



TAMPERE UNIVERSITY OF TECHNOLOGY

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**BIODEGRADABLE ELECTRONICS; MATERIALS AND
CURRENT APPROACHES**

Master of Science Thesis

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ABSTRACT

This master's thesis is a part of 'Human Spare Parts' research program by BioMediTech. The aim of the research program is to integrate different branches of biomedical engineering and stem cell research to discover new and better therapies and treatments. However, this thesis concentrates on biomaterials and sensor technology. The first part of the thesis, entitled the theoretical part is dedicated to a detailed investigation of the biodegradable electronics. This part gives an introduction to materials, existing technologies and area of applications. Polymers as organic materials, biodegradable materials, their classifications, and scope for biodegradable electronics are discussed in this part. A discussion of currently developed devices for medical and other applications are also documented. New organic materials such as, conducting, semiconducting and dielectric polymers have been developed for the facilitation of biodegradable electronics. Their ease in processing and fabricating has made them a potential candidate for organic electronics. Inorganic materials are being used as well, but the dependence is reducing with the emergence of new materials. Extremely flexible, bendable, thermally well stable and fully degradable electronic components have been demonstrated successfully.

The second part of the thesis involves an experimental part. The feasibility of biodegradable encapsulation of LC resonance sensor and reliability of extractable features to monitor the water absorption and degradation processes in the polymeric materials were studied. Biodegradable encapsulation of polycaprolactone (PCL) was found to be a potential candidate for such sensor configurations. PCL exhibited a low processing temperature and was found to be stabilized after taking up water into its matrix. Based on the results, further studies are needed in order to sort out prospects in biosensor technology based on the concept of biodegradable encapsulation of LC resonance circuit.

PREFACE

This thesis was accomplished as a part of Master's Degree in Biomedical Engineering, at the Department of Biomedical Engineering, Tampere University of Technology. A three month of fulltime funding was financed by TEKES, Academy of Finland and Council of Tampere Region.

All praises due to Allah, the almighty, peace and blessings upon Prophet Muhammad.

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ABBREVIATIONS

BJT	Bipolar junction transistor
CVD	Chemical vapor deposition
DNTT	Dinaphthothienothiophene
ESD	Electrostatic charge dissipation
GAG	Glycosaminoglycan
HA	Hyaluronic acid
HDPE	High density polyethylene
ICP	Intrinsically conducting polymers
MEMS	Microelectromechanical Systems
MOSFET	Metal oxide semiconductor field effect transistor
OFET	Organic field effect transistor
OLED	Organic light emitting diode
OTFT	Organic thin-film transistor
PAC	Poly (acetylene)
PAH	Polyanhydrides
PANI	Polyaniline
PCA	Poly (alkyl cyanoacrylates)
PCL	Polycaprolactone
PDMS	Polydimethylsiloxane
PDO/PPDO	Polydioxanone or poly (p-dioxanone)
PEDOT	poly (ethylenedioxythiophene)
PEN	Polyethylene naphthalate
PET	Poly (ethylene terephthalate)
PHA	Polyhydroxyalkanoates

PHB	Polyhydroxybutyrate
PI	Polyimide
PLA	Poly lactide
PLCL	Poly L-lactide caprolactone
PLGA	Poly L-lactide glycolide Acid
PLLA	Poly L-lactide
PMMA	Poly (methyl methacrylate)
POE	Poly (ortho esters)
PPS	Poly (p-phenylene sulfide)
PPV	Poly (p-phenylenevinylene)
PPy	Polypyrrole
PT	Polythiophene
PTMC	Poly trimethylene carbonate
PVA	Polyvinyl alcohol
RFID	Radio frequency identification
SAM	Self-assembled monolayer
SMD	Surface mounted device
SS	Stainless steel
THA	Total hip arthroplasty
TJR	Total joint replacements
UMWPE	Ultrahigh molecular weight polyethylene
VAD	Ventricular assist devices

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THEORETICAL PART

The theoretical part presents the review part of the thesis. The current technologies, devices and demonstrations are discussed with all necessary background studies.

1. INTRODUCTION

Biodegradable electronics is a new branch of electronics that offers the solutions for the existing limitations regarding conventional silicon electronic technology. Thus it has attracted attention of the scientists and research groups to develop new materials and manufacturing techniques. Compatibility with flexible substrates and low manufacturing cost are seemingly the key features that biodegradable electronics are offering in contrast with silicon electronic technology. Some of the technologies regarding biodegradable electronics are under development and some are close to a commercial success. Although performance efficiency and manufacturing consistency remain a great challenge, the current achievements hold a promise of becoming a part of the mainstream electronics. These devices appeared to be promising particularly when medical implant devices, environmental monitoring devices and consumer electronics are considered.

The journey of organic electronics started with the emergence of conducting polymers which can be dated back to early 1970s with the discovery of partially oxidized state of polymers with high electrical conductivity. Polymer or plastic conducting electricity cannot be well explained without the chemistry the polymers possess. Not long ago, any type of electrical conduction in polymer was regarded as undesirable phenomenon. But, later, in the last few decades, this phenomenon of polymers has left us with the promise of new history in the field of electronics. New organic degradable, dissolvable and absorbable electronic devices are developed by scientists and researchers to develop organic to biodegradable materials for electronics.

Thin, flexible and biodegradable electronics have great potential in biomedical applications such as chemical sensors, biosensors etc. These characteristics may allow device insertion into the body with ease to establish a conformal contact with the curvilinear tissue surface of various organs. These characteristics could be enabled by recently reported organic materials and small molecules. So far, the researchers have demonstrated electronic system that almost completely dissolves inside the body.

The primary aim of the thesis is to present a review study of biodegradable electronics. Biodegradable electronics could be an emerging field for both consumer electronics to medical electronic applications. The most up to date technologies were studied to find prospect in medical applications. This study required a necessary investigation of currently developed materials. Several organic materials, properties and candidacy as biomaterials for organic electronics were also studied.

2. BACKGROUND

The current era is encountering an emergence of new technologies and devices every single day. The lifetime of electronic devices is becoming shorter due to the technological advancement [1] falling prices and planned obsolescence [2] e.g. in case of the smart phones. These factors have resulted in fast growing surplus of electronic waste in the modern world [1]. Environmental Protection Agency estimated that 80-85% of these electronic devices go directly into landfills and incinerators. [3]



Figure01: Pictographic example of electronic waste [1].

Modern electronics utilize inorganic materials, such as Silicon (Si) and non-degradable materials like plastic and metals. Some plastics degrade in a very slow manner. It can take up to 1000 years [10, 11] to completely degrade. In the United States alone 70% of estimated metals in the landfills come from discarded electronic devices [12]. The United States is leading in producer electronics waste with a yield of 3 million tons every year. With a yield of 2.3 million tons, China has acquired the second [20].

Inorganic materials are said to be the basis of modern electronic technology. But, the researchers of Tel Aviv University in Israel [4] claim that silicon and inorganic materials are most likely to be outdated soon by organic materials to replace the entrenched electronics to produce less harmful devices to the environment. Alternative production methods are needed to reduce the current amount of waste due to electronic devices. The utilization of biodegradable and organic materials in manufacturing electronic devices is one possibility to address the issue of this growing ecological problem.

Many organic materials and biologically originated compounds have seen to be biodegradable and nontoxic [1]. Additionally, many organic materials have shown excellent electrical properties [17]. These features suggest that organic materials could be used in electronics to endorse properties such as softness, flexibility, biodegradability and non-toxicity [5]. This furthermore enables the development of bioresorbable electronics for environmentally friendly biodegradable devices and for medical applications [2, 4, 5].

Biodegradable electronics are readily offering potential in the cases of [8]:

1. Active implantable medical devices perform important diagnostic and therapeutic functions. After the desired operation, when they are no longer useful, these are simply going to dissolve and resorb in the body.
2. Environmental monitors, detector or sensors would disintegrate over time to ensure minimum ecological impact.
3. Consumer electronics to be bioresorbable to reduce electronic waste, especially generated by frequently upgradable consumer electronics

In general fashion, electronic devices are designed and built to last, e.g. TV, laptops, etc. are expected to serve for a longer time. And most of the time, the quality of an electronic product is measured on the ground of durability and robustness in operation and service. But the researchers at the University of Illinois are instead taking planned obsolescence to an extreme concept of developing a class of electronic devices which would be built to dissolve, degrade, and decompose over time. On the 27th of September, 2012, The News Bureau-Illinois, online publications of University of Illinois published an article regarding the invention of transient electronic device [7]. Senior physical science editor Liz Ahlberg has said [8]:

“.....researchers have demonstrated a new type of biodegradable electronics technology that could introduce new paradigms for medical implants, environmental monitors and consumer electronics.”

Prof. Martin Goosey, researcher from the Innovative Electronics Manufacturing Research Centre at Loughborough University commented about organic thin film transistors fabricated on resorbable biomaterial substrate [6, 9]:

“This route offers the possibility of biodegradable electronics, thereby avoiding all the common issues with existing electronics. Plastics from electronic waste is currently a problem”

Biodegradable electronics or organic electronics are most likely to outdate the entrenched technologies and getting into mainstream electronics market in near future. It is seen to have a versatile usability in a wide range of applications such as conventional electronic devices, photovoltaic and biomedical applications. Disposable RFID tags, printable circuits, large-area photovoltaic cells, high-resolution flexible displays are at the final stage of commercialization [14].

2.1. Biodegradable electronics

Electronics devices which are subjected to degrade in a desired manner after its operation to avoid discarding

Scientifically, biodegradable refers to a term to explain the biologically mediated degradation processes e.g. enzymatic degradation and/or cellular processes. Unlike biodegradable, bioresorption refers to a degradation process which is chemically mediated not biologically, such as hydrolysis. The degradation byproducts from

bioresorption are then disintegrated into normal metabolism. Such pathways may include Krebs cycle and other metabolic systems. Bioabsorbable is another chemically mediated degradation process but dissimilarity lies with the disintegration of the degradation byproducts. Unlike bioresorbable, the degradation by products is generally excreted through one or more route of excretion of human body instead of metabolically, resorbs in body metabolism [21].

However, organic electronics is the term commonly used to refer biodegradable electronics, plastic electronics or polymer electronics. Organic electronics is called ‘organic’ because the dominating materials e.g. polymers and small molecules are carbon-based. Organic electronics is subjected to be developed as biodegradable electronics. Development of degradable polymeric materials and small molecules is crucial to design the future electronic technology.

2.2. Thin Film Transistor (TFT)

A thin-film transistor (TFT) is a special kind of field effect transistor (FET) is made by deposition of thin films of a semiconductor layer, dielectric layer and metallic contacts known as stack.

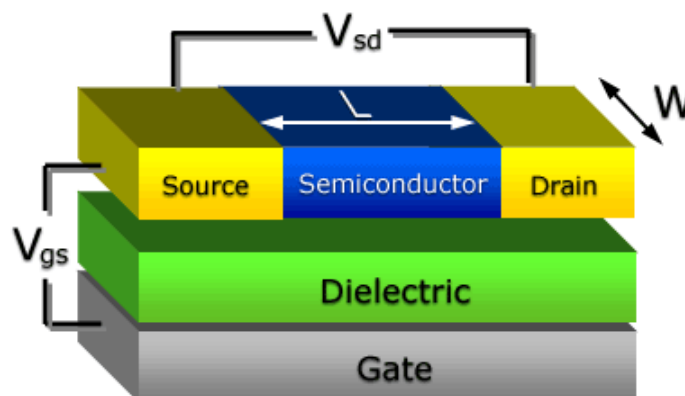


Figure 02: basic configuration of a TFT

Glass was being used as a common substrate on which TFTs were built; for example, liquid crystal displays. However, with the continuous demand for flexible electronics, organic active and substrate materials are becoming more common. This differs from the conventional FET, where inorganic materials are utilized. Several materials can be used to make the TFTs and the most common of them is silicon. TFTs have also been fabricated using organic materials which are referred to as an Organic TFT or OTFT. The patented idea of the field-effect transistor (FET) of J.E. Lilienfeld in 1930 was later demonstrated by and designed by Kahng and Atalla in 1960 using a metal-oxide-semiconductor [152]. Metal oxide semiconductors are expensive and they follow an expensive mean of manufacturing and processing. Thus, the rising costs of materials and manufacturing processes and the concept of developing environmentally friendly electronics have ignited the idea of organic based electronics later in recent years.

Scientist Koezuka with his groups has reported the first organic field-effect transistor made from a polymer of thiophene molecules in 1987[152]. Several other conjugated polymers such as polythiophenes, polyacetylene etc. have shown semi-conducting properties for such applications. This has led to the improvement of OFET design during the past decades and they are now designed based on the TFT model [146, 147, 151-153, 164]. OFETs are utilizing many aromatic and conjugated materials as their active semiconducting including small molecules such as tetracene, pentacene, diindenoperylene and perylenediimides [153].

There are three important parameters of transistor or thin film transistor to evaluate performance. These are, the charge carrier mobility (μ), the current on-off ratio ($I_{on}:I_{off}$) and Turn-On Voltage (V_{on}). Furthermore, for maximizing the transistor speed, two important points should be noted; the charge carrier mobility should be as high as possible and the channel length (distance between the source and drain electrodes) should be as short as possible [17].

Mobility (μ): Charge carrier mobility stands to express how fast holes or electron moves when subjected to an electric field. This parameter is measured in m^2/Vs . commonly reported mobilities are in the order of 10^{-1} . However, research groups and companies are facilitating mobility very close 1.

On/Off Ratio ($I_{on}:I_{off}$): Current on-off ratio stands for the expression of the measure of the relative difference in the source-drain current at two fixed gate voltages. Two fix voltages are usually 0V to 20V but generally specified. This parameter is unit less; ratio of 10^6 is usable for most transistor applications.

Turn-On Voltage (V_{on}): this parameter indicates the gate voltage at which the transistor switches 'ON'; this is defined by the rapid increase in source to drain current. It is measured in volts; ideally, V_{on} is 0V.

3. MATERIALS

Biomaterials are materials intended to interface with biological systems to evaluate, treat, augment, or replace any tissue, organ, or function of the body [21]. However, certain criteria and regulatory requirements must be met for the qualification of biomaterials to be used in medical applications. Biocompatibility is one of the most important requirements and the criteria for determining the biocompatibility of the biomaterial depend on the end use application. A wide range of biomaterials have been investigated as biomaterials which include metals, ceramics, glasses, and polymers. Polymers possess a versatile class of biomaterials investigated extensively for medical and other applications. Inherently possessing ease in synthesizing and modifying properties to match desired scope for applications have left polymer a unique biomaterial to be studied and investigated.

3.1. Biodegradable polymers

The last two decades have seen a paradigm shift from biostable polymers to biodegradable polymers to yield several advantages and scopes in biomedical and other applications as well. Biodegradable polymers are extensively studied class of polymers which degrade in vitro and in vivo into products which can be completely eliminated from the body. This may require further metabolic transformations. Both natural and synthetic biodegradable polymeric materials are being used widely in implantable medical devices. Biodegradable polymers were developed to enable the access of tailoring properties. Sutures, dental devices, drug delivery devices, orthopedic fixation devices, tissue engineering scaffolds and biodegradable vascular stents are main applications areas for biodegradable polymers [22, 23].

