Polylactide Growth on Various Oxides: Towards New Materials

Thesis

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By

Alexandre Bernard
Graduate Program in Chemistry

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Thesis committee
Dr Malcolm H. Chisholm, Advisor
Dr Patrick Woodward
Abstract

Poly(lactide) is a biodegradable, biocompatible material coming from renewable resources. Such properties, added to a more and more competitive cost makes it a very interesting material for current industries. Coupled with other materials, properties can be fine tuned for different fields, ranging from construction materials to biomedical applications.

Poly(lactide) was grown on the surface of various oxide particles through ring-opening polymerization of lactide, using lactic acid as surface modifier. The aim was to determine what materials were compatible with this method to make cost-efficient materials with new properties. To this end, a simple, one-pot reaction under very mild conditions was developed and tested with various materials.

Particles containing about 40% polymer were successfully obtained from silica gel particles. Poly(lactide) growth was confirmed through Fourier-transform infrared and solid state $^{13}$C nuclear magnetic resonance analysis. Scanning electron microscopy showed a polymer growth on the particles, although it was shown part of the growth comes from the surface initiator polymerizing on its own. It was also shown that polymer did not smoothly coat the particles but rather grew in random pattern.
White quartz, basic alumina, titanium oxide and montmorillonite clay all successfully grew poly(lactide), while iron oxide, cobalt oxide, barium titanate and starch did not within the chosen reaction conditions. It is also possible to vary the monomer being used or the surface modifier, as was shown by growing poly(caprolactone) or by using glycolic acid on silica gel particles.
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Vita

July 2002
French Baccalauréat

2002 to 2004
Classes Préparatoire CPE Lyon, France

2004 to 2006
CPE Lyon, Chemistry and Chemical Engineering Division, France

2006-2007
One Year Placement, Johnson-Matthey Catalysts, Middlesbrough, UK

2007 to present
Graduate Teaching Associate/Graduate Research Associate, Department of Chemistry, Ohio State University

September 2009
MS Chemistry and Chemical Engineering, CPE Lyon, France

Fields Of Study

Major Field: Graduate Program in Chemistry
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Introduction

1. Polylactide in industry

Polylactide, also called poly(lactic acid) and often abbreviated as PLA, is a polyester that has been known since 1780 when it was first isolated from sour milk by Sheele. It was first produced industrially in 1881\cite{1}, but had only recently become of great interest, because its biodegradability, its renewable resources origins and improvements in manufacturing processes are starting to lower its production cost as compared to fossil fuel derived polymers.

First patented in 1954 by DuPont\cite{2}, work on PLA was discontinued because of the susceptibility to hydrolytic degradation. In 1972, Ethicon reinstated interest in PLA through high-strength, biocompatible fibers made from poly(glycolic-co-lactic) acid and usable as resorbable medical sutures. The cost of making those polymers kept them from being used in other applications until the late 1980s, where new, more cost-efficient methods for producing lactic acid were discovered\cite{3}.

In 2007, the demand for polylactide in the US was of 90 millions pounds, representing 26% of the biodegradable plastics, and was expected to increase 25% annually through 2012. The main PLA producer is NatureWorks LLC (joint venture of Cargill and Teijin), and other companies involved in its production include Toyota and PURAC.
PLA is used for a broad range of applications. Because of its biodegradability\textsuperscript{[4]}, it has been used in packaging films, rigid thermoformed containers and coated papers. It also has created a lot of interest for biomedical applications, from drug delivery\textsuperscript{[5,6,7,8]} to biocompatible material used in helping tissue regeneration\textsuperscript{[9,10,11]}.

2. Chemistry of polylactide

2.1 Living Polymerization and Ring Opening Polymerization

The term "living polymerization" is applied to ionic polymerizations in which the capacity to terminate has been removed\textsuperscript{[12]}. This in theory makes it possible for the polymer chains to grow as long as some monomer is present, including if some monomer is added afterwards, be it the same or another one\textsuperscript{[13]}. In practice, though, a small amount of terminating agent is always present, and increase in viscosity and insolubility will slow down the reaction at some point. Living polymerizations are of interest because they yield high molecular weight polymers with narrow polydispersity indexes, allow good end-group control and provide access to block polymers.

