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TAMPERE UNIVERSITY OF TECHNOLOGY

ANNI ANTNIEMI

EVALUATION OF THE FEASIBILITY OF BIODEGRADABLE POLYMERS FOR ENCAPSULATING RESONANCE CIRCUITS

Master of Science Thesis

Examiner:
Professor Minna Kellomäki
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ABSTRACT

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The properties and the structure of biodegradable polymers alter during degradation. The conventional way to study material properties and degradation requires direct contact with the material. For example monitoring the degradation of biodegradable implants inside a human body is challenging. Changes in the biodegradable polymers can be wirelessly monitored using resonance circuits. However, the circuits have to be protected from the surrounding environment in order for them to work properly. A protective layer around the circuit prevents water penetration to the circuits and enables observing the material changes.

The aim of this work was to evaluate the feasibility of three biodegradable polymers for encapsulating resonance circuits. The circuits were encapsulated by poly(L-lactide-co-glycolide) (PLGA 80/20), poly(D,L-lactide-co-glycolide) (PDLGA 85/15), and poly(L-lactide-co-glycolide) (PLGA 10/90) using compression molding. The resonance behaviors of the encapsulated circuits were wirelessly measured in order to evaluate the success and the duration of the encapsulation. In addition, a degradation test series was carried out to compare the resonance behavior and the degradation. The comparison was done in order to find out if changes in material properties could be obtained by measuring wirelessly the resonance behavior of the encapsulated circuits.

The study revealed that the encapsulation using compression molding was possible with PLGA 80/20 and PDLGA 85/15 materials. The PLGA 80/20 capsules worked even for 14 weeks and the PDLGA 85/15 capsules for 7 weeks. The PLGA 10/90 capsules lasted only few days and failed due to rapid degradation of the capsules. The degradation test showed that the properties and the appearance of the PLGA 80/20 hardly changed. The properties of the PDLGA 85/15 decreased continuously during the degradation test and were weaker than the properties of the PLGA 80/20. The structure of the PDLGA 85/15 samples changed significantly due to autocatalysis. The study also revealed that the properties of the PLGA 10/90 samples were the weakest and the samples were totally fragmented after six weeks.

The visual characterization of the encapsulated circuits and the degradation test samples suggested that water absorption could have caused the characteristic resonance behavior of each material. However, the results from the degradation test series do not explain the resonance behavior even though some similarities could be obtained. Consequently further studies are needed to solve the reason for the resonance behavior.

TIIVISTELMÄ

ANNI ANTNIEMI: Biohajoavien polymeerien soveltuvuuden arviointi resonanssipiirien kotelointiin
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Biohajoavien polymeerien ominaisuudet ja rakenne muuttuvat polymeerien hajoamisen aikana. Tavallisesti materiaalien ominaisuuksien ja hajoamisen tutkiminen vaatii kontaktin tutkittavan materiaalin kanssa. Esimerkiksi biohajoavan implantin tarkkaileminen ihmisen sisällä on haastavaa. Biohajoavien materiaalien muutoksia voidaan seurata langattomilla mittauksilla käyttämällä resonanssipiirejä. Resonanssipiirit pitää kuitenkin suojata ympäristöltä, jotta ne toimivat kunnolla. Suojakerros piirin ympärillä estää veden tunkeutumisen piiriin ja mahdollistaa materiaalimuutosten tarkkailemisen.

Työn tavoitteena oli tutkia kolmen biohajoavan polymeerin soveltuvuutta koteloida resonanssipiiri. Piirit koteloitiin ahtopuristimella seuraavilla materiaaleilla: poly(L-laktidi-co-glykolidi (PLGA 80/20), poly(D,L-laktidi-co-glykolidi) (PDLGA 85/15) ja poly(L-laktidi-co-glykolidi) (PLGA 90/10). Koteloiduista piireistä mitattiin langattomasti resonanssikäyttäytyminen, jonka avulla arvioitiin koteloinnin onnistumista ja kestoa. Lisäksi materiaalien hajoamiskäyttäytymistä tutkittiin. Tarkoituksena oli vertailla resonanssikäyttäytymistä ja materiaalien hajoamista, jotta voitaisiin selvittää voidaanko muutokset materiaaliominaisuuksissa havaita pelkästään mittaamalla langattomasti koteloitujen piirien resonanssikäyttäytymistä.

Tutkimuksessa huomattiin, että kotelointi PLGA 80/20 ja PDLGA 85/15 materiaaleilla onnistui. PLGA 80/20 kotelot toimivat jopa 14 viikkoa ja PDLGA 85/15 kotelot 7 viikkoa. PLGA 10/90 kotelot toimivat vain muutaman päivän. Kotelointi epäonnistui PLGA 10/90 koteloiden nopean hajoamisen vuoksi. Hajoamistesti kertoi, että PLGA 80/20 näytteiden ominaisuudet ja ulkonäkö eivät juuri muuttuneet. PLGA 85/15 näytteiden ominaisuudet heikkenivät tasaisesti koko testijakson ajan, ja olivat huonompia kuin PLGA 80/20 näytteiden ominaisuudet. PLGA 85/15 näytteiden rakenne muuttui huomattavasti autokatalyysin vuoksi. Testissä paljastui myös se, että PLGA 10/90 näytteillä oli heikoimmat ominaisuudet ja kuuden viikon aikana näytteet olivat kokonaan fragmentoituneet.

Koteloitujen piirien ja hajoamistestin näytteiden visuaalisen karakterisoinnin mukaan materiaaleille ominaiset muutokset resonanssikäyttäytymisessä voisivat johtua veden absorptiosta kuhunkin materiaaliin. Hajoamistestin tulokset eivät kuitenkaan selitä muutoksia resonanssikäyttäytymisessä, vaikka joitakin yhtäläisyyksiä voidaan havaita. Resonanssikäyttäytymisen syyn selvittämiseksi tarvitaan lisätutkimuksia.

PREFACE

This study was performed in the Biomaterials and Tissue Engineering group in the Department of Electronics and Communication Engineering in the Tampere University of Technology. The study is also related to the Human Spare Parts project.

First, I would like to express my gratitude to Professor Minna Kellomäki for offering me this opportunity and for her guidance and help during my thesis. I am grateful to Maiju Hiltunen, who instructed me at the beginning of this project. I am also thankful to Timo Salpavaara for his help and guidance regarding the resonance behavior measurements. I would like to thank all my colleagues at the Department of Electronics and Communication Engineering for their help during this project and for making a pleasant working environment. I am also very grateful to thank Suvi Heinämäki and Heikki Liejumäki for their help in the laboratory.

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Anni Antniemi

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ABBREVIATIONS

ΔH	Melting enthalpy
^oC	Celsius degree
σ_f	Flexural strength
ε_f	Flexural strain
CAS number	Chemical Abstracts Service Number
DSC	Differential scanning calorimetry
E	Modulus
GPa	Gigapascal
Hz	Hertz
i.v.	Inherent viscosity
kN	Kilonewton
PCL	Polycaprolactone
PDLA	Poly(D-lactide)
PDLGA	Poly(D,L-lactide-co-glycolide)
PE	Polyethylene
PGA	Polyglycolide
PLA	Polylactide
PLCL	Poly(L-lactide-co-caprolactone)
PLDLA	Poly(D,L-lactide)
PLGA	Poly(lactide-co-glycolide)
PLLA	Poly(L-lactide)
PP	Polypropylene
PVC	Polyvinyl chloride
min	Minute
mg	Milligram
MPa	Megapascal
M_w	Weight average molecular weight
SD	Standard deviation
T_g	Glass transition temperature
T_m	Melting temperature

1. INTRODUCTION

Synthetic biodegradable polymers are commonly used as temporary materials in biomedical applications due to their easy and systematic processing, large variety of different properties and biodegradability. The properties and the structure of biodegradable polymers change during time as the polymers degrade. The degradation of biodegradable polymers has been widely studied. However, there are still plenty of unknown factors regarding the degradation mechanisms. The conventional way to study biodegradable materials *in vitro* requires contact with the studied material. The degradation behavior *in vivo* can differ compared to the *in vitro* degradation and hence it is harder to observe and predict. For example monitoring the degradation of biodegradable implants inside a human body is challenging. (Nair & Laurencin 2007; Göpferich 1997)

Currently, resonance circuits are used to monitor changes of biodegradable polymers *in vitro*. By embedding the circuits into test materials, the changes in materials can be detected by wirelessly measuring the resonance behavior of the encapsulated circuits. The resonance behavior of the circuits is prone to environmental effects and thus enables monitoring the material changes. The circuits need to be encapsulated in order for them to work in aqueous environment. However, there are some challenges regarding the encapsulation process. Also the reason why the measured resonance behavior changes as it does is unclear. In the future, similar method could be used to detect changes in material properties and monitor the degradation of implants in real-time *in vivo* if the used circuits were also biodegradable. (Salpavaara et al. 2012)

In this work, resonance circuits were encapsulated with three different poly(lactide-co-glycolide) based copolymers. The resonance behavior of the capsules was measured to evaluate the success and the duration of the encapsulation. For comparison, a degradation test series was done using the same three biodegradable materials. The purpose was to look for similarities between the resonance behavior and the degradation test results in order to find out if the degradation or changes in material properties could be observed by wirelessly measuring the resonance behavior of the encapsulated circuits.

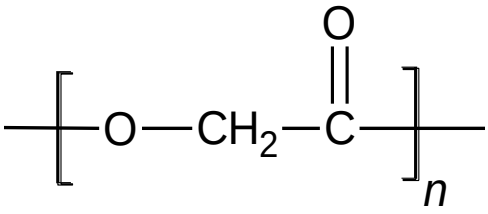
2. SYNTHETIC BIODEGRADABLE POLYMERS

Polymers are long chain molecules derived from repeating units, monomers. Polymers can be categorized to synthetic and natural polymers based on to their origin. Synthetic polymers such as polyethylene (PE), polyvinylchloride (PVC), polypropylene (PP) and polycaprolactone (PCL) are mainly produced from petrochemically manufactured monomers. Protein based polymers like collagen, keratin and albumin, or carbohydrate based polysaccharides such as chitin, chitosan, starch and cellulose are natural polymers. Polymers can also be divided to biostabile and biodegradable polymers based on their interactions. Biostabile and non-degradable polymers such as PE, PP and PVC are commonly used in packaging food and pharmaceutical products. Their high consumption is based on good physical and chemical properties such as stability, durability and strength. However, the lack of biodegradability and biocompatibility restricts their use in biomedical applications such as implant materials (Nair & Laurencin 2006; Shah et al. 2008)

Biodegradable polymers degrade in biological environment to harmless non-toxic molecules. Biodegradation of polymers includes cleavage of enzymatically or hydrolytically delicate bonds in the polymer backbone resulting in polymer erosion. In this thesis, mainly aliphatic polyesters such as polyglycolide (PGA), polylactide (PLA) and their copolymers are discussed. In aliphatic polyesters different monomers are connected to polymer chains via ester linkages. Aliphatic polyesters are normally biodegradable and susceptible to hydrolysis due to their easily hydrolysable ester bonds. (Premraj & Doble 2005; Shimao 2001; Ulery et al. 2011; Fonseca et al. 2014)

2.1 Polyglycolide

Polyglycolide is a synthetic biodegradable polymer and it is the simplest poly(α-hydroxy acid). The structure of PGA is presented in Figure 1. PGA is a highly crystalline polymer with 45-55 % crystallinity. Due to the high crystallinity, PGA shows a good mechanical properties and have a very low solubility in organic solvents except to highly fluorinated organic solvents like hexafluoro isopropanol. In addition, the melting point of PGA is high because of the high crystallinity. The melting point (T_m) of PGA is higher than 200 ºC and the glass transition temperature (T_g) varies between 35 and 40 ºC. (Nair & Laurencin 2006; Gunatillake & Adhikari 2003)



Polyglycolide

Figure 1. *Structure of polyglycolide.*

Polyglycolide is a hydrophilic polymer and therefore degrades comparatively fast. Within 1-2 months PGA loses its strength and within 6-12 months PGA starts to loss mass. PGA degrades by hydrolytic degradation. Water causes scissions of the ester backbone. During the hydrolysis, acidic degradation products such as alcohol and carboxyl groups are produced. The acidic degradation products accelerate the hydrolysis rate. PGA can also degrade partially by enzymes like esterase. (Nair & Laurencin 2007; An et al. 2000; Yu et al. 2010)

Despite the fact that PGA has a low solubility, it can be manufactured into different shapes and structures. Polyglycolide based materials can be processed for example by using extrusion, injection and compression molding and solvent casting. PGA has also an excellent fiber forming ability. PGA is very sensitive to hydrolytic degradation and thus the processing conditions need to be controlled. The properties and the degradation rate of PGA are influenced by the choice of processing method. (Gunatillake & Adhikari 2003) The use of PGA in biomedical applications is limited due to the high rate of degradation, acidic degradation products and low solubility. Consequently PGA is often copolymerized to get a wider range of properties and to alter the degradation rate. (Nair & Laurencin 2007)

2.2 Polylactide

Polylactide is a biodegradable, linear aliphatic polyester and the second simplest poly(α-hydroxy acid). PLA consist of lactic acids. Lactic acids exist in two stereoisomeric forms, L-lactic acid and D-lactic acid, which are presented in Figure 2. L-lactic acid is a natural occurring polymer and produced by humans and other mammals whereas D-lactic acid is only produced by bacteria. The chemical and the physical properties of lactic acids are similar apart from the ability to rotate plane-polarized light to opposite sides. Lactides can be formed from L-lactic acid, D-lactic acid or from their combination. Consequently there are three possible configurations of lactides: L-lactide, D-lactide and mesolactide (D,L-lactide). L- and D-lactides are optically active since stereochemical centres of the dimers are identical. The rasemic mixtures of both L-and D-lactides have different stereochemical centres and thus it is optically inactive. Different lactides are used to polymerize poly(L-lactide), poly(D-lactide) and poly(D,L-lactide),

PLLA, PDLA, PDLLA respectively. The structure of polylactide can be seen in Figure 3. (Carrasco et al. 2010; Groot et al. 2010)

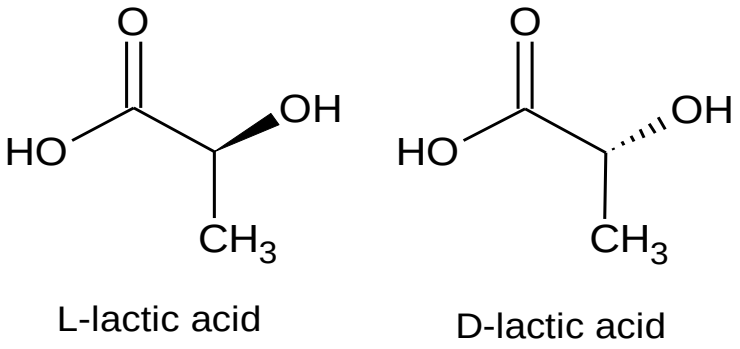


Figure 2. *Isomers of lactic acid.*

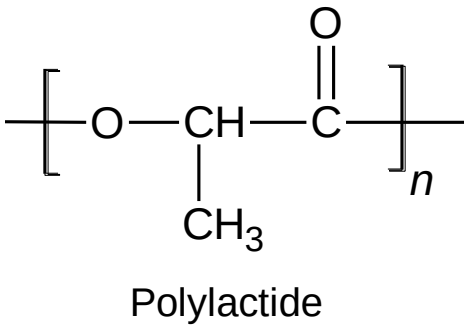


Figure 3. *Structure of polylactide.*

The properties of different polylactides vary to a large extend depending on the ratio of L- and D-isomers, crystallinity, polymer structure and molecular weight. (Auras et al. 2004; Avérous & Pollet 2012; Nampoothiri et al. 2010) Particularly PLLA and PDLLA are widely studied. PLLA is a semicrystalline polymer. The crystallinity of PLLA is approximately 37 %. The degree of crystallinity depends on the polymer composition and molecular weight. The crystallinity of PLLA can be decreased for examples by adding D-lactides which hinder the formation of organized crystals. PLLA has a melting temperature of about 180 ºC and a glass-transition temperature of about 55 ºC. PLLA has a good tensile strength, a low extension and a high modulus. PLLA is a slow degrading polymer. PLLA loses its strength in about 6 months but the mass will stay relatively the same for quite a long time. The total degradation of PLLA *in vivo* takes 2 to 5 years. (Nair & Laurencin 2007; Middleton & Tipton 2000; Södergård & Stolt 2002)

PDLLA is an amorphous transparent polymer that has equal amounts of L- and D-lactide units. The glass transition temperature of PDLLA is between 55-60 ºC. Being an amorphous polymer PDLLA does not have a melting point and exhibits relatively low strength compared to PLLA. PDLLA degrades rather fast in comparison to PLLA due to the lack of crystalline regions in the polymer structure. Within 1-2 months PDLLA

loses its strength and within 6-12 months PDLLA undergoes a mass loss. (Nair & Laurencin 2007; Jiang & Zhang 2013) PDLLA is often used in drug delivery applications due to its amorphous nature, fast degradation rate and low strength. (Gupta & Kumar 2007; Lasprilla et al. 2012)

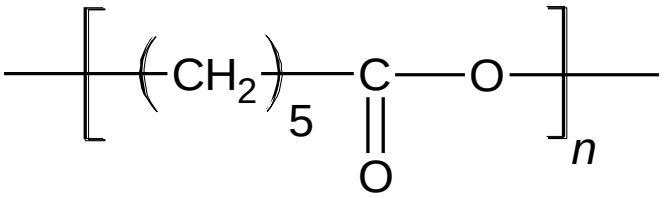
The difference between the structures of PGA and PLA is the methyl group in the PLA monomer. This makes PLA more hydrophobic than PGA and hence the water uptake and the hydrolytic degradation of PLA are slower compared to PGA. Because of the methyl side groups, PLA is less crystalline compared to PGA. The mechanical properties of PLA are better in comparison to PGA but not adequate for load-bearing applications. (Auras et al. 2004)

Polylactides undergo hydrolytic degradation via bulk erosion by the random scission of the ester backbone. The ester linkages in PLA backbone are susceptible to hydrolysis but also to enzymatic chain scission. (An et al. 2000; Ashammakhi et al. 2004) The degradation is autocatalyzed by carboxylic acid end groups. PLA degrades into lactic acids, normal human metabolic by-products, which are further broken down into water and carbon dioxide via the citric acid cycle. The crystallinity of polymer has a vast effect on the degradation. High temperature and humidity enhance the degradation rate of PLA. (Jain 2000; Tsuji 2010; Huttunen & Kellomäki 2013)

PLA is a thermoplastic polymer and possesses a good processability. PLA can be processed into several forms such as rods, fibers and plates using for example extrusion, injection molding, compression molding, and solvent casting. (Woodruff & Hutmacher 2010) Also blow molding, thermomolding and film forming can be used to process PLA. The biggest challenge during the processing of polylactides is the restricted thermal stability. Ester linkages in the polymer are very susceptible to heat. Even short contact with heat leads to degradation of polymer backbone to smaller fractions. (Gupta & Kumar 2007; Maurus & Kaeding 2004; Rydz et al. 2015; Avérous & Pollet 2012) The composition and the structure of PLA polymer chains have a great effect on the processing (Lim et al. 2008).