S. Nair et al (2007) stated some requirements for biodegradable polymers for them to be considered as biomaterials. Biodegradable polymers should not elicit either sustained inflammatory or toxic response upon implantation into human body and it should have a necessary shelf life. The degradation time and mechanical properties should serve the desired operation, e.g. healing. The degradation byproducts must be non-toxic and desirably metabolized inside the body. The material should also have appropriate permeability and processability for the intended application [22].

Synthetic biodegradable polymers

Various synthetic biodegradable polymers are currently investigated for diverse applications. The section discusses the synthetic biodegradable polymers, processing, mode of degradation and their applications.

Poly (alpha-esters)

Poly (alpha-esters), also known as aliphatic polyesters are one of the main classes of representatives of synthetic biodegradable polymers [23]. This class of biodegradable polymers is reported to be the earliest and most investigated polymers. They are thermoplastic polymers with aliphatic ester linkages in their backbone of chemical structures. These ester linkages are susceptible to hydrolytically degradation. Unlike other polyesters, they have relatively short aliphatic chains between the ester bonds [22]. This has made them suitable for many biomedical applications [22] These polymers are unique because of their diversity and versatility in synthesis [22]. Polyesters are now synthesized by the means of polycondensation or the ring-opening polymerization (ROP) depending on the monomer units [22, 23, 25]. Bacterial bioprocessing routes have also been reported [25]. Lactide, glycolide and caprolactone are the more commonly used monomer units for the synthesis of aliphatic polyesters [26].

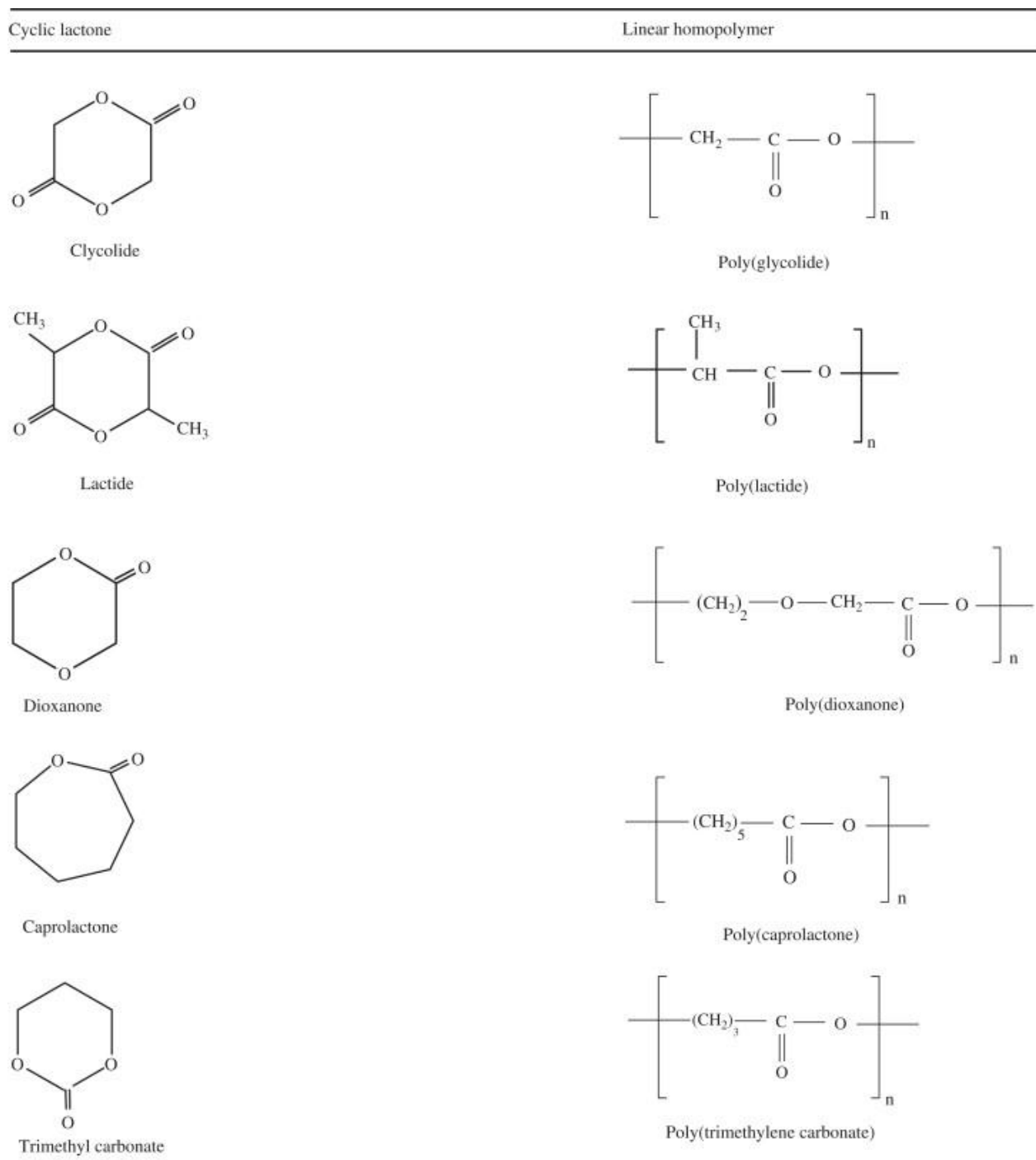


Figure 03: Structures of cyclic lactones and their derivative homopolymers [22].

Polyglycolide (PGA) is one of the first biodegradable synthetic polymers investigated for biomedical applications. The glass transition temperature (T_g) of the polymer ranges from 35 to 40 °C and the melting point is greater than 200 °C. PGA is a highly crystalline polymer (45–55% crystallinity) and due to this it exhibits a high tensile modulus and excellent mechanical properties with very low solubility in organic solvents. A self-reinforced PGA is stiffer than any other degradable polymeric system used clinically and has been shown to exhibit a modulus of approximately 12.5 GPa [24]. Polyglycolide is a bulk degrading polymer that degrades by the non-specific

scission of the ester backbone. The polymer is known to lose its strength in 1–2 months when hydrolyzed and it loses its mass within 6–12 months. In the body, polyglycolides are broken down into glycine which can be excreted in the urine or converted into carbon dioxide and water via the citric acid cycle. The high rate of degradation, acidic degradation products and low solubility however, limit the biomedical applications for polyglycolide. [22, 23]

The lactic acid is a chiral molecule. Lactide unit includes two lactic acid units. The polymeric lactide exists in three different stereoisomeric forms: L-lactide, D-lactide, and meso-lactide [22]. Among these monomers, L-lactide is the naturally occurring isomer. Hence, four different types of poly (lactic acid) (PLA) are available: poly (L-lactic acid) (PLLA), poly (D-lactic acid) (PDLA), and poly (dl-lactic acid) (PDLLA). It should be noted that with PDLLA is an equimolar racemic mixture of L-lactic acid, D-lactic acid isomers and the meso-poly (lactic acid) [23]. The polymerization of L-lactide and D-lactide monomers leads to the formation of semi-crystalline polymers. The polymerization of racemic (D, L)-lactide and meso-lactide however, results in the formation of amorphous polymers. Similar to polyglycolide, poly (L-lactide) (PLLA) is also a crystalline polymer (about 37% crystallinity) and the degree of crystallinity depends on the molecular weight and polymer processing parameters. It has a glass transition temperature of 60–65 °C and a melting temperature of approximately 175°C. Poly (L-lactide) is a slow-degrading polymer compared to PGA. It has good tensile strength, low extension and a high modulus (approximately 4.8 GPa). However, being more hydrophobic than polyglycolide, the degradation rate of PLLA is very low. Poly (DL-lactide) (PDLLA) is an amorphous polymer due to the random distribution of L- and D-lactide units, and has a glass transition temperature of 55–60 °C. Due to its amorphous nature the polymer shows much lower strength (1.9 GPa) compared to poly (L-lactide). This polymer loses its strength within 1–2 months when hydrolyzed and undergoes a loss in mass within 12–16 months. The degradation rate of PLLA is very low due to its hydrophobicity. It degrades into lactic acid a normal human metabolic by-product, which is broken down into water and carbon dioxide via the citric acid cycle. [22, 23]

Poly (lactide-co-glycolides) (PLGA) is a co-polymer of lactide and glycolide. Both L- and DL- lactides have been used for co-polymerization. Different ratios of poly (lactide-co-glycolides) have been investigated for various biomedical applications [22]. The composition range of 25/75 poly (L-lactide-co-glycolide) forms amorphous polymers. The intermediate co-polymers were found to be much more unstable compared to the homopolymers. The 50/50 PLGA is hydrolytically very much unstable degrades approximately within 1-2 months. Other compositions 75/25 PLGA and in 4-5 Months and 85/15 PLGA degrades in 4-5 months and 5-6 months respectively. PLGA has been shown to undergo bulk erosion through hydrolysis of the ester bonds and the rate of degradation depends on a variety of parameters including the LA/GA ratio, molecular weight, and the shape and structure of the matrix. [22, 27]

Poly (caprolactone) (PCL) is semicrystalline polyester, which can be obtained by the ROP of 'ε-caprolactone'. It has a melting temperature around 55–60 °C and Tg of – 60 °C. It has drawn attention because of cheap martial source (caprolactone), high solubility in organic solvents, low melting and glass transition temperature. It possesses an exceptional ability of forming blends with a variety of polymers, e.g. with lactides

(poly (ϵ -caprolactone-co-lactide)) (PLCL) [28]. However, PCL has low degradation rate making it suitable for long-term applications.

The aliphatic polyesters degrade via bulk erosion and the rate of degradation depends on the extent of water diffusion into the polymer matrix rather than the intrinsic rate of ester cleavage [22]. The water diffusion into the matrix depends on factors such as the hydrophobicity or hydrophilicity, the crystallinity, and the dimension [29]. These aliphatic polyesters degrade to give acidic degradation products, which have been identified to be resulting in adverse tissue reactions in some cases biomedical applications [22, 23]. There have been also reports of unusual release pattern [30] and the inactivation of sensitive macromolecules e.g. proteins [31] have led to further development of polyesters [22, 23]. This has led to the development of different block copolymers, multi-block copolymers using combination of lactide, glycolide, lactone and other monomer units to form poly (ether ester), poly (ester carbonates), poly (ester amide), poly (esters urethanes) etc. [29, 31].

Other polyesters

Polydioxanone or poly (p-dioxanone) (PDO/PPDO) is colorless semi-crystalline aliphatic polyester. It has a glass transition temperature ranging from -10 to 0 °C. It is prepared by ROP of p-dioxanone [22, 32]. PDO possesses a low tensile modulus of approximately 1.5GP and low thermal stability [32]. However, increasing the molecular weight may improve the thermal stability [32, 33]. PDO degrades via hydrolysis similar to other polyesters. It is considered as moderately degrading polyester due to its hydrophobicity and high crystallinity. [22]

Poly trimethylene carbonate (PTMC) is well known example of poly (ester carbonates) [23]. It is high molecular weight polyester prepared by the ROP of trimethylene carbonate. It is elastomeric aliphatic polyester; hence it possesses excellent flexibility but very poor mechanical strength. It undergoes surface erosion unlike other poly esters [22].

Poly (ester amides) are aliphatic polyesters possessing very good mechanical and thermal properties. This is due to their polar nature [23] hydrogen bonding capability of the amide bonds in their chemical structure and biodegradability impaired by ester bonds in their backbone [22, 23]. Poly (ester amides) undergo hydrolytic degradation; likewise other polyesters, they hydrolytic cleavage attacks the ester bonds but leaving the amide bonds more or less intact [22].

Poly (ortho esters)

Poly (ortho esters) are hydrophobic polymers with hydrolytically sensitive backbones and can undergo surface erosion [22]. They are excellent thermoplastic materials that can be easily fabricated by extrusion, injection molding or compression molding [34]. Poly (ortho esters) are divided into four different families or classifications, all of them depending on the time they were developed, and they present different properties and behavior; POE I, POE II, POE III and POE IV [34, 35].

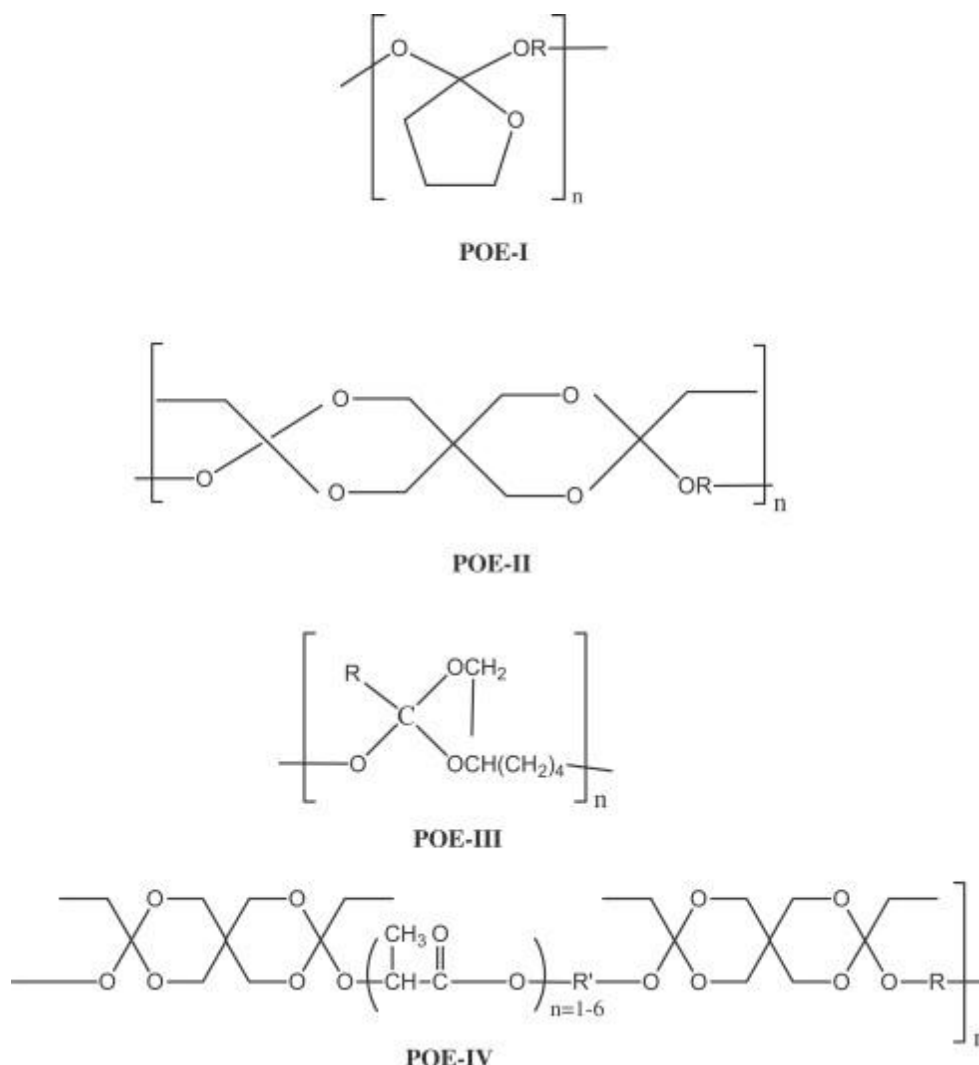


Figure 04: Structures of poly (ortho esters) [22].