Ring opening polymerization (ROP) is an example of living polymerization. The principle is that an initiator will open a cyclic molecule, giving a new charged moiety at the end of the opened cycle, which will in turn open a new cycle\textsuperscript{[12]} (See figure 1). One advantage of ROP is that, in contrast to condensation reactions, there is no elimination of small molecules which have to be removed or left as impurities. ROP is used to make polylactide, poly(propylene oxide), poly(caprolactone), and many other polyesters.
2.2 Polylactide synthesis

There are two different synthesis routes for making high molecular weight PLA, as shown in figure 2. In both routes, a condensation polymerization of lactic acid leads to a low molecular weight, brittle, glassy polymer. Then, in one route, the polymer is enhanced by adding coupling agents that lengthen the chains. This is not ideal because the low concentration of reactive end-groups leave low concentration of water or other impurities in the polymer. The other route consists of obtaining lactide rings by depolymerization of the obtained polymer, purification and ring-opening polymerization of those lactide units to yield high molecular weight PLA\textsuperscript{[14]}. The ROP of lactide method was the only way of making pure, high-molecular-weight PLA until recent development by Mitsui Toatsu.
Chemicals, in which lactic acid and catalyst are azeotropically dehydrated in an aprotic solvent under reduced pressures\(^{15,16,17,18}\). We will here focus on the ROP of lactide, as it is still more widely used for preparation of PLA, and was for this reason used in our experiments.

The polymerization of lactides can follow different mechanisms, depending on the type of initiators used\(^{19}\). These mechanisms are:

- enzymatic polymerizations
- cationic polymerizations
- anionic polymerizations
- coordination-insertion polymerizations

Enzymatic polymerizations are interesting in the medical field, because enzymes are biocompatible. It has been shown that enzymatic polymerization can produce polylactide with molecular weights of up to 126,000 Da\(^{20}\).

The mechanism for the cationic polymerization is shown in figure 3. It consists of a protonation or alkylation of one of the carbonyl oxygen atoms which results in the electrophilic activation of the O-CH bond. This bond will cleave by nucleophilic attack of another lactide ring, and the reaction will propagate following this process, until a monofunctional nucleophile causes termination. It has been shown\(^{19}\) that only extremely strong acids or carbenium ion donors will initiate this process. It is also a rather slow reaction below 50°C, and it yields low to moderate molecular weights.
Figure 4 shows the mechanism for the anionic polymerization of lactide. In this case, the chain growth occurs through nucleophilic attack on the carbonyl group of the lactide, followed by cleavage of the CO-O bond. Termination occurs by protonation of the alkoxide. This process involves the possibility of chain transfer and trans-esterification mechanisms, resulting in low to moderate molecular weights and the possible presence of macrocycles.
Finally, the coordination-insertion mechanism is based on coordinating a lactide monomer onto a metal center (figure 5), enhancing electrophilicity of the CO-group and nucleophilicity of OR groups, resulting in an insertion of the monomer onto the growing chain. This process allows for less side reactions, making it possible to reach higher molecular weights (higher than 200,000 Da\[^{21}\]) and keep a better control on the reaction.

**Figure 5: Lactide ROP coordination-insertion mechanism**

2.3 Stereochemistry

Lactide exists under three forms, shown in figure 6. Those three isomers have different properties on their own: D-lactide and L-lactide melt at 97° C, meso-lactide melts at 52° C.

The most common isomers found are L-lactide and rac-lactide, which is a racemic mixture of D- and L-lactide. In turn, the polymers will have different physical properties: pure poly-D-lactide (PDLA) and pure poly-L-lactide (PLLA) have equilibrium crystalline melting points of 207° C\[^{22}\] while poly-rac-lactide (rac-PLA) melts at 126-127° C\[^{1,3}\]. Reeve et al.\[^{23}\] showed the ratio of D- to L- lactide in PLA influences the enzymatic
degradability of the polymer, with optimal degradability occurring for a ratio of 92% L-
to D- isomer. Wanamaker et al.\cite{24} showed the physical properties of triblock copolymers
with PLA at both end of the chain were very different depending on the stereoisomer used
for PLA.

Stereochemistry for PLA goes farther than a simple differentiation between polymers
made from the different lactide stereoisomers. To study the stereoselectivity of a catalyst,
it is indeed important to know the exact stereosequence of the polymer. To that end, it is
common in PLA literature to designate assignments by pair, as isotactic ("i") for -RR- and
-SS- pairs, and syndiotactic ("s") for -RS- and -SR- pairs. From there, it is common to
study tetrads (a combination of four stereocenters). All possible tetrads are given in table
1.