2.3 Polycaprolactone

Polycaprolactone is a semicrystalline, hydrophobic, non-toxic, biocompatible and synthetic aliphatic polyester. The structure of PCL is presented in Figure 4. Because of the five methylene groups in the caprolactone monomer, its mechanical and processing properties resembles polyolefins such as polypropylene and polyethylene. For example high molecular weight PCL has similar mechanical properties than PE, having a tensile stress about 13-30 MPa and elongation at breakage about 400-650 %. (Jiang & Zhang 2013)



Polycaprolactone

Figure 4. *Structure of polycaprolactone.*

PCL is soluble in many organic solvents such as chloroform, benzene and cyclohexanone, and it is easy and quite inexpensive to process. Melting temperature (55-60 ºC) and glass transition temperature (-60ºC) are low and thus PCL is flexible at room temperature. PCL has a low strength and a very high elongation at breakage. (Nair & Laurencin 2007; Kricheldorf 2001) PCL is highly processable because of low T_g and T_m. PCL can be processed using for example extrusion, injection molding, compression molding, solvent casting and electrospinning. (Woodruff & Hutmacher 2010) PCL has a quite good water diffusion coefficient and it stabilizes quickly in the aqueous environment and consequently PCL is a good candidate for encapsulation material. The diffusion coefficient of PCL is higher compared to PLLA and PGA. PLLA has a higher diffusion coefficient in comparison to PGA. The crystallinity of polymer structure influences the water diffusivity. (Yoon et al. 2000)

Polycaprolactones degrade quite slowly. The degradation of PCL takes about 2-3 years and mass loss occurs after 4 to 6 months, consequently PCL can be used for long-term applications. Because of the high crystallinity and the long methylene chains in the PCL backbone, it has a much lower degradation rate than PLA or PGA. PCL degrades by hydrolytic erosion the same way as PGA and PLA. PCL has hydrolytically unstable ester linkages in its polymer chain. Degradation starts from amorphous regions and it is accelerated by autocatalysis. Water absorption into polymer matrix is a restricting factor in the degradation. (Nair & Laurencin 2007; Perrin & English 1998) PCL can also degrade enzymatically under specific conditions. This is known as enzymatic surface erosion. (Zhang et al. 2014)

2.4 Polylactide-based copolymers

Copolymerization is a useful way to enhance the properties of different polymers. The properties such as mechanical and thermal properties, solubility, degradation rate and crystallinity can be tailored and improved by copolymerization or by blending PLA with other biodegradable polymers. Different types of lactides can be copolymerized with each other but most often PLA is copolymerized with PGA and PCL. (Rydz et al. 2015; Södergård & Stolt 2002)

2.4.1 Poly(lactide-co-glycolide)

Poly(lactide-co-glycolide) (PLGA) is a group of biodegradable and biocompatible copolymers. In the copolymers lactide and glycolide monomers can be arranged in different ways. The structure of alternating copolymer of PLGA is presented in Figure 5. Other possible copolymer types are for example random copolymer, block copolymer and graft copolymer. Properties of PLGA can be modified by changing the composition of PLA and PGA monomers and by the choice of lactide monomer. PLGA is well known and it can be easily processed into different structures, sizes and shapes by using for example solvent-casting, compression molding or extrusion. PLGA is soluble in large range of solvents such as chlorinated solvents and acetone (Makadia & Siegel 2011).

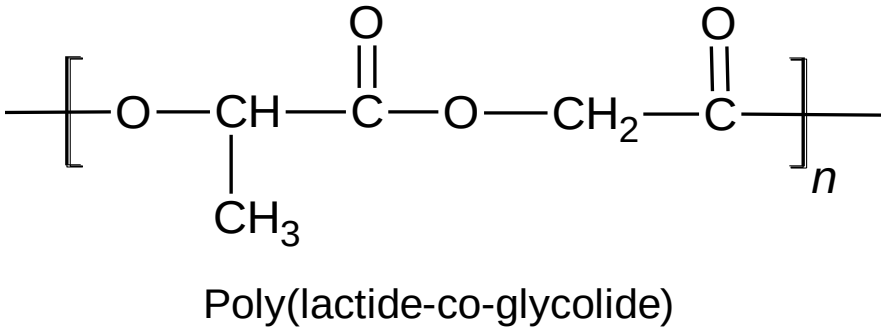


Figure 5. *Structure of alternating poly(lactide-co-glycolide) copolymer.*

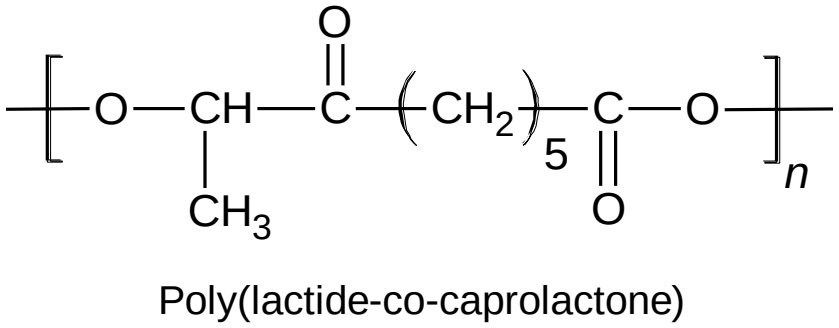
PLGA degrades into lactide and glycolide acids which are non-toxic and metabolized through normal metabolic pathways. The degradation occurs by bulk erosion through hydrolysis of ester bond in the polymer backbone. The degradation rate depends on many different parameters including comonomer ratio, molecular weight and the structure and form of the polymers. (Nair & Laurencin 2007) PLGA contains carboxylic end groups which are noted to catalyze the degradation process. During the degradation, polymer chains are broken down and consequently carboxylic end groups grow in number and accelerate the degradation even more. (Jain 2000) Because of the presence of methyl side groups in PLA, it is less hydrophilic than PGA. Therefore lactide rich PLGA copolymers absorb less water, are more hydrophobic and consequently degrade more slowly. As a rule, higher amount of polyglycolide results in faster degradation rate with an exception of 50:50 ratio of PGA/PLA. PLGA consisting of same amount of polylactide and polyglycolide is the most unstable and fastest degrading PLGA. (Ashammakhi et al. 2004; Jain 2000; Makadia & Siegel 2011; Nair & Laurencin 2007)

2.4.2 Poly(lactide-co-caprolactone)

The physical and the chemical properties of polycaprolactone can be tailored via copolymerization, blending or crosslinking with other polymers. Usually the copolymeriza-

tion of PCL is done using hydrophilic monomers such as glycolides and lactides to increase the slow degradation rate of PCL. Also the low strength of PCL is enhanced by copolymerization.

PLA is often copolymerized with PCL to toughen the PLA which is quite brittle. Copolymerization of PLA and PCL leads to remarkable increase in ductility and toughness of the polymers. (Jiang & Zhang 2013; Zhang et al. 2014) The structure of alternating copolymer of PLCL is presented in Figure 6. The lactide and caprolactone monomers can also be arranged in different ways to form different types of copolymers. The properties of different poly(lactide-co-caprolactones) (PLCL) can be tailored by changing the monomer ratio and by the choice of lactides. (Avérous & Pollet 2012; Lasprilla et al. 2012; Puppi et al. 2010) Increasing the amount of polycaprolactone in PLCL results in a lower rate of hydrolytic degradation and a lower glass transition temperature and consequently leading to more flexible products. (Kricheldorf 2001)



Poly(lactide-co-caprolactone)

Figure 6. *Structure of alternating poly(lactide-co-caprolactone) copolymer.*

3. DEGRADATION

Degradation can be defined as chemical modification of materials by a living organism which results in changes in mechanical and physical properties. In biological environment degradation can for example be induced by oxidation, photolysis, radiation or hydrolysis. In the body biodegradable polymers degrade into harmless by-products and are resorbed through normal metabolic pathways. (Ikada & Tsuji 2000) This thesis focuses on the degradation of synthetic biodegradable polymers which degrade mainly by hydrolysis.

3.1 Hydrolytic degradation

Typically synthetic biodegradable polymers degrade by hydrolytic degradation. The hydrolytic degradation of biodegradable polymers means cleavage of chemical bonds by hydrolysis in aqueous environment resulting in polymer erosion. This occurs due to the fact that polymer backbone consists of plenty of hydrolytically susceptible labile chemical bonds. Functional groups that are sensitive to hydrolysis are ester, orthoester, carbonates, amides, anhydrides, urethanes and ureas for example. (Nair & Laurencin 2007; Lucas et al. 2008; Ashammakhi et al. 2001)

The hydrolytic degradation of biodegradable polymers starts with water absorption into the polymer matrix and continues by chain scission of the hydrolytically unstable bonds in the polymer backbone. Chain scission can occur via chain end scission or random scission. The chain end scission and the random scission are illustrated in Figure 7 and Figure 8, respectively. In the chain end scission, the last amino acid at the end of the polymer backbone is removed. In the random scission, as the name says, the breakage of the bonds occur randomly along the polymer chains and the polymer is first degraded into oligomers and further into monomers. The cleavage of the chemical bonds in the polymer backbone via chain end scission is accelerated by the increasing number of acidic chain ends during the degradation. (Hasırcı et al. 2001; Södergård & Stolt 2002)

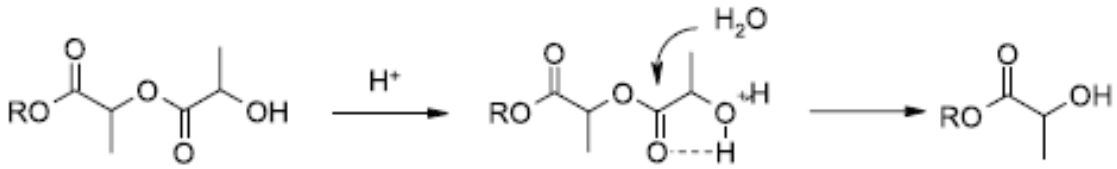


Figure 7. *Chain end scission of polylactide oligomer. Modified from (van Nostrum et al. 2004).*

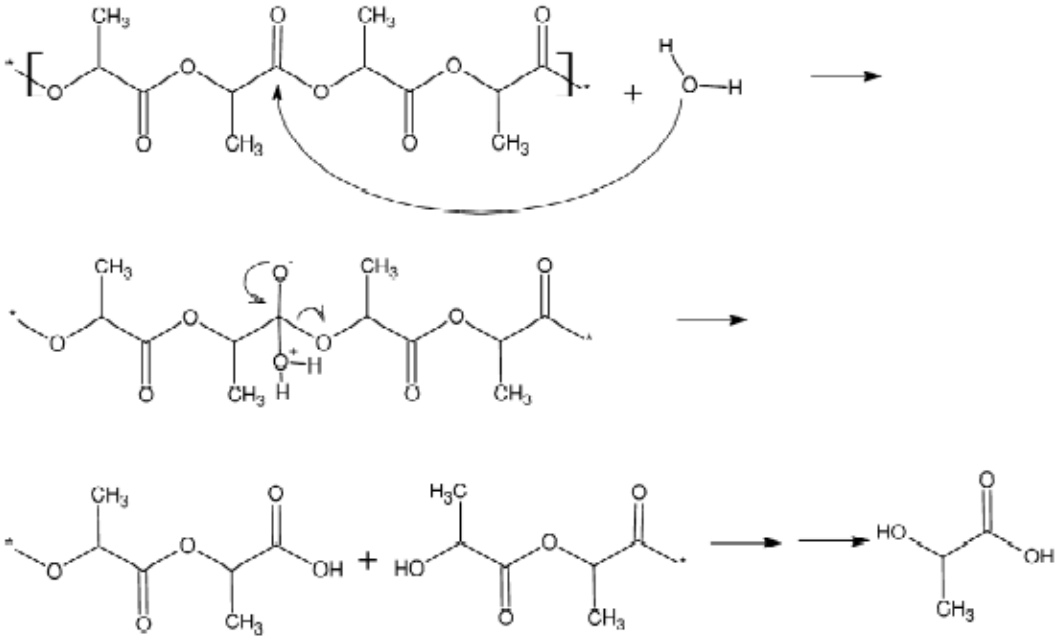


Figure 8. *Random chain scission of polylactide backbone. (Edlund & Albertsson 2003)*

During degradation monomers and oligomers, low molecular weight by-products, are produced and dissolved to surrounding environment. The degradation via chain scission occurs until the molecular weight of the oligomers is less than 5000 Da. After that the oligomers are able to dissolve to the surrounding environment and the material begins to loss mass. (Zhang et al. 2014)

The degradation might occur faster at the middle of the polymer matrix than at the surface. This is due to acidic degradation products, carboxylic and alcohol end groups, which have an autocatalytic effect and thus increase the degradation rate by breaking remaining ester bonds. From the surface, the degradation products are able to dissolve to the surrounding environment whereas in the interior part of the polymer the acidic degradation products are trapped and hence increase the degradation rate. (Hennink et al. 2004; Han & Pan 2011; Li et al. 1990a)

Enzymatic degradation occurs mainly in natural polymers but it has also an important role catalyzing the hydrolysis of synthetic polymers. Enzymes decrease the activation energy and consequently accelerate the hydrolytic degradation rate by attaching to polymer fragments. The enzymes affect only at the surface of the polymers because they cannot diffuse to the interior part. In order the synthetic polymers to degrade enzymatically or enzymes to catalyze the degradation, the active site of the enzymes must be able to attach to the polymer substrate. Aliphatic polyesters can be catalyzed by enzymes due to flexible chains whereas rigid aromatic polyesters, such as poly(ethylene terephtalate), do not degrade enzymatically. Aromatic polyesters are normally considered to be bioinert because of their unfavorable polymer structure for enzymes to attach. (Göpferich 1996; Chandra & Rustgi 1998; Anderson & Shive 1997)

The hydrolytic degradation of biodegradable polymers can occur via bulk or surface erosion but the other degradation mechanism contributes the other one. Figure 9 shows the schematic presentation of the bulk and the surface erosion. In the bulk erosion the polymer degrades throughout the entire polymer, whereas the degradation of the surface eroding materials occurs only via surface. The main reason for that is diffusion of water to the polymer matrix. The water absorption of the bulk eroding polymers is faster than the degradation of the polymer bonds and thus the degradation is not limited to the polymer surface. On the other hand, the water absorption of the surface eroding polymers is lower than the hydrolytic degradation therefore blocking the diffusion of the polymer matrix. (Tamada & Langer 1993; von Burkersroda et al. 2002; Timmins & Liebmann-Vinson 2003; Lao et al. 2011)

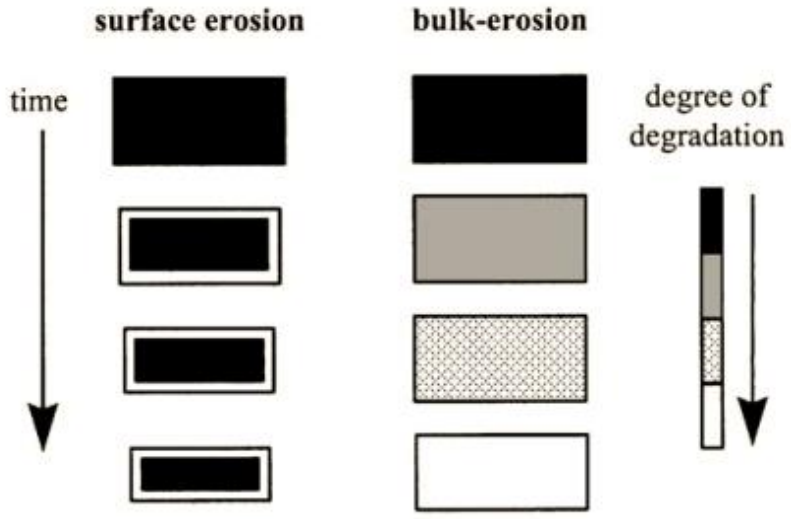


Figure 9. *Schematic presentation of surface and bulk erosion. Modified from (von Burkesroda et al. 2002)*

3.1.1 Bulk erosion

In the semi-crystalline polymers, the bulk erosion has two phases. First, water penetrates to bulk of the polymer attacking to the chemical bonds of the amorphous phase. This leads to a decrease in the molar mass without a loss in physical properties because the crystalline matrix holds the structure together. After the decrease in the molar mass, the physical properties of the polymer also decrease because the water starts to break the polymer chains into smaller pieces and the polymer fragments start to move among each other. In the second phase, the mass of the polymer decreases rapidly until the polymer chains are degraded into oligomers and monomers which are small enough to diffuse to the surrounding environment. (Timmins & Liebmann-Vinson 2003; Middleton & Tipton 2000)

For the bulk eroding polymers, the size and shape of the polymer will stay relatively uniform or even grow during the degradation due to the swelling of the material (Timmins & Liebmann-Vinson 2003; Göpferich 1996). Normally during the bulk erosion, cleaved monomers, oligomers and by-products diffuse to the surrounding environment and consequently the bulk erosion proceeds gradually and achieve equilibrium. If this equilibrium is interfered, by-products such as carboxyl end groups are unable to diffuse from the interior part of the polymer to the surrounding environment. The concentration inside the polymer increases due to the accumulating acidic by-products which accelerates the internal degradation and leads to a higher molecular weight of the outer part in comparison to the interior part. PLA, PGA and PCL are bulk eroding materials. (Woodruff & Hutmacher 2010)

3.1.2 Surface erosion

In the surface erosion, the rate of the hydrolysis is faster than the water absorption into the polymer. The size and the mass of the polymer start to decrease as a function of the time due to the hydrolytic degradation at the surface. The mass loss of the polymer continues over time. The degradation products are easily dissolved from the surface of the material to the surrounding environment without accumulating to the bulk material. The properties of the polymer below its surface stay relatively constant throughout the degradation. However, the mechanical properties weaken when the dimensions of the polymer decrease. Even then the mechanical properties of the surface eroding polymers remain better significantly longer in comparison to the mechanical properties of the bulk eroding polymers. (van Nostrum et al. 2004; Wuisman & Smit 2006; Ekholm et al. 2006)

Polyanhydrides and polyorthoesters degrade by surface erosion. They are hydrophobic even though the chemical bonds are highly susceptible to hydrolysis. For the surface eroding polymers, the rate of the hydrolysis is constant during the whole degradation. In the case of bulk eroding polymers it is more complex situation due to the changing ve-

locity of erosion. The surface eroding materials would be ideal to use as an encapsulating materials due to their predictability and because they have a lower water absorption rate in comparison to the bulk eroding materials. (Timmins & Liebmann-Vinson 2003; Middleton & Tipton 2000)

3.1.3 Factors affecting hydrolytic degradation

The main factors affecting the rate of hydrolytic degradation are water absorption to the polymer matrix and structure of the polymer backbone. In addition, crystallinity, molecular weight, copolymer composition, and processing method of the polymer have an effect on the degradation rate. (von Burkersroda et al. 2002; Göpferich 1996) Factors affecting the water absorption of biodegradable polymers and factors affecting polymer processing are discussed in more detail in section 3.1.4 and in section 4.4, respectively.

Chemical composition within the polymer backbone mainly determines the rate of hydrolysis. The chemical bonds in the polymer backbone resist the hydrolysis in different ways. Anhydride and ortho-ester bonds are the most reactive ones, followed by esters and amides. The ester bonds are more sensitive to hydrolysis than the amide bonds. (Göpferich 1996; Amsden 2010) Chirality of polymer has an effect on the biodegradation. According to Chandra & Rustgi (1998) pure L-isomers synthetized from phenylalanine degrades a lot faster than D, L-phenylalanine isomers.