POE I was the first type of POE developed. It undergoes autocatalytic reaction. In hydrolysis it degrades to γ -butyrolactone, which rapidly turns into γ -hydroxybutyric acid. Thus it has low glass transition temperature. However, POE I is no longer under development. [34, 35]

Likewise, POE I, hydrolysis of POE II also produce acids. POE II to biodegrade into small water soluble molecules and this property is unique among POEs. By using diols thermal and mechanical properties of POE II can be adjusted into several degrees from flexible to hard and glassy. However, POE II is very much stable in physical conditions because of its higher hydrophobicity. It follows mainly surface erosion and long erosion times can be achieved using a stabilizer like $Mg(OH)_2$ [34, 35, 36].

POE III is semi-solid with very flexible back bone. This enables incorporations of therapeutic agents in a simple mixing process without solvents. POE III is viscous at room temperature; hence, these kinds of materials can easily be injected. Hydrolysis proceeds as breaking into isomers which follows by slower hydrolysis of monoesters to carboxylic acid and triols, and no autocatalysis occurs. Unlike other POEs, POE III is very hydrophilic. By changing diol level of hydrophobicity can be changed. Due to the

difficulties in processing and controlling molecular weight, POE III is no longer under investigation [22, 34, 35].

POE IV is the most common POE used as biomaterials. It's a modification of POE II and requires no acids to control erosion rates. This ability to vary thermal and mechanical properties of POE IV has made it popular when devising applications. It differs from POE II as it may have a mono, or a dilactide or a mono, or a diglycolide segment in its back bone. [22]. Thermal and mechanical properties can be modified by choosing the right R-group in the diol and latent acid [35]. Choosing of diol affects greatly the glass transition temperature of POE IV, and it can be made hard, viscous etc. They are also thermally stable and soluble in different solvents. POE IV follows usually the surface erosion, and erosion rates can be controlled. Also sterilization does not affect badly its properties. These properties have made POE IV very much promising in medical applications. [22, 34, 35]

Polyanhydrides

Polyanhydrides are one of the most widely studied hydrolytically labile polymers due to the highly sensitive aliphatic anhydride bonds on the polymer backbone. The chemical structure contains hydrolytically labile backbone coupled with the hydrophobicity. This precludes water penetration into the matrix allowing polyanhydrides to truly undergo surface erosion [22]. They have a well-defined polymer structure with controlled molecular weight and degrade hydrolytically at a predictable rate. These polymers can be accordingly manipulated to release bioactive agents at a predictable rate for periods of weeks [38]. Polyanhydrides have been synthesized by melt condensation, ring opening polymerization, interfacial condensation, dehydrochlorination and dehydrative coupling agents. With solution polymerization low molecular weight polymers are achieved [38]. They are processible by low temperature injection molding or extrusion for mass production and have versatile properties, which can be varied by monomer selection, composition surface area, and additives. Polyanhydrides can be classified into aliphatic, unsaturated, aromatic, aliphatic-aromatic polyanhydrides, poly(ester anhydrides) and poly(ether anhydrides), fatty acid based polyanhydrides, terminated polyanhydrides, amino acid based polyanhydrides, branched polyanhydrides, cross linked polyanhydrides and polyanhydride blends [22, 38].

Polyanhydrides degrade rapidly in the body into their non-toxic and non-mutagenic diacid counterparts, which body metabolizes in weeks (in the case of aliphatic polyanhydrides) or months [38]. It has been noticed, that PAHs degrade rapidly in aqueous environment. Hydrolytic degradation is therefore a main mechanism in polymer bond cleavage and enzymatic degradation mechanisms are in minor role [22]. PAHs degrade as their respective diacids and exit the body in few weeks or months [22]. They have also usually almost linear mass loss kinetics, which means that they physically degrade by surface erosion [38] However, the erosion isn't completely limited to the surface with some PAHs, so mass loss can also be exponential. Fatty-acid based anhydrides degrade into natural components occurring in the body [38]. They degrade by bulk erosion because they take up so much water [39].

Poly (alkyl cyanoacrylates)

Poly (alkyl cyanoacrylates) (PCA) possesses cleavage of the carbon–carbon bonds in this polymer by hydrolysis. This has resulted in a new class in biodegradable synthetic polymers [23]. This can be attributed to the high inductive activation of methylene hydrogen atoms by the neighboring groups possessing electron-withdrawing nature [22, 23]. Poly (alkyl cyanoacrylates) is usually processed by the moisture initiated anionic polymerization of alkyl cyanoacrylic monomers [23]. Unlike other biodegradable polymers, PCA exhibits high rates of degradation which can be ranged from hours to days depending on the alkyl chain length of the polymer [41]. Ease in preparation and processing, eradication of solvent residues, ability to form stealth nanoparticles, high utility size ranges, and the ability of PCAs to absorb drug or protein molecules; these characteristics of PCAs have made them very interesting and advantageous over other polymers for drug delivery devices [22].

Synthetic Poly (amino acids)

Synthetic poly (amino acids) has a similar chemical structure as naturally occurring proteins [23]. Several forms of homopolymers and copolymers have been studied [78], but, the high crystallinity, low degradation rate, poor mechanical strength in practice have influenced their potential use in biomedical applications [79]. However, attempts were taken to develop synthetic amino acids to facilitate good physiochemical and biological properties such as amino acid derived synthetic polymers, copolymerizing amino acids with other monomers were demonstrated [79]. Also, routes of block copolymers synthesis with amino acid sequences and poly (ethylene glycol) were investigated for this purpose [80]. They are also called pseudo poly (amino acid) or pseudo amino acid polymers [22]. The most extensively studied pseudo amino acid polymer is the tyrosine-derived pseudo poly (amino acid) [80]. Tyrosine can provide good mechanical strength to the corresponding polymers. They degrade into tyrosine and diols used in the esterification of side chains. It shows excellent tissue compatibility but possess low degradability which makes them suitable for long term applications in drug delivery devices. They also exhibit good osteoconductivity [82]. However, L-tyrosine and its derivatives have seen to exhibiting amorphous biodegradability with high mechanical strength and stiffness [82]. Poly (amino acids) has been investigated for different biomedical applications [23].

Polyphosphoesters

Polyphosphoesters are phosphorus atom containing class of biodegradable polymers developed as biomaterials [84]. These polymers can be synthesized by ROP, polycondensation, and polyaddition. There are three different classes of polymers belonging to the polyphosphoester family: polyphosphates, polyphosphonates, and polyphosphates. The properties of such polymers can be manipulated copolymerizing with other monomers. For instance, copolymerizing of polyphosphoesters and DL-lactide [poly (lactide-co-ethyl phosphate)] and poly [bis(hydroxyethyl) terephthalateethyl orthophosphorylate/terephthaloyl chloride] (Poly [BHET-EOP/TC])

found to be interesting and thus investigated extensively for medical applications [84, 85]. Polyphosphoesters degrade into phosphate, alcohol, and diols, under physiological condition because of the presence of the hydrolytic and enzymatic cleavage of phosphate bond in the backbone structure. It is found interesting because the ease of physicochemical properties alteration by varying backbone or side-chain of organic components. Another advantage is the pentavalency of phosphorus atoms which allows drug or protein installation in the backbone making it suitable for drug delivery vehicles. Most of the polymers of this class have been seen to be cytocompatible in vitro and tissue compatible in vivo [85]. The near-zero-order releasing manner of the matrices of poly (lactide-co-ethyl phosphate) has been proved to be interesting as chemotherapeutic agent vehicles [86].

Natural biodegradable polymers

Various nature-originated or natural biodegradable polymers are currently investigated for diverse applications. The section discusses the natural biodegradable polymers, processing, mode of degradation, and their applications.

Polysaccharides

Polysaccharides are high molecular weight polymers made of one or more monosaccharide repeating units. Polysaccharides are widely available, cost effective, and it offers wide range of properties and structures. In addition to that, mostly polysaccharides are easily modified because of the presence of reactive functional groups along the polymer chain. Their biodegradability, biocompatibility, and water solubility and the ability of forming hydrogels have made them excellent candidates for medical applications, such as, tissue engineering, drug delivery devices etc. [22, 23]

Cellulose is the reason of forming the structural framework in plants. It is a linear polymer with repeating units consisting of d-glucose in 4C_1 configuration. It may undergo enzymatic degradation and the degradation products give result in d-glucose units. Cellulose is insoluble to common solvents due to strong hydrogen bonding between polymer chains in the structure. However, the presence of hydroxyl groups in cellulose structure can make them reactive. Different forms and derivatives of cellulose in the form of ethers, esters, and acetals have been investigated as candidates for various biomedical applications; for instance, methyl cellulose, hydroxypropyl cellulose, hydroxypropyl methyl cellulose, and carboxymethyl cellulose etc. These cellulose derivatives are soluble in different solvents. They can be fabricated into membranes, sponges, and fibers easily and possess potential in biomedical applications. For example, Cellulose based membranes have been extensively investigated as hemodialysis membranes, due to the diffusional permeability of toxic metabolic agents [54]. Different types of cellulose derivatives have been studied and investigated for dressings in treating surgical incisions, burns, wounds, and various dermatological disorders [56].

Starch has many potential uses in polymer technology. It can be converted into chemicals like ethanol, acetone and organic acids, used in the production of synthetic polymers and it can produce biopolymer through fermentative processes or be hydrolyzed and employed as a monomer or oligomer. Finally, it can be grafted with a variety of reagents to produce new polymeric materials, used as such or as fillers for other polymers. Starch is deposited in the form of semi-crystalline granules which are insoluble in cold water and resemble spherulites alternating amorphous and crystalline lamellae. Native starch is composed of two main macromolecular components, amylose and amylopectin [49]. Starch is unique among carbohydrates because it occurs naturally as discrete granules. This is because the short branched amylopectin chains are able to form helical structures which crystallize. Starch granules exhibit hydrophilic properties and strong intermolecular association via hydrogen bonding due to the hydroxyl groups on the granule surface. [50] Starch can be found in the botanical world in seeds, roots, tubers, leaves, trunks, stems, fruits, pollen, etc. [51]. Origin of the plant is very important because starches from different sources have distinct properties [51]. Thin films, fibers, or porous matrices made from modified starch are suitable for various biomedical applications. Due to biocompatibility and biodegradability, biodegradable starch-based blends have recently been suggested as potential candidates for biomedical applications. The degradation products comprise of low molecular weight starch chains, fructose, and maltose have made them suitable candidate as well [52]. Different fabrication methods are also developed for making porous scaffolds for tissue engineering [53]. Starch possesses good cytocompatibility which has also been investigated in vitro [52].

Hyaluronan or hyaluronic acid (HA) is a natural polysaccharide, or more specifically mucopolysaccharide. Glycosaminoglycans (GAGs), or mucopolysaccharides, are long and un-branched polysaccharides containing a derivate of an aminosugar. Usually GAGs are linked to a protein to form large macromolecules called proteoglycans, but HA exists without the protein part [57]. Hyaluronic acid is a naturally occurring biopolymer, which has important biological functions in bacteria and higher animals including humans [58]. It is found as a constituent of all body fluids and tissues, in higher concentrations in the vitreous humor of the eye and in synovial fluid in the joints; the highest reported concentration in mammals is found in the umbilical cord. Hyaluronan is synthesized by many types of cells and extruded into the extracellular space to interact with extracellular matrix constituents to create the supportive and protective structure around the cells. [57] The repeating disaccharide units are d-glucuronic acid and N-acetyl glucosamine linked by $\beta(1,4)$ and $\beta(1,3)$ glucosidic bonds [59]. The structure of disaccharide is energetically very stable. This disaccharide polymer can be 25 000 repeating units long and its size ranges from 5 000 to 20 000 000 Da [58]. Hyaluronic acid (HA) can be modified in two main ways: Cross-linking or conjugation. In cross-linking different HA chains are linked together by two bonds or more, whereas in conjugation a compound is grafted onto one HA chain by a single bond only. The chemical modification of HA can be performed on the two available functional sites of HA: the carboxylic acid group and the hydroxylic group (probably mainly on the hydroxyl group of the C& of the N-acetylglucosamine moiety). Also an amino group can be modified after deacetylation of the N-acetyl group. [59]. Being a naturally occurring polymer, it follows enzymatic degradation.

Karl Meyer introduced the term “hyaluronidase” to denote the enzymes that degrade HA. In enzymatic degradation disaccharides are the major end products of HA degradation and these can be transported and metabolized intracellularly to supply needed nutrients (as a carbon source) for a pathogen as it replicates and spreads [60]. It may also follow spontaneous deesterification. Hyaluronan esters undergo spontaneous de-esterification when in an aqueous environment, while from the quantification of the presence of N-acetyl-glucosamine the hyaluronan backbone chain appears to be more stable under the same conditions [61]. The large quantities of hyaluronan are metabolized in the human body [63]. Due to its excellent biocompatibility and biodegradability, it is an attractive component for building new polymers for medical applications such as tissue repair, tissue engineering and drug delivery devices [22]. The hyaluronan derivatives may have physicochemical properties that significantly differ from the native polymer, but most derivatives retain the biocompatibility and biodegradability, and in some case the pharmacological properties, of native hyaluronan [62].

Chitosan is a linear polysaccharide which is composed of randomly distributed Beta-(1-4) linked D-glucosamine and N-acetyl-D-glucosamine. It is biodegradable and the by-product of degradation is biocompatible and metabolizable. Chitosan doesn't dissolve in water but as a polymer it is dissolvable in water-lactic acid solution. Chitin is produced commercially by the deacetylation of chitin, the structural elements in exoskeleton of crustaceans. The deacetylation is done by using sodium hydroxide in excess as a reagent and water as a solvent [65]. It undergoes biodegradation in vivo enzymatically by lysozyme and gives result to nontoxic products. The rate of degradation of Chitosan depends inversely on the degree of acetylation and crystallinity of the polymer [69]. However, Chitosan has seen interest in biomedical application for wound healing, bone filler etc. [64]. Chitosan exhibits bioadhesive property and allows it to rapidly clot blood, and has been used in bandages and other hemostatic agents, recently being approved by USA and UK to be used [66]. It is mucoadhesive and reactive which allows it to be used in transdermal drug delivery [67].

