposed coordination-insertion mechanism involves a hydroxyl group from an alcohol and a monomer coordinating with the Sn(Oct)₂. This, in turn, initiates the polymerization of lactide. Sn(Oct)₂ at high concentrations and temperatures produce transesterifications. High catalyst concentrations increase the number of sites for ester interchange reactions, while high temperatures result in alkyl-oxygen bond cleavage, leading to racemization.

![Figure 2.9](image)

**Figure 2.9** Two points where ester bond can break: a) if this bond is broken during transesterification, no racemization is observed and b) if this bond is broken, racemization occurs.

Other tin based compounds have been successfully used as catalysts or initiators for the ring-opening polymerization of lactides. Such examples include cyclic tin-based catalysts, and divalent tin(II) alkoxides such as tin(II)butoxide (Sn(OBu)₂). Other examples include Bu₃SnOMe or Bu₂Sn(OMe)₂, BuSnCl₃, and tetraphenyl tin.

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Other developments in tin-based initiators include a tin(II) macroinitiator synthesized through the reaction of a cyclic ester monomer, such as L-lactide, rac-lactide, or caprolactone with Sn(OEt)$_2$ as reported by Story, et. al.$^{72}$ This initiator yielded high molecular-weight polyesters of about 500,000 g/mol with narrow polydispersions (PDI = 1.1-1.5), suggesting that transesterification had been minimal. Penczek, et al. reported controlled synthesis of ultrahigh molecular weight aliphatic polyesters of about 100,000 g/mol with the use of Sn(OBu)$_2$. However, Storey, et al. indicated the insolubility of Sn(OBu)$_2$ in common organic solvents in comparison to the solubility of the macroinitiator.

2.3.4 Biodegradation of Polylactides

One of the most appealing characteristics of polylactides is their biocompatibility, allowing for a vast array of biomedical applications. Aliphatic polyesters can degrade in contact with living tissues or under outdoor conditions. Research conducted over the last two decades has led to several applications in surgery and pharmacology. Outdoor applications include packaging or mulch films and plant therapy, whereby controlled

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delivery of pesticides or insecticides in agriculture have sparked interest. Emphasis in this chapter will be placed on the medical applications and properties of interest for such applications. It was not long after their introduction that interest was generated in this class of biomedical polymers for temporary therapeutic applications in surgery and pharmacology.

The term “biodegradable polymer” has been widely used for polymers that undergo \textit{in vivo} degradation.\textsuperscript{73} Williams defined biodegradation as a biological breakdown.\textsuperscript{74} Graham and Wood defined biodegradable materials as those that can degrade in vivo, but extended the definition to denote materials that form soluble products that can be easily removed from the implantation site and excreted from the body.\textsuperscript{75} A consensus was reached on the following terms at the Second International Scientific Workshop on Biodegradable Polymers and Plastics (Montpellier, France).\textsuperscript{76}

- **Polymer degradation** is a deleterious change in the properties of a polymer due to a change in the chemical structure;
- **Biodegradable polymer** is a polymer in which the degradation is mediated at least partially by a biological system
- **Bioabsorbable polymer** is a polymer that can be assimilated by a biological system;
- **Erosion** reflects the process of dissolution or wearing away of a polymer from the surface.

\textsuperscript{74} Ibid.
\textsuperscript{75} Ibid.
\textsuperscript{76} Ibid.
The prefix “bio” will be considered as reflecting phenomena resulting from contact with living elements such as tissues, cells, bodily fluids or microorganisms. Accordingly, water, oxygen and enzymes are regarded as biological elements, although a lot of authors still tend to limit discussions of biodegradation to enzymatic attack only.

Most of the attractive biodegradable polymers discovered thus far contain hydrolyzable linkages such as amide, ester, urea and urethane along the polymer chains.77 Aliphatic polyesters such as polylactides prove to be the most attractive class, and this is due in part to their versatility in terms of their physical, chemical and biological properties. Biodegradation or depolymerization of polylactides involves the chemical cleavage of the polymer backbone, which results in a reduction in the mechanical properties. Cleavage may result from either enzymatic attacks or simple hydrolysis of the ester bond or a combination of both.78

There is physical and chemical evidence of enzymatic attacks on polylactides even though information is limited. Williams and Mort examined the role of 15 enzymes in the in vitro degradation of Dexon® sutures and found that four of them increased the hydrolytic rate.79 PLA was also investigated and it was shown that proteinase K caused PLA hydrolysis.80 Reed indicated that there could be considerable enzymatic involvement in PLA degradation since there was a substantial difference between in vitro and in vivo molecular weight changes.81 Later, work by Williams showed that lactate dehydrogenase produced ambiguous results with PLA, but proteinase K, pronase and

77 Ibid.
80 Ibid.
81 Ibid.
bromelain had significant effects, as shown by the detection of lactic acid in solution.\textsuperscript{82} Schakenraad, et al. investigated tissue reactions toward PLA implants by studying the activity pattern of seven enzymes as a function of time.\textsuperscript{83} The authors concluded that the main degradation mechanism of these PLA implants was hydrolysis which took place in tissue fluids. However, intracellular breakdown of small molecular debris could not be excluded. The conclusion that the process is not enzyme-mediated is supported by another study which showed that the degradation rates measured \textit{in-vivo} (sheep, dogs, and rats) were essentially the same as measured \textit{in-vitro}.\textsuperscript{84} Younes, et al. also claimed the absence of enzymatic activity in the course of LLA/ethylene oxide block copolymers.\textsuperscript{85} Makino, et al. examined effects of plasma proteins on the degradation characteristics of polylactide homopolymers and showed the degradation rates in aqueous media were accelerated by the addition of albumin, $\gamma$-globulins and fibrinogen.

Polylactide degradation can also occur hydrolytically. From a molecular viewpoint, ester hydrolysis is a well-known mechanism in organic chemistry:

$$
\text{RCOOR}^{'} + \text{H}_2\text{O} \rightleftharpoons \text{RCOOH} + \text{R'}\text{OH}
$$

This reaction can be catalyzed by either acids or bases. The reaction product, RCOOH, is able to accelerate ester hydrolysis according to a phenomenon known as autocatalysis. In the case of aliphatic polyesters, chain cleavage at the ester bond can be autocatalyzed by carboxyl endgroups initially present or generated by the degradation reaction:

$$
\sim\text{COO}\sim + \text{H}_2\text{O} \rightleftharpoons \sim\text{COOH} + \text{HO}~
$$

\textsuperscript{82} Ibid.
\textsuperscript{83} Ibid.
\textsuperscript{84} Ibid.
\textsuperscript{85} Ibid.
The kinetics of the hydrolytic reaction can be expressed by the following rate equation:

\[ \frac{d[E]}{dt} = -\frac{d[COOH]}{dt} = -k[COOH][H_2O][E] \]

where \([COOH]\), \([H_2O]\) and \([E]\) represent carboxyl endgroup, water, and ester concentrations in the polymer matrix, respectively.\(^{86}\) By using the following relationships:

\[
[COOH] = \frac{W}{(M_n*V)} = \frac{\rho}{M_n},
\]

\[
[COOH] = \frac{[E]}{(DP-1)},
\]

\[
M_n = m*DP
\]

where \(W\) is the polymer molecular weight, \(V\) is volume, \(\rho\) is density, \(M_n\) the number average molecular weight, and \(DP\) the number average degree of polymerization and \(m\) the repeat unit weight, one obtains the following equation:

\[
\frac{d(1/DP)}{dt} = k(\rho/m)[H_2O](DP-1)DP^{-2}
\]

Integration of this equation leads to the following:

\[
\ln\{(1-\frac{DP}{DP_0})\} = k't
\]

where \(k' = k[H_2O](\rho/m)\) and \(DP_0\) is the average degree of polymerization at time zero. This kinetic expression is valid provided there is no weight loss. If \(DP >> 1\), this equation can be simplified:

\[
\ln(DP)/(DP_0) = \ln(M_n/M_n0) = -k't
\]

According to this expression, semilog plots of \(DP\) or of \(M_n\) versus time of hydrolysis are linear prior to the onset of weight loss.\(^{87}\)

\(^{86}\) Ibid.
From the macroscopic viewpoint, the degradation of aliphatic polyesters has been viewed as homogeneous (bulk erosion) or as resulting from surface erosion. Bulk hydrolysis of the ester bonds in the polymer chains follows the general two-stage degradation profile for semicrystalline aliphatic polyester bioabsorbable polymers.\(^8\)\(^8\)

The hydrolysis of aliphatic polyesters initially involves water uptake followed by random hydrolytic chain scission according to the Flory principle, which postulates that all linkages have the same reactivity. However, a growing amount of chain ends leads to an increased probability of chain scission at the chain ends over time.\(^8\)\(^9\) The initial degree of crystallinity of the polyesters influences the rate of hydrolytic degradation as the crystal segments slow down the water permeation in the matrix. The amorphous parts of the polyesters have been shown to undergo hydrolysis before the crystalline regions due to a higher rate of water absorption. The first stage of hydrolytic degradation is accordingly in the amorphous regions, where the molecular fragments that are tie the crystalline segments together are hydrolyzed. The remaining undegraded chain segments, therefore, obtain more space and mobility, which leads to reorganization of the polymer chains and increased crystallinity.\(^9\)\(^0\)

The second stage commences when most of the amorphous regions are exhausted and the crystalline regions are attacked.\(^9\)\(^1\) Work by Li examining the degradation of PDLLA conclusively showed that degradation could be more rapid in the center than at

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\(^8\)\(^7\) Ibid.