Morphology generally means the study of form and structure. Polymer morphology describes how polymer chains are arranged in macromolecular solids and describes microscopic order of polymer molecules meaning the degree of crystallinity. Amorphous polymers and the amorphous regions of semicrystalline polymers are more susceptible to degradation than crystalline regions due to their lower chain density, ability to absorb more water into the matrix and higher degree of free motion. (Timmins & Liebmann-Vinson 2003) Crystalline regions of polymers degrade slower because their structure is well-organized. There is also less free volume and tougher secondary bonds between polymers chains in the crystalline regions compared to the amorphous parts of the polymers. For examples the degradation of semicrystalline PLLA takes years while amorphous PDLLA degrades in 12-16 months. (Wuisman & Smit 2006; Middleton & Tipton 2000; Södergård & Stolt 2002) Higher crystallinity makes it harder for enzymes to access hydrolysable groups thus decreasing the degradation rate. Also size, shape and number of crystallites affect the chain movements thus influencing to the degradation rate. (Chandra & Rustgi 1998) The relative crystallinity of the polymers increases during degradation due to the fact that the amorphous regions degrade faster than the crystalline regions. Remaining regions gain more space leading to reorganization of the polymer chains. (Wuisman & Smit 2006; Södergård & Stolt 2002; Duek et al. 1999)

High molecular weight polymers usually express slow degradation rates due to long polymer chains containing more ester bonds that need to be cleaved. Thus longer poly-

mers chains need more time to degrade into water soluble monomers or oligomers than shorter ones. (Makadia & Siegel 2011; Wuisman & Smit 2006; Woodruff & Hutmacher 2010) For example, the degradation of a high molecular weight PCL (number average molar mass 50 000 g/mol) is significantly slow, taking 3 years to degrade completely (Rezwan et al. 2006).

By altering the copolymer composition the degradation rate of copolymers can be changed. In Table 1 are presented degradation times for different polylactide and polyglycolide based biodegradable polymers. The composition of PGA is an important factor because it affects the hydrophilicity and the degradation rate of polymers. The degradation rate of poly(lactide-co-glycolide) copolymers can be accelerated by increasing the polyglycolide content. An exception is 50:50 ratio of PLA/PGA which exhibits the fastest degradation rate. (Anderson 2001; Göpferich 1996; Makadia & Siegel 2011; Engineer et al. 2011)

Table 1. *Degradation times for different polylactide and polyglycolide based biodegradable polymers. Modified from (van Nostrum et al. 2004; Gunatillake & Adhikari 2003).*

Polymer	**Degradation time (months)**
Poly(L-lactide)	18-24
Poly(D,L-lactide)	12-16
Poly(glycolide)	6-12
Poly(D,L-lactide-co-glycolide) 50/50	1-2
Poly(D,L-lactide-co-glycolide) 75/25	4-5
Poly(D,L-lactide-co-glycolide) 85/15	5-6
Poly(D,L-lactide-co-caprolactone) 90/10	2

Also environmental factors (pH, temperature and mechanical loading), porosity and particle dimensions (geometry, size, shape and surface to volume ratio) have a great influence to the degradation. (Timmins & Liebmann-Vinson 2003; Anderson 2001) During degradation of aliphatic polyesters acidic by-products are formed. This decreases the pH and consequently increases the degradation rate. (Zhang et al. 2014) The pH of the surrounding environment may change the degradation mechanism. Usually PLLA degrades by bulk erosion but after being in high pH solution, PLLA degrades by surface erosion. (Hennink et al. 2004) Pan & Ding (2012) showed that pH of environment affects the degradation rate of PLGA. Very high or a low pH catalyzes the hydrolysis of ester linkages in the polymer backbone. The pH also affects the chain scission mechanism of polylactides. In acidic conditions chain end scission is dominant, whereas in

alkaline conditions more random scission occurs. (Södergård & Stolt 2002; Pan & Ding 2012)

Temperature affects a lot to the polymers morphology and to the microscopy order of polymer chains and consequently has an effect on the degradation rate. As the temperature increases the degradation rate also increases. This is due to the fact that at elevated temperatures, above T_g, polymer is flexible and in rubbery state and thus polymer chains are able to move more freely. This facilitates the degradation of polymer chains. Therefore T_g is an important parameter because it changes significantly the properties of polymers (from glassy to rubbery). (Wuisman & Smit 2006; Södergård & Stolt 2002; Lucas et al. 2008).

The mechanical loading of material has an effect on the rate of degradation. For example if material is exposed to stress, degradation rate is faster. Stress induces microstructural cracks into the material leading to a larger surface area and hence the degradation rate increases. (Maurus & Kaeding 2004)

The porosity and the surface area of the polymers have a vast effect on the degradation of polymers. Water access inside to the polymer is easier and faster with larger surface area and with the presence of pores in the polymer surface. (Maurus & Kaeding 2004). Although water access is easier into porous polymers, the degradation rate of porous polymers is generally lower than the degradation of a solid polymer. This is due to the fact that the degradation by-products are released more easily from the interior part of the porous polymers than from the core of the solid polymers. Autocatalysis happens via acidic by-products that accelerate the degradation rate of remaining polymer chains inside the solid polymers. (Rydz et al. 2015; Pan & Ding 2012) Physical size of the polymer matrix has an effect on the degradation rate. Thicker samples are more susceptible to autocatalysis due to the fact that the acidic degradation by-products dissolve slower from the matrix to the surrounding media. (Li et al. 1990a; Li et al. 1990b)

3.1.4 Factors affecting water absorption

Absorption of water into polymers is a complicated process because small water molecules form hydrogen bonds with each other and with polar groups in the polymer structure. (Auras et al. 2004) The degradability of polymers is in direct contact with water absorption to the polymer. To the water absorption affects factors such as chemical structure, stability, crystallinity and porosity of the polymer backbone and possible impurities or additives. Also temperature and pH of the environment influence on the water absorption of the polymers. (Middleton & Tipton 2000; Rezwan et al. 2006)

Hydrophilic materials absorb water more easily in comparison to the hydrophobic materials because the polar side groups in the polymer structure attract water molecules leading to better water absorption. In contrast hydrophobic materials reject water and are

usually non-polar. Water absorption to polymer also depends on chain flexibility of the polymer. Water diffusivity increases as the chain flexibility increases. (Amsden 2010)

As a rule, if crystallinity increases the water absorption decreases. Water cannot penetrate the crystalline parts of the semicrystalline polymers as easily than it can penetrate to the amorphous parts of the polymer. The crystalline parts are chemically more stable compared to the amorphous parts and thus diminish water penetration into the polymer matrix (Rezwan et al. 2006; An et al. 2000).

Water access inside polymers is easier with porous surfaces of the polymers. Consequently the porosity increases the water absorption. Effects of the impurities and additives depend on their structure and character. For example long glass-fibers can induce water penetration deep to the polymer matrix because of the capillary phenomenon. (Middleton & Tipton 2000)

3.2 Mechanisms to study polymer degradation

Degradation of polymers can be monitored with many parameters such as changes in mass, molecular weight and mechanical properties. Even though mass loss is simple to measure, it does not necessarily describe the actual polymer degradation. Mass loss might indicate the dissolution of low molecular weight oligomers and monomers to the surrounding environment. Molecular weight, on the other hand, refers to the chemical degradation of the polymers. However, molecular weight of the surface eroding polymers might alter only a little during degradation. When combining multiple parameters such as the molecular weight, the changes in mass loss, crystallinity and mechanical properties more information and more extensive description of the degradation can be achieved. (Timmins & Liebmann-Vinson 2003; Göpferich 1996)

The degradation behavior of biodegradable polymers is challenging to predict because several parameters affect the degradation kinetics of the polymers. (Ikada & Tsuji 2000; Jain 2000) Consequently different mathematical models have been developed by several researchers to predict the degradation behavior of polymers. Han & Pan (2011) created a model that predicted specific parameters such as molecular weight distribution and weight loss as a function of time during the degradation of polymers. Gleadall et al. (2014) used another mathematical model to gain information about the hydrolysis mechanisms. The mathematical model of Gleadall et al. (2014) showed that the mass loss of polymers occurs due to chain end scissions and the decrease of molecular weight was caused by random scissions in the polymer backbone.

Studying the degradation of biodegradable polymers *in vitro* typically requires a contact with the studied samples meaning that pieces from the test samples are taken away and further studied. However, currently the changes in polymers can be monitored with wireless measurements. The measurements are based on the ability of resonance circuits

to detect changes of the surrounding environment. During the degradation the structure of biodegradable polymers alters and for example water absorbs into the polymer matrix. By encapsulating the resonance circuits with biodegradable polymers, the changes in the polymers can be monitored during the degradation. The wireless measurements enable monitoring the materials in real-time. In Figure 10 is illustrated a measuring set-up that can be used to measure the resonance behavior of the encapsulated circuits. Reader device detects the changes in the encapsulated resonance circuits that are immersed in a buffer solution. (Salpavaara et al. 2012)

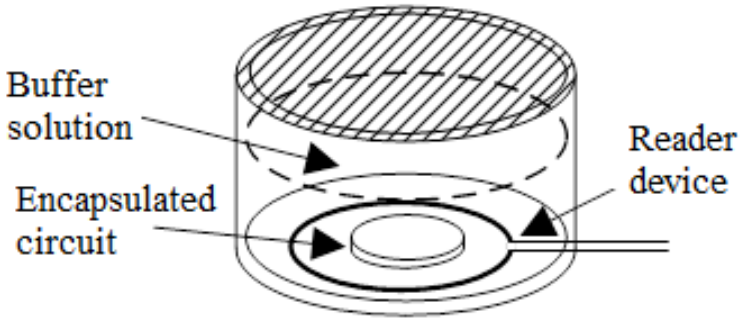


Figure 10. *Wireless measurement setup for monitoring material changes. Modified from (Salpavaara et al. 2012)*

4. ENCAPSULATION METHODS

Biodegradable polymers can be processed in the same way as any other thermoplastic polymers. Biodegradable polymers can for example be melted and formed into rods, fibers, capsules and molded parts. Injection molding, extrusion and compression molding are widely used for processing aliphatic polyesters. (Middleton & Tipton 2000) Encapsulation must provide sufficient temporary support and protect the core against moisture and external distractions. The selection of material and suitable processing method is a key factor for processing a proper products and capsules.

During processing, biodegradable thermoplastic polymers must be in a molten state and flow into final shape where solidification happens. Thermoplastic polymers are heated over their softening temperatures. Amorphous polymers are heated above their glass transition temperatures where polymers are rubbery and polymer chains are flexible compared to temperature below T_g where polymers are glassy, often brittle and polymer chains are less mobile. Semicrystalline polymers are heated above their melting temperatures. (David & Misra 2001; Timmins & Liebmann-Vinson 2003; Middleton & Tipton 2000; Lucas et al. 2008)

4.1 Injection molding

In injection molding process a fluid polymer melt is forced through nozzle into a mold cavity at elevated temperature. Injection molding can be used for both thermoplastics and thermosets. The injection molding equipment consists of a feed hopper, a barrel, a screw, a nozzle and a mold. The raw material, polymer granulates are fed through the feed hopper. The granules move to the heated barrel where one or two screws rotate and carry the molten polymer forward. The screws have three zones: feeding zone, compression zone and homogenous zone. In the feeding zone non-melt plastic granulates are heated and some melting can be detected. In the compression zone polymer granulates melt completely. The molten and mixed polymer is homogenized in the homogenous zone by continuous movement of the screw. Homogeneity of the polymer melt affects the filling process and the quality of the final product. Finally melted polymer is injected into the mold via the nozzle. The mold is cooled under high pressure until the material is solidified and takes the shape of the mold cavity. (David & Misra 2001; Vlachopoulos & Strutt 2003; Lim et al. 2010)

Injection molding can be used to manufacture complex products with different shapes using many different materials. Injection molding is a low cost process and spare materials from the process can be re-used. Disadvantages of injection molding are that manu-

facturing products is time-consuming and investing into machinery requires money. (Tadmor & Gogos 2006)

4.2 Extrusion

Extrusion is a widely used method for processing lactide-based polymers. Extrusion is a continuous process where a molten polymer is forced through a shaped die using pressure. Extrusion can be used to produce a plenty of different products with constant cross-section such as sheets, films, pipes and wire coating. The aim of the extruder is to prepare a homogenous molten polymer in a certain temperature, pressure and flow rate. The biggest difference between injection molding and extrusion is that the extrusion process takes place in a lower temperature and works continuously. (David & Misra 2001)

The main components of the extruder are a feed hopper, a barrel, a screw and a die. The first part of the extrusion process is similar to the injection molding. The raw polymer goes via hopper to the barrel where it is heated into a molten state by a combination of rotating screw and a high temperature. When the molten polymer has gone through the whole screw and becomes homogenous, the screw pushes the polymer mixture into the forming die. After the die, the extruded material, extrudate, is solidified by cooling. Cooling can be done using for example a water bath or cooled air. (Tadmor & Gogos 2006; Makadia & Siegel 2011)

Important parameter, in addition to properties of the screw, temperature and cooling which are handled in the injection molding chapter, is a design of the extrusion die. To design a proper die is difficult and needs significant experience. (David & Misra 2001) Advantages of extrusion are low initial setup cost, fast setup time and low production costs. Disadvantages are mediocre production speed and that extrusion is limited to parts with a constant cross section. (Tadmor & Gogos 2006) During extrusion polymers are exposed to the high temperatures and shear forces. This can affect polymer properties and results to loss of molecular weight.

4.3 Compression molding

Compression molding is a forming process where material is formed using heat and pressure. A proper amount of raw polymer material such as polymer granulates or pellet, is placed in a heated cavity and a hydraulic press compresses the mold together. When the mold is closed the pressure increases and force the material to fill up the whole mold cavity. The mold is heated for a predetermined time after which the mold is cooled and the formed part is removed from the mold. (Tadmor & Gogos 2006; Callister 2007, pp. 565-571)

In general, better mechanical properties can be achieved with compression molding than with injection molding. Also parts with large surface areas can be manufactured because the molding pressure is lower compared to injection molding. Parts with complicated cross-sections or exactly identical products are difficult to produce using compression molding. Both thermoplasts and thermosets can be produced by compression molding. However, for thermoplasts it is more time-consuming and more expensive compared to extrusion or injection molding. (Tadmor & Gogos 2006; Callister 2007, pp. 565-571)

4.4 Effects of the polymer processing

Processing method and conditions of biodegradable polymers have an effect on the chemical and physical properties and the degradation rate of the processed polymers. (Anderson 2001) Important factors during melt processing are for example processing temperature, moisture content in the polymer, thermal degradation and melting behavior of the polymer. (Södergård & Stolt 2002)

Usually processing of polymers occurs at high temperatures with application of pressure. Poly(α-hydroxy acids) are very susceptible to elevated temperatures because of the sensitive ester bonds in the polymers backbone. Consequently thermal degradation is the limiting factor in thermal processing of poly(α-hydroxy acids). Also the presence of moisture exposes the polymer to hydrolytic degradation. If the polymer is not dried properly before processing or it is contact with moisture, the final properties of the processed polymer might alter. For example the decrease of molecular weight is faster at the presence of moisture. (Middleton & Tipton 2000; Weir et al. 2004; Södergård & Stolt 2002; Gomes & Reis 2004)

Morphology and surface properties of the used polymer affect the properties of the final product. Degree of crystallinity can alter depending on processing method. Rapidly cooled polymers often have less crystallinity and thus are more prone to biodegradation compared to slowly cooled polymers which are more crystalline. Non-polymer parts in the product such as additives may also have an impact to the biodegradability. Plasticizers might promote the chain mobility and consequently improve the degradation rate. Mineral fillers increase the degradation because of acidic degradation products. (Timmins & Liebmann-Vinson 2003)

5. MATERIALS AND METHODS

In this study, resonance circuits were encapsulated with three different poly(lactide-co-glycolide) based polymers using compression molding machine. Resonance behavior was measured from the encapsulated circuits in order to see how the encapsulation method functioned and to monitor changes in the materials. For comparison, a degradation test series was carried out. The same three biodegradable polymers were used to manufacture test samples and to study the material properties. The following material properties were studied during the degradation test series: water absorption, mass loss, melting and glass transition temperatures, mechanical properties and inherent viscosity. Also visual characterization of the test samples was done.

5.1 Materials

5.1.1 Biodegradable polymers

Three different poly(lactide-co-glycolide) based biodegradable copolymers were used. 80L/20G poly(L-lactide-co-glycolide), 85DL/15G poly(D,L-lactide-co-glycolide) and 10L/90G poly(L-lactide-co-glycolide), abbreviated as PLGA 80/20, PDLGA 85/15 and PLGA 10/90 respectively. The material data is presented in Table 2.

Table 2. *Material data.*

Information	**PLGA 80/20**	**PDLGA 85/15**	**PLGA 10/90**
Batch number	DL 779HA	302000158	DL 659FL
Form	Granule	Granule	Granule
Inherent viscosity (dl/g)	5.8[A]	2.5-3.5[B]	- [C]
Manufacturer	Purac Biochem B.V.	Purac Biochem B.V.	Purac Biochem B.V.
Ratio	80/20	85/15	10/90

[A] Measured at Tampere University of Technology

[B] According to the manufacturer

[C] Could not be measured and the data sheet not available

5.1.2 Resonance circuit

Inductively coupled LC-circuits were used to measure changes in the polymers. The resonance circuits were fabricated by using a four-layer circuit board. The capacitance of the circuit consisted of a finger capacitor and a plate capacitor connected in parallel. The finger electrodes sensed the environment and the plate capacitor was presumed to be constant. The thickness of the circuit was 1.60 mm and the thickness of copper layer 35 µm. LC-circuits were manufactured by Prinel Piirilevy Oy. In Figure 11 can be seen the upper side and the bottom side of the resonance circuits used.

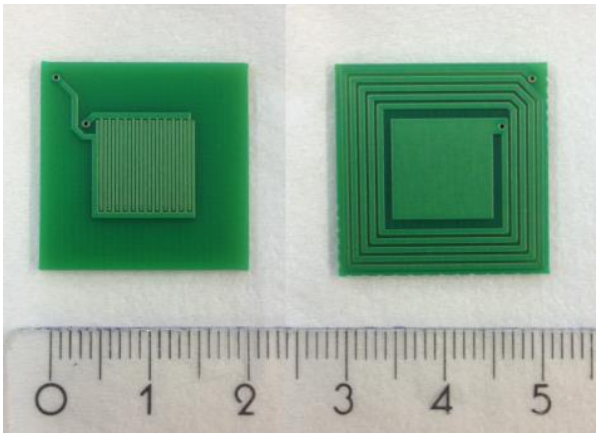


Figure 11. *Upper side (left) and bottom side (right) of the LC-circuit.*

5.1.3 Buffer solution

The test samples were immersed in a buffer solution during tests. The buffer solution simulated conditions similar to physiological environment, pH and salts of body fluids, and provided the fluid where samples were placed during the tests. A phosphate buffer solution, Sörensen buffer, was prepared according to the standard ISO 15814 Implants for surgery – Copolymers and blends based on polylactide – In vitro degradation testing (ISO 15814). The buffer solution was made from sodium hydrogen phosphate (Na_2HPO_4) and potassium dihydrogen phosphate (KH_2PO_4) substances. Specific information about the reagents can be found in Table 3. The manufacturer of both reagents was Mallinckrodt Baker B.V. The pH of the prepared buffer solution was between 7.46-7.49.

Table 3. *Reagents used for preparation of phosphate buffer solution.*

Reagent	**CAS number**	**Mw (g/mol)**	**Mass (g)**
Na_2HPO_4	7558-79-4	141.96	15.48
KH_2PO_4	7778-77-0	136.09	3.3

5.2 Methods

5.2.1 Manufacturing of capsules

Two different types of capsules were manufactured. The capsules were used as test samples for the resonance behavior measurements and for the degradation test series. Three different biodegradable polymers were used as raw materials for both capsules: PLGA 80/20, PDLGA 85/15 and PLGA 10/90. The capsules were manufactured using a compression molding machine NIKE Hydraulics (Type ZB110, NIKE Hydraulics Ab, Eskilstuna, Sweden). Prior to the compression molding, the PLGA 80/20 polymer granules were vacuum-dried in a vacuum chamber (WTB Binder 78532 Tuttlingen, Germany). Heating rate of the vacuum was 1 ºC/min and the polymer granules were kept at 80 ºC for 8 hours. The vacuum was cooled down to room temperature and the polymer granules were taken out under a nitrogen atmosphere. The PLGA 10/90 and the PDLGA 85/15 polymer granulates were dried in a vacuum at room temperature for one week. Compression moldings were performed in ambient conditions.