<table>
<thead>
<tr>
<th>stereosequence</th>
<th>iii</th>
<th>sii</th>
<th>ssi</th>
<th>iss</th>
<th>iis</th>
<th>isi</th>
<th>sis</th>
<th>sss</th>
</tr>
</thead>
<tbody>
<tr>
<td>subunits</td>
<td>SSSS</td>
<td>SSR</td>
<td>SRSS</td>
<td>SSRS</td>
<td>SSSR</td>
<td>SSRR</td>
<td>SRRS</td>
<td>SRSR</td>
</tr>
<tr>
<td></td>
<td>RRRR</td>
<td>RRRS</td>
<td>RSRR</td>
<td>RRSR</td>
<td>RRRS</td>
<td>RRSS</td>
<td>RSSR</td>
<td>RSRS</td>
</tr>
</tbody>
</table>

Table 1: Possible stereosequence tetrads in PLA

The polymerization mechanism will determine the stereochemistry of the polymer. It has
been shown that cationic polymerization of L-lactide only yields optically pure PLLA

![Figure 6: Lactide stereoisomers: a) D-lactide b) L-lactide c) meso-lactide](image)
under 50°C and induces racemization above that temperature. Anionic polymerization always leads to racemization, because of the planarity of the delocalized anion. In the case of coordination-insertion mechanism, the catalyst will determine if racemization will occur, and to what extent. This method therefore allows good control on the stereochemistry of the final polymer by fine-tuning of the catalyst.

2.4 Polylactide properties

Mechanical properties and crystallization behavior of PLA are very dependent on the molecular weight and stereochemistry of the backbone. Since both those variables can be controlled quite easily, the overall properties of the polymer can be tuned to different applications.

C. Perego et al. studied the effect of molecular weight of PLLA and rac-PLA on physical properties of the polymer. Their results, summarized in table 2, show how control on molecular weight and stereochemistry allow control on a wide range of physical properties. In this table, viscosity was measured in chloroform at 25°C at a concentration of 0.20 g/dL, and was used to determine the molecular weights.

Infrared peak band assignments for PLA have been reported in the literature and are given in Table 3.
<table>
<thead>
<tr>
<th>Assignment</th>
<th>Peak position, cm⁻¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>-CH- stretch</td>
<td>2995 (asym.), 2944 (sym.)</td>
</tr>
<tr>
<td>-C=O carbonyl stretch</td>
<td>1759</td>
</tr>
<tr>
<td>-CH- deformation</td>
<td>1382, 1362, 1453</td>
</tr>
<tr>
<td>-C-O- stretch</td>
<td>1194, 1130, 1093, 1047, 1268</td>
</tr>
<tr>
<td>-C-C stretch</td>
<td>868</td>
</tr>
</tbody>
</table>

Table 3: Peak Band Assignments for PLA Infrared Spectra

A very useful tool to analyze PLA and its stereochemistry is nuclear magnetic resonance (NMR). Indeed, in the NMR spectrum of a given polymer, the observed resonances can be assigned to stereosequence combinations in the polymer, although the exact reason why the different chemical shifts arise is still unknown[27]. Many articles are available in the literature discussing the assignment of peaks with stereochemistry[28,29,30,31,32], using...
either $^1$H NMR, $^{13}$C NMR or both, and not all agree on said assignment, so we will not expand upon this here. Table 4 gives a general assignment for PLA peaks in chloroform.

<table>
<thead>
<tr>
<th>Chemical Shift (ppm)</th>
<th>Multiplicity</th>
<th>Assignment</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^1$H NMR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.5-1.6</td>
<td>doublet</td>
<td>methyl</td>
</tr>
<tr>
<td>5.1-5.2</td>
<td>quartet</td>
<td>methyne</td>
</tr>
<tr>
<td>$^{13}$C NMR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>169-170</td>
<td>-</td>
<td>C=O</td>
</tr>
<tr>
<td>69-70</td>
<td>-</td>
<td>methyne</td>
</tr>
<tr>
<td>16-17</td>
<td>-</td>
<td>methyl</td>
</tr>
</tbody>
</table>

*Table 4: Chemical shifts for PLA NMR in chloroform-D*

Research has shown[33] tin and lead oxide are very effective catalyst for ring-opening lactide. Tin, antimony and bismuth octanoate catalysts are also very efficient as far as yield and viscosity are concerned. Finally, tin and bismuth octanoate are both very good at preventing racemization for reaction times under 12h, while still giving >95% conversion. Tin is widely used because of its low toxicity, making it compatible with biomedical applications.