Protein

Proteins are high molecular weight polymers having amino acid repeating units. Amino acid segments are joined together by peptide linkages. These materials have been extensively investigated for diverse medical applications such as sutures, hemostatic agents, scaffolds for tissue engineering, and drug delivery.

The term “collagen” refers to proteins that form a characteristic triple helix of three polypeptide chains. All members of the collagen family form these supramolecular structures, although their size, function and tissue distribution vary greatly. Collagens can be grouped into fibril-forming collagens, basement membrane collagens, microfibrillar collagens, anchoring fibrils, network forming collagens, fibril-associated collagens (FACIT), transmembrane collagens and multiplexins. The various types of collagen show different susceptibility to collagenolytic degradation [72]. Collagen is a protein found in the body. Collagen can be processed into sheets, tubes, sponges, foams, nano fibrous matrices, powders, fleeces, injectable viscous solutions and dispersions due to its vast versatility in properties. Collagen degrades through

enzymatic degradation but collagen is particularly resistant to attacks by neutral proteases, probably due to its function as the primary structural protein in the body. However, Collagen I is one of the most studied polymer, because it has a great impact on mammals [72]. In bones, it takes an important role in defining biomechanical properties concerning load bearing, tensile strength and torsion stiffness specifically after calcification [70]. Natural crosslinking gives high tensile strength and proteolytic resistance to collagen. Due to dissociation of crosslinks, reconstituted forms of collagen such as films, fibers, or sponges can lack sufficient strength and may disintegrate upon handling or collapse under the pressure from surrounding tissue in vivo. Furthermore, the rate of biodegradation has to be customized based on the specific application. So it is often necessary to confer mechanical firmness and collagenase resistance by introduction of exogeneous crosslinking into the molecular structure [71]. The flexibility of collagen increases with the increasing content of glycine [72]. Collagen is insoluble in organic solvents [71] and soluble in acidic aqueous solutions [72]. The covalent crosslinks between molecules is the major impediment to dissolution of collagen I [71]. Collagen is hydrophilic which makes them able to swell and have more rapid release of drugs in drug delivery applications as compared with synthetic polymers [71]. Because of its high reactivity, collagen can be cross-linked by various cross-linking agents like di-functional or multifunctional aldehydes, carbodiimides, hexamethylene-diisocyanate, polyepoxy compounds and succinimidyl ester polyethylene glycol [72]. Collagen is also highly thrombogenic; it is one of the initiators of the coagulation cascade and for that reason have applications as a hemostatic agent [72]. Finally, collagen binds to different growth factors and cytokines; it can be used as transport vehicles for drug delivery [70].

Albumin can be found in blood plasma in highest concentration as protein. It carries hydrophobic fatty acid molecules in the bloodstream. An α -helical form of single polypeptide chain constitutes albumin. It is soluble to water and various solvents. Due to its solubility and the association of reactive hydroxyl functional groups along the polymer chain allows the modification of albumin into membranes, microspheres, or nanospheres. Since albumin allows the adsorption of fibrinogen and the aggregation of platelets, it has seen to be investigated to be used as a coating of devices to improve hemocompatibility. Intravascular drug delivery systems have been reported to develop due to its hemocompatibility [77].

Bacterial Polyesters and Polyamides

Bacterial polyesters and polyamides are polymers produced by microorganisms. These are nontoxic, biocompatible, biodegradable materials and are being investigated for a variety of medical applications.

Polyhydroxyalkanoates (PHAs) are thermoplastic or elastomeric polyesters (polyoxoesters) of R-hydroxyalkanoic acid (HA) monomers that are biosynthesised by a wide range of Gram-positive and Gram-negative bacteria as intracellular carbon and energy storage compounds. Structurally, these polymers are classified on the basis of the length of chain which is defined by the number of carbon atoms. For example, poly

(3-hydroxybutyrate), P(3HB) and poly(4-hydroxybutyrate), P(4HB) are small chain PHAs. Polyhydroxybutyrate (PHB) is short chain length PHA and probably one of the most used PHA group in different applications [43]. There are well over 100 different types of hydroxyl acid monomers which may occur in the PHA polymers [45]. Usually, PHA polymers are produced in vivo by fermentation from sugars or oils (often using co-feeds) and with rather high molecular weights (100 000-500 000, even 3 000 000 Da, depending on the type of microorganism and growth conditions) [44, 46]. PHAs can be thermoplastic or elastomeric polymers. PHAs can be degraded by PHA hydrolases and PHA depolymerases and the degradation rate can vary from months to years. Some scl-PHAs have higher tensile strength than polypropylene and polystyrene Mcl-PHAs. On the other hand are thermoplastic elastomers with low crystallinity and tensile strength but high elongation to break. They have lower melting points and glass transition temperatures when compared with scl-PHAs and polypropylene [47]. PHAs are processed via injection molding, blow molding and extrusion process [48].

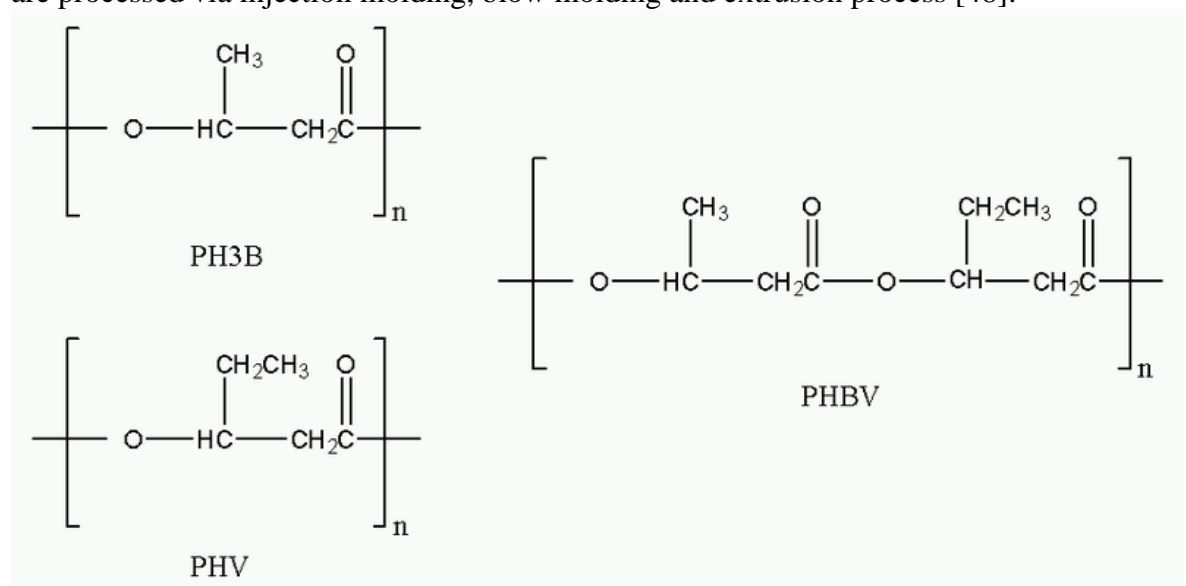


Figure 05: structure of different PHAs [22]

PHB for example is highly crystalline (60 %) but very brittle and stiff (5% extension to break). PHB is homopolymer, but the copolymers such as PHB48, PHBV and mcl-PHA, PHBHx are less brittle and stiffer than PHB, but they retain most of the other mechanical properties of PHB [47]. PHBs degrade by enzymatic hydrolysis. PHB has a rather low degradation rate in the body compared to synthetic polyesters presumably due to its high crystallinity [22, 46, 47]. As PHBs possess high melt viscosity, it makes processing harder than that of PHAs.

Poly(γ -glutamic acid) is a homopolyamide. It is produced by various strains of Bacillus. The d- and l-glutamic acid constitutes the polymer and the units are connected by amide linkages. Water solubility, biodegradability, and nontoxic nature of degradation products have made this polymer a very good candidate for medical applications such as drug delivery. In addition to that, the presence of reactive carboxyl groups on the polymer chains has allowed the covalent immobilization of drug molecules, which enables designing and developing anticancer drug delivery vehicles [73]. This polymer has also been investigated for surgical adhesive, hemostatic agent [74, 75]. It has also studied for hydrogel preparation due to its good water solubility.

For instance, poly (glutamic acid) based hydrogels formed by γ -irradiation are under investigation for drug delivery purposes [76].

3.2. Non-biodegradable polymers

Synthetic polymers have been widely used for various applications including medical applications such as disposable supply lines, implants, drug delivery systems and tissue engineering scaffolds. These polymers are more easily manufactured into various sizes and shapes compared to metals and ceramics. Polymers are light in weight and exhibit a wide range of mechanical properties for different applications.

3.2.1. Synthetic polymers

Polyethylene

There are three forms of polyethylene widely known: High density polyethylene (HDPE), low density polyethylene (LDPE) and ultrahigh molecular weight polyethylene (UHMWPE).

Linear high density polyethylene or high density polyethylene (HDPE) is very inert material in nature and in the body it possesses very low tissue reactivity. HDPE has become a standard reference material for biocompatibility testing because of showing 30 years of favorable tissue response [87]. It is 60-80% crystalline synthetic non degradable polymer. The molecular density of HDPE ranges from 0.05-0.25 g/mol. It has a melting temperature of 130-137°C. Tensile modulus of elasticity ranges from 0.4 to 4.0 GPa. The tensile yield strength and ultimate tensile strength may vary from 26 to 33 MPa and from 22 to 31 MPa respectively at 23°C [88]. HDPE has been used as bone and bone substitute for over 60 years. The porous scaffolds of HDPE allow fibrous tissue growth into the implant. Porous HDPE has been successfully used for craniofacial applications, such as chin, nasal reconstruction, ear reconstruction, and the correction of craniofacial contour deformities [89-91].

Ultrahigh Molecular Weight Polyethylene UHMWPE is manufactured in powdered form and should be consolidated under high temperature and pressure because of its high melt viscosity due to the high molecular weight. Compression molding is the most common method to manufacture UHMWPE. It is 39-75% crystalline polymer. The molecular density of UHMWPE ranges from 2.0-6.0 g/mol. It possesses a melting temperature about 125-138°C. Tensile modulus of elasticity ranges for UHMWPE from 0.8 to 1.6 GPa. The tensile yield strength and ultimate tensile strength may range 21-28 MPa and 39-48 MPa respectively at 23°C [88]. UHMWPE possesses notable properties which makes it suitable for diverse applications including biomedical applications [87, 92]. For instance, in arthroplasties; the high abrasion resistances, low friction, excellent

toughness, and biostability of UHMWPE are utilized. In fact, UHMWPE is the only material used in total hip arthroplasties (THAs), tibial inserts and total knee arthroplasties. This remains the preferred material because of its exceptional mechanical properties, chemical inertness, impact resistance, and low coefficient of friction. However, UHMWPE possesses a concern of wear problem which may elicit undesirable effect on tissue [93, 94].

Poly (methyl methacrylate)

PMMA is a strong and lightweight material with a density of 1.17–1.20 g/cm³. The glass transition temperature values of commercial grades of different PMMA range from 85 to 165 °C. PMMA is generally produced by radical polymerization and it is completely amorphous. Common processes may be used for the processing of PMMA which include injection molding, compression molding, and extrusion [87]. PMMA is seen to swell and dissolve in many organic solvents. PMMA has a water absorption ratio up to 0.3–0.4% by weight and the strength decreases with increased water absorption [97]. A protocol for the chemical production of bone cement was established in 1943. After a lot of research and development work, in 1958, Sir John Charnley had succeeded to develop self-polymerizing PMMA in femoral prosthesis [95, 96]. The PMMA bone cement and commonly known as bone cement has become a major synthetic biomaterials in orthopedics and currently the only biomaterial used for cemented arthroplasties in contiguous bones [88, 89].

Polyester

Polyesters are polymers with ester linkage in their chemical structure. Among all of the polyesters, poly (ethylene terephthalate) PET is the most commonly known. The typical synthetic reaction of PET uses dimethyl terephthalate (C₆H₄(CO₂CH₃)₂) or terephthalic acid and ethylene glycol [99]. The amorphous PET has a molecular density of 1.38g/cm³ at 20⁰C. It has a modulus ranging from 2.8 GPa to 3.1 GP and a tensile strength from 55 MPa to 75MPa. PET has a glass transition temperature of 67 – 81⁰C and melting temperature may range from 250- 260⁰C. PET is practically insoluble in water. PET is considered to be biocompatible and PET fibers and fibrous structures (e.g. woven, knitted, felted and braided structures) are used in biomedical applications such as sutures, internal patches, ligament prosthesis, artificial blood vessels, heart valve sewing cuffs, etc. [98].

Polycarbonate

Polycarbonate family of polymers have carbonate linkages in their polymer chains. It is synthesized by the reaction of phosgene with bisphenol A [2,2-bis(4-hydroxyphenyl) propane]. The polycarbonate is tough and transparent plastic with a molecular density 1.20 -1.22 g/cm³. It possesses a modulus of 2.0-2.4 GPa and tensile strength of 55-75MPa. It has a glass transition temperature of 147⁰C and melting temperature of 155⁰C [100, 101]. In medical applications, polycarbonate is used in oxygenator for

open heart surgery, venous reservoir, and arterial filter due to its sterilizability, easy processability, biocompatibility, and transparent texture [87].

Polysulfones

Polysulfones belong to the family of thermoplastics. Polysulfone is generally produced by the reaction of a diphenol typically bisphenol-A or, 1, 4-dihydroxybenzene. Andbis (4-chlorophenyl) sulfone forms a polyether by elimination of sodium chloride [102]. Polysulfones have good mechanical properties and chemical resistance. They are also preferred when toughness and high thermal stability is required. It has a glass transition temperature of 1850°C and heat deflection temperature (HDT) of 174°C. It has an excellent chemical resistance to inorganic acids & bases making it suitable for various applications. It also exhibits food, water and medical contact compliance [102]. Polysulfones allow easy manufacturing of membranes for hemodialysis machine and they have been used as orthopedic biomaterials due to their good mechanical properties (tensile modulus of 2.4 GPa). However, to improve their bone-bonding properties, polysulfones are used to make composites with bioactive glass [87].

Poly amides

Polyamide polymers have amide linkages in their polymer chains. The first polyamide Nylon 6,6 was synthesized by the polycondensation process of hexamethylenediamine and adipic acid [103]. Nylon is tough, with high tensile strength, elasticity and luster. Nylon typically has a melting temperature ranging from 190 to 350 °C depending on the different class of nylon. The molecular density of nylon is 1.15 g/cm³. It possesses high elongation and excellent abrasion resistance. Nylon has been used as surgical sutures, matrix material in composite materials, with reinforcing fibers like glass or carbon fiber [87].