First, polymer sheets were manufactured using the compression molding machine by applying temperature and pressure. The polymer sheets were manufactured using a mold (see Figure 12). Opening screws were used to open the mold after compression. Size of the manufactured polymer sheets was 32 x 32 x 2 mm.

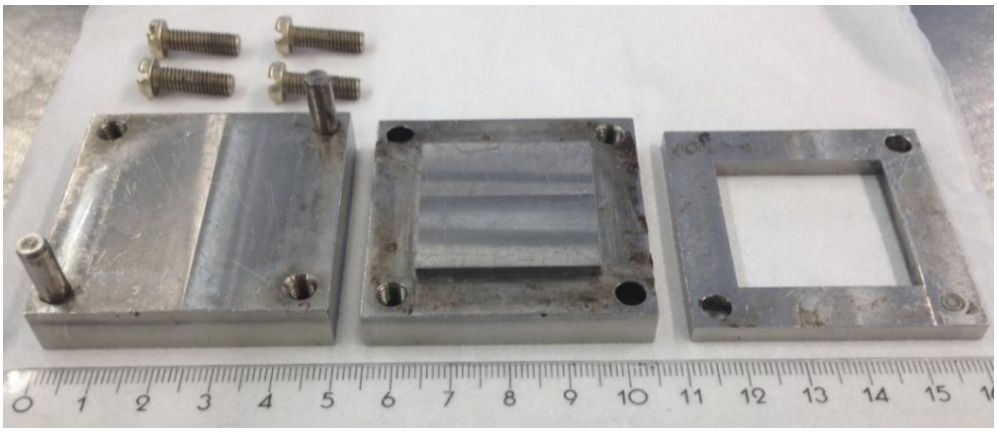


Figure 12. *Mold used for manufacturing sheets and capsules using compression molding.*

The parameters for manufacturing the polymer sheet are shown in Table 4. The correct amount of polymer granulates was weighed using an analytical scale (Mettler Toledo AB-265-S/FACT, Switzerland). The polymer granulates inside the mold were first melted (melting time) after which the mold was compressed together (pressing time) to prepare a sheet. During cooling the mold was kept between the plates of the compression molder under pressure.

Table 4. *Parameters for the polymer sheet manufacture.*

Raw material	Amount of raw material (mg)	Temperature (°C)	Melting/Pressing time (min)	Pressure (MPa)
PLGA 80/20	2390.0-2410.0	180	3/5	10
PDLGA 85/15	2440.0-2470.0	160	2/3	10
PLGA 10/90	2590.0-2610.0	215	3/5	10

After the manufacture of the sheets, two different types of capsules were manufactured using the mold. The capsules used for the resonance behavior measurements were prepared using two polymer sheets and a resonance circuit. The capsules used for the degradation test series were manufactured using two polymer sheets and six pieces of non-working circuit material (size of one piece 5x5 mm). The pieces of non-working circuit material were glued to the polymer sheet before compression to maintain their correct position using glue called Eri Keeper (Akzo Nobel Decorative Coatings Ab, Sweden). From one manufactured capsule (see Figure 13) three different samples for the degradation tests were gained by cutting the capsule into three pieces along the black dash lines.

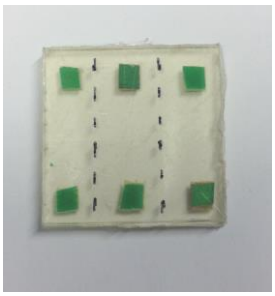


Figure 13. *Capsule for degradation test series. The capsule was cut into three pieces along the black dash lines.*

The manufacture of the biodegradable capsules using the compression molding was done in two phases. The parameters for both phases are presented in Table 5. Temperatures of upper and lower plates of the compression molding machine were set separately. In the first phase (phase I) the circuit/the pieces of non-working circuit material were compressed to the polymer sheet. Metal pieces between the mold parts were used to prevent the sinking of the circuit and the pieces to the bottom of the polymer sheet. In the second phase (phase II) another polymer sheet was compressed on the top of the circuit or the pieces and thus forming a capsule. In the second phase the proper amount of pressure needed to form the capsules was so small that the pressure gauge was not able to show the pressure value.

Table 5. *Parameters for the capsule manufacture.*

Material	Parameter	Phase I	Phase II
PLGA 80/20	Temperature of the upper/ lower plate (°C)	160/160	160/160
	Time of melting/pressing (min)	3/5	2/3
	Pressure (MPa)	10	Small
	Metal piece (mm)	0.7	-
PDLGA 85/15	Temperature of the upper/ lower plate (°C)	140/140	125/125
	Time of melting/pressing (min)	2/3	1/2
	Pressure (MPa)	10	Small
	Metal piece (mm)	0.7	-
PLGA 10/90	Temperature of the upper/ lower plate (°C)	190/190	195/190
	Time of melting/pressing (min)	2/3	1/2
	Pressure (MPa)	10	Small
	Metal piece (mm)	1.0	-

5.2.2 Measurement of resonance behavior and signal processing

The changes in the resonance behavior of the LC-circuits encapsulated with biodegradable polymers were studied. The capsules were prepared using the same compression molder previously described. The measurements were done by wirelessly using a portable reader device, a coil (diameter 35 mm). The capsulated circuit was put into a measuring cup and 100 ml of the Sörensen buffer solution was poured into the cup. Measurement setup can be seen in Figure 14. The buffer solution was changed and monitored every other week using a calibrated Mettler Toledo SevenMulti MP 225 pH-meter (Mettler-Toledo International Inc., Greifensee, Switzerland). The measurements cup was placed on the reader device always the same way to gain reliable and reproducible results. The samples were stored in a non-shaking incubator (37 ºC) during the measurements. The capsules were also visually observed during the measurements.

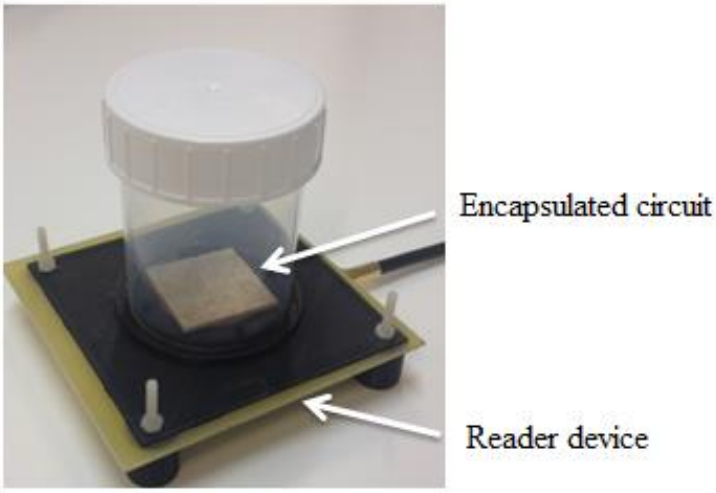


Figure 14. *Measurement setup including reader device, measuring cup and encapsulated circuit.*

Three different biodegradable capsules were measured: PLGA 80/20, PDLGA 85/15 and PLGA 10/90. The number of parallel samples for each material was five. The resonance behaviors of the circuits were measured as long as the circuits inside the capsules were still working. The circuits did not work in an aqueous environment and thus the circuits stopped working when they were in contact with the buffer solution.

The reader device measured the phase and the magnitude responses of the encapsulated circuit at different frequency values. The responses were gained over a range of 20 MHz. The signal processing was done by M.Sc. Timo Salpavaara. The features that changed during the water diffusion into the polymer capsules were extracted and studied from the measured phase and magnitude responses. Shift of frequencies and bandwidth values were further gained from the data.

5.2.3 *In vitro* degradation test

In vitro degradation test series was done in order to follow the degradation behavior of the three different biodegradable polymers: PLGA 80/20, PDLGA 85/15 and PLGA10/90. The samples were prepared using the compression molding machine previously described. Used test methods included weighing of wet and dry masses, pH measurements, mechanical and thermal testing, viscosity measurements and visual characterization of the test samples. Microscope images were taken using Olympus light microscope (Olympus BH-2, Olympus Optical Co., Ltd. Tokyo, Japan). With these test methods the reasons behind the changes in the resonance behavior were investigated by comparing the degradation test results to the characteristic resonance behavior of the encapsulated circuits.

During the degradation test the manufactured test samples were embedded in the Sörensen buffer solution. The amount of the buffer solution was calculated according to the

standard ISO-15814 (volume/weight ratio was greater than 30:1 ml/g). The pH of the buffer solution was measured with the calibrated pH-meter to maintain pH values near to 7.4. The buffer solutions of the PLGA 80/20 and the PDLGA 85/15 samples were changed every other week and the buffer solution of the PLGA 10/90 samples every week due to more rapidly decreasing pH values. The degradation test series lasted 8 weeks. Used time points for test series were 0, 2, 4, 6 and 8 weeks. During the degradation the test samples were kept at 37 °C in a static incubator. Four parallel test samples were used for each material.

5.2.4 Measurements of mass loss and water absorption

Weights of the degradation test samples were measured in wet and dry conditions with an accuracy of 0.01 mg using an analytical scale. The PLGA 10/90 samples were measured only in weeks 0, 2 and 4. After that the samples were too degraded to be weighted. Mean values and standard deviations were calculated using four parallel samples.

The wet weights were measured immediately after taking the samples out from the buffer solution. Before weighting both surfaces of the samples were rinsed with distilled water and gently wiped with tissue paper. The dry weights were measured when the samples had been entirely dried, for three days under a fume hood and for one week in a vacuum chamber. After vacuum drying the dry weights of the samples were weighed. Every test sample was measured the same way to gain reliable results. The water absorption and the mass loss were calculated according to the equations (1) and (2).

$$Water\ absorption\ (\%) = \frac{wet\ weight - dry\ weight}{dry\ weight} \times 100\% \quad (1)$$

$$Mass\ loss\ (\%) = \frac{dry\ weight - initial\ weight}{initial\ weight} \times 100\% \quad (2)$$

5.2.5 Measurement of mechanical properties

Three-point bending test was used as a mechanical testing method to measure mechanical properties of the PLGA 80/20, PDLGA 85/15 and PLGA 10/90 test samples. The three-point bending was done using an Instron 4411 Materials Testing Machine (Instron Ltd. High Wycombe, England). Flexural strength (σ_f), flexural strain (ε_f) and modulus (E) were measured. The test parameters used in the three-point bending test can be seen in Table 6. The three-point bending test was done according to the standard SFS-EN ISO 178 Plastics - Determination of flexural properties (SFS-EN ISO 178 2011).

Table 6. *Parameters of the three-point bending test.*

Load cell	5 kN
Crosshead speed	5 mm/min
Radius of the loading edge	1.5 mm
Length of bending span	22 mm

The three-point testing was performed at ambient conditions right after the samples were taken out from the buffer solution. Before testing the samples were rinsed with distilled water to remove residual salts and both sides of the test samples were gently dried with tissue paper. All the samples were tested in wet conditions except the zero week samples which were tested dry. The mean thickness and width of the test samples were measured with a slide gauge with an accuracy of 0.01 mm. The number of the parallel samples was 3-4 for each material and time point. Mean values and standard deviations were calculated. After the mechanical testing all the sample pieces were collected and dried, under a fume hood for three days and in a vacuum for one week, before further analysis.

5.2.6 Measurement of thermal properties

The measurement of the thermal properties was done using a differential scanning calorimetry (DSC) (Q1000, TA Instruments, New Castle, Delaware, USA). The DSC was used to solve the melting temperature, the glass transition temperature and the melting enthalpy (ΔH) of the PLGA 80/20, PDLGA 85/15 and PLGA 10/90 test samples. The first heating cycle was used to determine T_m and the melting enthalpies and the second heating cycle was used to determine T_g. During the second heating melting peaks were not visible anymore due to rapid cooling of the samples. Analyzing the DSC data was done using a TA Universal analysis 200 program.

The DSC samples were prepared using a standard aluminum pans and lids. The thermal analysis was performed with 4 to 7 mg vacuum dried samples. The samples were put between the pan and the lid and they were compressed together with an encapsulating press. The samples were heated twice from 0 °C to 220 °C using the heating rates 5 °C/min and 20 °C/min. Cooling rate was 50 °C/min. The samples were heated twice to ensure that all the samples had the same thermal history. The PDLGA 85/15 samples were prepared separately from the core and from the shell of the capsules. Two parallel samples were used for each material and time point.

5.2.7 Measurement of inherent viscosity

The inherent viscosity (i.v.) was measured using an automatic viscometer (LAUDA, Lauda-Königshofen, Germany) with Ubbelohde 4, 0c capillary viscometer tubes (Schott-Instruments, Mainz, Germany). For the i.v. measurements 20 ± 0.8 mg of material was weighed from the dried samples and dissolved overnight in 20 ml of chloroform. The measurements were carried out in ambient conditions. The viscosity measurements were run for the PLGA 80/20 and the PDLGA 85/15 materials. The i.v of the PDLGA 85/15 samples was measured separately from the core and from the shell of the capsules. Two parallel samples were used for PLGA 80/20 and PDLGA 85/15 materials and every time point. The PLGA 10/90 samples did not dissolve in chloroform due to their high glycolide content and consequently the i.v. of the PLGA 10/90 could not be measured.

6. RESULTS AND DISCUSSION

6.1 Effects of the encapsulation

Three different biodegradable polymers were used to manufacture sheets and capsules using a compression molding machine. In Figure 15 can be seen the compression molded capsules used in the degradation test series and capsules used in measuring the resonance behavior of the circuits. The manufacture of the PLGA 80/20 and the PDLGA 85/15 sheets and capsules was relatively easy. Almost all the sheets and the capsules had smooth surfaces except a couple of the PDLGA 85/15 sheets that had a few small air bubbles. The PLGA 80/20 and the PDLGA 85/15 samples appeared clear and transparent. The manufacture of the PLGA 10/90 sheets and capsules was more complex due to the narrow processing window of the PLGA 10/90. The processing temperature of copolymers containing a notable amount of glycolide is usually low. Most surfaces of the PLGA 10/90 sheets and capsules were slightly rough and uneven. The PLGA 10/90 samples were opaque and the color was darker compared to the PLGA 80/20 and the PDLGA 85/15 samples.

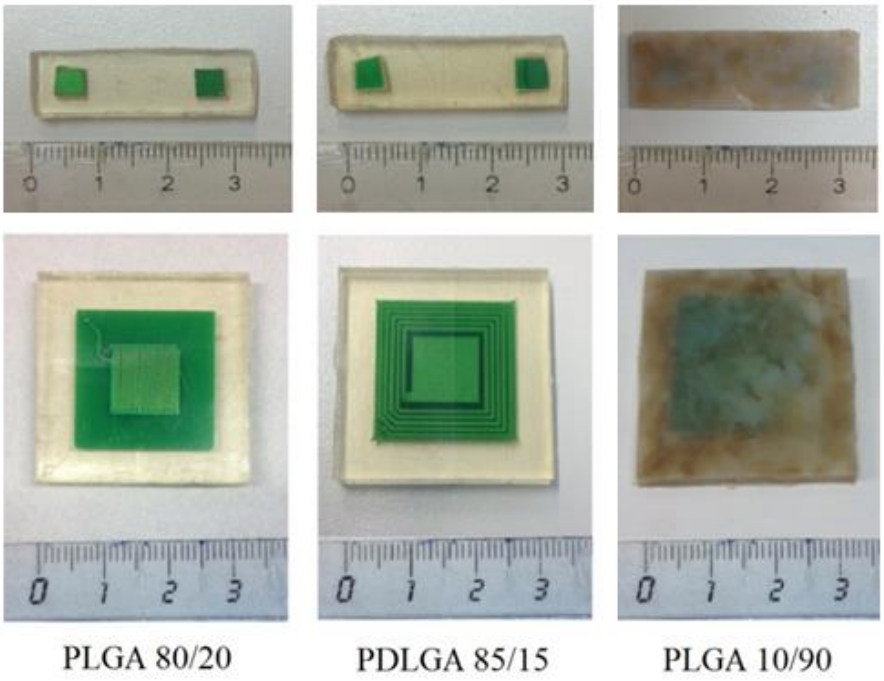


Figure 15. *Compression molded PLGA 80/20, PDLGA 85/15 and PLGA 10/90 capsules used in the degradation test series and for measuring the resonance behavior of the circuits.*

The manufacture of the capsules consisted of several steps and multiple parameters. Hence there might have been slight deviations between the different capsules. The capsules used in the degradation test series were cut into three pieces. Thus the height of the samples varied over a wider range compared to the other dimensions. Also the sides of the cut samples were not exactly uniform. Dimensions of the manufactured capsules are presented in Table 7.

Table 7. *Dimensions of the manufactured capsules.*

Capsule	Width (mm)	Height (mm)	Thickness (mm)
Degradation test sample	32.0 ± 0.2	10.5 ± 1.0	3.8 ± 0.4
Encapsulated circuit	32.0 ± 0.2	32.0 ± 0.2	4.0 ± 0.4

In phase I when manufacturing capsules, the circuit was placed on the polymer sheet and compressed into it. The circuit was placed by hand and might have moved slightly during the compression. Therefore the place of the circuit might have been a little different between the different capsules and consequently affecting the results. In phase II when attaching two polymer sheets, the pressure had to be strong enough to get tight and compact capsules. This was challenging to achieve when using the PLGA 10/90. Because of the narrow processing window, the material easily slid out of the mold if too much pressure was applied, too high temperature or too long time was used. In comparison, if the pressure was too low, the polymer sheets would not attach properly to each other.

Overall the encapsulation was possible with PLGA 80/20 and PDLGA 85/15 using compression molding. Using a compression molder, capsules with eligible properties can be achieved. However, for some materials, such as PLGA 10/90, the encapsulation was challenging and it was important to know the right manufacturing parameters in order to get a good, reliable and reproducible outcome.

6.2 Resonance behavior of the encapsulated circuits

The resonance behaviors of the circuits encapsulated with the three different biodegradable polymers was studied. Frequency changes and bandwidth values were obtained from the wirelessly measured data of each encapsulated circuit. The feasibility of the encapsulation and the degradation of the materials used were examined in the measurements. Frequency shifts of the encapsulated resonance circuits are shown in Figure 16. All the five parallel samples are marked with the same color.