2.5 Biodegradability

According to the US Environmental Protection Agency website, plastic waste accounted for 30 millions tons (12.0%) of the total municipal solid waste. In the USA, the most common method of municipal solid waste disposal is landfill (54%), followed by recycling (24%), combustion (13%) and composting (9%). However, landfilling results in the generation of greenhouse gases and takes up and may contaminate land that could be used otherwise. It would therefore be desirable to develop recycling or composting...
methods. Biodegradable polymers are therefore of great interest in nowadays environmentally-concerned society.

In general, polymer degradation takes place through scission of the chain. Such scission can occur through chemical or biological mechanisms. Factors that influence degradation are\[4\] first-order structural factors (molecular weight, structure), higher order structural factors (crystallinity, elasticity, melting point) and surface conditions (surface area, hydrophobicity). Exposure conditions, such as moisture, acidity, temperature, aerobic or anaerobic conditions and enzyme specificity will also influence degradation.

PLA degradation has been intensively studied\[^{[34,35,36]}\] and it has been showed that it is highly dependent on crystallinity and does vary with stereochemistry. R.T. McDonald et al. showed that, with regard to proteinase-K-mediated degradation, highly crystalline samples degrade much slower than low-crystallinity samples and PDLA degrades faster than PLLA\[^{[35]}\].

3. Polylactide hybrids

PLA is an interesting polymer on its own, but there are a lot of applications that could use hybrids. Used in copolymers, blends, or attached to non-polymeric materials, it gains new properties, it can be used for different applications.

Starch is a natural product both renewable and degradable. It is easily extracted from a variety of botanical sources, and it has some polymeric properties. It however has limited mechanical performance. Combining it with PLA would improve its mechanical properties while improving PLA’s biodegradability. Several ways of combining starch and
PLA have been explored, including starch acetylation\textsuperscript{[37]}, PLA functionalization with acrylic acid\textsuperscript{[38]} or maleic anhydride\textsuperscript{[39]}, inclusion of diisocyanates\textsuperscript{[40]}, or plain simple grafts\textsuperscript{[41]}. E. Schwach et al. studied the benefits of several methods of compatibilization of Starch and PLA\textsuperscript{[42]}, and showed that peroxide reticulation and addition of copolymer compatibilizer (PLA-grafted amylose) best improved tensile mechanical and thermal properties of the blend.

Similarly, PLA properties have been modified using clays\textsuperscript{[43,44]}, sugars\textsuperscript{[45,46]}, or natural fillers\textsuperscript{[47]}. Another way to modify the polymer's properties is by adding another monomer to the polymerization, producing copolymers with properties usually somewhere in between the properties of the polymers produced from each type of monomer. Examples of co-monomer that have been used include $\varepsilon$-caprolactone\textsuperscript{[48]}, glycolide\textsuperscript{[49,50]}, trimethylene carbonate\textsuperscript{[51]} and dioexpanone\textsuperscript{[52]} each inducing changes in the properties of the polymer\textsuperscript{[53]}.

4. Polylactide and nanoparticles

Nanoparticles have applications in many important fields of research: catalysis\textsuperscript{[54,55,56]}, solar cells\textsuperscript{[57,58]}, biochemistry\textsuperscript{[59]}, biomedicine\textsuperscript{[60,61]}, etc. Very often, nanoparticles are either made of polymer or coupled with polymers to improve on their physical properties. Polylactide is often used in such applications, especially where biochemistry is concerned.
A. Pfister et al. used a blend of polylactide and difluoroboron dibenzoylmethane to make nanoparticles with fluorescent and phosphorescent properties, as well as biocompatibility and the ability to be processed into fibers and films. Interestingly, this material also gains temperature-sensitive delayed fluorescence and green oxygen-sensitive room-temperature phosphorescence that are not properties of either of the starting materials. Such a material could be very useful for imaging or optical sensing[62].