Polyurethane

Polyurethanes are a class of polymer with carbamate or urethane linkage in their backbone. Generally, polyurethane is synthesized by the synthetic reaction of dihydric alcohols and di-isocyanates. Polyurethane elastomers are often used as biomaterials due to their excellent fatigue resistant properties, biocompatibility, low toxicity, good thermal and oxidative stability, and anti-adhesive nature [104, 105]. Because of exhibiting such properties, segmented polyurethanes have been used as blood contacting materials, such as totally implantable artificial hearts and left ventricular assist devices (VADs). Poly (ester urethane) has been used as catheters and gastric balloons which only need to be used for a short period of time [87, 105].

3.3. Organic conducting polymers

Conducting polymers can be defined as a class of organic polymers which conducts electricity [111]. Such compounds may exhibit metallic level conductivity or may elicit semiconducting behavior. However, tailoring and fine-tuning of the electrical properties are the important advantages of conducting polymers. Several techniques such as organic synthesis, advanced dispersion techniques are usually used to alter the electrical properties of conducting polymers [112, 113]. The conducting polymers are possible substitutes for metallic conductors and semiconductors. They exhibit highly reversible redox reaction behavior as well as the unusual combination of properties of metals and plastics [115]. They possess unique conduction mechanism and good environmental stability in presence of oxygen and water. They could be highly promising for many technological uses because of their chemical versatility, stability, processibility and low cost manufacturing process [108, 114].

Electrical conductivity of intrinsically conducting polymer (ICPs) results from its positive or negative charged macromolecules through oxidation or reduction by charge transfer agent (electron acceptor or donor), termed dopant. Charge in ICPs is transported along and between polymer molecules by the generated charge carriers e.g., holes, electrons. They have drawn much attention in the last few decades not only because of their potential applications in diverse fields but also due to their lower processing cost and enhanced physical and electrical properties. However, ICPs have successfully kept their ground in the field of electronic devices such as, organic solar cells, organic light emitting diodes (OLEDs), flexible displays, printed circuits, chemical and biosensors, rechargeable batteries, smart windows, electrostatic charge dissipation (ESD) coatings [108]. There are publications, patents and several ongoing research activities in the field of conducting polymers, yet the number of commercially available ICPs is still small. Lack of stability and reasonable processing methods are considered as the main obstacles of the commercialization of ICPs.

Conducting polymers are classified on the basis of the presence of heteroatoms in the polymer backbone. The table 01 illustrates the classification of conducting polymers.

The main chain contains	Heteroatoms present		
	No heteroatom	Nitrogen-containing	Sulfur-containing
Aromatic cycles	Poly(fluorene)s polyphenylenes polynaphthalenes	The N is in the aromatic cycle: poly(pyrrole)s (PPY) polycarbazoles polyindoles The N is outside the aromatic cycle: polyanilines (PANI)	The S is in the aromatic cycle: poly(thiophene)s (PT) poly(3,4-ethylenedioxythiophene) (PEDOT) The S is outside the aromatic cycle: poly(p-phenylene sulfide) (PPS)
Double bonds	Poly(acetylene)s (PAC)		
Aromatic cycles and double bonds	Poly(p-phenylene vinylene)(PPV)		

Table 01: Classification of conducting polymers [108]

PEDOT

Poly (2,3-dihydrothieno-1,4-dioxin) (PEDOT) exhibits good electrical conductivity and stability. PEDOT/PSS is one of the most widely studied and used PEDOT based materials in organic electronics. It has been used in organic light emitting diodes (OLEDs) technology. High conductivity of 1000 S/cm can be achieved in case of PEDOT [116].

Polythiophenes

One of the most extensively studied conjugated polymers is polythiophene (PT) and polythiophene based conjugated conducting polymers. Polythiophene is a sulfur heterocycle, when doped it becomes conducting in nature because of the adding

or removing of electron which results in conjugated π -orbitals. For instance, when poly (3-dodecylthiophene) is doped with iodine 1000 S/cm of conductivity can be reached [119]. The mono-, di- and ring substituted polythiophenes possess good solubility. These derivatives also allow tuning the band gaps for achieving the desired conduction. Polythiophenes are widely used in OLEDs, organic field effect transistors (OFETs) and other organic electronic devices [117, 118].

Oligothiophenes

Oligothiophenes exhibit high charge carrier mobility and on/off ratios as semiconductors [120]. The first all-organic transistor was fabricated based on α -sexithiophene (6T) [120, 122]. When the α and ω -positions on sexithiophene are altered with alkyl chains, it results in increase in the charge carrier mobility. The alkyl chain substitution to polythiophenes improved their solubility too rganic solvents which also aids the processibility [122, 125]

Polyanilines

Polyaniline (PANI) is one of the most studied conducting polymers in the last 50 years [127]. It exhibits unique physical and chemical properties. Light weight, good conductivity, mechanical flexibility and low processing cost have made it a versatile conducting polymer with diverse range of applications. PANI can be easily processed by melt or solution processes. Polyaniline hydrochloride has reported to exhibit conductivity of about 2.9- 6.1 S/cm depending on the ratio of chemical constituents [128]. PANI is environmentally and thermally stable. Fully oxidized form known as pernigraniline is environmentally unstable in nature. Doped emeraldine form of PANI has reported to exhibit very high conductivities [126].

Polypyrroles

Polypyrroles (PPy)are also called pyrrole blacks or polypyrrole blacks. PPy exhibits high conductivity upto 1 S/cm and good stability [129, 130]. Ethylene and propylene substituted pyrrole enhances the electronic properties and alkyl substitutions improve processability [136]. PPy films have been fabricated on a number of surfaces. The scientists from Brown University have reported fast charging and discharging based battery chemistry of PPy [131]. Other applications of PPy include chemical sensors, ion selective electrodes, and conductive coatings for nanomaterials [133], nano wires [135] and carbon nanotubes applications [134]. Polypyrrole has been studied as a material for "artificial muscles" together with other conjugated polymers, which supposedly offer an advantage over present motor nerve actuating elements [132].

Polyacetylenes

Polyacetylenes (PACs) are the simplest conjugated polymers with a band gap of 1.5eV. Polyacetylene exhibits conductivity upon doping with bromine or iodine vapor [137]. Polyacetylene can be regarded as an intrinsic semiconductor. The processible derivatives of polyacetylenes, polythioacetylenes exhibit solubility in organic solvents. When they are irradiated with laser light, the conductivity may range from 10-200 S/cm. Polydiacetylenes are produced by the photopolymerization of diacetylene. They find applications in the development of organic films [138].

3.4. Organic dielectric material

Numerous organic materials have been investigated and identified as promising substrate materials for the fabrication of organic electronics. Many of these materials exhibit excellent insulating properties making them suitable for gate electrode dielectric layer of OFET, OTFT etc. Additionally, the availability and easy processability of these organic materials are opening vistas for applications such as biomedical applications etc.

Organic and inorganic-organic hybrid materials have been investigated for gate dielectric layer materials for organic electronics. Poly (methyl methacrylate) (PMMA), poly(styrene), poly(vinylphenol), silsesquioxane (glass resin), and benzocyclobutene (BCB) etc. materials are found to be promising for such application [139-141]. However, cross-linked polymers are generally found to be more robust as ultrathin dielectric materials [142]. Well-ordered and densely packed self-assembled monolayer (SAM) could also be used as possibly thinnest and high quality dielectric layer [143]. In addition to that, dielectric surface treatment with self-assembled monolayer may also affect the nucleation organic semiconductors; for instance, pentacene organic semiconductor readily exhibits the highest thin film charge carrier mobility. However, charge carrier mobility of pentacene can be changed dramatically. This depends on the types of hydrophobic surface treatment of the dielectric [145]. Incorporating inorganic nanoparticles of high dielectric constant into a polymer matrix is also reported to boost the overall dielectric constant of the polymeric thin film [144]. Table 02 in Appendix presents newly developed dielectric polymers for organic transistors and thin-film transistors.

3.5. Organic semiconducting polymer

There are two types of organic semiconductors based on the types of charge carriers; p-type semiconductors, where holes as major charge carriers and n-type semiconductors, where the electrons as major charge carriers. The organic semiconductor layer usually

consists of π - conjugated oligomers or polymers that facilitates the charge transportation. However, the π - π stacking direction and the current flow direction should ideally be in the same direction. To ensure this, the semiconductor molecules should be self-assembled into a certain orientation during their deposition process. Also, the semiconductor thin film should be densely packed and well-interconnected [108].

In conducting polymers, electrons are delocalized along the conjugated backbones, usually through overlap of π -orbitals. And this results in an extended π -system with a filled valence band. However, the p-type semiconducting polymers are produced by the removing electrons from the π -system. This process is done by simultaneous oxidation of conducting polymers. This is called oxidative doping or p-doping. By doping a conducting polymer when it is synthesized, a thick film can build up on an electrode [108, 114].

Similarly, adding electrons into the π -system of a conducting polymer gives result in n-type semiconducting polymers. This process is done by reduction reactions; hence the process is called reductive doping or n-type doping [108, 114].

3.6. Inorganic Materials

Beside organic materials, inorganic materials have been playing an important role as biomaterials. Alkaline, earth alkaline, metal, transitional metal, metalloid etc. elements are studied and investigated for potential as biomaterials.

Some of the metals are used as biomaterials because of their physical properties and fair biocompatibility. Physical properties of metals include high mechanical strength, resistance to fracture and corrosion etc. A number of metals used in biomedical applications, exhibit good biocompatibility, i.e. they do not cause toxic reaction in human body upon exposure to biological tissue. Such metals include noble metals such as platinum, gold, silver, cobalt, palladium, titanium, aluminum etc. Metal alloys such as stainless steel (SS), titanium alloy, cobalt alloys etc. are also used in medical applications [87]. Metal contacts are still being used in organic and biodegradable electronics [146-153, 158, 162-164]. Cadmium, zinc [203] and magnesium [7, 15] have also been reported as biomaterials to be used in organic to biodegradable electronics.

Metalloids are also reportedly used in biodegradable electronic applications. Silicon (Si), germanium (Ge), boron (B) elements are used in doped form to yield a desired semiconductivity for switching and amplifying devices in electronic applications. Iodine (I) and bromine (Br) have been reported as a doping material for conducting polymers as well [119, 137].

4. CURRENT APPLICATIONS

This chapter is going to investigate the most latest organic and degradable electronic devices. Both, active and passive electronic components have been demonstrated. The devices are categorized according to the characteristics they offer.

4.1. Passive Electronic Component: Transistor

Transistors being the building block of modern electronic technology have attracted attention to be developed for biodegradable electronics. Organic thin film transistors, Organic light emitting diode, Organic MOSFETs, Organic CMOS switching devices, transistor arrays and ring oscillators are transistor based electronic devices. Furthermore, more organic configurations are currently under investigation.

4.1.1. High thermal stability of Organic transistor

High thermally stable organic transistors were developed by the research groups from Japan, USA and Germany. The focus of their research was to utilize the flexibility of organic materials for different applications such as robotic sensors, flexible displays and medical electronic applications. Still the issue of thermal instability of the organic materials was a great concern. Low melting temperatures and large thermal expansion coefficients of organic materials enabled the thermal degradation during the operation. This research has demonstrated the necessity of thermally stable TFT[146].

The dinaphthothienothiophene (DNNT) transistor (Figure 06), the electrode coated with gold was encapsulated in parylene due to its mechanical flexibility. Au, Al and Si/SiO₂ were inorganic materials used in this configuration. The high mobility organic semiconducting layer and thin gate dielectrics layer consisting of a 2 nm thick self-assembled monolayer (SAM) and a 4 nm thick aluminum oxide layer facilitates charge carrier mobility of $1.2\text{cm}^2\text{V}^{-1}\text{s}^{-1}$ with in operating voltage of 2 volts. However, dinaphthothienothiophene DNNT used here as the organic semiconductor [146]. DNNT semiconductor has been reported to use in other transistor configurations [147, 151]. The figure 06 shows the structure of DNNT based transistor. Alkylphosphonic acid molecules, such as n-octadecylphosphonic acid and n-tetradecylphosphonic acid organic materials have been used as dielectric layer of gate coating [146, 147].

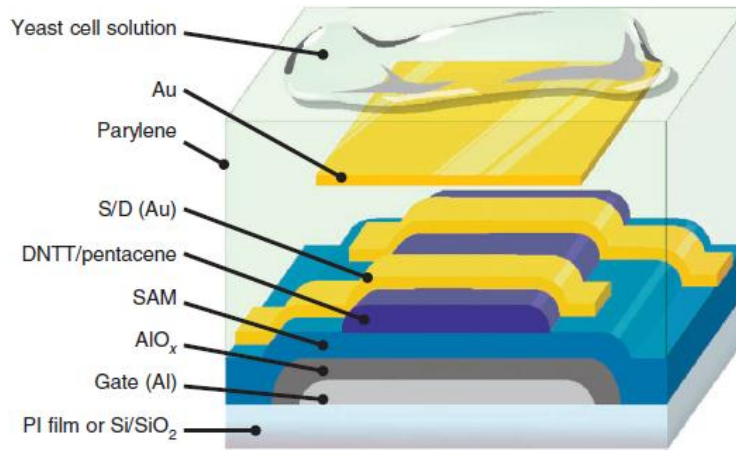


Figure 06: 3D cross-sectional view of dinaphthothienothiophene (DNTT) transistor [146]

The use of these heat-resistant and flexible organic transistors for medical sterilization and other instrumentations were demonstrated. For instance, one of the most common processes of sterilization is the treatment of implantable medical devices at 150 °C for 20 seconds in presence of moisture at an atmospheric pressure. To demonstrate the thermal stability of DNTT TFT, three individual tests were made and the transfer curves were recorded before and after the heat-treatment tests. The test were performed at 100° C in boiling water for 30 minutes at 150° C for 20 minutes and at 121 °C for 20 minutes in the air. The figure illustrates the transfer curves to be very much stable even during the exposure to different heat applications (Figure 07) [146]. The results showed high thermal stability and sustained electrical performance. Parylene as the encapsulation materials improved the thermal stability and protected the conductive Au-layer. [146].