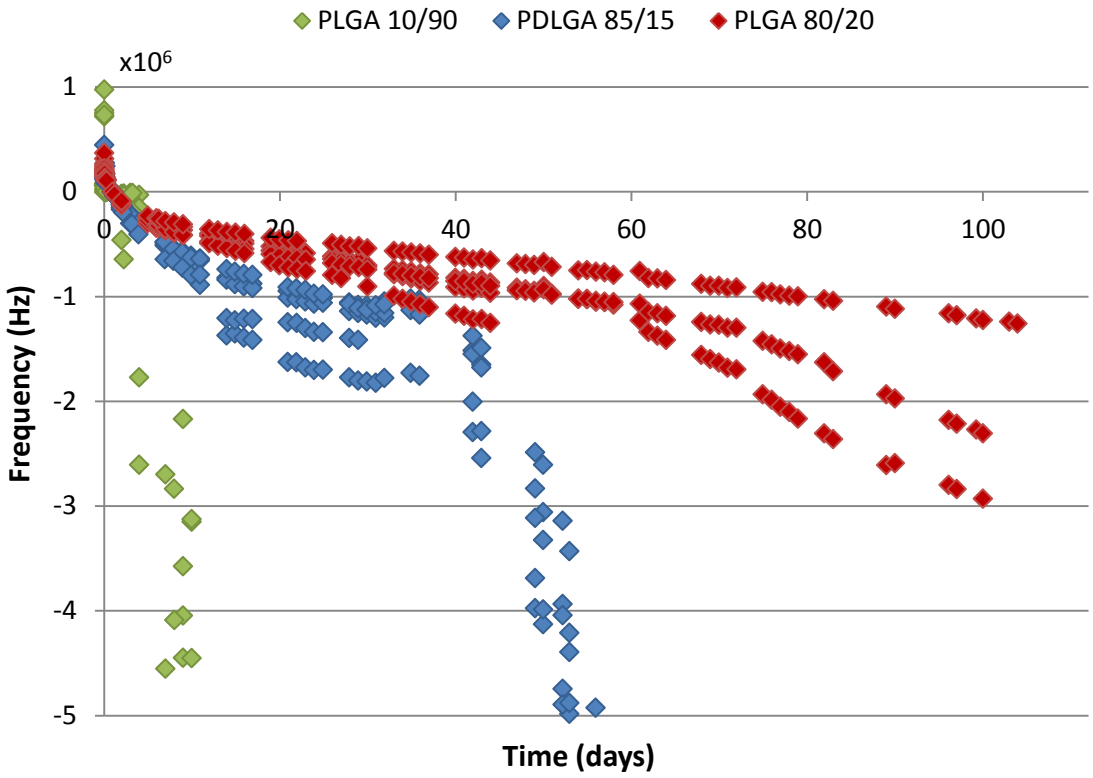


Figure 16. *Frequency shifts of the encapsulated resonance circuits.*

The resonance circuits encapsulated by PLGA 10/90 lasted only a few days. The frequency values started to drop dramatically already after a couple of days and the drop continued for 10 days until all the parallel samples had stopped working. This indicates that the buffer solution had been in contact with the resonance circuit already after a few days. Thus it can be said that the encapsulation of the resonance circuits using PLGA 10/90 failed.

All the PLGA 80/20 capsules resisted the buffer solution over 40 days. Three of the capsules were still working even after 100 days. There was a remarkable drop in the frequency change during the first days just after immersion. After day 5 the decrease of frequency stabilized and continued steadily for 60 days. After day 60 there was a larger deviation between the parallel samples and the frequency decreased faster compared to the beginning of the measurement. The circuits encapsulated with PLGA 80/20 stopped working at higher frequency values compared to the two other materials.

All five of the PDLGA 85/15 capsules resisted the buffer solution approximately 55 days. Also PDLGA 85/15 capsules had a clear shift in the frequency during the first days after the capsules were immersed in the buffer solution. Between days 10 and 40 the frequency values decreased somewhat linearly. The frequency values between the parallel samples had more variance and were a bit lower compared to the frequency values of the PLGA 80/20 capsules. After day 40 a clear change in the frequency values of PDLGA 85/15 capsules can be observed when the frequency values started to drop

dramatically. The decrease in the frequency continued until the circuits stopped working.

Salpavaara et al. (2012) studied the behavior of resonance circuits encapsulated by PLC and PLCL. They found out that the frequency decreased during the measurement and they observed a clear shift of frequency during the first days of the measurement. Consequently similar behavior of frequency was detected when compared to circuits encapsulated with poly(lactide-co-glycolide) based polymers.

In Figure 17 can be seen the bandwidth values for each encapsulated circuit. Bandwidth curves were very different for the PLGA 80/20, PDLGA 85/15 and PLGA 10/90 materials. The bandwidth of the PLGA 80/20 capsules increased throughout the measurements. After day 60, the bandwidth values increased faster than at the beginning of the measurements and deviations between the parallel samples were larger. When comparing the frequency changes and the bandwidth values similar behavior can be observed in the PLGA 80/20 capsules.

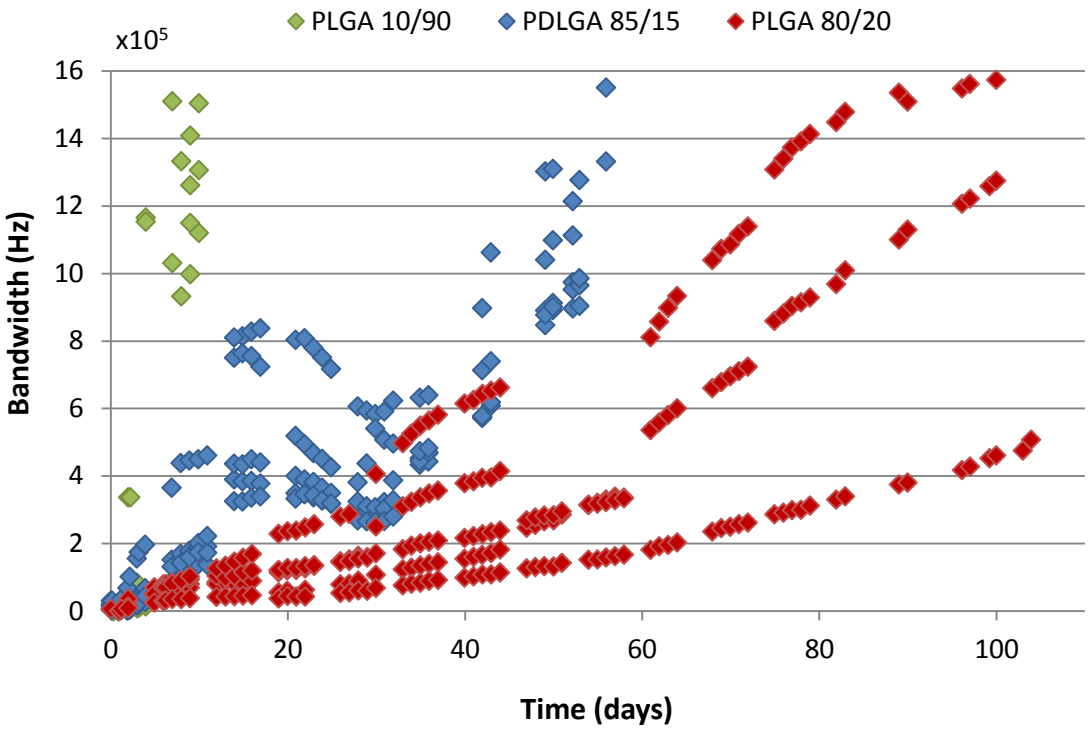


Figure 17. *Bandwidth values of the encapsulated resonance circuits.*

For the PDLGA 85/15 capsules the bandwidth values changed more dramatically compared to the PLGA 80/20 capsules. A clear pattern can be seen between the parallel PDLGA 85/15 samples. One explanation for this pattern could be the degradation of polymer chains. During days 0-15 the bandwidth increased. During that time the long polymer chains started to degrade due to hydrolysis and a plenty of different sized polymer chains were formed. After day 15, when the bandwidth decreased, short enough polymer chains were able to diffuse from the polymer matrix to the surrounding envi-

ronment. After day 30, there were only remaining the high molar mass polymer chains and the bandwidth started to increase again. At the same time cleavage of the remaining polymer chains continued as the hydrolysis proceeded. This could be one explanation but the actual reason for the changes in bandwidth is unknown. The bandwidth of the PLGA 10/90 samples started to increase after a couple of days. The increase in bandwidth was much faster compared to the bandwidth values of PLGA 80/20 and PDLGA 85/15. Also the behavior of frequency change and bandwidth of the PLGA 10/90 capsules was similar. In all three materials the bandwidth values were approximately at the same level when the circuits stopped working.

The encapsulated resonance circuits were on a stand which kept the samples stationary during the tests and enabled the buffer solution to surround the capsules from every side. Even though the encapsulated circuits were lying still on the stand at the bottom of the measuring cups during the measurements, there might have been a slight change in the position of the circuits in relation to the reader device. This could have an effect on the results and cause differences between the parallel samples. Also small air bubbles might have been under the circuits and thus affecting the results. After day 60 the deviation between the parallel samples of the PLGA 80/20 were larger compared to the deviations of the PDLGA 85/15 and the PLGA 10/90. Thus the reliability of the PLGA 80/20 frequency values was questioned.

From the results can be seen that the frequency values changed daily. The reason to this and the explanation of the phenomena of why this kind of change happened is studied in more detail in the section 6.3 by combining the results from the degradation test series with the resonance behavior. An assumption was that the resonance behavior changed because the water penetrated into the polymer. However, no certain facts can be said based on the resonance behavior measurements alone.

6.2.1 Visual characterization of the capsules

Visual characterization of the capsules was done using the writer’s own eyes and by taking pictures after measuring the resonance behavior of the circuits. The PLGA 80/20 capsules maintained their size and shape throughout the whole measurement period. The degradation could not be observed by using eyes only, however, on the surface of the capsules some changes were clearly seen. White crystallization was formed on the surfaces of the capsules as can be seen in Figure 18. Also some superficial fractures were observed on the surfaces of the capsules. On the right side of Figure 18 cracks can be distinguished. The cracks were larger and more easily detectable on the top of the capsules (upper side of the circuit). Heat treatment affects the material behavior and properties and thus cooling of the capsules during the compression molding may have caused the linear fractures.

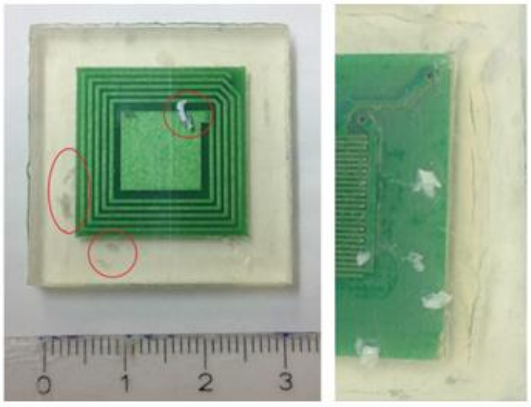


Figure 18. *PLGA 80/20 capsules after 100 days in buffer solution. Crystallization and cracks can be observed on the surfaces.*

The resonance behavior of the PLGA 80/20 changed continuously during time even though visibly no major degradation was observed. The buffer solution had probably diffused into the material and caused malfunction of the circuit even though the capsule itself had not been degraded. The degradation was homogeneous and the water penetration was faster than the hydrolysis rate, as it often is in bulk eroding materials like PLGA 80/20 (van Nostrum et al. 2004).

During the resonance measurements, the PDLGA 85/15 capsules remained quite unchanged except during the last two weeks. Shape of the PDLGA 85/15 capsules started to change after 40 days and the corners of the PDLGA 85/15 samples turned whitish. Also the circuit inside the capsules started to move during the last week. Autocatalysis reaction enabled movements of the circuits inside the capsules. The core of the capsules degraded faster than the shell of the capsules because acidic degradation products accelerated the degradation. Thus the core becomes more viscous liquid, gel-like allowing the circuit to move. The shell of the capsules became thinner, rigid and was easily breakable. When taking the capsules out of the buffer solution, they were swollen and sticky liquid from the core was draining out as seen in Figure 19.

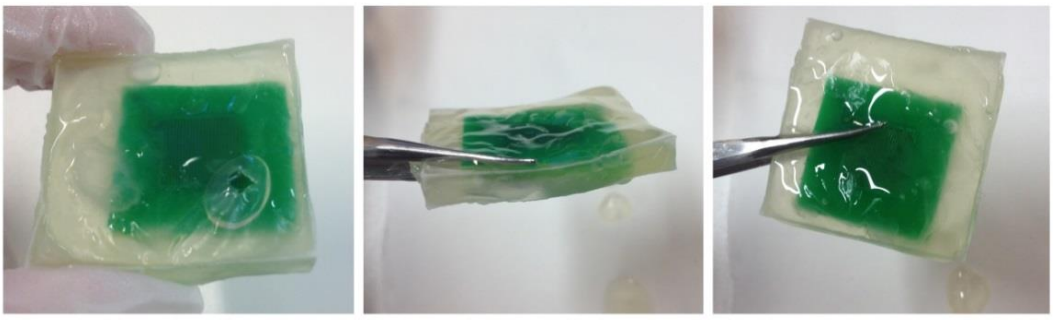


Figure 19. *PDLGA 85/15 capsules right after taking them out from buffer solution after 7 weeks.*

After the capsules had been in the air approximately 30-120 seconds, the capsules turned whiter and opaque although they were rinsed twice with distilled water as seen in Figure 20. From some of the capsules viscous liquid from the core had drained out and the corners of the capsules bent after being short time in air. Some capsules stayed swollen keeping the degradation products inside them. After the capsules had been dried for two weeks at room temperature the shell and the core were able to be distinguished even better as seen in Figure 21. Even though the capsules were dry, the core was still sticky and gel-like. The shell was still very fragile and thin. From the dried capsules can be seen how the circuit had moved from the middle nearer to the edges.

Figure 20. *Empty (left) and swollen (right) PDLGA 85/15 capsules after a short time in air (30-120s).*

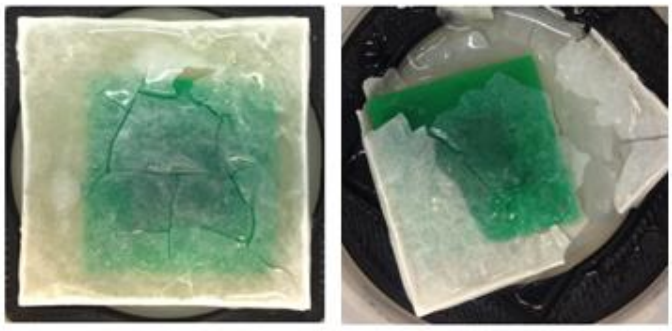


Figure 21. *PDLGA 85/15 capsules after drying at room temperature for 2 weeks.*

The frequency of the PDLGA 85/15 capsules changed remarkable during the measurements. Autocatalysis could explain the dramatic drop of frequency values. The decrease in frequency change values can be observed at the same time when the appearance of the capsules started to change and circuits moved inside them. The core of the capsules became viscous liquid which could have had an effect to the functionality of the circuit or might have affected the electrical conductivity of the resonance circuit and thus changed the resonance behavior. The resonance circuits were prone to environmental effects and consequently when the structure of the polymer core changed from solid to viscous liquid the circuit reacted to that which can be seen as changes in the resonance behavior.

The PLGA 10/90 capsules were in buffer solution for 2 weeks, some capsules even less than that. During that time visible cracks were formed on the both sides of the capsules. The cracks were deep, extending down to the circuit, not just at the surface of the capsules. The surfaces of the capsules were uneven and rough. The dried PLGA 10/90 capsules after measurements can be seen in Figure 22. After drying the capsules were very fragile. From the surfaces small material pieces were fragmented. The cracks in the PLGA 10/90 capsules could explain the behavior of the frequency change. Because of the cracks, buffer solution easily penetrated into the circuits and caused the decrease in the frequency values.

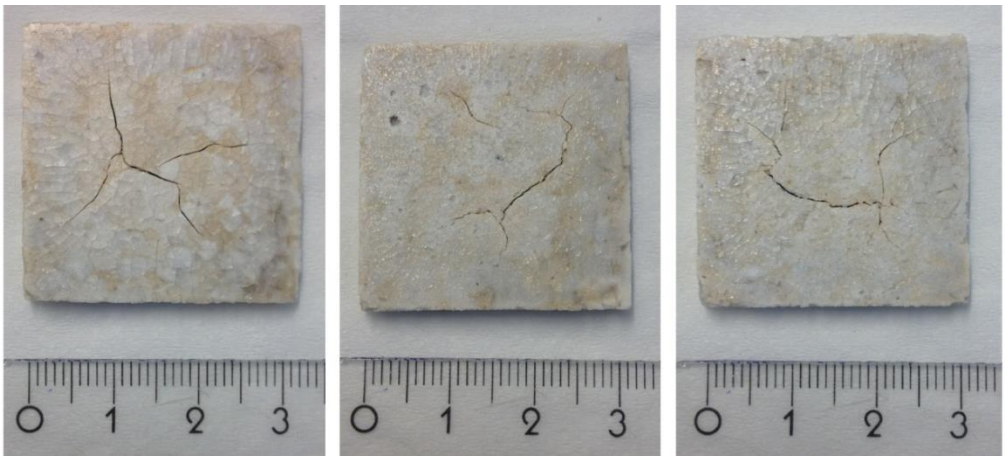


Figure 22. *PLGA 10/90 capsules after drying.*

When comparing the resonance behavior and the visual characterization of the capsules it can be suggested that the water absorption into the polymer matrix could have caused the changes in frequency. For example, the rapid drop in frequency change values of both PLGA 80/20 and PDLGA 85/15 capsules during the first days was probably due to water absorption into polymer capsules. However, the rest of the resonance behavior cannot be this unambiguously explained.

6.3 *In vitro* degradation of the materials

The degradation test series was done using three different materials (PLGA 80/20, PDLGA 85/15 and PLGA 10/90). The aim was to compare the degradation test results with the resonance behavior measured using the encapsulated circuits and to solve which properties affected the resonance behavior of the circuits. Properties of the PLGA 10/90 measured during the degradation test series were not analyzed and compared with the resonance behavior as closely as the properties of PLGA80/20 and PDLGA 85/15 because the encapsulation failed and lasted only for a few days.

During the degradation test the samples were immersed in a phosphate buffer solution. The measured pH values of the buffer solutions at different test weeks are presented in Table 8. After measuring the pH, the buffer solution of every test samples was changed.

The pH of the new buffer solution was 7.46-7.49. The measured pH of the PLGA 80/20 and the PDLGA 85/15 samples fluctuated between 7.48-7.56 and the pH of the PLGA 10/90 varied between 6.56-7.05. The low pH of the PLGA 10/90 samples corresponds to the fact that it degraded faster than the two other materials. During the degradation acidic degradation products were formed and released into the surrounding environment and consequently the pH of the PLGA 10/90 buffer solution decreased.

Table 8. *Mean pH values and standard deviations (SD) of three different buffer solutions, n=4.*

Test week	PLGA 80/20	SD	PDLGA 85/15	SD	PLGA 10/90	SD
2	7.54	0.01	7.54	0.01	6.97	0.06
3	-	-	-	-	6.56	0.15
4	7.56	0.01	7.55	0.01	6.99	0.12
5	-	-	-	-	7.05	0.25
6	7.48	0.01	7.49	0.01	6.77	0.19
7	-	-	-	-	6.76	0.10
8	7.50	0.01	7.51	0.01	6.78	0.12

6.3.1 Water absorption and mass loss

The wet and dry weights of the samples were measured in order to calculate mean mass loss and mean water absorption of the samples. The results of the water absorption measurements and the mass loss measurements are presented in Figure 23 and Figure 24, respectively. The results are presented in different tables for clarity. The PLGA 10/90 samples were measured only at weeks 0, 2 and 4 due to rapid fragmentation and degradation of the samples. The wet weights of the samples were constantly changing due to evaporating water. In order to get good results every sample was weighed the same way.