\(^9\)\(^0\) Ibid.

\(^9\)\(^1\) Ibid.
the surface. This phenomenon is known as heterogeneous degradation and is widely accepted as occurring in both lactide and glycolide polymers. The extent of this degradation is dependent upon both polymer geometry and pH of the degradation medium. The heterogeneous degradation or autocatalysis mechanism results from the hydrolytic cleavage of the ester bonds forming a new carboxyl endgroup. It was explained that as degradation progressed, the soluble oligomers produced close to the surface could escape, while those in the center could not diffuse out of the polymer. It was reasoned that this could lead to a higher internal acidity, with carboxyl endgroups catalyzing ester hydrolysis and a differentiation between surface and interior degradation rates.

The degradation of PLA is generally regarded as a bulk hydrolysis process. The polymer retains its volume for a considerable time throughout degradation with a loss of molecular weight observed, followed by mechanical strength and finally mass. The degradation rate and mechanical properties of PLLA are highly dependent upon different material properties such as crystallinity, orientation, molecular weight and molecular weight distribution, as well as the presence of impurities and unreacted monomer.

While poly(L-lactide) has been regarded as outstanding for its non-toxicity, biodegradability and biocompatibility, there is room for improvement in the biomedical field in terms of its hydrophilicity. Poly(ethylene glycol) (PEG) is also an attractive biopolymer due to its non-toxicity, biodegradability and biocompatibility. Terminal

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94 Ibid.
95 Ibid.
96 C. C. Chu, Polymer, 26, 591 (1985).
hydroxyl groups of PEG can readily react with a variety of compounds, thus allowing copolymerization with lactones such as chiral lactides, glycolide and $\varepsilon$-caprolactone to yield block copolymers. PEG segments are often introduced into PLLA chains to improve their hydrophilicity and reduce the crystallinity of the PLLA. Diblock and triblock copolymers of PLLA/PEG can be prepared via ring-opening polymerization of L-lactide in the presence of hydroxyl-functional PEG and certain catalysts.\textsuperscript{97} Co-initiators such as Zn metal or CaH$_2$ can be utilized in addition to stannous octoate.\textsuperscript{98} The increasing degree of hydrophilicity of the copolymers correlates directly with the increase in PEG composition. High molecular weight copolymers can be obtained by using long PEG blocks, but this increases the likelihood of accumulation of polymer fragments in the body when utilized in vivo. It is suggested that multiblock copolymers constructed with short blocks might overcome this limitation.\textsuperscript{99}

2.4 Poly(lactide)-(siloxane) Copolymers

Poly(L-lactide)s impart excellent biocompatibility and biodegradability with many potential applications. One of these applications includes controlled drug delivery, where they would serve as a matrix that would contain the drug and then function as a bioerodible system. The matrix would contain a labile bond that would further erode, thus liberating the drug of choice.

Copolymerization of two materials allows for adjusting biodegradation rates and mechanical properties. Copolymerization of PLLA with an elastomer may lead to a large variety of materials ranging from reinforced thermoplastics to thermoplastic elastomers. Improved impact strength and elongation at the break are desired for orthopedic applications. More rubbery materials are desired for material implants and drug delivery. Polysiloxanes are of particular interest to the research described in this thesis. Polysiloxanes have a low $T_g$ and a higher permeability for oxygen and water in the polymeric materials, making it biocompatible and serving as the rubber phase in a copolymer with poly(L-lactide).

There has been minimal published research performed on the formation of block copolymers of L-lactide and siloxanes. Zhang, et al. studied the ring-opening polymerization of L-lactide in the presence of $\alpha,\omega$-hydroxy-terminated PDMS macrorinitiators, resulting in a PLLA-PDMS block copolymer. PDMS that was terminated with hydroxyalkyl groups were utilized to ring-open lactide cyclic monomers in the presence of stannous octoate. They investigated the concentration of SnOct$_2$ used for preparing the triblock copolymers, keeping the reactions at a constant temperature (100 °C) and time (24 h). Reducing the amount of SnOct$_2$ did not raise the molecular weight of the products. When altering the ratio of PDMS to LLA, there was a change in the molecular weight distributions of the resulting polymers according to GPC. A low content of PDMS reduced the availability of hydroxyl groups, and the authors attributed this to more initiation of lactide by impurities. They inferred that two sets of

coordination-insertion mechanisms occurred during the polymerization reaction. One included SnOct$_2$, the lactide monomer, and hydroxyl groups in PDMS, while the other occurred by reaction with impurities in the system. Zhang, et al. concluded that low concentrations of SnOct$_2$ and high contents of PDMS optimally initiated the lactide monomer. After modifying their purification procedures, they were able to obtain a narrower molecular weight distribution from washing out low molecular weight chains. Zhang, et al. tried the polymerization of LLA initiated by the hydroxyl groups on the PDMS in the absence of SnOct$_2$ catalyst. The reaction was very slow and the final product was yellow and did not solidify.$^{102}$

2.5 Ene-Thiol Addition

It was of interest to incorporate carboxylic acid groups into the polylactide-siloxane copolymers focused described in this research. Carboxylic acid groups would allow for interesting surface properties and provide a means for stabilizing dispersions of various nanoparticles. The method of choice was to synthesize polysiloxane precursors having vinyl pendent groups, and then introduce carboxylic acid groups through an ene-thiol addition reaction.

The reaction of mercaptoacetic acid with vinyl-containing polysiloxanes was first studied by Scioborek, et al. on a polysiloxane with regularly-spaced vinyl groups.$^{103}$ The reaction, initiated with azo-bis-(isobutyronitrile) (AIBN), proceeded smoothly with the transformation of vinyl groups into an anti-Markovnikov addition product. Scioborek

$^{102}$ Ibid.

found that almost no vinyl groups were present after the chemical modification. The addition reaction proceeds in accordance with a free radical mechanism, thus no polysiloxane chain cleavage occurs during the reaction. After several days the chemically modified polysiloxane remains stable. However, after 100 days, Scioborek found evidence of cleavage of the siloxane bond by the carboxyl groups through SEC chromatography.104

2.6 Magnetic Nanoparticles

2.6.1 Background

Magnetism is a property that changes significantly as size decreases from bulk to nanoscopic. Materials that demonstrate this property are separated into domains with specific magnetic spins, whose orientations can be altered with the presence of an external magnetic field. These magnetic spins will align with that external field, thus inducing an overall magnetic moment. If there is complete randomization of the orientations of the particle magnetic moments when the applied magnetic field is removed, the material is considered to be superparamagnetic.105

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104 Ibid.
2.6.2 Magnetite Nanoparticles

Magnetite is a ferrimagnetic iron oxide, Fe₃O₄, with an inverse spinel crystalline structure in which part of the iron atoms are octahedrally coordinated to oxygen and the rest are tetrahedrally coordinated to oxygen. Advantages that magnetite has over other magnetic particles are that it is less susceptible to oxidation and loss of magnetization than the magnetic metals. However, one potential disadvantage is that it has a lower specific saturation magnetization when compared to the magnetic transition metals.

At a neutral pH, the surface of magnetite primarily consists of hydroxyl groups. This surface can be altered by adjusting the pH of the medium. At low pH, surface hydroxyl groups become protonated and at high pH they are deprotonated (Figure 2.11).
\[
\begin{align*}
\text{FeOH}_2^+ & \quad \text{FeOH} \quad \text{FeO}^- \\
\text{(low pH)} & \quad \text{(high pH)}
\end{align*}
\]

**Figure 2.11** Surface chemistry of magnetite as a function of pH

At low pH, it is also possible for water to leave, thus forming cations on iron. Counterions balance positive or negative surface charges at any particular pH to maintain electro-neutrality, resulting in an electrostatic double layer.\(^{109}\) This double layer promotes repulsion of the magnetite particles resulting from the decreased entropy of counterion distribution as the two surfaces approach each other. The isoelectric point of magnetite is at a pH of 6.8; that is, there is an equal number of positive and negative surface charges.\(^{110}\) Surfactants on the surface of magnetite nanoparticles are desirable to stabilize dispersions of such materials via a steric mechanism (Figure 2.12).\(^{84}\)

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\(^{109}\) Ibid.