Another useful application of nanoparticles including polylactide is in drug delivery. By using magnetic materials, usually iron oxide, it would be possible to direct drugs embedded in polylactide to certain area of the body by using magnetic fields. This would make it possible to reduce the quantity of drugs injected, since the concentration in the targeted area could be higher than in the rest of the body, and to reduce any toxicity issues such as those seen in chemotherapy's treatment against cancer. There are here several approaches to making such nanoparticles. A magnetic material is needed to give magnetic properties, and polylactide helps holding the nanoparticles together and opens possibilities as to attaching drugs to the particles, but research has been done both on making nanoparticles out of a blend of those materials[63], or on coating magnetic nanoparticles with polylactide[63,64].

The biodegradable and biocompatible properties of PLA have been found to be of great interest in drug delivery systems[65]. The possibility to trap a drug in polylactide copolymers (or a polylactide composite) and to have it be released upon degradation of the polymer has been thoroughly investigated[8,66].
5. Goals

Seeing as how PLA is of so much interest, we tried to explore the possibility to develop new types of materials by coating PLA around nanoparticles and powder particles. One goal was to explore how feasible that was with a variety of materials that could be used in different applications. To fulfill that goal, a wide range materials were investigated, from iron oxide to sand.

One major problem nowadays with everything that touches renewable "green" resources is their cost. Customers are in majority ready to pay a little extra for environment-friendly materials if those materials compare with what they are used to, but being able to make those materials as cost-efficient as possible would be a great improvement. That is why our secondary goal was to develop a cost-efficient, if possible easy way of coating our materials with PLA. To fulfill this goal, we have used a pretty simple way of synthesis, and stuck with it – with slight variations if needed – for the whole study.
Surface Growth Of PLA

1. Particles coating

Several ways of preparing nanoparticles involving PLA can be found in the literature. One way is through evaporation and solvent emulsification method. It consists of making nanoparticles out of a homogeneous blend of PLA and nanoparticles of interest\(^{[8, 67]}\). The advantages of this method are that it gives a good control on the particle sizes, and it starts from polylactide, rather than lactide, allowing for a good control on the polymerization, since it can be done under whatever conditions desired. However, it is rather tedious and asks for accurate settings in order to obtain satisfying results. It will also be a blend, not an inorganic core in a polymeric shell.

Another way is through surface-grafting of polymer on nanoparticles\(^{[68]}\). It consists of attaching polylactide to the surface of the particles. It allows for a good control of the polymerization here again, since the polymer is also prepared separately and it results in a core-shell structure. However, it requires separate steps for the polymerization and the functionalization of the particles.

The last method is the surface growth method\(^{[64]}\). In this method, polylactide is grown from lactide directly on the surface of the nanoparticles. For this to happen, there needs to be active hydroxide groups on the surface of the particle to ring-open lactide and initiate chain growth. Most metal oxide particles will have those hydroxides on their surface, but
they are not active enough to ring-open lactide. That's why the metal oxide starting particles have to be pretreated with some surface agent that will both attach easily to the surface hydroxides and provide an active alkoxide, such as titanium isopropoxide, glycolic acid\cite{64} or lactic acid\cite{68}. Although there is not as much control on the particles size and the polymerization, this method is much simpler, since it consists only of blending reagents together in a one-pot preparation. It will also produce particles with a core/shell structure instead of the blend structure.

Because of its simplicity, which results in better cost efficiency, the surface-growth method was selected to be used for this study. When surface modifiers would be needed, research had already been done on using glycolic acid on magnetic nanoparticles\cite{64}. Lactic acid is very similar in structure to glycolic acid, but using it as surface modifier makes it easier to manage toxicity and bioproperties of the particles, because it will be indistinguishable from the grown PLA chains (as shown in figure 7).

2. Initial test

As an initial test, to get an initial feeling of how the reaction behaved, TiO$_2$ nanoparticles were coated with PLA, using titanium isopropoxide as surface modifier, following a mechanism indicated in figure 9. This gave quite satisfactory results, with particles on which a melting point could clearly be observed around 130°C, and with a solid state $^{13}$C
NMR giving sharp peaks at 170, 74 and 16 ppm, characteristic of PLA (data not shown). A FT-IR spectrum also gave a very sharp peak at 1750 cm\(^{-1}\) (figure 8), confirming presence of PLA on the particles’ surface.