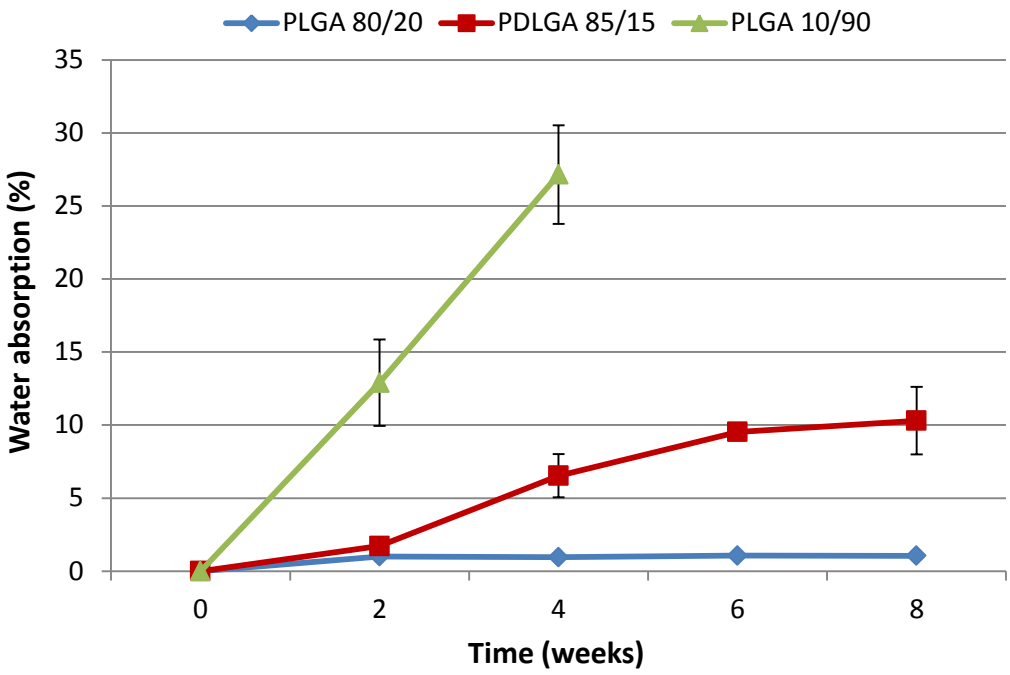


Figure 23. *Mean water absorption of the PLGA 80/20, PDLGA 85/15 and PLGA 10/90 degradation test samples, n=4. Error bars represent standard deviations.*

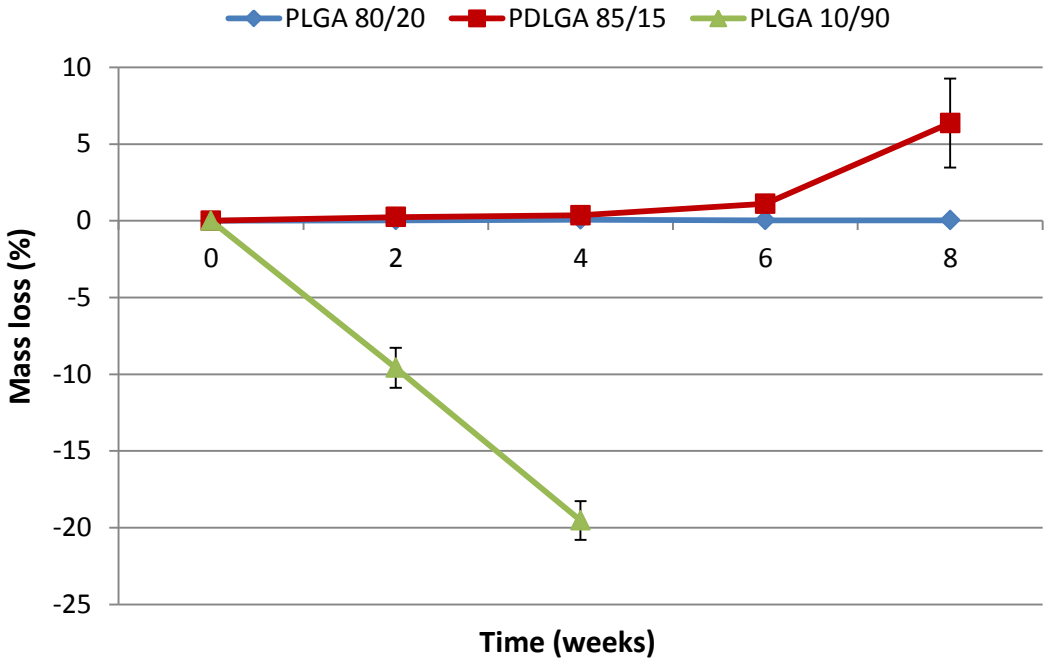


Figure 24. *Mean mass loss of the PLGA 80/20, PDLGA 85/15 and PLGA 10/90 degradation test samples, n=4. Error bars represent standard deviations.*

The water absorption of the PLGA 80/20 samples stayed fairly constant during the degradation test. The PLGA 80/20 samples absorbed water approximately one percent of their original weight throughout the whole degradation test. The mass losses of the

PLGA 80/20 samples were slightly positive (0.03-0.07 %) at every time point. In an ideal case mass loss should be negative during degradation because the cleavage of polymer chains enables dissolution of small oligomers and monomers into surrounding environment. Gained mass might have been due to interference with the analytical scale. Another explanation could be that the test samples were not dried properly and there might have been moisture between the circuit and the polymer matrix. It should be noticed that the size and appearance of the PLGA 80/20 samples hardly changed during the test. However, because PLGA degrades by bulk erosion, some degradation of the PLGA 80/20 samples might have occurred without a change in the size or the shape of the samples (Timmins & Liebmann-Vinson 2003).

The water absorption of the PDLGA 85/15 samples increased at every time point. At week 8 the samples were swollen and the water absorption could be seen clearly. Also the PDLGA 85/15 samples gained mass during the degradation test. Mass was gained slowly during the first 6 weeks of the test series. At week 8 a clear increase in the mass can be seen. Interior part of the PDLGA 85/15 samples degraded faster than the outer part of the samples because of autocatalysis and the samples became extremely swollen. Apparently the degradation products were not yet dissolved into the surrounding environment because the mass loss was positive at week 8.

The water absorption of the PLGA 10/90 samples was the highest and the fastest compared to the PLGA 80/20 and the PDLGA 85/15 samples. The mass loss of the PLGA 10/90 samples was negative, meaning that samples physically degraded during the test series. The PLGA 10/90 samples changed a lot more compared to the two other material. The wet and dry masses could not be weighed after week 4 due to massive fragmentation of the test samples to small pieces. At week 4 the dry and wet masses were hard to weight because of the fragmented pieces were at the bottom of the test tubes. Thus the results from the week 4 were not as reliable as the results from weeks 0 and 2. Also the standard deviations were clearly higher in the PLGA 10/90 samples in comparison to the PLGA 80/20 and the PDLGA 85/15 samples.

Overall, the changes in mass and water absorption were clearly seen in the PLGA 10/90 samples. The appearance of the PLGA 80/20 samples hardly changed during the 8 week period of time. The PDLGA 85/15 samples uptake water constantly during the degradation test but a clear change in mass loss was not observed until at week 8.

When comparing the resonance behavior of the PLGA 80/20 encapsulated circuits to the water absorption and the mass loss of the PLGA 80/20 degradation test samples, can be observed that the frequency change values and the bandwidth values changed somewhat linearly during the first 60 days of the measurement whereas the water absorption and the mass loss remained almost at the same level throughout the whole degradation test period (56 days). Thus no obvious connection can be made between them.

There can be seen some similarities between the gained mass of the PDLGA 85/15 and the resonance behavior of the encapsulated circuits. The frequency changes and the gained mass of the PDLGA 85/15 can be connected together as seen in Figure 25. During the first 6 weeks, the PDLGA 85/15 test samples gained mass slightly at every time point. At week 8 a higher increase in the mass can be detected. The frequency decreased slowly at the beginning of the experiment and a huge drop can be seen in the frequency values after day 40.

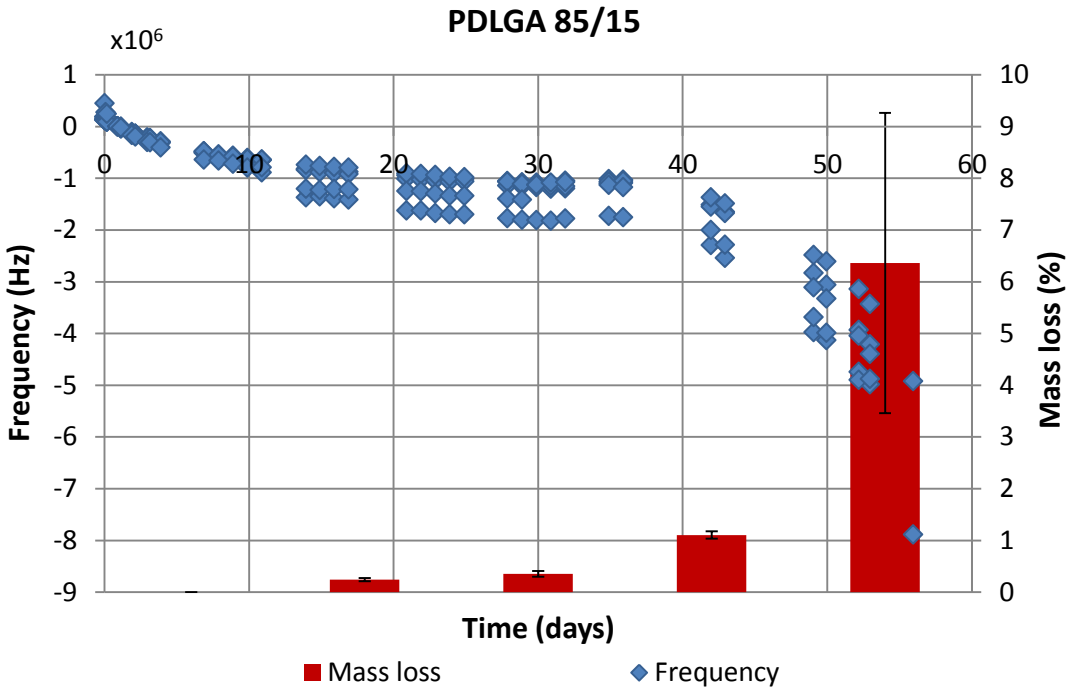


Figure 25. *Frequency change and mean mass loss of the PDLGA 85/15 capsules.*

However, when comparing the water absorption and the resonance behavior of the PDLGA 85/15 samples, no connection or similarities can be seen. The water absorption of the PDLGA 85/15 increased at every time point whereas the frequency did not change significantly until the day 40. The bandwidth of the PDLGA 85/15 fluctuated and consequently no connection could be made.

In conclusion, the water absorption and the mass loss of the PDLGA 85/15 do not explain why bandwidth changes so dramatically during measurements. If the bandwidth describes the material degradation and reflects the release of shorter chains into surrounding environment, there should be seen more changes in the water absorption and mass loss.

6.3.2 Mechanical properties

Mechanical properties of the PLGA 80/20, PDLGA 85/15 and PLGA 10/90 samples were studied using three-point bending test. The number of parallel samples was four,

except for the PLGA 10/90 the number of parallel samples was three at weeks 2 and 4. The PLGA 10/90 samples were very fragile and some of them broke already before bending when taking them out from the buffer solution. The PLGA 10/90 could not be measured at weeks 6 and 8 due to massive fragmentation and degradation of the samples. The PDLGA 85/15 samples could not be measured at week 8 due to the deformation and swelling of the samples. The PLGA 80/20 and the PDLGA 85/15 samples behaved in ductile manner whereas the PLGA 10/90 samples behaved in brittle manner.

The mean flexural strength values of the PLGA 80/20, PDLGA 85/15 and PLGA 10/90 are shown in Figure 26. Flexural strength describes the ability of a material to resist applied load. Consequently the flexural strength is the highest stress that a test sample bears during bending test. In practice, the flexural strength value is reached right before test sample breaks or cracks (Callister 2007, pp. 447-448).

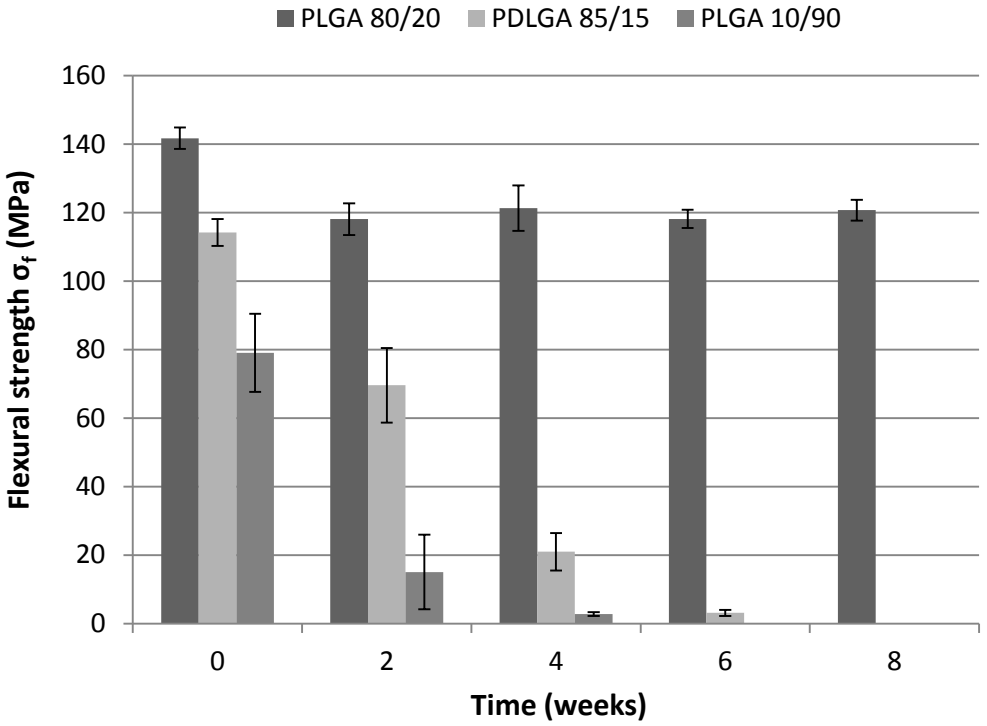


Figure 26. *Mean flexural strength of the PLGA 80/20, PDLGA 85/15 and PLGA 10/90 samples, n=3-4. Error bars represent standard deviations.*

The PLGA 80/20 samples showed the highest values of the flexural strength. The flexural strength of the PLGA 80/20 dropped after two weeks by 16.7 % (from 142 MPa to 118 MPa), after which the flexural strength maintained almost at the same level for the rest of the degradation test period.

The flexural strength of the PDLGA 85/15 and the PLGA 10/90 samples changed more dramatically during the degradation test compared to the PLGA 80/20. A remarkable drop of the flexural strength can be seen at every measured week in both the PDLGA 85/15 and the PLGA 10/90 samples. The flexural strength of the PLGA 10/90 decreased

faster compared to the flexural strength of the PDLGA 85/15. After two weeks the flexural strength of the PDLGA 85/15 had dropped by 39.0 % (from 114 MPa to 69.6 MPa) whereas the flexural strength of the PLGA 10/90 had decreased by 81.0 % (from 79.1 MPa to 15.0 MPa). After six weeks the flexural strength of the PDLGA 85/15 had dropped by 97.4 % (from 114 MPa to 3.1 MPa) from the initial value. At week 8 the PDLGA 85/15 samples could not be measured any more due to deformation of the samples. After four weeks the flexural strength of the PLGA 10/90 had dropped by 96.5 % (to 2.8 MPa) from the initial strength (79.1 MPa) after which the PLGA 10/90 samples were too degraded to be tested.

Flexural strain describes the deformation of the samples and represents how much the samples yield during the bending test. The mean flexural strain values of the PLGA 80/20, PDLGA 85/15 and PLGA 10/90 can be seen in Figure 27. The PLGA 80/20 samples had the highest flexural strain values. The flexural strain of the PLGA 80/20 maintained approximately at the same level (between 6.3 % - 6.8 %) throughout the whole degradation test series. At week 2 the highest flexural strain value of the PLGA 80/20 can be observed. However, this can be due to large standard deviations.

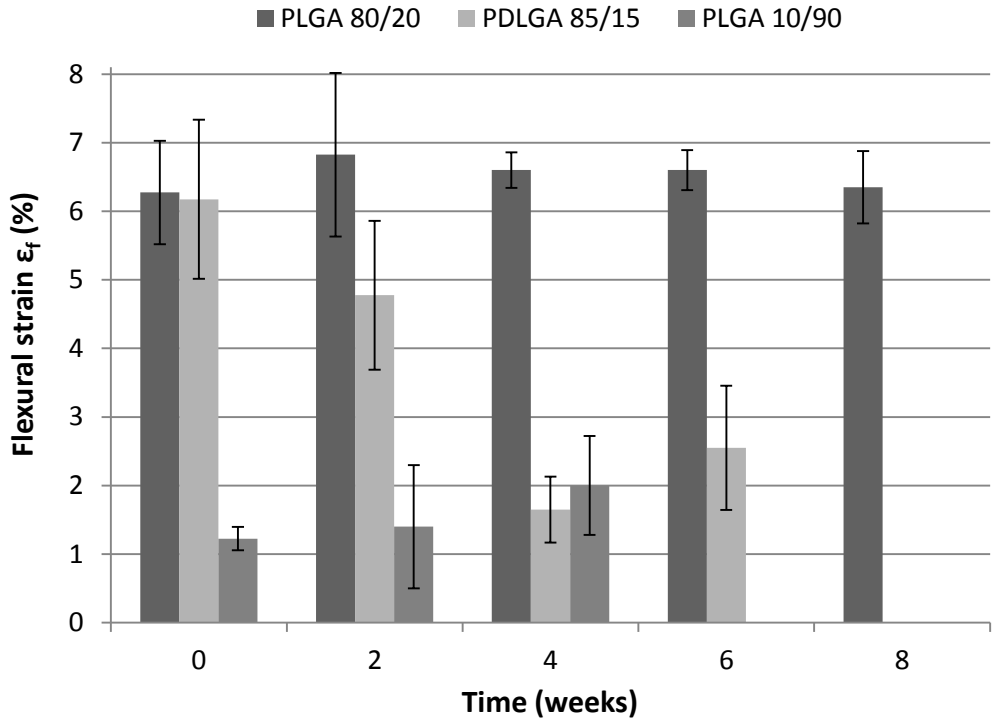


Figure 27. *Mean flexural strain of PLGA 80/20, PDLGA 85/15 and PLGA 10/90 samples, n=3-4. Error bars represent standard deviations.*

At the beginning of the degradation test series the flexural strain values of the PDLGA 85/15 were almost as high as the flexural strain of the PLGA 80/20 samples. However, the flexural strain of the PDLGA 85/15 decreased remarkable during the degradation. The flexural strain values dropped after 4 weeks by 72.6 % of the initial value (from 6.2

% to 1.7 %). At week 6 the strain had slightly increased in comparison to week 4, however, the standard deviations of the PDLGA 85/15 samples were quite high. The flexural strain values of the PLGA 10/90 samples were much lower compared to the two other materials. The flexural strain of the PLGA 10/90 increased slightly during every measured week (from 1.3 % to 2.0 %). However, it should be noted that standard deviations were moderately high also at the flexural strain values of the PLGA 10/90.

Modulus describes stiffness of the test samples and it is the relation between the flexural stress and flexural strain. The mean modulus values of the PLGA 80/20, PDLGA 85/15 and PLGA 10/90 can be seen in Figure 28. At the beginning of the degradation test series the PLGA 10/90 had the highest values of modulus. The high modulus was probably due to the crystallinity of the material. However, the modulus values of the PLGA 10/90 decreases substantially after two weeks and after four weeks the modulus had dropped by 95.3 % from the initial modulus (from 6.4 GPa to 0.3 GPa). The PLGA 80/20 and the PDLGA 85/15 had approximately the same modulus at week 0. The modulus of the PLGA 80/20 virtually maintained at the same level during the whole degradation series. The modulus of the PDLGA 85/15 decreased evenly during the test period. After six weeks the modulus of the PDLGA 85/15 samples had dropped by 94.6 % (from 3.7 GPa to 0.2 GPa) from the initial value.