\(^{110}\) Ibid.

**Figure 2.12** Steric repulsive forces between particles
Polymeric surfactants can be used to overcome any attractive forces between the nanoparticles, producing stabilized magnetite dispersions. These surfactants must be prepared with a functionalized portion that can bind to the surface of magnetite with the rest of the polymer being solvated in a dispersion medium or carrier fluid. When the magnetite particles approach each other, they encounter repulsive forces caused by the presence of polymer chains, losing their conformational entropy. This process is known as entropic, or steric, stabilization.\textsuperscript{111}

Research has shown that the functional portion of a polymer that can bind to the surface of magnetite tend to be organic ligands (carboxylic acids) and inorganic ligands (phosphates). Massart, et al. investigated the magnetite-carboxylate bond using magnetite with oleic acid. Based on FTIR spectrometry results, he concluded that the bond was a chelating bidentate configuration (Figure 2.13).\textsuperscript{112}

\begin{figure}[h]
\centering
\includegraphics[width=0.5\textwidth]{figure2.13.png}
\caption{Two forms of bidentate chelation of carboxylic acid on magnetite surface\textsuperscript{113}}
\end{figure}

\textsuperscript{111} Ibid.
\textsuperscript{112} Ibid.
\textsuperscript{113} Ibid.
CHAPTER 3

Synthesis and Characterization of Polylactide-siloxane Block Copolymers

3.1 Synopsis

The synthesis of the polylactide-siloxane triblock copolymers comprises three reactions. First, difunctional, controlled molecular weight polymethylvinylsiloxane oligomers with either hydroxybutyl or aminopropyl endgroups were prepared in ring-opening redistribution reactions. Second, these oligomers were utilized as macroinitiators for ring-opening L-lactide to provide triblock materials with polymethylvinylsiloxane central blocks and poly(L-lactide) endblocks. The molecular weights of the poly(L-lactide) endblocks were controlled by the grams of L-lactide relative to the moles of macroinitiator. Third, the vinyl groups on the polysiloxane center were further functionalized with carboxylic acid groups by adding mercaptoacetic acid across the pendent double bonds in an ene-thiol free radical reaction.
3.2 Materials

1,3,5,7-Tetravinyl-1,3,5,7-tetramethylcyclotetrasiloxane (Gelest), tetramethylammonium hydroxide pentahydrate (Aldrich, 99%), 1,3-bis(hydroxybutyl)tetramethyldisiloxane (Gelest), and bis(aminopropyl)tetramethyldisiloxane (Gelest) were used as received. Toluene (Aldrich, 98%) was washed twice with concentrated sulfuric acid and neutralized with water. It was dried over MgSO₄ for one hour, then over calcium hydride overnight and distilled just before use. Chloroform, stannous octoate, diethyl ether, trifluoromethanesulfonic acid, and mercaptoacetic acid were obtained from Aldrich and used as received. Methanol (HPLC grade) was obtained from EM Science (distributed by VWR, Inc.) and used as received. L-lactide (Purac) was recrystallized in ethyl acetate (Aldrich), filtered, and dried at room temperature in a round-bottom flask under vacuum. Nitrogen gas was obtained from AIRGAS, Inc. and used as received. Millipore water was obtained from Millipore (distributed by VWR, Inc.) and used as received. FeCl₃ · H₂O and FeCl₂ · H₂O (Aldrich) were used as received. Ammonium hydroxide 50 v/v % aqueous solution (Alfa Aesar) was deoxygenated prior to reaction. Concentrated hydrochloric acid (EM Science) was diluted to 4M.

3.3 Synthesis

3.3.1 Synthesis of tetramethylammonium disiloxanolate catalyst
The procedure used was based on work done by Hoyt.\textsuperscript{114} To prepare the tetramethylammonium disiloxanate catalyst, the apparatus was equipped with a mechanical stirrer, a nitrogen inlet running through the solution, and a flame-dried Dean Stark trap equipped with a condenser linked to a drying tube. Tetramethylammonium hydroxide pentahydrate (0.685 g, 0.0038 mol) was added to the reaction vessel followed by addition of octamethylcyclotetrasiloxane (13.7 g, 0.046 mol) via syringe. This represents a 5 weight \% (TMAH·5H$_2$O) dispersion in D$_4$. The reaction mixture was stirred with nitrogen bubbling through it for 24 h at 80 °C. The nitrogen flow was high enough to aid in the removal of water to the Dean-Stark trap (Figure 3.1). After 24 h, the catalyst was syringed immediately from the reactor into the desired reaction mixture to avoid moisture absorption.

\begin{figure}[h]
\centering
\includegraphics[width=0.5\textwidth]{figure3.1.png}
\caption{Dean-Stark apparatus for preparing tetramethylammonium disiloxanolate Catalyst}
\end{figure}

3.3.2 Synthesis of hydroxybutyl-terminated polymethylvinylsiloxane

Polymethylvinylsiloxane is produced via a cationic ring-opening equilibration of 1,3,5,7-tetramethyl-1,3,5,7-tetravinylcyclotetrasiloxane catalyzed by trifluoromethanesulfonic acid and end-capped with a difunctional hydroxyl-terminated siloxane. A procedure for preparing a 1000 g/mol molecular weight oligomer is provided. All other oligomers were prepared in similar procedures, but with appropriately different ratios of endcapping reagent relative to cyclosiloxane monomer. 1,3,5,7-Tetramethyl-1,3,5,7-tetravinylcyclotetrasiloxane (30 g, 0.087 mol), followed by 1,3-bis(hydroxybutyl)tetramethyldisiloxane (6.68 g, 0.024 mol) was charged to a flame-dried, 500-mL, one-neck, round-bottom flask equipped with a magnetic stir bar and septum. Once the mixture dissolved at 65 °C, trifluoromethanesulfonic acid catalyst (0.04 mL, 0.44 mmol) was added. The reaction was heated for approximately 48 h at 65 °C to allow the mixture to equilibrate. The reaction mixture was cooled to room temperature. The acid catalyst was neutralized by dissolving the reaction mixture in diethyl ether and repeatedly washing with deionized water until litmus tests indicated the mixture was neutral. The product was vacuum stripped to remove solvents, water and any remaining cyclics.

3.3.3 Synthesis of aminopropyl-terminated polymethylvinylsiloxane

The procedure was based on work done by Hoyt.\textsuperscript{115} Polymethylvinylsiloxane is produced via an anionic ring-opening equilibration of 1,3,5,7-tetramethyl-1,3,5,7-

tetravinylecyclotetrasiloxane catalyzed by tetramethylammonium disiloxanolate catalyst and end-capped with a difunctional aminopropyl-terminated siloxane. A procedure for preparing a 1000 g/mol molecular weight oligomer is provided. All other oligomers were prepared in similar procedures, but with appropriately different ratios of endcapping reagent relative to cyclosiloxane monomer. 1,3,5,7-Tetramethyl-1,3,5,7-tetravinylecyclotetrasiloxane (15 g, 0.044 mol) was added to a flame-dried, 500-mL, one-neck, round-bottom flask equipped with a magnetic stir bar and septum followed by 1,3-bis(3-aminopropyl)tetramethyldisiloxane (2.98 g, 0.012 mol). Once the mixture dissolved at 80 ºC, tetramethylammonium disiloxanolate catalyst (0.255 g) was added. The reaction was heated for approximately 48 h at 80 ºC to allow the mixture to equilibrate. The reaction was heated at 140 ºC for 3 h while bubbling nitrogen through it to decompose the catalyst and evolve the trimethylamine byproduct. The reaction mixture was heated at 125 ºC under vacuum (1-2 mm pressure) for 5 h to remove cyclics. The polymer was stored under nitrogen in a flame-dried round-bottom flask until used.

3.3.4 Synthesis of a Polylactide-siloxane Copolymer utilizing α,ω-Dihydroxybutyl-terminated PMVS

The copolymerization was conducted in bulk according to the following representative procedure for preparing a triblock copolymer containing 6,000 g/mol poly(L-lactide) tail blocks. α,ω-Dihydroxybutyl-terminated PMVS (0.53 g, 0.53 mmol), L-lactide (5.35 g, 0.047 mol), stannous octoate (2.1 mg Sn based on grams monomer) and toluene (10 mL) were charged to a flame-dried, nitrogen-purged, round-bottom flask equipped with a magnetic stir bar. The flask was placed in an oil bath at 65 ºC for 5 h.
The temperature of the oil bath was increased to 100 °C and the reaction mixture was stirred for another 15 h. The reaction progress was monitored by $^1$H NMR. After 20 h, the monomer had reacted to >70% conversion. The copolymer was purified by precipitation into methanol followed by washing several times with methanol. The copolymer was vacuum dried in a one-neck round-bottom flask.