This was however somewhat outside the goals that were chosen for this study, since using titanium isopropoxide involves working under closely controlled atmosphere, which is not exactly easy or cost-efficient.

3. Methods

From the initial test with titanium oxide, a method was developed to be used with every test from here on. Unless stated otherwise, this method was followed for every experiment described later on.
3.1. Surface functionalization

Surface functionalization was not always implemented. However, when it was, it was done in accordance with the following method:

Nanoparticles were suspended in tetrahydrofurane by ultrasounds or vigorous stirring, depending on the size of the particles. A large excess of the surface modifier was then added slowly while stirring the nanoparticles in the solvent. The reaction was left stirring overnight, and the nanoparticles were then washed repeatedly with tetrahydrofuran and dried.

The solvent and nanoparticles were kept away from air during most of the reaction, to prevent too large input of water that could offset lactide ring-opening in the next step.

3.2. Polymerization

Polymerization was done in accordance with the following method:

Nanoparticles were dried for 8h under vacuum at 80°C. If a surface modifier was needed, the particles were dried before functionalization and kept under nitrogen most of the time to avoid moisture input.

The nanoparticles, with or without surface modifier, were then suspended in toluene by ultrasound (or vigorous stirring for bigger particles). The monomer was then added, usually with a 3:1 weight ratio, and left to dissolve at 60°C for a couple of hours. The catalyst was then added, and the reaction left to reflux for 8 hours. The final particles were then washed twice with toluene and twice with chloroform to wash away any free polymeric chain, then dried under vacuum.
3.3. Analysis

Analysis of the final product was done with several methods:

Fourier-Transform InfraRed spectroscopy (IR) was used in most cases to determine whether PLA was present, characterized by a peak at 1750 cm\(^{-1}\). Those were run on a Perkin-Elmer Spectrum GX instrument.

An experiment was devised to determine the quantity of polymer that grew on the particles. It consisted in weighting the particles before and after burning them in an Coorstek high-density alumina crucible over a Bunsen burner. Any weight-loss would be due to polymer decomposition, leaving only the inorganic particles.

Solid state \(^{13}\)C nuclear magnetic resonance (\(^{13}\)C NMR) was run on select samples with a Bruker DSX 300 MHz instrument, using magic angle spinning.

A Jeol JSM-5500 scanning electron microscope (SEM) was used for imaging of the particles.

4. Silica and derivatives

The possibility of coating silica or sand with polymer can have interesting applications in areas such as construction work, because it would make a very cost-effective materials that would have the handling properties of a powder with the physical properties of the polymer.

4.1. Silica

Reflecting lactide directly with silica gel having proved unsuccessful, the surface modification of lactide with lactic acid was then experimented with.
Lactic acid was reacted onto silica gel, and the resulting particles were then reacted with lactide, using different catalysts known to promote ring-opening polymerization, namely 4-dimethylaminopyridine (DMAP), tin octanoate (Sn(oct)$_2$) and zinc oxide (ZnO). Figure 14 shows FT-IR spectra for, from bottom to top, silica gel, silica gel reacted with lactic acid, and PLA-coated silica gel made using DMAP, Sn(oct)$_2$ and ZnO as catalyst. A peak at 1750 cm$^{-1}$ is clearly visible for each catalyst used, confirming their efficiency for this reaction. Results also showed at least 30% weight content of polymer on the final particles, as shown in table 5. Finally, a solid state $^{13}$C NMR spectrum of the reaction using Sn(oct)$_2$ as catalyst confirms presence of PLA (figure 12). This showed that for coating silica gel with PLA, either of the three catalysts tested worked fine, although DMAP gave a lower conversion. It should be noted that the reaction with DMAP produced more free polymer than either of the other catalysts. Whether this was due to DMAP ring-opening lactide on its own or to a better catalysis of ring-opening with water has not been determined.