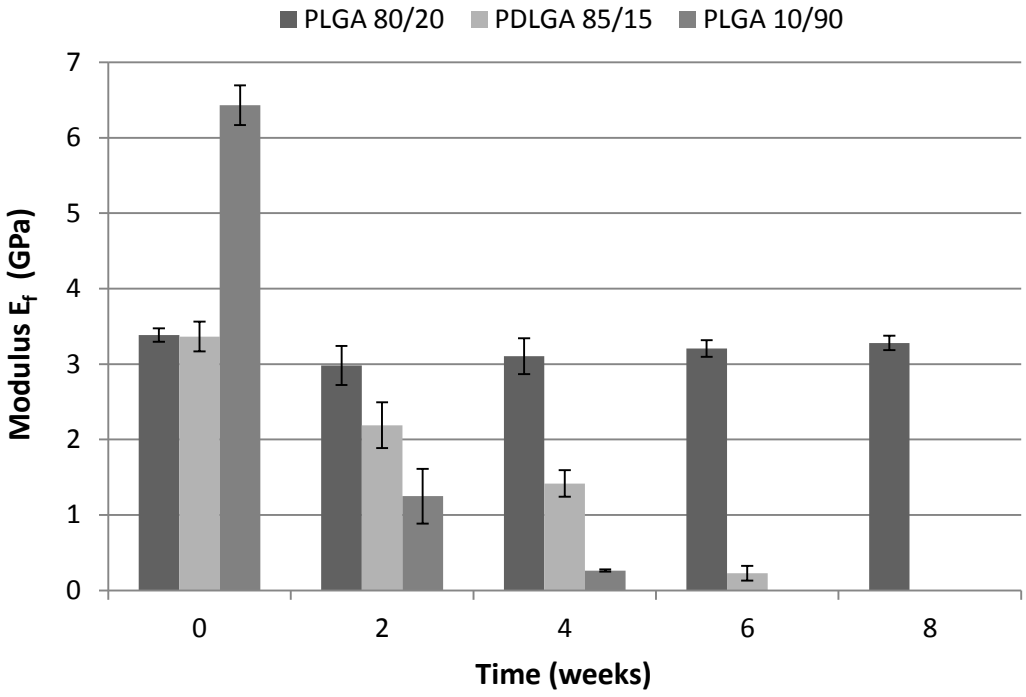


Figure 28. *Mean modulus of the PLGA 80/20, PDLGA 85/15 and PLGA 10/90 samples, n=3-4. Error bars represent standard deviations.*

Similar modulus values were reported by Gunatillake & Adhikari (2003). According to them PGA and PLLA have modulus values of 7.0 GPa and 2.7 GPa, respectively. They also said that PDLGA 85/15 has modulus of 2.0 GPa. However, Gunatillake & Adhikari

(2003) did not report the exact test methods which were used to study the modulus values. It should be noticed that bending test usually gives higher values of mechanical properties compared to tension test for example.

In conclusion, the mechanical properties of the PLGA 80/20 were very good throughout the whole degradation test series and no considerable changes were seen in the flexural strength, flexural strain or modulus of the PLGA 80/20 samples. Thus it can be said that the PLGA 80/20 retained its mechanical properties for 8 weeks. The mechanical properties of the PDLGA 85/15 were good at the beginning but decreased quite fast during time. The properties of the PLGA 10/90 except the modulus were fairly poor already at the beginning of the test series and decreased even more during the next four weeks. After four weeks the samples were fragmented and degraded so much that mechanical testing could not be performed any more.

When comparing the resonance behavior measured from the encapsulated circuits and the mechanical properties of the degradation test samples, a weak connection can be seen between the flexural strain and the bandwidth values of the PDLGA 85/15. The bandwidth and the flexural strain values of the PDLGA 85/15 are presented in Figure 29. From the figure can be seen that when the flexural strain increased also the bandwidth increased apart from the beginning. Consequently around day 20 when the bandwidth started to decrease also the flexural strain decreased. The connection is not unambiguous although some similarities can be observed. Also standard deviations are high and thus the connection is not very reliable.

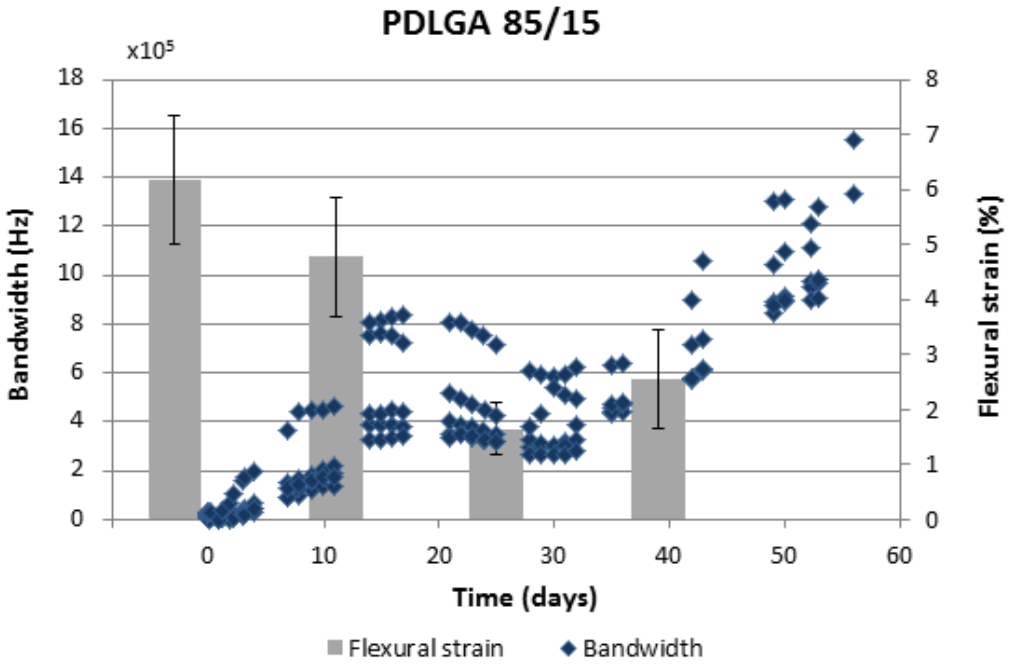


Figure 29. *Bandwidth and mean flexural strain of PDLGA 85/15.*

However, no other similarities can be observed between the mechanical properties and the resonance behavior in the used materials. The mechanical properties of the PLGA 80/20 remained quite unchanged during the degradation whereas the resonance behavior changed continuously during the measurements. The mechanical properties of the PDLGA 85/15 samples decreased at every time point during degradation. The frequency changes of the PDLGA 85/15 decreased slowly and steadily to the day 40 after which a dramatic drop in the frequency change can be seen. Thus the results of mechanical properties cannot be connected to the frequency changes.

6.3.3 Thermal properties

Melting temperature, glass transition temperature and melting enthalpy were analyzed using DSC. Two different heating rates were used. The heating rate was 20 °C/min at weeks 0, 2, 4 and 8. The week 6 samples were heated with the heating rate 5 °C/min because no glass transition temperatures or melting temperatures were seen with the faster heating rate. The PDLGA 85/15 samples were measured separately from the core and from the surface of the capsule but there were no notable differences between the results. However, it should be noted that the separation of the core and the surface was challenging and the prepared samples might have contained pieces of each other.

Glass transition temperature values of the PLGA 80/20, PDLGA 85/15 and PLGA 10/90 can be seen in Figure 30. The dots represent the two parallel sample values and the line is the mean of those. PLGA 80/20 had the highest T_g values. The T_g of the PLGA 80/20 samples slightly decreases during the degradation test series. The glass transition temperature of the PDLGA 85/15 decreased slowly during the first 4 weeks. After week 4 a clear decrease in the T_g can be seen. The glass transition temperature of the PLGA 10/90 samples was clearly lower than the T_g of the PLGA 80/20 and the T_g of the PDLGA 85/15 samples during the first 4 weeks. T_g of the PLGA 10/90 varied from 35.4 °C to 43.3 °C during the degradation test period. The fact that a lower heating rate was used at week 6 could have slightly affected that week's results.

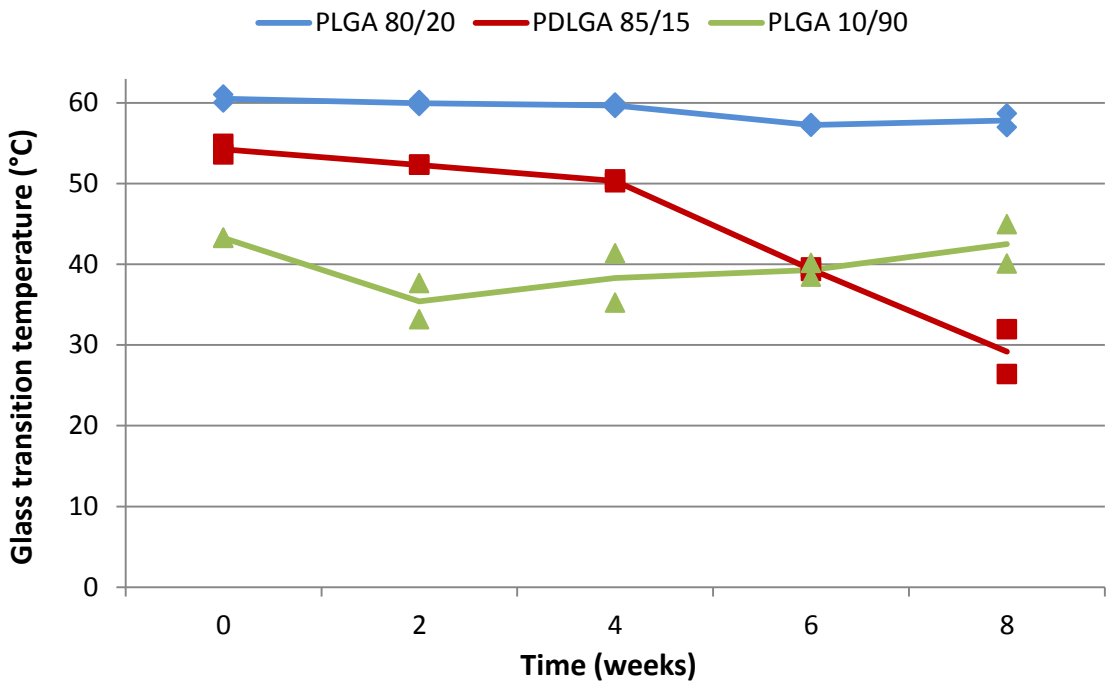


Figure 30. *Glass transition temperatures of the PLGA 80/20, PDLGA 85/15 and PLGA 10/90 degradation test samples, n=2. The dots represent parallel sample values and the lines are the mean of those values.*

The PLGA 80/20 and the PDLGA 85/15 samples were amorphous throughout the whole degradation test series and consequently did not have melting points and no melting enthalpies were observed. The PLGA 10/90 samples were semicrystalline. The melting temperatures of the PLGA 10/90 fluctuated between 204 - 207 °C throughout the whole test series. The melting enthalpies of the PLGA 10/90 increased every week (from 52 J/g to 114 J/g) apart from week 8. The melting enthalpies can be used to estimate the crystallinity of the samples. Crystallinity often increases during degradation because amorphous parts degrade first and the mobility of remaining polymer chains increase as they get shorter. The more mobile polymer chains are able to rearrange themselves and form new crystals. (Södergård & Stolt 2002; Wuisman & Smit 2006) The melting temperatures and the melting enthalpies of the PLGA 10/90 samples can be seen in Appendix 1.

When comparing the DSC results to the resonance behavior, there can be seen clear connections between the PLGA 80/20 and the PDLGA 85/15 samples. The frequency changes and the glass transition temperatures of the PLGA 80/20 and the PDLGA 85/15 samples are presented in the Figure 31. The frequency and the T_g of the PLGA 80/20 samples slightly decreased during the measurements. During the first 30 days the T_g of the PDLGA 85/15 decreased slowly and somewhat linearly. After that a clear difference was obtained when the T_g started to decrease much faster. The frequency values of the PDLGA 85/15 behaved in a similar way decreasing slowly until day 30 after which a faster decrease in frequency values was seen. The transition of polymers from brittle and glassy state to soft and rubbery state happens at glass transition temperature. The

polymer chains become more flexible and soft above T_g. The resonance circuits might have detected the changes in the polymer structure and consequently the measured frequency change and the glass transition values of the PLGA 80/20 and PDLGA 85/15 behaved in similar manner.

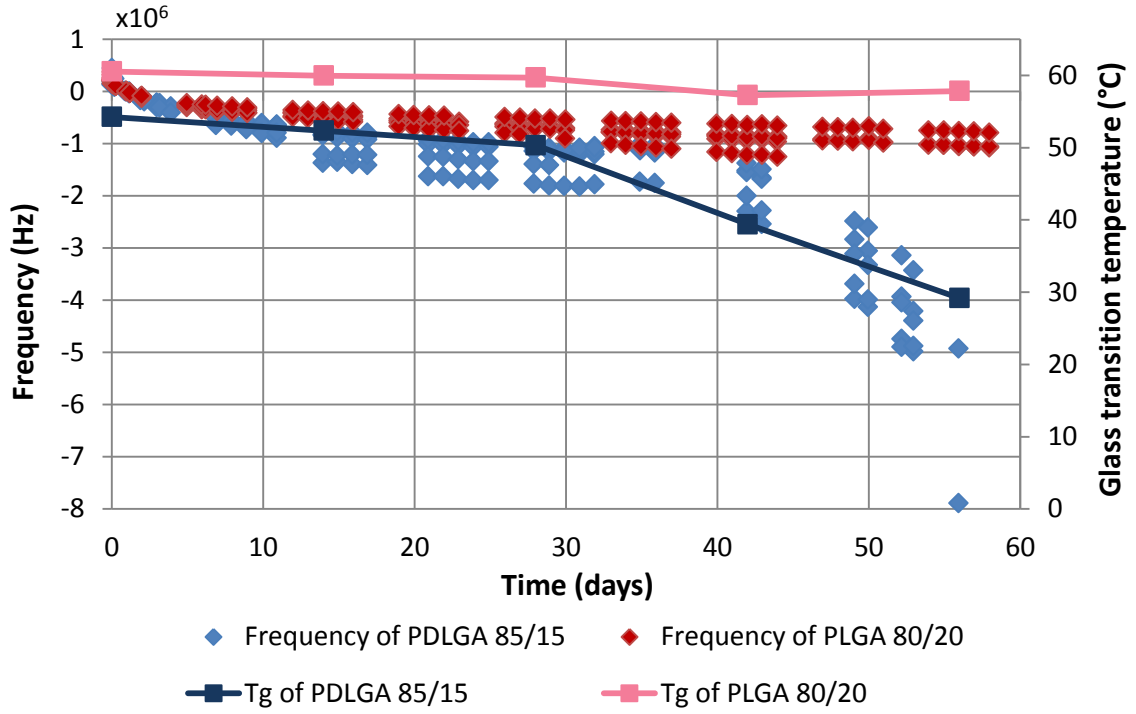


Figure 31. *Frequency change and mean glass transition temperatures of the PLGA 80/20 and the PDLGA 85/15 samples.*

6.3.4 Inherent viscosity

The i.v. values were measured for the PLGA 80/20 and for the PDLGA 85/15 materials. For the PDLGA 85/15 samples the i.v. values were measured separately from the shell and the core of the samples. The inherent viscosity values of the PLGA 80/20 and the PDLGA 85/15 are shown in Figure 32. The dots represent the two parallel sample values and the line is the mean of those. During the manufacturing of the test samples using compression molding the i.v. of the PLGA 80/20 dropped 19 % (from 5.8 dl/g to 4.7 dl/g). The i.v. of the PDLGA 85/15 dropped 40 % - 57 % (from 2.5-3.5 dl/g to 1.5 dl/g) during the manufacture process.

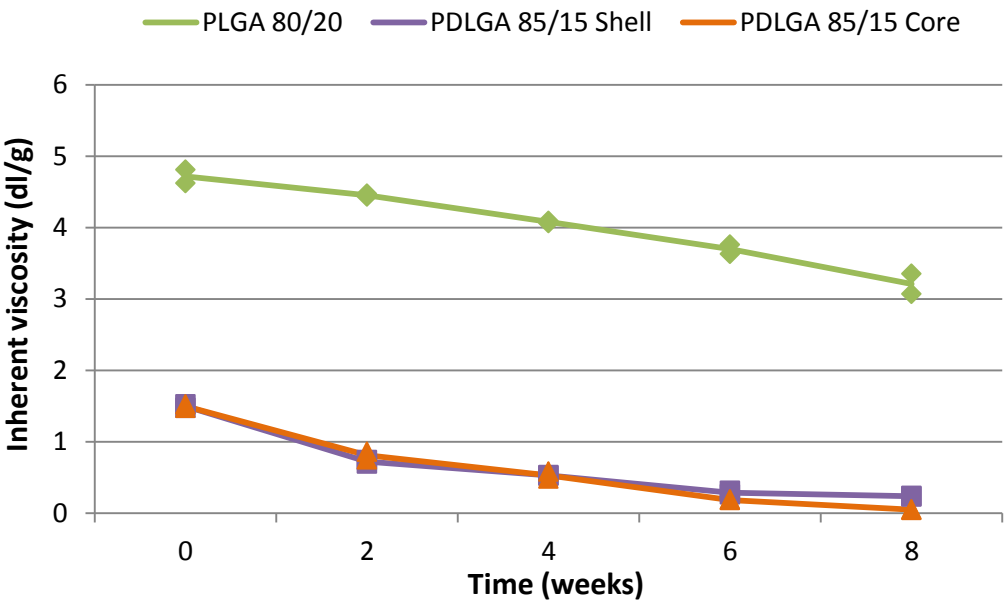


Figure 32. *Inherent viscosity values of the PLGA 80/20 and the PDLGA 85/15 samples, n=2. The dots represent parallel sample values and the lines are the means of those values.*

Inherent viscosity of the both PLGA 80/20 and PDLGA 85/15 decreased during the degradation. The PLGA 80/20 had higher i.v. values compared to the PDLGA 85/15. The i.v. of the PLGA 80/20 decreased from 4.7 dl/g to 3.2 dl/g. The i.v. values of the PDLGA 85/15 shell and core decreased from 1.5 dl/g to 0.2 dl/g and from 1.5 dl/g to 0.05 dl/g respectively. The i.v. values of the shell and core of the PDLGA 85/15 were almost the same. There was no remarkable difference between them even though the appearance of the shell and the core were totally different. At week 8 the core was viscous liquid, gel-like and the shell was white, thin and rigid. However, the preparation of the i.v. samples from the thin core and the shell was challenging. The core samples might have contained pieces of the shell and the other way around. Thus the reliability of the results was questioned.

Assumption was that the core should have a lower i.v. than the shell due to autocatalysis. In the core, polymer chains should have been shorter due to faster degradation and consequently the short chains should flow faster and have a lower i.v. However, at small viscosity values the reliability of the results can be questioned. In practice and within the limits of measuring accuracy, the results of the PDLGA 85/15 can be assumed to be the same. If the i.v. values of the shell and the core truly were the same, the autocatalysis does not explain the difference in the degradation behavior of the shell and the core of the PDLGA 85/15 samples. In this case, perhaps crystallinity might have caused the dissimilar degradation behavior between the core and the shell of the samples.

The i.v. values and the frequency change of the PLGA 80/20 samples are presented in Figure 33. An obvious connection between them can be seen even though the rapid drop

of the frequency at the beginning cannot be obtained from the i.v. results. Both parameters decreased somewhat linearly during the 60 days period of time.