3.3.5 Synthesis of a Polylactide-siloxane Copolymer utilizing Aminopropyl-terminated PMVS

The copolymerization was conducted in bulk according to the following representative procedure for preparing a triblock copolymer containing 5,000 g/mol poly(L-lactide) tail blocks. L-lactide (14.99 g, 0.13 mol), and toluene (30 mL) were charged to a flame-dried, nitrogen-purged, round-bottom flask equipped with a magnetic stir bar. The flask was placed in an oil bath at 65 °C and the lactide monomer dissolved. Aminopropyl-terminated PMVS (3.99 g, 1.50 mmol) was added and allowed to stir for 45 min. at 65 °C. Stannous octoate (6.0 mg, 2.1 mg Sn based on grams of monomer) was charged to the flask and the temperature of the oil bath was increased to 100 °C. The reaction progress was monitored by $^1$H NMR. After 48 h, the monomer had reacted to >94% conversion. The copolymer was purified by precipitation into hexanes followed by washing several times with hexanes. The copolymer was vacuum dried at 40 °C for 18 h.

3.3.6 Ene-thiol Addition of Mercaptoacetic Acid to a Polysiloxane-lactide Copolymer Prepared from the Hydroxybutyl Terminated Polymethylvinylsiloxane
The 15,500 g/mol PLLA-PMVS-PLLA (10.58 g, 6.80 x 10⁻⁴ mol) copolymer was weighed into a round-bottom flask equipped with a magnetic stir bar. Toluene (100 mL) was added via syringe and the solution was bubbled with dry nitrogen. AIBN (13.4 mg, 8.16 x 10⁻⁵ mol) was added and the flask was the mixture was purged with nitrogen. Mercaptoacetic acid (1.14 mL, 0.016 mol) was added via syringe and the reaction flask was placed in an oil bath at 80 °C. The reactions were monitored via ¹H NMR by following the disappearance of the peaks corresponding to the vinyl protons at 5.8 and 6.0 ppm. Once the reaction was complete as indicated by ¹H NMR, the polymer was precipitated into methanol. Iced methanol was used to filter and wash the polymer, which was then vacuum dried at 40 ºC and for 18 h.

3.3.7 Ene-thiol Addition of Mercaptoacetic Acid to a Polysiloxane-lactide Copolymer Prepared with an Aminopropyl Terminated Polymethylvinylsiloxane

The 11,500 g/mol PLLA-PMVS-PLLA (10.31 g, 8.93 x 10⁻⁴ mol) copolymer was weighed into a round-bottom flask equipped with a magnetic stir bar. Toluene (105 mL) was added via syringe and the solution was deoxygenated by bubbling dry nitrogen through the reaction mixture. AIBN (48.4 mg, 2.95 x 10⁻⁴ mol) was added and the flask was again purged with nitrogen. Mercaptoacetic acid (8.19 mL, 0.118 mol) was added via syringe and the reaction flask was placed in an oil bath at 80 °C. The reactions were monitored via ¹H NMR by following the disappearance of the peaks corresponding to the vinyl protons at 5.8 and 6.0 ppm. Once the reaction was complete as indicated by ¹H NMR, the polymer was precipitated into hexanes. Further iced hexanes were used to filter and wash the polymer, which was then vacuum dried at 40 ºC for 18 h.
3.3.8 Synthesis of Magnetite-Copolymer Complexes

Millipore water and a 50% aqueous solution of NH$_4$OH were deoxygenated by purging with N$_2$ for 30 min prior to the reaction. The reaction flask was purged with N$_2$ prior to the reaction to ensure an anaerobic environment. The iron salts were dissolved in 20 mL H$_2$O. Aqueous solutions of FeCl$_3$·6H$_2$O (2.0 g in 20 mL H$_2$O, 0.389 M) and FeCl$_2$·4H$_2$O (0.736 g in 20 mL H$_2$O, 0.195 M) were prepared separately under N$_2$ and syringed into a three-neck, 250-mL, round-bottom flask equipped with a mechanical stirrer and a pH electrode connected to a pH meter. The pH was adjusted to ~9.5 by adding 10 mL of the NH$_4$OH solution while stirring. The solution immediately turned black indicating the formation of magnetite particles. The reaction mixture was stirred under N$_2$ for 60 min. The reaction was neutralized to pH ~7.0 using a 4M HCl solution and allowed to continue stirring under N$_2$ purge for an additional 30 min. The appropriate amount of copolymer dissolved in 90% CH$_2$Cl$_2$ / 10% MeOH v/v (25 mL) was injected into the reaction flask. The N$_2$ purge was removed and the reaction mixture was stirred for 18 h.

The reaction mixture was transferred to a one-neck, 250-mL, round-bottom flask. The reaction flask was washed with 90% CH$_2$Cl$_2$ / 10% MeOH v/v to ensure the complete transfer of the product. The CH$_2$Cl$_2$ / MeOH solution was removed under vacuum and the remaining product was collected by holding a magnet to the bottom of the flask and decanting the water. The magnetite complex was washed with Millipore water three times to remove any salts. The complex was dried at room temperature then redispersed in CH$_2$Cl$_2$ / MeOH solution (100 mL). The dispersion was centrifuged to
remove any aggregates. The CH₂Cl₂ / MeOH solution was removed under vacuum and the complex was stored in a sealed 250-mL, one-neck, round-bottom flask.

3.4 Characterization Methods

3.4.1 Nuclear Magnetic Resonance (NMR)

3.4.1.1 ¹H NMR

¹H NMR spectra were obtained on either a Varian Unity 400 or a Varian Inova 400 NMR spectrometer operating at 400 MHz. The NMR parameters included a pulse width of 28.6º and a relaxation delay of 1.000 s at ambient temperature. The samples were dissolved in d-CHCl₃ for obtaining the spectra.

3.4.1.2 ²⁹Si NMR

²⁹Si NMR spectra were obtained on a Varian Unity 400 NMR spectrometer operating at 80 MHz. The samples for ²⁹Si NMR were prepared with 0.30 g copolymer, 0.05 g Cr(Acac)₃, and 2.4 mL d-CHCl₃. Quantitative silicon NMR spectra were obtained with the aid of the relaxation agent, Cr(Acac)₃ with a pulse width of 168.0º and a relaxation delay of 10.000 s. Inverse gated proton decoupling was used with scans ranging 500-1500.

3.4.2 Gel Permeation Chromatography (GPC)

Gel permeation chromatography was employed to investigate the molecular weights and molecular weight distributions of the polymethylvinylsiloxane oligomers and
the polylactide-siloxane copolymers. A Waters 2690 GPC equipped with four Waters Styragel HR columns (HR4 7.8x300mm, HR3 7.8x300mm, HR2 7.8x300mm, and HR0.5 7.8x300mm), an online Viscotek 100 differential viscometric detector, and a Viscotek laser refractometer was used for chromatographic analysis. Chloroform was employed as the mobile phase at 25 °C and a flow rate of 1.0 mL min\(^{-1}\). Polystyrene standards were used to construct a universal calibration plot. The molecular weights of the samples were determined using a universal calibration.

A Waters SEC (515 pump, 717 autosampler) with an external 2410 refractive index detector was also used. Three PLgel 5 micron MIXED-C columns were utilized. ACS grade THF was used at a flow rate of 1.0 mL min\(^{-1}\) and 40 °C. Multi-angle laser light scattering (MALLS) was utilized with an in-line Wyatt Minidawn. Samples were filtered prior to runs through a 0.2 micron PTFE filter.

### 3.4.3 Differential Scanning Calorimetry (DSC)

DSC scans were performed on a TA Instruments DSC Q1000 under constant Helium flow. The samples (10-15 mg) were ramped from -150 °C to 200 °C using hermetically sealed DSC pans. Two scans were performed on each sample and the T\(_g\)'s were taken from the inflection points on the second scans.

### 3.4.4 Transmission Electron Microscopy (TEM)

A Philips 420T TEM operated at 400kV was used to obtain photomicrographs of the magnetite-copolymer complexes. Polymer-stabilized magnetite was dispersed in
chloroform and diluted to the appearance of a “weak tea,” then deposited on carbon-coated copper grids and allowed to air dry.

3.4.5 Vibrating Sample Magnetometry (VSM)

Magnetite properties were measured in the solid state using a Standard 7300 Series Lakeshore Vibrating Sample Magnetometer. The saturation magnetization value was determined from the plateau region of the magnetic flux density of a solid sample at 8000 Oe applied field with a sensitivity of 0.1 emu.