<table>
<thead>
<tr>
<th>Surface Modifier</th>
<th>Monomer</th>
<th>Catalyst</th>
<th>Weight Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lactic acid</td>
<td>Lactide</td>
<td>DMAP</td>
<td>30%</td>
</tr>
<tr>
<td>Lactic acid</td>
<td>Lactide</td>
<td>Sn(oct)$_2$</td>
<td>38%</td>
</tr>
<tr>
<td>Lactic acid</td>
<td>Lactide</td>
<td>ZnO</td>
<td>39%</td>
</tr>
<tr>
<td>Glycolic acid</td>
<td>Lactide</td>
<td>Sn(oct)$_2$</td>
<td>16%</td>
</tr>
<tr>
<td>Lactic acid</td>
<td>$\varepsilon$-caprolactone</td>
<td>Sn(oct)$_2$</td>
<td>18%</td>
</tr>
</tbody>
</table>

*Table 5: Relative weight of polymer on silica gel, using different surface modifier, monomer or catalyst*
An optical image of the particles was obtained through scanning electron microscopy (see figure 10). Each steps shows a difference in the aspect of the particles. Two observation should be noted: First, coating with lactic acid is quite important, and probably involves some degree of polymerization of lactic acid. Secondly, the so-called "coating" doesn't coat the particles uniformly. Rather, polylactide seems to grow at certain spots, giving a very heterogeneous surface. This is further discussed in the Discussion section.

Although lactic acid as the surface modifier and lactide as the monomer worked very well and were to be benchmarks for all other experiments, variations were tested on silica. Using glycolic acid as surface modifier gave 16% weight polymer, which is in the range of the 13.3% obtained on iron oxide nanoparticles in the literature[64]. Similarly, using ε-
caprolactone as the monomer yielded 18% polymer on the particles. (FT-IR spectra for those two experiment are given in Appendix A).

Sand is composed mostly of silica, and would provide for an even more cost-effective material than silica gel. Experiments showed however than using any sand would not work. Initial experiments involved plain beach sand, and no polymerization at all was observed using Sn(oct)$_2$ as catalyst, with and without surface modifier. Trying to wash the sand with a base to activate the surface hydroxides didn’t improve the reaction. It is assumed too many impurities were present in the sand, and that surface hydroxides were too few to provide with any initiator for the reaction.

White quartz was then bought from Aldrich.

This material induced polymerization, although an infrared spectrum could not be obtained. 20.2% of the particles were polymer. PLA growth on the sand surface was however confirmed by SEM (figure 11).

4.2. Metal oxides

Following the procedure used for silica, an attempt at coating iron oxide was made. Starting from nanoparticles bought from Sigma-Aldrich, using either lactic acid or glycolic acid did not give any results: FT-IR did not show any PLA peaks, and weight determination were always below 5%.
Figure 12: Solid state 13C NMR spectrum of PLA-coated silica gel particles

Figure 13: FT-IR, SEM and NMR analysis of PLA-coated alumina
An attempt to reproduce results from F. Chen et al.\textsuperscript{64} did not lead to better results. For this, nanoparticles were synthesized in the lab: Iron (II) and iron (III) were mixed in a 1:2 ratio in water and nanoparticles were formed by adding ammonia under vigorous stirring. The particles were washed and dried, then reacted immediately with glycolic acid. The rest of the procedure was done according to previous experiments. FT-IR again did not show any results, and SEM confirmed no polymer growth had happened. Other particles were experimented upon without more success. BaTiO\textsubscript{3} and Co\textsubscript{3}O\textsubscript{4} never grew polylactide.

Basic alumina, however, successfully grew PLA up to 11\% of the oxide's weight, without any surface modifier. Both FT-IR and NMR confirm presence of PLA, as shown on

\begin{figure}
\centering
\includegraphics[width=\textwidth]{figure14.png}
\caption{FT-IR spectra of SiO\textsubscript{2}-PLA compounds made from different catalysts}
\end{figure}
The idea to try basic alumina came from the fact that some surfaces seemed to be better than other for ring-opening lactide. This shows that basic character of the surface hydroxide is needed to achieve polymerization without using surface modifiers. Finally, TiO$_2$ was tested with lactic acid and lactide. This gave 12% weight polymer on the nanoparticles. FT-IR confirmed presence of PLA with a peak at 1750 cm$^{-1}$, as shown in appendix A.