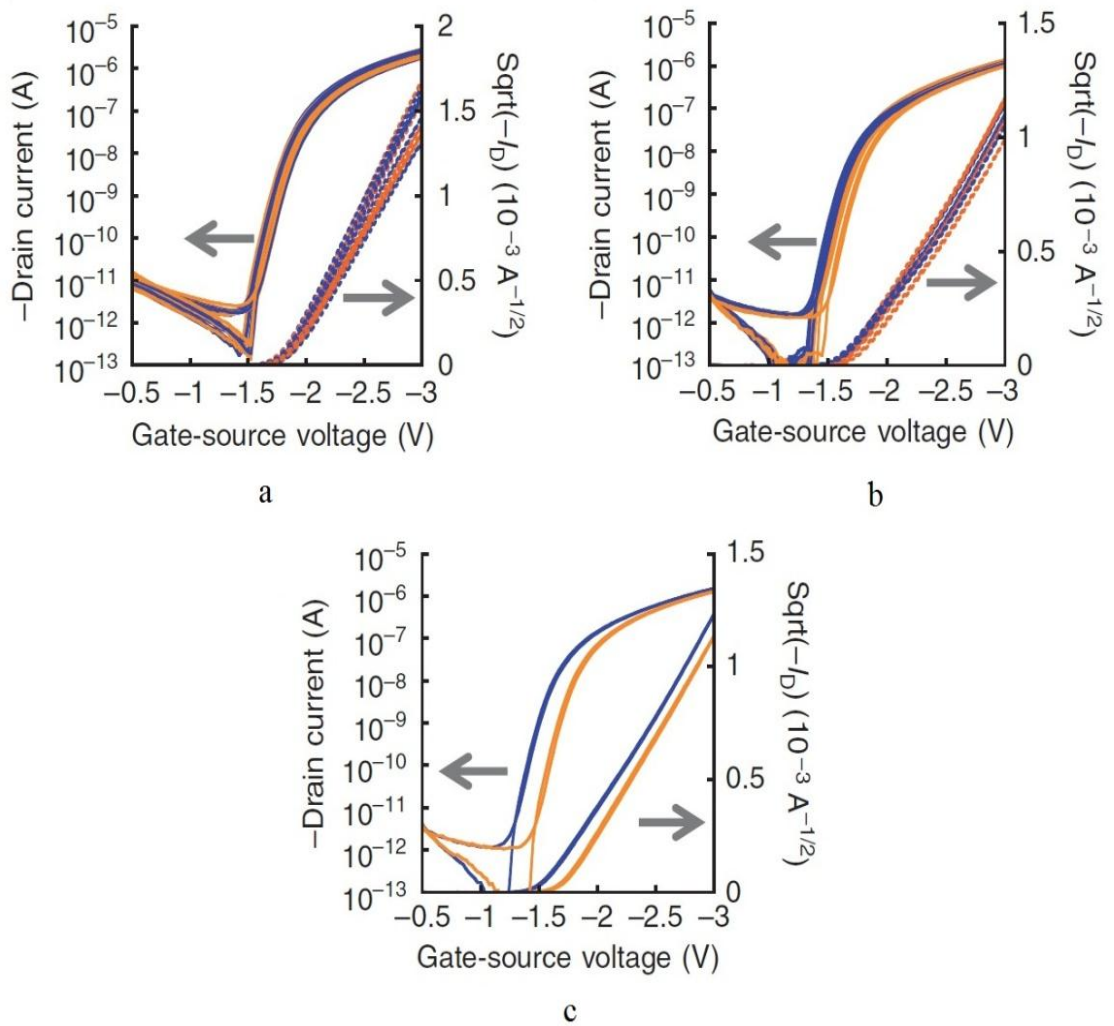


Figure 07: a) Transfer curves of a DNTT TFT before (blue line) and after (orange line) immersion in boiling water (100 °C) for 30 min; (b) before and after heat treatment at a temperature of 150 °C; and (c) before and after heat treatment at a temperature of 121 °C for 20 min in air. Right axis labels in gate current, square root of drain current [146].

4.1.2. Flexible organic transistor

A Japanese research institute and a German research center demonstrated the flexibility and extreme bending stability of the organic transistor thin film structure shown in Figures 08 & 09. Polyimide substrate based organic transistors were studied for several applications which included also medical applications [149].

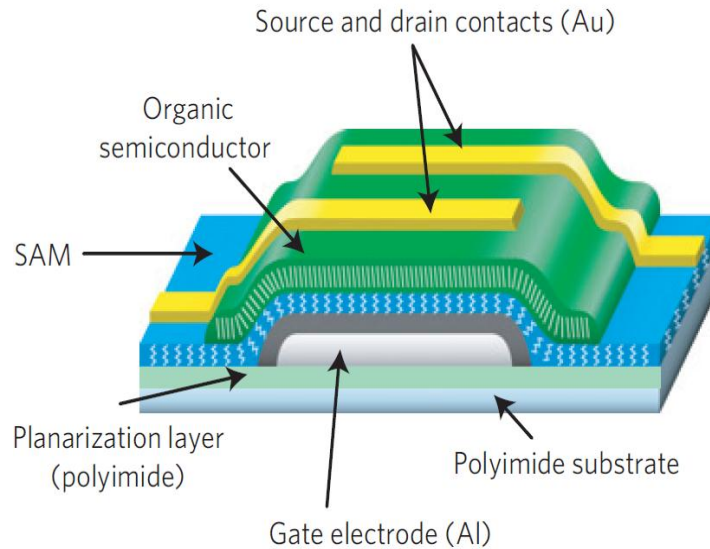


Figure 08: cross-section of polyimide substrate coated Organic TFT [149]

Polyimide is used in insulating layer and passivation layer in digital semiconductor and MEMS chips. Polyimide layer provides good mechanical and tensile strength to the transistor structure. This enhances the adhesion between different layers such as, polyimide to polyimide layers and polyimide to deposited metal (Au) layers [148]. Polyimide has a high temperature stability, which offers reliable insulation during processing and against the environmental stresses [150]. Pentacene was used as a semiconducting material in this OTFT configuration. Pentacene consists of five linearly-fused benzene rings, which makes it highly conjugated compound and suitable to be an organic semiconductor layer in OTFT configuration [149].

A hexadecafluorophthalocyanine ($F_{16}CuPc$) n-channel TFT based five-stage complementary ring oscillator was fabricated on a 500nm polyimide substrate. With a supply voltage of 3V, it was demonstrated in normal state and while bent into 300 μ m radius (figure 10 a). The circuit shows similar response in both cases.

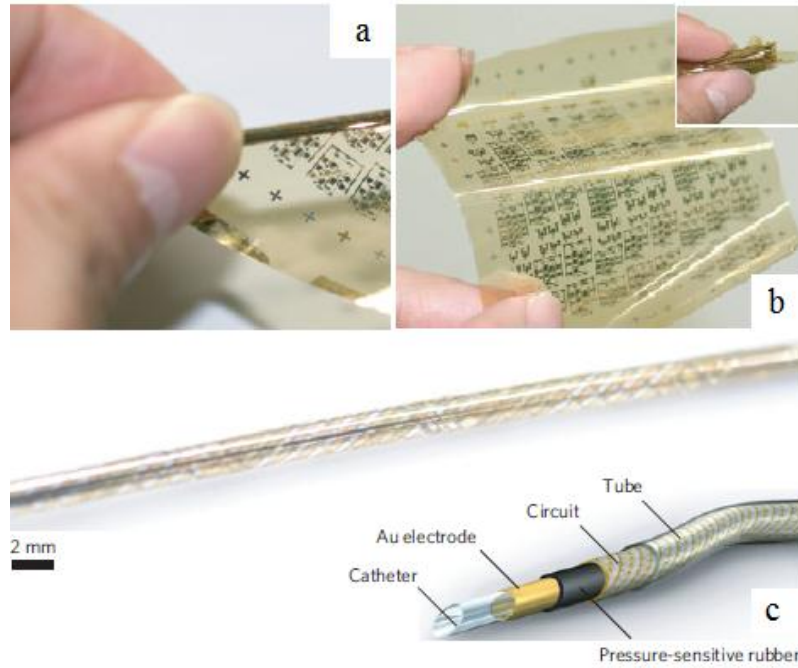


Figure 09: a) Rolled organic TFT printed circuit, b) extremely bendable and foldable organic TFT printed circuit, functions quite nicely c) Printed circuit fed rolled in catheter for detecting spatial detection of pressure along its length. [149]

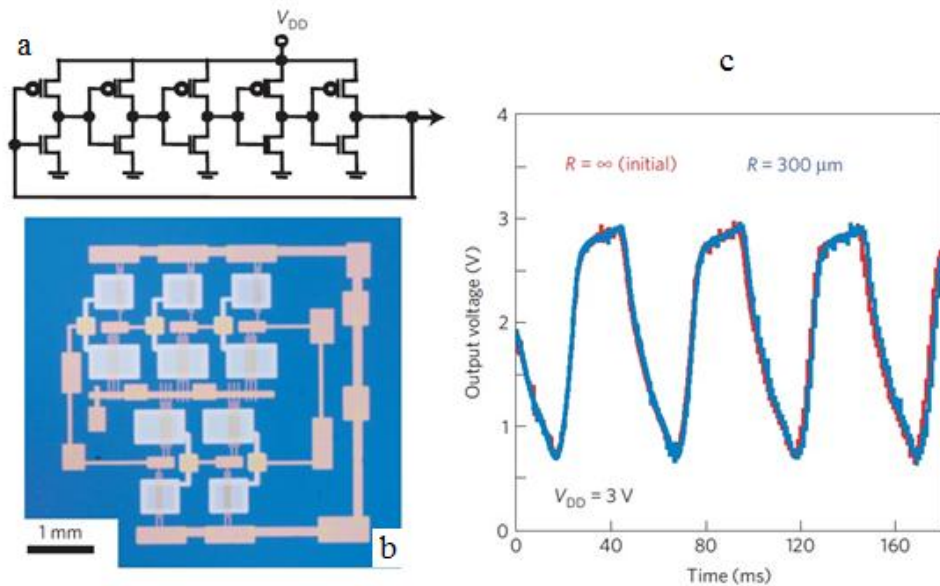


Figure 10: a) Schematic of five-stage complementary ring oscillator, b) Printed layout deposited on substrate, c) output signals the complementary ring oscillator operated with a supply voltage (V_{DD}) of 3 V in the flat state (red line) and while bent into a radius of $300 \mu\text{m}$ (blue line) [149].

Bendability and Flexibility of OTFT was reported in other publications, where OTFTs were fabricated on a variety of substrate materials that included foils, [154] fibers, [10] and paper [11-13]. Figures 11 & 12 represent applications of flexible operations.

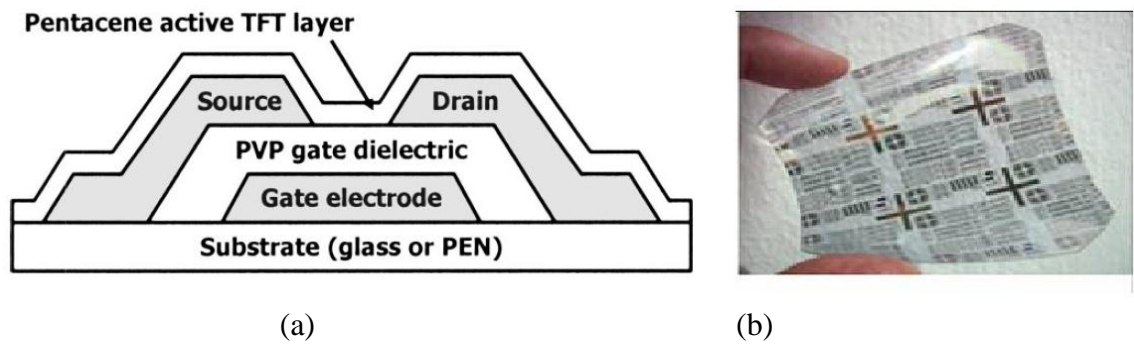


Figure 11: a) schematic cross section of a pentacene TFT. b) Photograph of flexible PEN substrate with pentacene TFTs and integrated circuits [13].

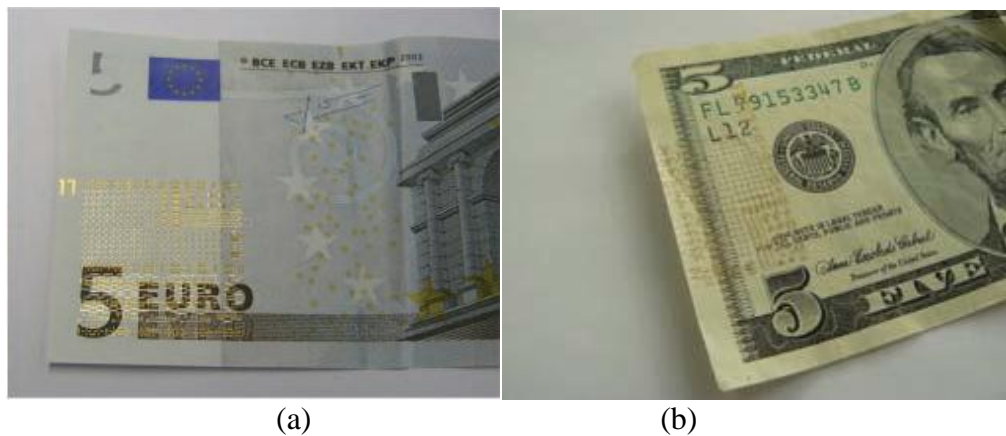


Figure 12: Pentacene semiconductor based organic TFTs embedded on a) 5 euro and b) a 5 USD banknote. [147]

4.1.3. Air stability of transistors

When exposing the organic thin film transistors (TFTs) to air the electrical performance of the devices often degrades over time. It is due to the oxidation of the conjugated molecules in the presence of e.g. oxygen, water vapor [159]. Oxidation affects the charge carrier transport because of the changes in energies of the molecular orbitals. Yamamoto and Takimiya have recently reported DNTT with good air stability for TFTs fabricated on Si/SiO₂ substrates. This DNTT and PEN based OTFT has been studied and the Figure 13 shows the carrier mobility of the DNTT TFT to be 50% of its initial state [160]. Figure 13 (a) shows the current–voltage characteristics of a DNTT TFT embedded on a PEN substrate recorded shortly after device fabrication to air exposure. The TFT showed charge carrier mobility of 0.6 cm²V⁻¹s⁻¹, on/off current ratio of 10⁶ and sub-threshold swing of 150 mV per decade which is similar to that of figure 13 (b)

except the decrease in carrier mobility to 50% ($0.3 \text{ cm}^2\text{V}^{-1}\text{s}^{-1}$). For the comparison pentacene TFT that is easily prone to oxidizing TFT was tested (Figure 13 c). Pentacene showed much less stable performance just in three month time span. [159]