3.4.6 X-Ray Photoelectron Spectroscopy (XPS)

Surface analysis of the magnetite-polymer complexes was investigated via X-Ray Photoelectron Spectroscopy (XPS). The data was obtained on a Perkin-Elmer X-Ray Photoelectron Spectrometer 5400 Series using a Mg anode operating at 300 watts (14kV) with the pressure of the system below $5 \times 10^{-6}$ Pa.

3.4.7 Thermogravimetric Analysis (TGA)

Thermogravimetric analysis was performed on a TGA Q1000 from TA Instruments, Inc. TGA samples were ramped from 50 °C to 800 °C at 10 °C / min in N$_2$ environments.
CHAPTER 4

Results and Discussion

A series of polymethylvinylsiloxanes were prepared with controlled molecular weights and tailored endgroups via ring-opening equilibrium polymerization. These homopolymers served as precursors for preparing block copolymers and for further chemical modification.

4.1 Synthesis of hydroxybutyl-terminated polymethylvinylsiloxane

A series of polysiloxanes with controlled numbers of pendent vinyl groups were prepared. Polymethylvinylsiloxane homopolymers were synthesized via an acid-catalyzed redistribution reaction and terminated with a hydroxybutyl functional endcapping reagent (Figure 4.2). Molecular weights were controlled through the weights of the cyclic monomers charged, relative to the numbers of moles of the 1,3-bis(hydroxybutyl)tetramethyldisiloxane endcapping reagent. The proposed mechanism for the acid catalyzed equilibration of $D_4^{Vi}$ involves triflic acid protonating the partially negative oxygen and propagation by the oxonium ion active species.
Figure 4.1 Synthesis of hydroxybutyl-terminated polymethylvinylsiloxane

$^{29}$Si NMR is a useful tool to characterize the hydroxyl-terminated polymethylvinylsiloxanes for confirming molecular weights (Figure 4.3). The silicon atoms of the methylvinyl repeat units are observed at ~ -34 to -36 ppm, depending on adjacent structures. The slight broadening of the peaks is indicative of the sensitivity the NMR has towards the proximity of the endgroups. The endgroups are observed at 9-10 ppm. By assuming that there are precisely two dimethylhydroxybutylsilyloxy endgroups, this peak could be used to standardize the integral values and thus determine the degree of polymerization. The integral areas for these peaks corresponded closely to the targeted chemical compositions.
$^1$H NMR is another method that was utilized to analyze the compositions and molecular weights of hydroxyl-terminated polymethylvinylsiloxane homopolymers (Figure 4.4). The methylene protons bonded to the terminal silicon atoms at ~1.1 - 1.2 ppm were used to standardize the integral values for calculations of molecular weight. The vinyl proton sets (denoted “a”) were used to calculate the degree of polymerization. The integrals corresponding to the vinyl protons in figure 4.4 have a value of 24.73 relative to the integral from peak “d” of 4.0. Thus, the degree of polymerization was calculated to be $24.73 / 3 = 8.24$ or approximately 8. This value corresponds with the degree of polymerization calculated from the corresponding $^{29}$Si NMR spectrum.
A series of hydroxybutyl-terminated polymethylvinylsiloxane homopolymers were synthesized and subsequently characterized by $^1$H NMR and $^{29}$Si NMR (Table 4.1). Analysis indicated reproducible control over the molecular weights with the targeted values corresponding well with the actual values obtained.
Table 4.1 A series of hydroxy-terminated PMVS was synthesized and characterized by 
$^{1}$H NMR and $^{29}$Si NMR.

<table>
<thead>
<tr>
<th>Target $M_n$ (g/mol)</th>
<th>$^{1}$H NMR $M_n$ (g/mol)</th>
<th>$^{29}$Si NMR $M_n$ (g/mol)</th>
</tr>
</thead>
<tbody>
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<td>500</td>
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<td>650</td>
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<tr>
<td>5000</td>
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</table>

Gel permeation chromatography was utilized to analyze the 1,000 g/mol homopolymer in tetrahydrofuran (THF) (Figure 4.4). GPC revealed a monomodal distribution with a retention time at ~ 22 - 26 min. The trace revealed a polydispersity index (PDI) of 1.7, characteristic of an equilibration reaction. Small shoulders on the low molecular weight (right) side of the trace indicate the individual species which can be resolved at the very low molecular weights.
Synthesis of tetramethylammonium disiloxanolate catalyst for base-catalyzed polysiloxane equilibrations

Tetramethylammonium disiloxanolate catalyst was utilized as a basic catalyst for anionic ring-opening polymerization of $D_4^{\text{Vi}}$ in the presence of bis(aminopropyl)tetramethyldisiloxane as an endcapping reagent. The catalyst was prepared by reacting $D_4$ with tetramethylammonium pentahydrate until all the water of hydration and reaction was removed. Vinyl groups on siloxanes withdraw electron density from the silicon atoms, increasing the partial positive charge on silicon, making it
more susceptible to attack by base (relative to D₄). D₄ was used to prepare the base catalyst as opposed to D₄^Vi to avoid any possible reaction of the vinyl groups during synthesis of the catalyst.

The disiloxanolate catalyst reacts with the methylvinylsiloxy substituents in at least three different types of reactions. With a partial positive charge on silicon, the base may simply ring-open D₄^Vi. This occurs rapidly during the early stages of the reaction to yield relatively high molecular weights (not controlled well by the endcapping reagent at early reaction stages). Another reaction involves the inter- or intra-molecular anionic attack on the growing chains. This process continues until equilibrium has been reached between the cyclic and linear species. The endcapping reagents used in the equilibrium reactions remain stable in the presence of the catalyst, as the base attacks only their Si-O bonds and the Si-C groups remain stable.\(^{117}\)

\(^{116}\) Ibid.  
\(^{117}\) Ibid.
Figure 4.5 Formation of the tetramethylammonium siloxanolate catalyst

4.3 Synthesis of aminopropyl-terminated polymethylvinylsiloxanes

The synthesis of aminopropyl-terminated polymethylvinylsiloxane was performed through a base catalyzed redistribution reaction. The base catalyzed equilibration of D$_4^{Vi}$ utilizes tetramethylammonium disiloxanolate to initiate the polymerization. The catalyst and byproducts were thermally decomposed with a nitrogen purge for approximately 4 h at 140 °C. The disiloxanolate catalyst reacts with the methylvinylsiloxane through three
different routes. A characteristic of base catalyzed equilibrations of the cyclomethylvinylsiloxanes is to achieve high molecular weight oligomers early in the reactions. As the reaction progresses chains begin to attack other chains or experience backbiting. This lowers the number average molecular weight of the chains. The reaction reaches equilibrium within 72 hours. A typical polydispersity of 1.5 - 2.0 is established once cyclics have been removed. The chains are terminated with an amino-functional endcapping agent, whereby the Si-C bonds remain stable during the redistribution reaction.

\[
\begin{align*}
\text{SiCH}_3\text{O} & \quad \text{SiCH}_3\text{O} \\
\text{Si} & \quad \text{Si} \\
\text{SiO} & \quad \text{SiO} \\
\text{SiCH}_3\text{O} & \quad \text{SiO} \\
\text{SiCH}_3 & \quad \text{SiCH}_3 \\
\text{CH}_3 & \quad \text{CH}_3 \\
\hline
\text{H}_2\text{N(CH}_2\text{)}_3\text{SiO} & \quad \text{SiO} \\
\text{H}_3\text{C} & \quad \text{H}_3\text{C} \\
\text{NH}_2 & \quad \text{NH}_2 \\
\end{align*}
\]

\[
\begin{align*}
\text{tetramethylammonium} & \quad \text{disiloxanolate catalyst (0.04 mol %)} \\
\text{80 C for 48 h} & \quad \text{150 C for 3 h with N}_2\text{ bubbling} \\
\text{Distill off cyclics} & \\
\end{align*}
\]

**Figure 4.6** Synthesis of aminopropyl-terminated polymethylvinylsiloxane

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\footnote{\textit{Ibid.}}
$^{29}$Si NMR was also used to characterize the amino-terminated polymethylvinylsiloxanes and determine the degree of polymerization (Figure 4.5). The silicon atoms of the methylvinyl repeat units are observed at -34 to -36 ppm, while the endgroups are observed at 9 - 10 ppm. Since there are two endgroups, this peak was utilized to standardize the integral values and thus determine the degree of polymerization. The targeted molecular weights and those analyzed by silicon NMR agreed well in all cases.