<table>
<thead>
<tr>
<th>Material</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fe$_2$O$_3$</td>
<td>No polymerization</td>
</tr>
<tr>
<td>Al$_2$O$_3$</td>
<td>11% polymer</td>
</tr>
<tr>
<td>Co$_3$O$_4$</td>
<td>No polymerization</td>
</tr>
<tr>
<td>BaTiO$_3$</td>
<td>No polymerization</td>
</tr>
<tr>
<td>TiO$_2$</td>
<td>12% polymer</td>
</tr>
</tbody>
</table>

Table 6: Summary of results for metal oxide particles

4.3. Other materials

Following the same basic idea of using surface hydroxide to ring-open lactide or react with some surface modifier, a couple other materials were tried. Starch is has a lot of properties that would make it interesting when combined with PLA, as has been mentioned before. Using either DMAP or Sn(oct)$_2$ as catalyst did not lead to any polymerization, as confirmed by NMR. It was deemed that using a surface modifier would not be useful, since starch structure does contain a large amount of hydroxides bound to organic molecules. Therefore, adding an organic molecule to starch should not improve the properties of available hydroxides in any way.
Clays also have free hydroxides in their structure. Combining clay and PLA could also lead to interesting properties. Montmorillonite was selected as it had been used for PLA-grafting before\textsuperscript{[69]}, although the polymer was not grown on the clay. Surface treatment by lactic acid followed by ring-opening polymerization of lactide gave 17% polymer on the final product. Presence of PLA was confirmed both by FT-IR and NMR, as shown in figure 15.

Montmorillonite, as most clays, has a layered structure. It was deemed possible that polymer chains would grow between layers, altering the structure of the clay. This was proven wrong, however. X-ray diffraction pattern (shown in Appendix B) proved exactly the same for the clay with or without PLA. This shows that PLA will grow on the outside hydroxides, lactide molecules being sterically prevented from getting between layers.
Figure 15: FT-IR and NMR spectra for montmorillonite coated in PLA
Discussion And Conclusion

A method for growing polylactide on nanoparticles was developed. The principle is that hydroxide groups on the material surface will ring-open lactide and induce polymerization. Experimentation showed that not every material will ring-open lactide. Surface hydroxide groups have to be both readily accessible and be able to ring-open lactide. Some will not induce reaction with lactide, probably because of a too great electronegativity character of the atom they are bound to.

In some cases, it is possible to use a surface modifier to provide with reactive hydroxide groups. Those surface modifiers will bind with surface hydroxides and provide a reactive hydroxide group to ring-open lactide. Glycolic acid or lactic acid act very well as such, since they can undergo esterification at the particle's surface and provide with a reactive hydroxide. They also are very close in structure to lactide, and do not interfere with the polymer biodegradability or toxicity. One observation that has been made is that lactic acid seems to polymerize to some degree on the surface of the particles. Mass measurements actually showed that around 40% of the final polymer weigh comes from lactic acid polymerizing. Since lactic acid and lactide polymers will have the same monomer, this will not influence the polymer backbone, but it will likely prevent any stereoselectivity in the polymer. Quantities of lactic acid used are large enough to assume
that polymer grown from lactic acid only would not grow longer than what has been observed, and shows that reacting additional lactide allows elongation of the backbone. During most experiments, a weight ratio of 3:1 lactide to particles was used. This was to prevent formation of free polylactide chains that made separation of the particles difficult. However, the possibility of using higher quantities of polymer was tested. A 3:1 weight ratio of lactide to silica particles leads to 23% polymer weight on the particles, while a 20:1 ratio leads to 38% polymer on the particles. Within experimental error, an increase can be seen, but it is not very significant. This seems to show there is a ceiling to the length of the polymer backbone.

Although some sort of coating of the particles was expected, what was actually observed was actually more random growth on the surface of the particles. That is most probably due to a larger particle size than what has been used in the literature. It is particularly visible on sand, which consists of bigger particles than other materials (see figure 11). This would be due to a preference for any incoming monomer to react with the end-alkoxide from the growing chain rather that with a new surface hydroxide.

In summary, polylactide can be grown from the surface of different particular materials, theoretically giving them properties from the polymer while retaining properties from the material and the particular shape. Silica-based materials reacts readily, and other usable materials have been listed.
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Appendix

A- FT-IR Spectra

A.1 Glycolic acid surface-treated silica gel reacted with lactide
A.2 Lactic acid surface-treated silica gel reacted with ε-caprolactone

![Graph showing the infrared spectrum of SiO2 and SiO2 + CL.]

A.3 Lactic acid surface-treated titanium oxide reacted with lactide

![Graph showing the infrared spectrum of lactide.]

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B – XRD Spectrum of Montmorillonite coated in PLA