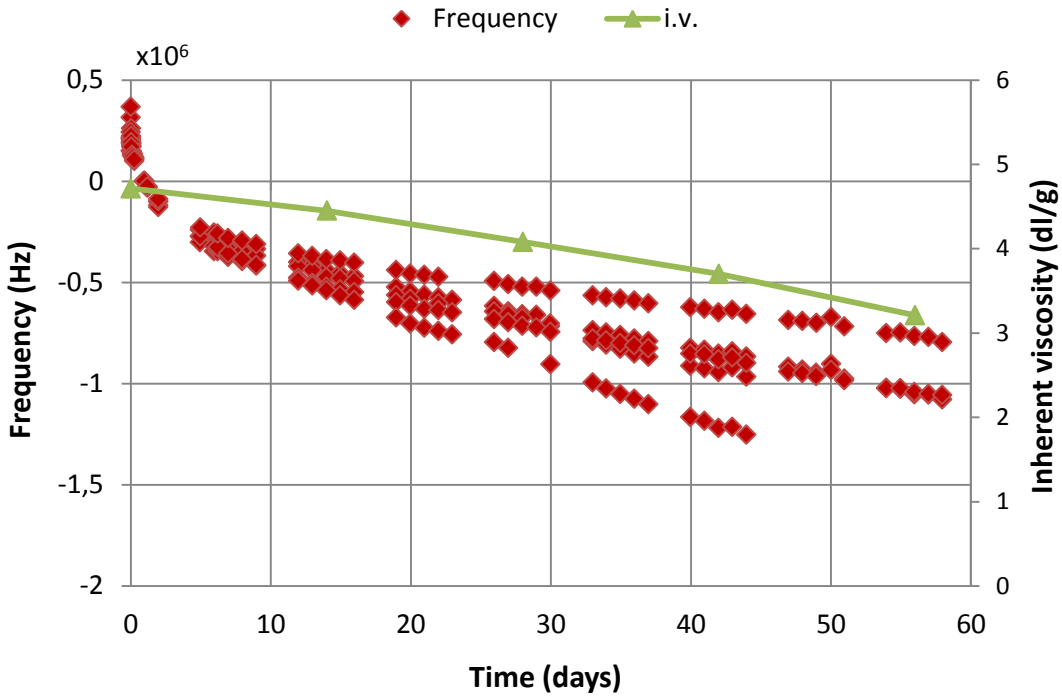


Figure 33. *Frequency change and mean i.v. values of the PLGA 80/20 samples.*

The i.v. values and the resonance behavior of the PLGA 85/15 cannot be connected to each other using results gained from this study. During the degradation test series the i.v. of the PDLGA 85/15 decreased slowly and continuously. The frequency change of the PDLGA 85/15 samples started the same way but the frequency dropped dramatically after day 40. Also no similarities were observed between the i.v. and the bandwidth values during the measurements. Thus the resonance behavior and the degradation test results of the PDLGA 85/15 cannot be connected to each other.

6.3.5 Visual observation

Visual characterization of the samples was done using the writer's own eyes and by taking pictures (photographs and microscope images) during the *in vitro* degradation test series. The visual appearance of the PLGA 80/20 samples hardly changed. The PLGA 80/20 samples maintained their size and shape throughout the whole test series. Also the properties of the PLGA 80/20 samples examined during the degradation test series maintained quite constant. However, some changes in the visual appearance were observed. The PLGA 80/20 degradation test samples from weeks 0 and 8 can be seen in Figure 34. During the degradation white crystallization was formed on the surfaces of the samples and the samples became slightly opaque but were still transparent. The same phenomena happened also to the capsules used for measuring the resonance behavior.

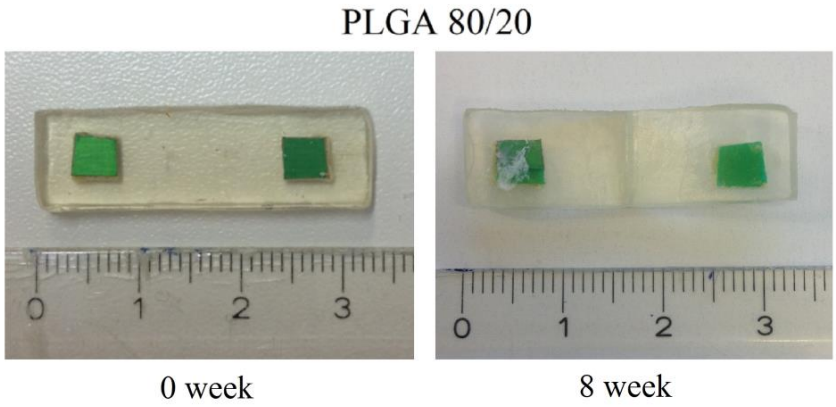


Figure 34. *PLGA 80/20 degradation test samples from week 0 (left) and week 8 (right). The picture of 8 week sample was taken after three-point bending test.*

In Figure 35 can be seen the PDLGA 85/15 degradation test samples at weeks 0, 4 and 8. The PDLGA 85/15 samples were initially transparent but already after two weeks the shell of the samples turned whitish and opaque. The samples remained quite unchanged, except for the color change, until week 6. The form of the PDLGA 85/15 samples changed remarkable during the last two weeks of the degradation test series due to auto-catalysis. The samples became swollen and viscous gel-like core ran to the bottom of the sample due to gravity and the thin shell in the upper part of the samples bent as seen in the Figure 35. In some samples the encapsulated pieces of non-working circuit materials dropped to the bottom of the samples. The core of the samples was still sticky and gel-like in the dried 8 week samples, hence similar to the PDLGA 85/15 capsules used to measure the resonance behavior. In this study was obtained that PLA containing rasemic D,L-lactide degraded faster than PLA containing L-lactide. It is commonly known that the ratio of L- and D- and D,L- isomers influences to the properties and degradation rate of PLA. For example PDLLA is an amorphous polymer and degrades faster compared to PLLA and PDLA which are semicrystalline polymers. (Nair & Laurencin 2007; Lim et al. 2008; Auras et al. 2004; Carrasco et al. 2010)

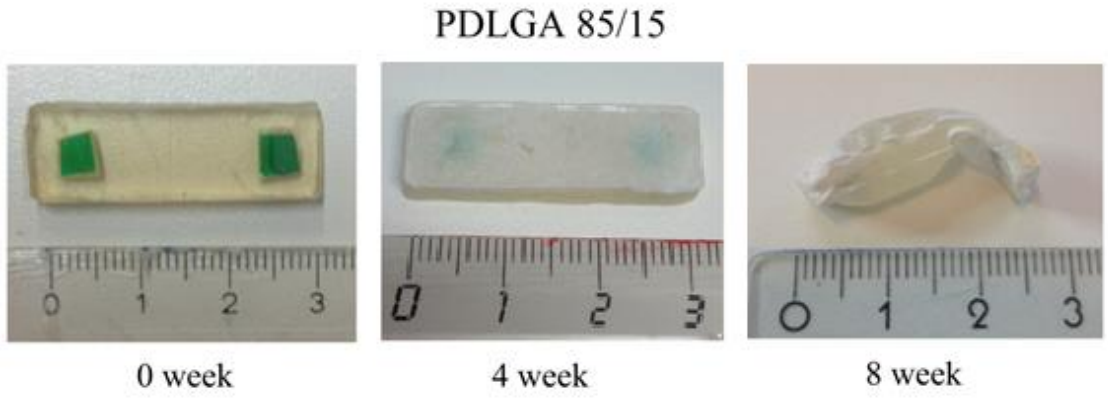


Figure 35. *PDLGA 85/15 degradation test samples from week 0 (left), week 4 (middle) and week 8 (right).*

In Figure 36 can be seen cross sections of the PDLGA 85/15 samples from week 2 and week 6. The test samples appeared to be heterogeneous already after two weeks. The surfaces of the samples turned whitish while the core remained transparent. The cross section of the week 6 samples shows that the samples were swollen, the white shell of the samples had become thicker and the core of the samples had turned yellowish.

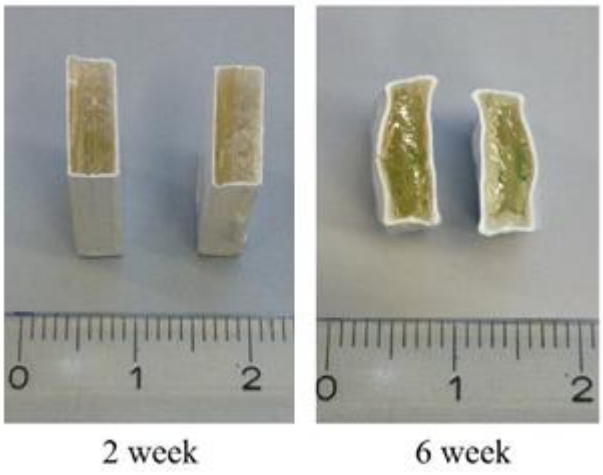


Figure 36. *Cross sections of the PDLGA 85/15 degradation test samples from week 2 (left) and week 6 (right).*

The autocatalysis reaction was visible in both PDLGA 85/15 capsules (the degradation test samples and the encapsulated circuits). Both capsules were manufactured using compression molder. During manufacturing the structure of the shell become slightly different in comparison to the structure of the core because the shell was cooled down faster inside the compression molder. The difference in the structure of the compression molded samples might have enabled the autocatalysis reaction and even promoted the appearance of it.

Li et al. (1990b) detected the same kind of autocatalysis reaction using poly(D,L-lactide-co-glycolide) (PDLGA 75/25). The test samples turned whitish after 10 days and the samples appeared to be heterogeneous after breaking having transparent inner part. After 20 days the inner part of the samples appeared as viscous liquid. The degradation was faster compared to the 85/15 PDLGA samples due to higher glycolide amount in the copolymer. Li et al. (1990a) studied the degradation of rasemic poly(D,L-lactide). Autocatalysis affected also the degradation of poly(D,L-lactide). Weight loss was observed at the end of the degradation when the surfaces of the samples become permeable for oligomers. Finally only empty shell from the sample was remaining. (Li et al. 1990a; Li et al. 1990b)

The PLGA 10/90 samples degraded more and faster than the two other materials. Already after two weeks small but visible material pieces were fragmented from the samples. At weeks 6 and 8 the initial capsules could not be distinguished anymore because the samples had fragmented to the bottom of the test tubes. In Figure 37 can be seen wet and dry PLGA 10/90 samples from week 4. The dried sample had been bended in mechanical testing. After drying the samples were very brittle and from the surface of the sample small material pieces were fragmented. Compared to the original color of the samples, they turned lighter after two weeks.

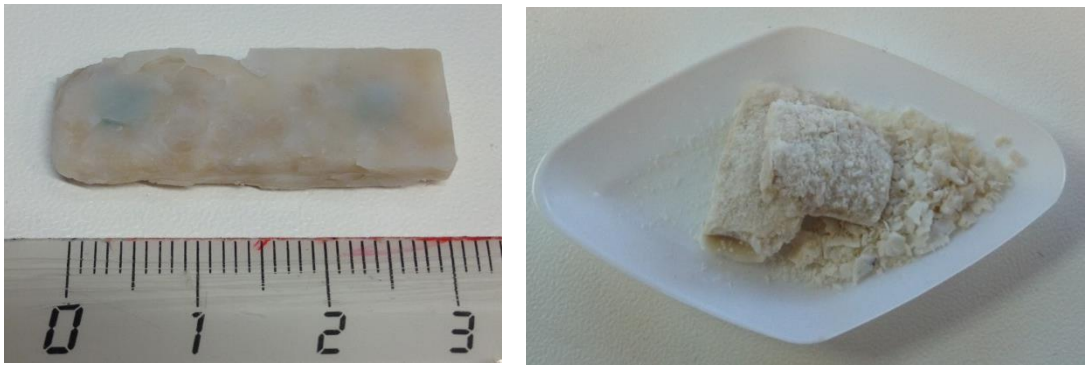


Figure 37. *Wet (left) and dry (right) PLGA 90/10 samples at week 4. The picture of the dry sample was taken after three-point bending test.*

Surfaces of the degradation test samples were more closely observed using light microscopy. In Figure 38 are shown light microscopy images of the PLGA 80/20, PDLGA 85/15 and PLGA 10/90 samples. At week 0 images were taken from the dry samples. At weeks 4 and 8 images were taken from the wet samples. Images of the PLGA 80/20 are from weeks 0 and 8. Images of the PDLGA 85/15 and the PLGA 10/90 are from weeks 0 and 4. The PLGA 10/90 samples were too degraded and the surfaces of the PDLGA 85/15 samples turned whitish after taking them out from buffer solution after week 4. Thus no images were possible to be taken after week 4.

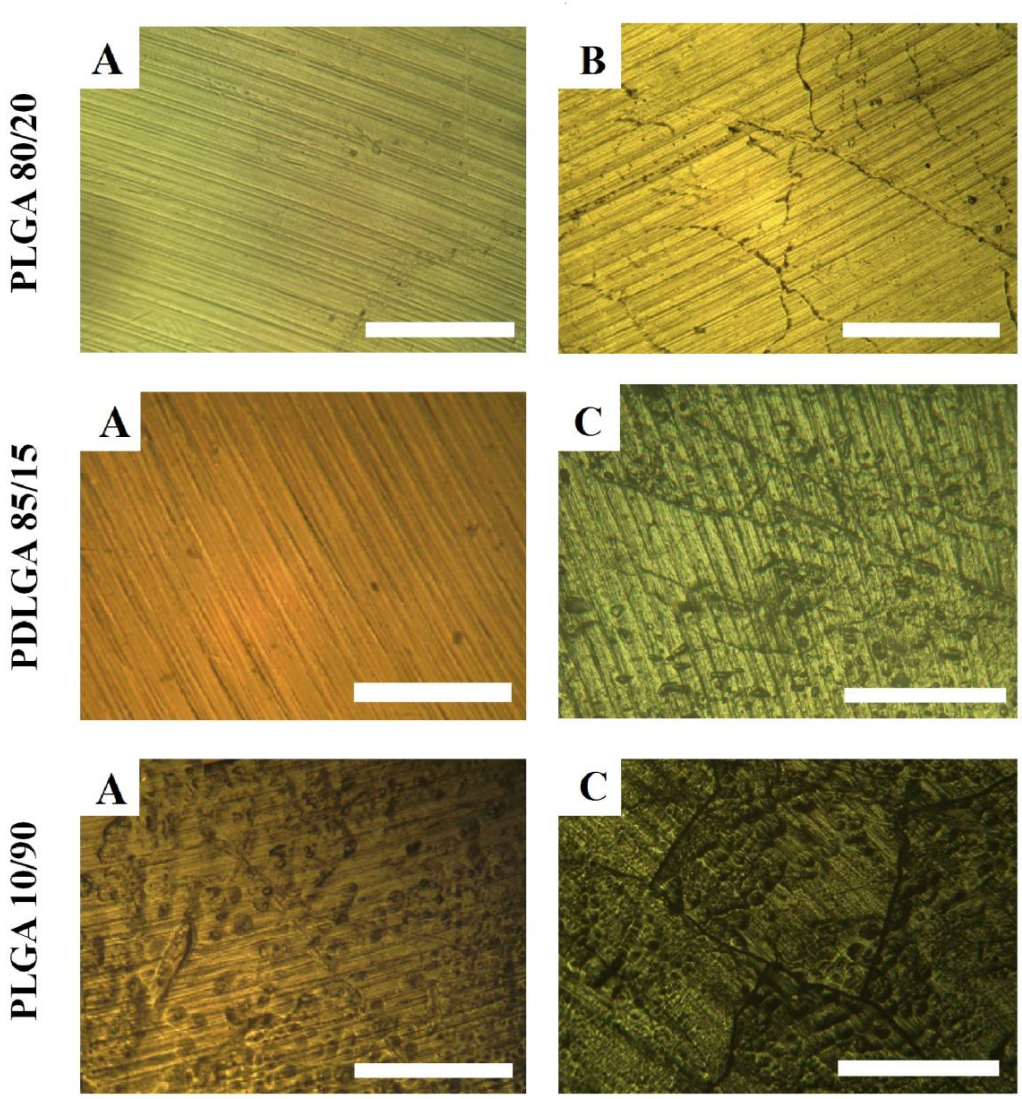


Figure 38. *Light microscopy images of PLGA 80/20, PDLGA 85/15 and PLGA 10/90 test samples (A) before degradation, (B) at week 8 and (C) at week 4. Scale bars 0.5 mm.*

In all images especially in the PLGA 80/20 and the PDLGA 85/15, the pattern of the mold surface can be distinguished on the surfaces of the samples. At the beginning the PLGA 80/20 and the PDLGA 85/15 samples had smooth surfaces. Surfaces of the PLGA 10/90 samples were already uneven and rough at week 0. The fact that the PLGA 10/90 is composed of two different monomers, mainly glycolide, affected the appearance of the surface. Also the grain boundaries might be seen in the image.

During 8 weeks small intergranular fractures were formed to the surfaces of the PLGA 80/20 samples. Etching of the grain boundaries probably induced the cracks. The surfaces of the PLGA 80/20 samples were the least changed during the degradation. In the PDLGA 85/15 samples a great difference can be seen already after four weeks. The degradation caused surface roughness and induced crack and holes. After 4 weeks the PLGA 10/90 samples were still rough and big intergranular fractures were formed on

the surfaces of the samples. Water likely penetrated into polymer matrix through the intergranular fractures. Cracks were biggest in the PLGA 10/90 samples.

7. CONCLUSION

The aim of this work was to evaluate the feasibility of the three different poly(lactide-co-glycolide) based biodegradable polymers for encapsulating resonance circuits using compression molding and to monitor the degradation behavior of the materials. The purpose was to find out if the degradation or a specific material property could be observed by measuring the resonance behavior wirelessly from the encapsulated circuits. In addition, a degradation test series was carried out in order to look for similarities between the resonance behavior and the degradation of the materials.

The study showed that the resonance circuits can be encapsulated with biodegradable polymers using a compression molder. The encapsulation was feasible using the PLGA 80/20 and the PDLGA 85/15 materials because the properties of the raw materials were favorable to the manufacture process. The resonance circuits encapsulated with the PLGA 80/20 worked up to 14 weeks and the resonance behavior of the PDLGA 85/15 capsules was possible to be measured for 7 weeks. The manufacture of the capsules using the PLGA 10/90 was challenging due to the narrow processing window. The measurements revealed that the encapsulation using the PLGA 10/90 lasted only for a few days and consequently failed due to rapid degradation of the capsules.

The degradation test series showed that the properties of the PLGA 80/20 samples hardly changed during the 8 week test period and the test samples remained almost unchanged. The properties of the PDLGA 85/15 samples weakened continuously during the degradation test and were weaker than the properties of the PLGA 80/20 samples. The appearance of the PDLGA 85/15 test samples changed significantly because of autocatalysis. The core of the samples turned to viscous liquid and the shell turned white and rigid. The study also revealed that almost all the properties of the PLGA 10/90 samples were quite poor already before the degradation test series and got even weaker during time. After six weeks, the PLGA 10/90 samples were entirely fragmented to the bottom of the test tubes.

The visual characterization of the encapsulated circuits and the degradation test samples suggested that water absorption could have caused the characteristic resonance behavior of each material. However, the results from the degradation test series did not explain the resonance behavior even though some similarities were observed. Based on this study can be said that the resonance behavior was not caused by any specific material property. Further studies are needed to solve the reason behind the resonance behavior. For the PLGA 80/20 samples a longer degradation test series is required to observe the changes in the degradation process and to compare the results with the resonance behav-

ior. The PDLGA 85/15 samples changed more than expected during the measurements. Thus more frequent time points and more parallel samples are recommended in further studies.

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APPENDIX A: DSC RESULTS OF THE PLGA 10/90

Material	Test week	Melting temperature T_m (°C)	SD	Melting enthalpy ΔH (J/g)	SD
PLGA 10/90	0	205.3	0.8	52.3	1.0
	2	204.2	3.2	68.0	7.8
	4	206.1	1.0	71.9	13.0
	6	205.9	1.3	114.5	13.6
	8	207.2	2.9	101.3	1.8