![Figure 4.7 Polymethylvinylsiloxane with aminopropyl endgroups analyzed via $^{29}$Si NMR (M_n = 1600 g/mol)](image)

$^{1}$H NMR was also employed to confirm the compositions and molecular weights of the aminopropyl-terminated polymethylvinylsiloxane homopolymers (Figure 4.8). The methylene protons bonded to the endcapping silicon atoms resonating at 1.1 - 1.2
ppm were utilized to standardize the integral values for molecular weight calculations. The integrals corresponding to the vinyl proton sets (denoted “a”) were, again, compared to the integral values for the endgroups, and the comparisons were used to calculate the degree of polymerization. In Figure 4.8, the vinyl protons integrated to 47.9, and this was compared to the integrals for the methylene peaks at ~0.5 ppm to calculate an average of approximately 16 vinyl groups per chain. This value corresponds well with the degree of polymerization calculated from the corresponding $^{29}$Si NMR.

Figure 4.8 Polymethylvinylsiloxane with aminopropyl endgroups analyzed via $^1$H NMR ($M_n = 1600$ g/mol)
A series of aminopropyl-terminated polymethylvinylsiloxane homopolymers were synthesized and subsequently characterized by $^1$H NMR and $^{29}$Si NMR (Table 4.2). Analysis indicated reproducible control over the molecular weights with the targeted values corresponding well with the experimental values obtained from the NMR measurements.

**Table 4.2** A series of amino-terminated PMVS was synthesized and characterized by $^1$H NMR and $^{29}$Si NMR

<table>
<thead>
<tr>
<th>Target $M_n$ (g/mol)</th>
<th>$^1$H NMR $M_n$ (g/mol)</th>
<th>$^{29}$Si NMR $M_n$ (g/mol)</th>
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<td>2000</td>
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</tr>
</tbody>
</table>

Gel permeation chromatography was used to analyze the 2,000 g/mol homopolymer in THF (Figure 4.9). GPC revealed a monomodal distribution with a retention time of ~ 22 - 26 min. The trace revealed a polydispersity index of 1.7,
characteristic of an equilibration reaction.

Figure 4.9 GPC was used to analyze 1600 g/mol homopolymer revealing a PDI of 1.7

In general, the redistribution reaction of cyclomethylvinylsiloxanes is reproducible, regardless of the use of acid or base catalysts via either a cationic or anionic equilibrium reaction. Materials synthesized by both methods indicated a reasonably close correlation between targeted number average molecular weights and those obtained through both $^1$H NMR and $^{29}$Si NMR. GPC indicated unimodal distributions of molecular weights with typical equilibrium polydispersity indices of 1.7.
4.4 Poly(L-lactide)-siloxane Triblock Copolymers Initiated with Polymethylvinylsiloxane Telechelic Oligomers

The polymethylvinylsiloxane homopolymers were synthesized with either hydroxybutyl or aminopropyl difunctionality, and these oligomers served as macroinitiators for preparing the poly(L-lactide) tail-blocks of the triblock copolymers. Poly(L-lactide) syntheses were conducted via a coordination-insertion mechanism in the presence of stannous octoate as the ring-opening catalyst.

One series of triblock copolymers involved using the hydroxybutyl-terminated polymethylvinylsiloxane as a macroinitiator (Figure 4.10). Attempts were made to prepare controlled molecular weight lactide blocks in these copolymers through adjusting the ratio of grams of lactide monomer to moles of the polymethylvinylsiloxane difunctional initiator.
Figure 4.10 Synthesis of a polylactide-siloxane block copolymer utilizing a hydroxybutyl terminated telechelic polymethylvinylsiloxane macroinitiator

$^1$H NMR served as a useful tool to monitor the progress of the reaction and characterize the final product. $^1$H NMR of the lactide monomer indicates that the methine proton on the ring resonates at ~5 ppm (Figure 4.11).
As ring-opening polymerization progresses, the methine proton peak shifts from ~ 5 ppm to ~ 5.2 ppm in the linear lactide repeat unit. The percent conversion of lactide monomer to form the block copolymer was calculated from the integral ratios of these two peaks. In the copolymerization reactions, the methylene proton set immediately adjacent to the silicon atom at ~ 0.2 ppm and was utilized to standardize the integral values for calculating block molecular weights and copolymer compositions. Once the reaction reached ~ 90% conversion, the polymerizations were terminated and the copolymers were isolated by precipitation in methanol, filtration and drying. \( ^1H \) NMR of the isolated copolymers helped to confirm the compositions and molecular weights by comparison of the lactide methine proton set at ~ 5.2 ppm with the resonances corresponding to the polysiloxane backbone and endgroup peaks (Figure 4.12).
For the copolymer corresponding to the NMR spectrum shown in Figure 4.12, the targeted molecular weight of the poly(L-lactide) tailblocks was 5,000 g/mol. The integral value of the linear lactide methine proton set was 169.4. Thus, the calculated molecular weight for a single lactide tail block was $169.4 \times 72.0 / 2 = \sim 6,000$ g/mol. The targeted values closely corresponded with the experimental values obtained from the spectra. A series of triblock copolymers were synthesized with varying lactide degrees of polymerization (Table 4.3).
**Table 4.3** A series of hydroxyl-initiated poly(L-lactide)-siloxane triblock copolymer was synthesized and characterized by $^1$H NMR

<table>
<thead>
<tr>
<th>Target $M_n$ [PLLA(g/mol)-PMVS(g/mol)-PLLA(g/mol)]</th>
<th>$^1$H NMR $M_n$ [PLLA(g/mol)-PMVS(g/mol)-PLLA(g/mol)]</th>
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GPC chromatograms of the PLLA-PMVS-PLLA copolymers were bimodal, suggesting that inefficient initiation of the lactide monomer by the hydroxybutyl terminated PMVS had occurred (Figure 4.13). Although several polymerization parameters were explored in efforts to minimize this effect, the results were not encouraging. It was reasoned that some loss of functionality on the polysiloxane macroinitiator was responsible for the incomplete initiation, and this led to a more thorough investigation of aminopropyl terminated oligomers as macroinitiators for these block copolymerizations.
Figure 4.13 GPC chromatogram of a poly(L-lactide)-siloxane copolymer suggests inefficient initiation by the hydroxybutyl terminated polymethylvinylsiloxane macroinitiator.

4.5 Triblock poly(L-lactide)-siloxane copolymers initiated with aminopropyl terminated polymethylvinylsiloxane oligomers

The lone electron pairs on a primary amine readily attack the carbonyl carbon on the lactide monomer, and this reaction will open one ring without the aid of a catalyst. Thus, aminopropyl-functional polymethylvinylsiloxane endgroups could be converted to
hydroxyalkyl terminal groups by adding one lactide dimer to the aminopropyl endgroups. Hydroxyl groups can then be utilized as described previously to propagate the polymerization of lactide through a coordination-insertion mechanism. The amino-terminated PMVS macroinitiator ensures efficient initiation of the lactide monomer. $^1$H NMR was used to monitor and confirm the amine-initiated ring-opening of a single lactide monomer per amine group in the absence of Sn(Oct)$_2$ (Figure 4.14). After reaction of the aminopropyl-functional oligomer for one hour at 65 °C, the lactide methine hydrogen peak corresponding to the open-chain structure appears at $\sim 5.2$ ppm in the proton NMR spectra. Integration confirmed that precisely one lactide cyclic dimer added onto each amine group. The amide hydrogen protons resonating at $\sim 6.5$ ppm appear during this addition, further confirming the opening of a single dimeric repeat unit on each end of the polymethylvinylsiloxane chain.
Figure 4.14 $^1$H NMR was used to confirm opening of one lactide monomer by an amine-terminated PMVS macroinitiator

Terminal methine protons on the linear lactide, with a chemical shift of $\sim 4.5$ ppm and integration of 2 per endgroup, were utilized to quantify these reactions.

Once the macroinitiator has opened one lactide monomer, then the stannous octoate catalyst is added at an approximate 400 ppm concentration based on grams of monomer and the percent conversion of lactide monomer is further monitored with $^1$H NMR. Once the reaction is complete, the copolymers were isolated by dissolution in
chloroform and precipitation into methanol. This procedure removes residual lactide cyclics. The compositions of the triblock poly(L-lactide-b-methylvinylsiloxane-b-L-lactide) copolymers were confirmed with \(^1\text{H}\) NMR after filtration and drying (Figure 4.15).

![Figure 4.15](image)

**Figure 4.15** \(^1\text{H}\) NMR of a poly(L-lactide-b-methylvinylsiloxane-b-L-lactide) triblock copolymer with 5,000-1,600-5,000 g/mole block molecular weights respectively.

The methine protons in the linear lactide repeat unit resonating at \(~ 5.2\) ppm were compared to the two terminal methine protons of the tail block resonating at \(~ 4.4\) ppm.
and utilized to calculate the molecular weights of the tail blocks. A series of triblock copolymers were synthesized utilizing the aminofunctional macroinitiators (Table 4.4). Table 4.4 shows reasonable correlation between the targeted molecular weights and those calculated from $^1$H NMR, thus confirming the reproducibility of the synthetic procedure.