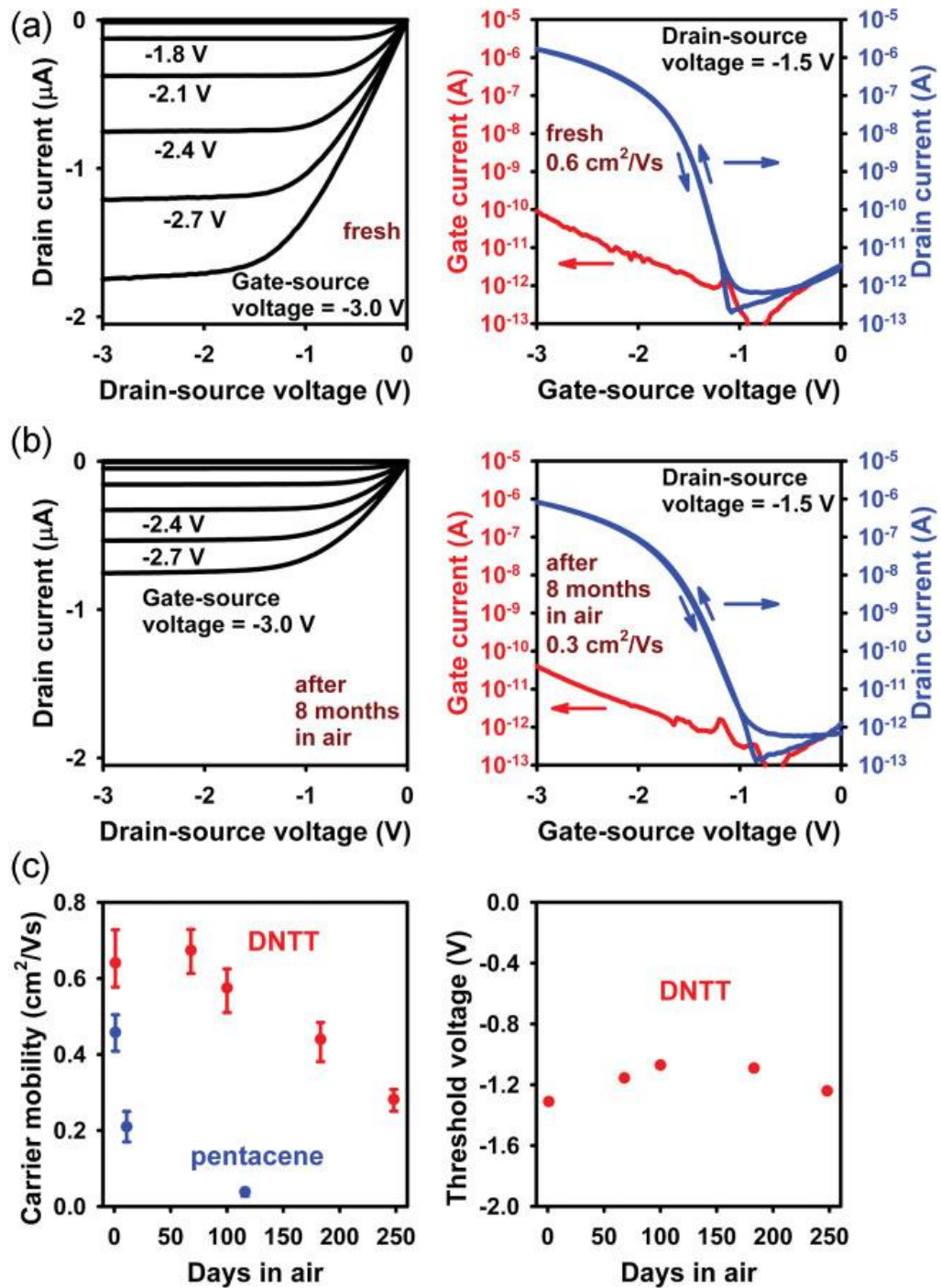


Figure 13: IV-characteristics (current-voltage) of a DNTT TFT on a flexible PEN substrate. a) Transistor characteristics curve right after device fabrication. b) Transistor characteristics curve after 8 months in air exposure. c) Charge carrier mobility (comparing charge carrier mobility of a pentacene TFT) and threshold voltage over time are shown in separate response curves [159].

4.1.4. Fully degradable transistor

Chemical engineers Bettinger and Zhenan from Stanford University successfully demonstrated an entirely degradable transistor deposited on resorbable substrate biomaterial.

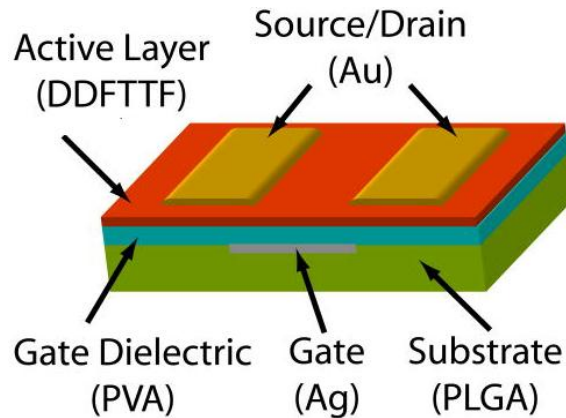


Figure 14: the device geometry of organic transistor deposited on PLGA substrate [164].

Figure 14 shows an organic PLGA substrate based organic transistor. In the device geometry, PLGA has $1 \times 1 \text{ cm}^2$ area and 2 mm of thickness, comprising the major part (99.89% mass of the device) of the device. PLGA used here is of high relative amount of lactic acid, PLGA 85:15) which enables glass-transition temperature [14]. However, Ag gate contacts were printed though shadow masking and thin layers of gold contacts were used. DDFTTF or [5, 5']-bis-(7-dodecyl-9H-fluorene-2-yl)-2, 2'-bithiophene] was used as semiconductor layer due to its favorable properties under aqueous conditions [164, 165]. PVA dielectric layer of 1mm was utilized to serve as an effective dielectric [164, 170, 171]. Non-cross-linked PVA (nPVA) and photo-cross-linked PVA (xPVA) films were used for separate configurations with roughness values of 0.31 and 0.24 nm, respectively. Conducting metals silver (Ag) and gold (Au) were used for electrical contacts with the consideration that both are potentially suitable for use in medical devices.

DDFTTF semiconducting layers exhibited high mobilities and on-off ratios for both (a) nPVA and (b) xPVA dielectrics (figure 15 a, b). Device performances are demonstrated by drain-source current (I_{DS}) to gate voltage (V_g) and drain-source voltage (V_{DS}) for both dielectric layers [164].

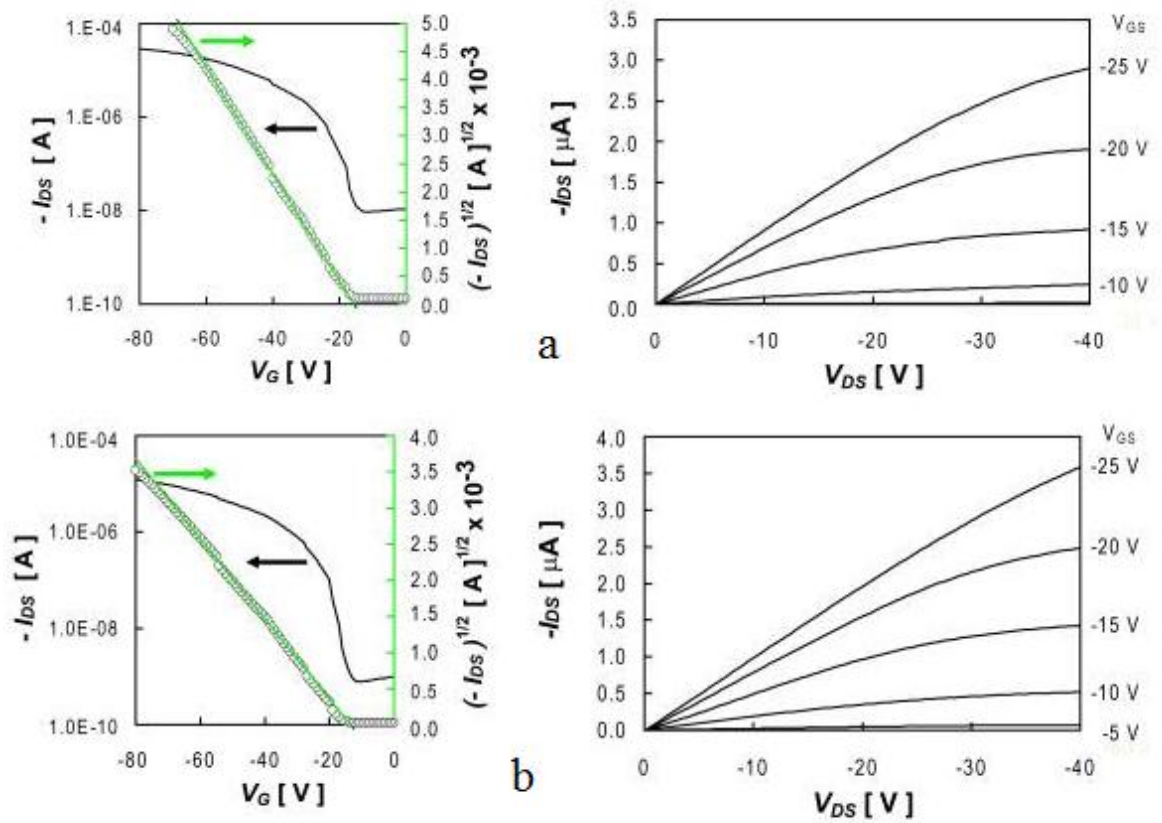
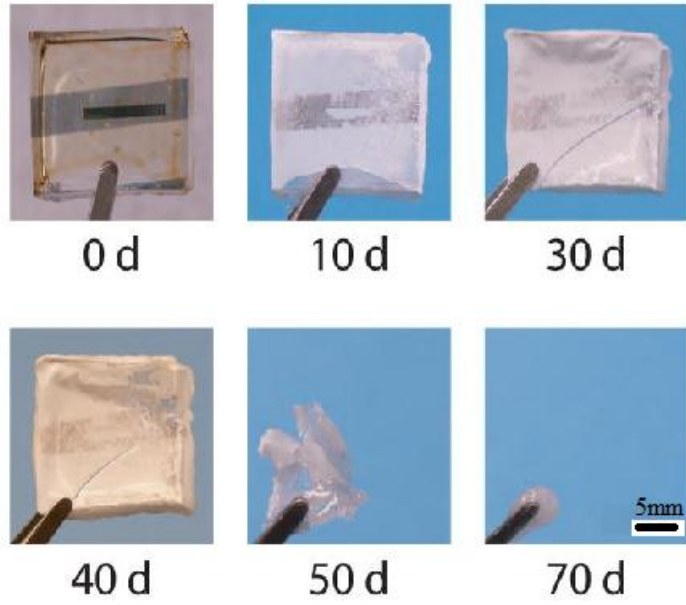
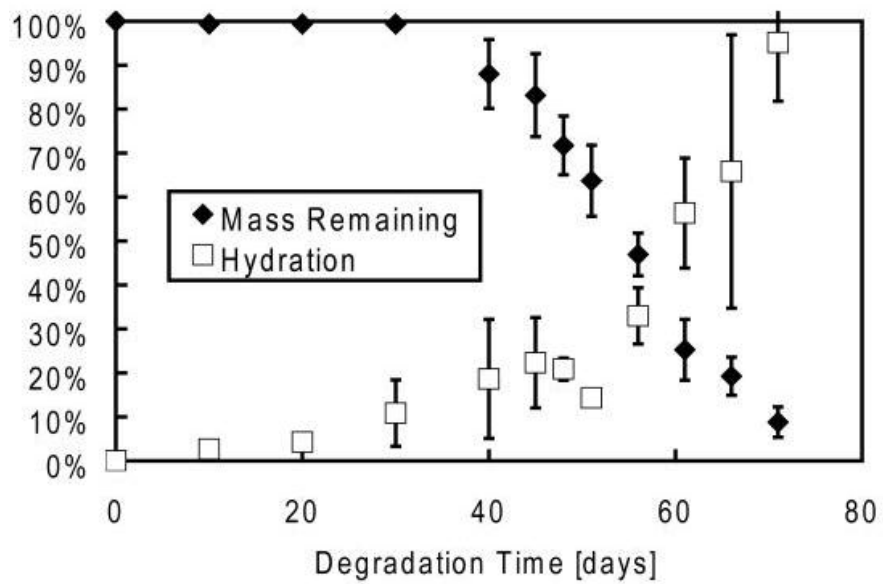


Figure 15: Dielectric based on (a) nPVA exhibits carrier mobility of $0.153 \text{ cm}^2\text{-sec}^{-1}\text{-V}^{-1}$, on/off current ratio of 3.49×10^3 with a threshold voltage of -15.6 V . in the case of xPVA dielectric based transistor shows (b) mobility of $0.060 \text{ cm}^2\text{-sec}^{-1}\text{-V}^{-1}$, on/off current ratio of 2.93×10^3 a threshold voltage of -13.6 V [164].

In vitro degradation of this organic transistor is shown in various stages of the degradation (Figure 16 a). The time line suggests that device integrity was intact up to 40 days with near total device resorption at 70 days. Devices also transitioned from being initially optically transparent (0 days) to opaque within 10 days. The mass reduction and water uptake (hydration) is demonstrated in Figure 16 (b). The device is deposited on PLGA substrate which is initially seen to be stable; resistant to water uptake and degradation. However, significant mass loss and water uptake were noted after 30 days of immersion in citrate buffer solution of $\text{pH} = 4.0$ at $37 \text{ }^\circ\text{C}$. Near total mass loss and 100% device hydration was observed at 70 days. They estimated that this device has a potential for biomedical or environmental applications due to the adequate performance of PVA dielectrics after direct exposure of the semiconducting layer to aqueous environment for prolonged time [164].



a



b

Figure 16: a) In Vitro Degradation of Organic transistor at various stages of the degradation (Scale bar represents 5 mm for all panels) b) A plot of mass remaining and water uptake by mass is demonstrated [164].

4.2. Active electronic components

Physically transient form of silicon electronics have been investigated by Rogers et al (2012). Magnesium (Mg) as conductors, magnesium oxide (MgO) as dielectrics, monocrystalline silicon (Si) nanomembranes (NMs) as semiconductors was embedded into silk substrate. Silk substrate is soluble in water and enzymatically degradable [189]. The schematic illustration of the entire system is shown in Figure 17(a), (b). The fabrication involves transfer printing of Si NMs, vapor deposition of Mg, MgO, and SiO₂ layer, and solution-casting of silk substrate [7].