**Table 4.4** A series of aminopropyl-initiated poly(L-lactide)-siloxane triblock copolymer was synthesized and characterized by $^1$H NMR

<table>
<thead>
<tr>
<th>Target $M_n$ [PLLA(g/mol)-PMVS(g/mol)-PLLA(g/mol)]</th>
<th>$^1$H NMR $M_n$ [PLLA(g/mol)-PMVS(g/mol)-PLLA(g/mol)]</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000-1600-2000</td>
<td>1900-1600-1900</td>
</tr>
<tr>
<td>5000-1600-5000</td>
<td>5000-1600-5000</td>
</tr>
<tr>
<td>2000-2600-2000</td>
<td>2100-2600-2100</td>
</tr>
<tr>
<td>5000-2600-5000</td>
<td>4500-2600-4500</td>
</tr>
<tr>
<td>8000-2600-8000</td>
<td>7800-2600-7800</td>
</tr>
</tbody>
</table>

GPC was used to characterize the molecular weights and distribution of the triblock copolymer series (Table 4.5). Molecular weight averages obtained from GPC traces correlated well with the targeted values. Consistently monomodal and narrow GPC peaks confirmed that the use of primary amines to initiate single lactide monomers improved the efficiency of the initiation (Figure 4.16).
Table 4.5 Comparisons of targeted and experimental molecular weights (GPC) for a series of triblock copolymers wherein the lactide tailblocks were initiated with aminopropyl terminated polymethylvinylsiloxane oligomers.

<table>
<thead>
<tr>
<th>Target Mn (g/mol)</th>
<th>GPC Mn (g/mol)</th>
<th>PDI</th>
</tr>
</thead>
<tbody>
<tr>
<td>5600</td>
<td>7400</td>
<td>1.01</td>
</tr>
<tr>
<td>11600</td>
<td>12400</td>
<td>1.05</td>
</tr>
<tr>
<td>6600</td>
<td>7400</td>
<td>1.16</td>
</tr>
<tr>
<td>12600</td>
<td>15600</td>
<td>1.10</td>
</tr>
<tr>
<td>18600</td>
<td>16600</td>
<td>1.23</td>
</tr>
</tbody>
</table>
Figure 4.16  GPC chromatogram of a poly(L-lactide)-siloxane triblock copolymer (M_n ~12,400 g/mol) suggests that aminofunctional macroinitiators provide efficient initiation and well-defined materials

Thermal properties of the PLLA-PMVS-PLLA triblock copolymers were analyzed through differential scanning calorimetry (DSC) (Figure 4.17). Triblock copolymers with 5,000 g/mol PLLA tailblocks displayed a glass transition temperature (T_g) at 43 °C, a crystallization temperature (T_c) of 83 °C, and a melt transition temperature (T_m) of 152 °C. A triblock copolymer with a 2,600 g/mol PMVS central
block appeared to have a $T_g$ corresponding to the polymethylvinylsiloxane phase at approximately -124 °C, but the lower $T_g$ was broad and difficult to quantify. The thermal data suggested that the PMVS central block did not disrupt the crystallinity of the PLLA tail blocks, and this was considered important to obtain structural properties in microspheres to be prepared from these materials adsorbed onto magnetite nanoparticles.

**Figure 4.17** DSC thermogram for the amine-initiated 5000 g/mol PLLA-2600 g/mol PMVS-5000 g/mol PLLA
4.6 Ene-Thiol Addition of Mercaptoacetic Acid to the PLLA-PMVS-PLLA Copolymers which were prepared with Hydroxybutyl Terminated Macroinitiators

Ene-thiol addition reactions were utilized to incorporate pendent carboxylic acid functional groups onto the PMVS central blocks of the copolymers (Figure 4.18). The reactions were monitored by following the disappearance of resonances associated with the vinyl proton sets in $^1$H NMR spectra at ~ 6 ppm. Results suggested that it was important to carefully deoxygenate these systems to obtain quantitative functionalization.

![Figure 4.18](image)

**Figure 4.18** Ene-thiol addition of mercaptoacetic acid to the central block of a PLLA-PMVS-PLLA triblock
The number of carboxylic acid groups per polymer chain was verified by $^{29}$Si NMR, by noting a shift of silicon resonances with vinyl pendent groups at $\sim$ -30 ppm to acid-functional silicon resonances at $\sim$ -23 ppm (Figure 4.19).

![Figure 4.19](image)

**Figure 4.19** $^{29}$Si NMR spectrum of carboxylic acid-functionalized 5000 g/mole PLLA-1700 g/mole P(COOH)-5000 g/mole PLLA triblock copolymers

The two terminal silicon atoms resonating at $\sim$ 10 ppm in the copolymer served as the standard for comparison of integrals corresponding to silicon atoms along the backbone of the polymer. Quantitative functionalization was confirmed by the disappearance of the vinyl-functional silicon resonance peak at approximately -35 ppm. The resonance peak at approximately -23 ppm corresponds to the major anti-Markovnikov product of the mercaptoacetic-acid-functional silicon atoms along the backbone of the polymer. The resonance at $\sim$ -20 ppm denotes a small degree of Markovnikov addition of mercaptoacetic acid across the pendant vinyl groups. These integrals correlate well with
the targeted values of acid groups, suggesting that quantitative functionalization can be achieved.

4.7 Ene-Thiol Addition of Mercaptoacetic Acid to Triblock Copolymers that were Formed with Aminopropyl Terminated Polymethylvinylsiloxane Macroinitiators

This ene-thiol addition reaction was similarly utilized to incorporate pendent carboxylic acid functional groups on the PMVS central blocks of the better defined block copolymers prepared from aminofunctional macroinitiators (Figure 4.20). The numbers of pendent vinyl groups on the PMVS central blocks was increased from 8 to 24 so that more acid groups per mole of copolymer could be achieved. As described previously, the reactions were monitored by following the disappearance of resonances associated with the vinyl proton sets in $^1$H NMR spectra at ~ 6 ppm.
The isolation steps for the amine-initiated series was modified due to changes in the solubility characteristics of these copolymers containing large numbers of carboxylic groups. Whereas methanol was utilized as the coagulation solvent when low concentrations of carboxylic acids were present, the copolymers with 24 acid groups per chain were soluble in methanol. Thus, hexanes served as a more non-polar solvent to precipitate the copolymers. To redissolve the acid-functional copolymers for analysis, chloroform or dichloromethane was mixed with a small percentage of methanol. The number of carboxylic acid groups per polymer chain was verified by $^{29}$Si NMR,

Figure 4.20 Ene-thiol addition of mercaptoacetic acid to PLLA-PMVS-PLLA triblock copolymers which were prepared from the aminopropyl terminated polymethylvinylsiloxane central blocks.
indicating a shift of vinyl-pendent silicon resonances at ~ -30 ppm to acid-functional silicon resonances at ~ -23 ppm (Figure 4.21).

![Figure 4.21](image)

**Figure 4.21** $^{29}$Si NMR of an acid-functionalized PLLA-P(COOH)-PLLA triblock copolymer having block molecular weights of 5000-2600-5000 g/mol where 2600 refers to the molecular weight before the addition of 24 acid groups.

4.8 Preparation and Characterization of Magnetite-Copolymer Nanoparticle Dispersions

One objective in this research was to prepare dispersions which were highly concentrated with magnetite nanoparticles so that they would have the highest possible magnetic susceptibility and saturation magnetization. For most medical applications,
these nanoparticles must be coated with biocompatible stabilizers that can be dispersed in biological fluids.

The magnetite nanoparticles were coated with the acid-functionalized poly(L-lactide)-siloxane triblock copolymers. During the formation of the magnetite-copolymer complex, the pH was adjusted to pH ~ 5-6 with dilute HCl. In this pH range, the magnetite surface was cationic (magnetite isoelectric point = pH 6.8) and the acid groups were partially ionized. Hence, this pH was utilized to promote adsorption of the carboxylate groups onto the magnetite surface. Once this was accomplished, the magnetite-copolymer complex was dispersible in chloroform and not water. This suggests that the particles were coated with the organic-soluble block copolymers having water-insoluble PLLA tail blocks.

To confirm that the magnetite nanoparticles were coated with the copolymer stabilizer, the surface properties of the magnetite were analyzed using X-ray photoelectron spectroscopy. XPS analysis was also performed on magnetite coated with a 5,000-2,600-5,000 g/mol triblock copolymer functionalized with an average of 24 acid groups per chain. Two complexes were prepared by charging 66 wt % and 50 wt % magnetite. These complexes were centrifuged to remove any uncoated magnetite or any magnetite that might have very little adsorbed copolymer. Aggregates that centrifuged out of the dispersion were collected and analyzed. Another complex was made targeting 50 wt % magnetite which was not centrifuged. XPS analysis was used to compare both centrifuged particles that remained in solution and aggregated with the particles that were not centrifuged. These samples were, in turn, compared with uncoated magnetite (Table 4.7).
Table 4.6 Elemental composition of the surfaces of magnetite nanoparticle complexes with the triblock copolymer via XPS analysis

<table>
<thead>
<tr>
<th>Elements (% conc)</th>
<th>C</th>
<th>O</th>
<th>N</th>
<th>Fe</th>
<th>Si</th>
<th>S</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uncoated Magnetite without stabilizer</td>
<td>23</td>
<td>46</td>
<td>0</td>
<td>27</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>w/ 5k-2.6k-5k (target 66 wt.% magnetite)</td>
<td>59</td>
<td>28</td>
<td>0</td>
<td>2</td>
<td>9</td>
<td>1</td>
</tr>
<tr>
<td>(dispersed after centrifugation)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>w/ 5k-2.6k-5k (target 66 wt.% magnetite)</td>
<td>34</td>
<td>41</td>
<td>0</td>
<td>18</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>(aggregated after centrifugation)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>w/ 5k-2.6k-5k (target 50 wt.% magnetite)</td>
<td>58</td>
<td>25</td>
<td>0</td>
<td>0</td>
<td>16</td>
<td>0</td>
</tr>
<tr>
<td>(dispersed after centrifugation)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>w/ 5k-2.6k-5k (target 50 wt.% magnetite)</td>
<td>29</td>
<td>46</td>
<td>0</td>
<td>19</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>(aggregated after centrifugation)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>w/ 5k-2.6k-5k (target 50 wt.% magnetite)</td>
<td>49</td>
<td>38</td>
<td>0</td>
<td>7</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>(no centrifugation)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The high iron (27 %) and oxygen (46%) on the surface of the bare magnetite particles suggested that they were relatively clean. Once the magnetite nanoparticles were coated with the copolymer, these surface compositions changed significantly. The iron content decreased from 27% to 2% suggesting that the particles were, indeed, coated with the triblock dispersion stabilizer. The presence of Si and S in the coated magnetite further confirms the presence of the stabilizer on the surface of magnetite. The complexes that were not centrifuged in the isolation procedure displayed iron surface compositions (7 % Fe) comparable to those complexes that were dispersed after centrifugation (2 % and 0 %). This suggests that centrifugation is not necessary in the work up of the complexation procedure.
Thermogravimetric analysis (TGA) is also investigated as a means for determining the efficiency of copolymer adsorption onto the magnetite nanoparticles (Figure 4.22). “Aggregated – 66 wt % magnetite” refers to the complex that was charged with 66 wt % magnetite and came out of solution during centrifugation. Subsequently “Dispersed – 66 wt% magnetite” refers to complex charged with 66 wt % and remained in solution. “Aggregated – 50 wt% magnetite” and “Dispersed – 50 wt% magnetite” refer to the complex charged with 50 wt % magnetite. “No centrifuge – 50 wt % magnetite” refers to complex charged 50 wt % magnetite and was not subjected to centrifugation.
Figure 4.22 TGA study of centrifuged and non-centrifuged magnetite-polymer complexes

TGA studies show that the magnetite-polymer complexes that remain dispersed after centrifugation contain approximately 20-30 wt% of polymer, while complexes without centrifugation have the charged composition of 50 wt% magnetite. Aggregated complexes collected after centrifugation show mild complexation with approximately 10-15 wt % polymer with the rest being magnetite (80-85 wt%). This analysis suggests that centrifugation may be important for isolating complexes with narrow compositional distributions.

Vibrating Sample Magnetometry (VSM) was utilized to determine the saturation magnetization of the resulting complexes. Dispersed complexes charged with 33 wt%
and 50 wt% yielded 14.4 emu/g and 17.4 emu/g, respectively. Non-centrifuged complexes yielded a higher value of saturation magnetization at 31 emu/g. This corresponds well with the compositions measured by TGA.
Well-defined polymethyvinylsiloxane homopolymers were prepared and characterized with controlled molecular weight and molecular weight distributions utilizing base catalyzed polysiloxane equilibrations in combination with bis(aminopropyl)tetramethyldisiloxane as an endcapping reagent. NMR was used to confirm the compositions of the resultant homopolymers. Acid catalyzed redistribution reactions were also investigated utilizing bis(hydroxybutyl)tetramethyldisiloxane as the endcapping reagent. Although the polymethylvinylsiloxane oligomers appeared to be well-functionalized and the molecular weight distributions of the oligomers were reasonable, these hydroxybutyl endgroups could not be used to quantitatively initiate L-lactide tailblocks. Thus, it is reasoned that some side reactions involving these particular endgroups may occur upon heating, and thus these oligomers are not recommended for the research discussed in this thesis.

These aminopropyl terminated polymethyvinylsiloxane telechelic oligomers were utilized as macroinitiators for the ring-opening polymerization of L-lactide through a coordination-insertion mechanism with stannous octoate as a catalyst to yield triblock copolymers of poly(L-lactide-\text{-}b\text{-}methylvinylsiloxane-\text{-}b\text{-}L-lactide). $^1$H NMR was used to monitor the progress of the L-lactide polymerizations by noting the shift of the methine proton in the L-lactide monomer to its linear analogue. The triblock compositions determined via $^1$H and $^{29}$Si NMR and GPC agreed well with the targeted values. The
amine-initiated PMVS-PLLA-PMVS copolymers had monomodal GPC chromatograms with narrow PDI values, suggesting well controlled polymerizations.

Successful functionalization of the triblock copolymers with mercaptoacetic acid was achieved through an ene-thiol addition. $^{29}$Si NMR proved to adequately dwas useful in confirming that quantitative functionalization of the pendent vinyl groups could be achieved.

A copolymer having $5,000-2,600-5,000$ g/mol poly(L-lactide-b-siloxane-b-L-lactide) blocks respectively where the central block was functionalized with 24 acid groups was utilized to prepare a series of magnetite nanoparticle-polymer complexes at pH 5-6. It was reasoned that under such conditions, the magnetite surface should have a net positive charge while the copolymer acid groups should be partially anionic. Thus, the anionic copolymer was expected to adsorb onto the cationic magnetite by electrostatic attraction, and the non-ionic PLLA tailblocks were expected to sterically prevent interparticle aggregation in solvents such as chloroform. XPS, VSM, and TGA were used to characterize the resultant complexes, and, although additional investigations of adsorption parameters are warranted, these studies confirmed good adsorption of the triblock materials onto the magnetite nanoparticles. Considerable additional research will be required to understand more of the parameters involved in controlling the complexation of magnetite with stabilizers. The exact method of complexation of carboxylic acid groups on the surface of magnetite needs to be better understood, and methods for separating any unbound copolymer from these dispersions should be addressed.
Incorporation of these magnetite-polymer complexes into microspheres serves as a potential avenue of study.

Magnetic microspheres also have potential for various biotechnological applications. Further study will also be required to optimize the block molecular weights and functionality of the copolymers for the dispersions and for their efficient incorporation into controlled-size microspheres. The incorporation of poly(ethylene oxide) blocks into the PLLA may also promote hydrophilicity and thus, render such nanoparticle complexes and their microspheres dispersible in water as well as other solvents.

Magnetic media with higher saturation magnetization values need to be investigated as potential media for stabilization with the functionalized polylactide-siloxane copolymers. It is also recognized that pendent moieties other than carboxylates need to be addressed as sites of functionalization along the backbone of the copolymers.
REFERENCES

VITA

Ragy Tadros Ragheb, son of Nadia and Raafat Ragheb, was born on February 16, 1979 in Cairo, Egypt. He is the first child with one brother, Daniel. He was raised in Dhahran, Saudi Arabia. His parents currently reside in Cairo, Egypt. He attended St. Paul’s School in Concord, New Hampshire and graduated in 1997. That same fall, he began his studies in Davidson College in Davidson, North Carolina where he became interested in organic and polymer chemistry. He spent two summers and a full academic year conducting research at Davidson College, under the advisement of Dr. David Blauch, Dr. David Brown, and Dr. Susan Hendrickson, respectively. He graduated with a Bachelor of Science degree in Chemistry in May of 2001. In the fall of 2001, he entered the graduate program at Virginia Polytechnic Institute and State University in pursuit of a Masters of Science degree in Chemistry. His Master’s thesis focused on the synthesis of novel polylactide-siloxane stabilizers for the formation of magnetite complexes under the advisement of Dr. Judy Riffle.