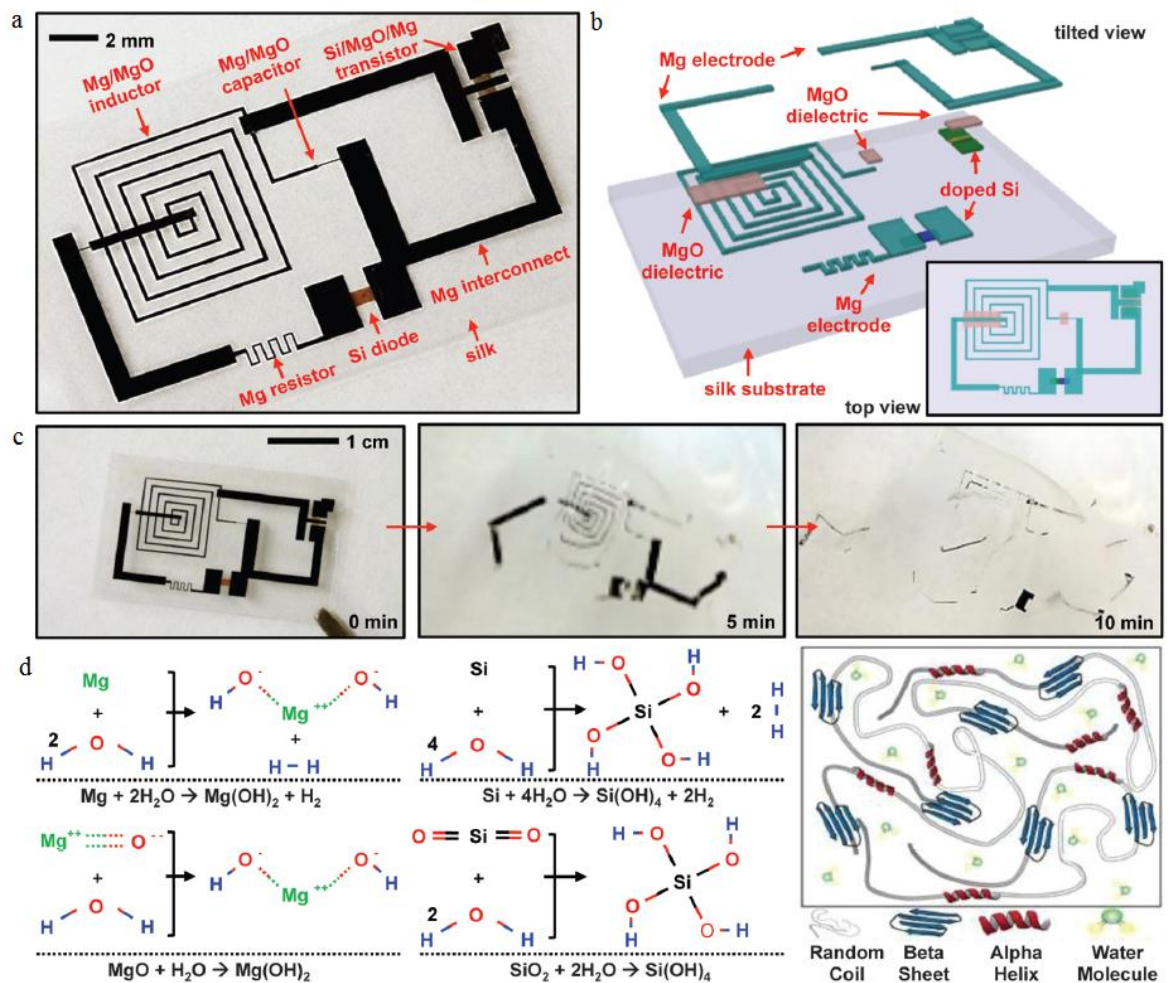


Figure 17: a) A device consisting of transistor, diode, inductor, capacitor, and resistor, with interconnecting wires and interlayer dielectrics embedded into silk substrate; b) schematic illustration of titled view, with a top view inset; c) dissolution in de ionized water in time frame of 0 to 10 minutes; d) Chemical reactions for each of the constituent materials with water [7].

The chemical reactions involved in the dissolution of the constituent materials appear in Fig. 17(d). The main membrane layer geometry of Si and SiO₂ is particularly important

and critical. It plays an important role in high performance transistors, diodes, photo detectors, temperature sensors etc. The planar configuration minimizes the use of material and provides mechanical stability. It further enables processing options that are favorable when integrating it into substrates like silk [189] or elastomers [190].

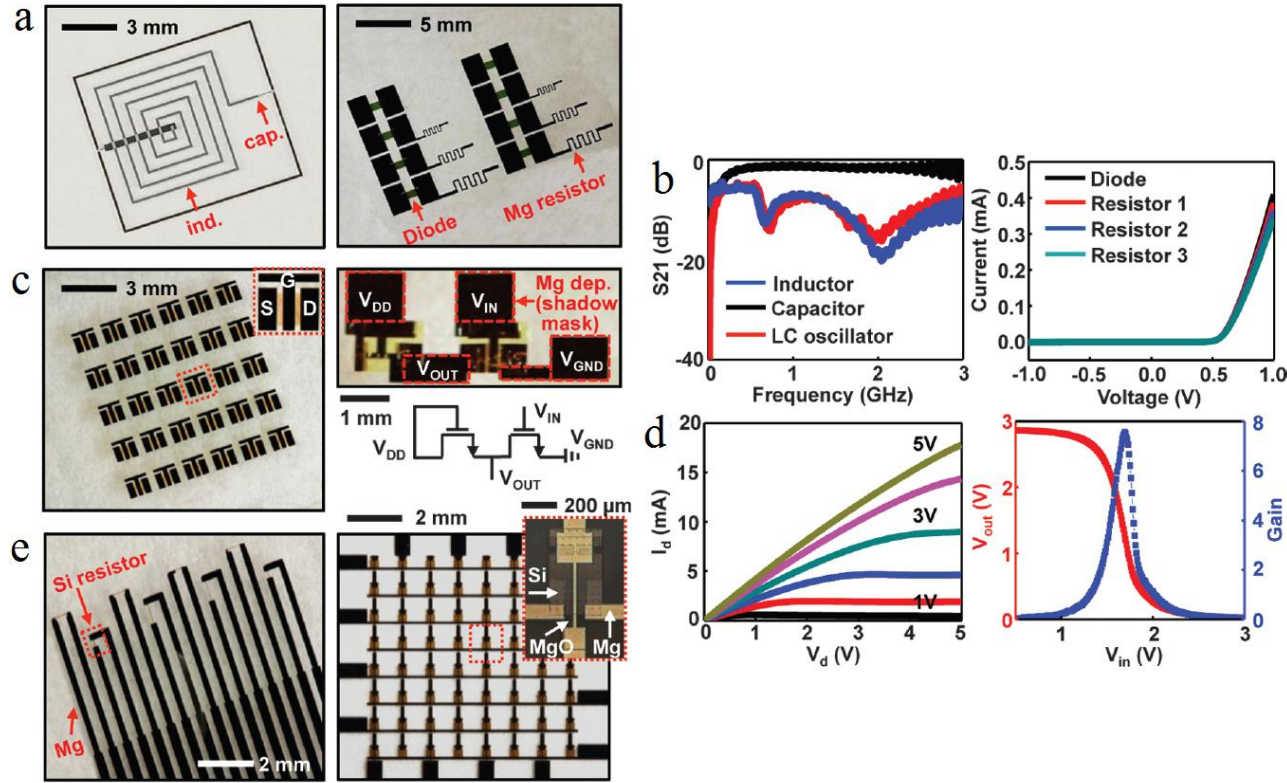


Figure 18: a) An LC (inductor-capacitor) oscillator made with Mg and MgO dielectric layer (left) and an array of Si nanomembrane diodes connected with serpentine Mg resistors (right). b) Measurement of scattering parameter of an inductor (blue line), capacitor (black line), and LC oscillator (red line) at different frequencies up to 3 GHz (left). I-V characteristics of diodes connected to three individual samples of Mg resistors. c) Array of p-channel MOSFETs (left) and logic gate inverter composed of n-channel MOSFETs (right). d) I-V characteristics of an n-channel MOSFET (left). The voltage gain for such transfer curve is about 8 (right). e) Si nanomembrane resistors (left) and an array of Si nanomembrane photodetectors with blocking diodes [7].

The p-channel MOSFETs utilize (figure 18 c) channel length (L_{ch}) and width (W) of 20 mm and 900 mm, respectively and the n-channel MOSFETs utilize L_{ch} and W of 20 mm and 700 mm for the input transistor and 500 mm and 40 mm for the load transistor, respectively. The MOSFETs use Mg as source (S), drain (D), and gate (G) material, MgO as gate dielectrics and Si as a nanomembrane for the semiconducting layer. The inverter uses Mg for interconnecting lines and Au for source, drain, and gate electrodes, in the circuit configuration. However, ever, in both cases, Mg serves as contact and interconnecting lines and MgO as the dielectric [7].

The three individual Si nanomembrane samples yield thicknesses 35nm, 70 nm and 100nm. The degradation profile at 37 °C has been illustrated in fig 19 (a). Various MgO and silk substrate has been used for the encapsulation, such as MgO of 400 nm and 800 nm and silk of different conditions. The thicknesses have impact on the degradation of the device. Fig19 (a), the thickness of 100 nm degraded later than 70nm thick nanomaembrane and so on. [7].

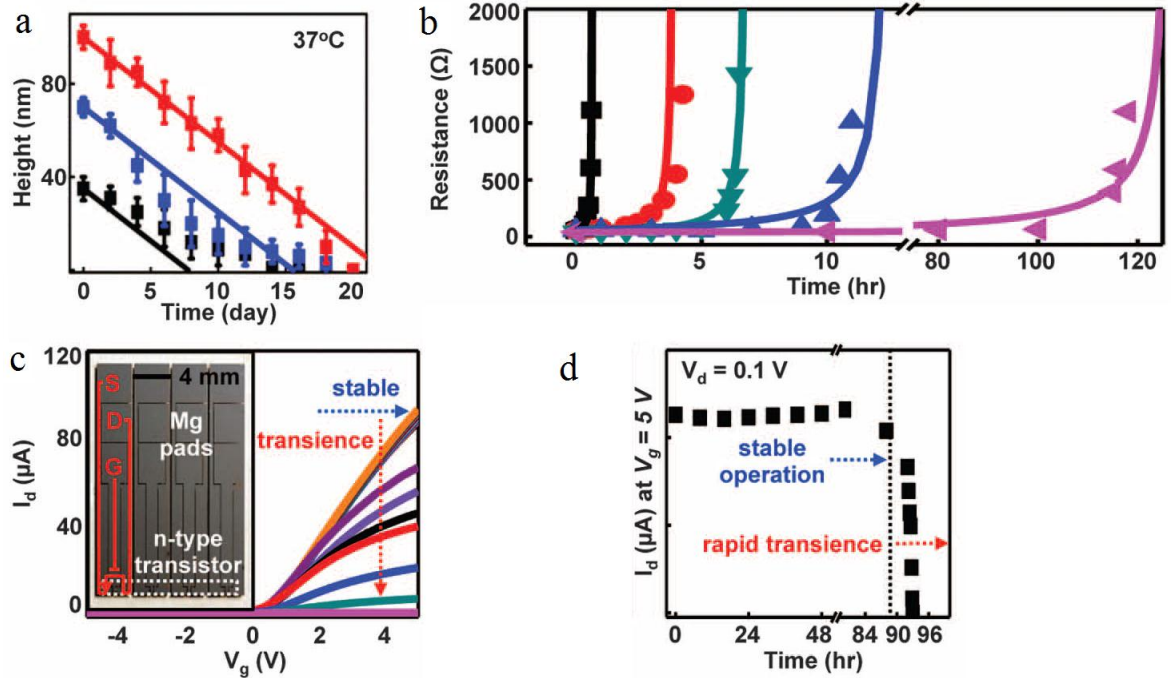


Figure 19: a) Experimental (square symbols) and theoretical (solid lines) results for time dependent dissolution of Si nanomembranes of different thicknesses; black, blue and red color indicates 35nm, 70 nm and 100nm Si NMs respectively at 37 °C. b) Experimental (symbols) and theoretical (solid lines) results of dissolution kinetics of similar traces of Mg with different encapsulating layers; MgO of 400 nm (red) and 800 nm (blue) and silk of different conditions are represented by cyan and purple c) Operational characteristics of n-channel transistors encapsulated by MgO and crystallized silk and then immersed in deionized water and the transience is studied [7].

4.3. Discussion (Current applications)

Polymers as organic compound are found to be very good candidate as conducting materials for organic to biodegradable electronics. Organic compounds have a wide range of conductivity; for example, from pure anthracene to metallic even superconductive in few cases such as charge transfer salt [114]. Polyacetylene, polythioacetylene, polypyrroles, polythiophenes, PEDOTs are being used widely in several transistor configurations. Beside organic compounds, inorganic materials still plays a very important role in organic and biodegradable electronics. Metals as

biomaterial are still used for effective conduction and enough carrier charge injection. Charge injection from the contact electrode must be efficient for the proper function of organic transistor. Work function of the electrode is required to be matched properly with organic semiconductor energy level, so that the energy barrier becomes low. High work function electrodes such as Au, Pd, or indium tin oxide are used. [199]. However, some metals don't evoke biofouling events in biological environment. For example, silver is used in organic transistors. Due to the biocompatibility and antimicrobial property that Ag exhibits in vitro and in vivo, it is always been preferred in medical applications [166, 167]. Gold being a bioinert material exhibits less biofouling in vivo and has been used in biomedical applications such as including cardiovascular [168] and BioMEMS devices [169]. Also, using self-assembled monolayer (SAM), electron surface modification can be achieved to can be used to improve the charge injection [199]. The source and drain electrodes utilize organic semiconductor deposition, interestingly, the organic semiconductor morphology differs significantly when deposited on self-assembled monolayer treated Au compared to bare Au layer. This observation helps to tune the organic semiconductor morphology; the organic interface to improve charge injection into organic semiconductor [200]. Cost in manufacturing processes yield solution processible electrode materials. Some of the research groups have developed Au or Ag nanoparticle inks. These nanoparticle inks can compatible with low cost plastic substrates, because they can be cured below 200 °C [201]. Conducting polymer solutions could also be potential electrode material candidates.

Organic semiconducting materials, such as p-type and n-type organic polymers are also used instead of silicon. Some transistor configurations utilize ultra-thin silicon sheet as well. Both types of organic semiconductor polymers are being developed to reduce the perdurable dependency of silicon in electronics. However, p-type organic semiconductors are more preferred than n-type organic semiconducting polymers. This is due to reduction of the conducting polymer or n-doping, is much less common than p-doping. Also, the number of cycle needed for the reductive doping is much higher than that of the oxidative doping. Moreover, the reductive doping appeared to be kinetically limited [202]. However, Appendix B and C state some newly developed organic semiconducting polymers.

Some of the material configurations are found to be very good candidate to build organic and biodegradable transistor with robust and consistent performance. High capacitive gate dielectric property is ensures better thermal stability in operation; for example DNNT and alkylphosphonic molecule combination facilitates such property. Good thermal stability can be achieved by transistor configurations utilizing the combination of pentacene semiconducting layer and polyimide (PI) dielectric layer to facilitate a good thermal stability even at the exposure of 160⁰ C. However, OTFTs utilizing pentacene and PI have reported to have limitations in their operation due to the oxidization of pentacene to 6, 13-pentacenequinone and polyimide requires an operating voltage 20V or more which limits the potential in medical applications because of exceeding safety limits of medical instrumentations [146]. In addition to that, Pentacene based TFTs possess less air stability. The larger ionization potential of DNNT can be utilized in such cases. DNNT exhibits ionization potential of 5.4 eV compared with that of pentacene (5.0 eV) may provide a dramatic improvement in the air stability of the transistors. Better air stability can be achieved by synthesizing

conjugated molecules with even larger ionization potential e.g. approaching 6.0 eV, with similar configuration to ensure large carrier mobility. However, such large ionization potential will cause a significant energy barrier at source and drain contacts, which may result in excessive contact resistance [161].

For organic thin-film transistor, densely packed and pin-hole free dielectric layer is crucial. Smooth aluminum gate electrode deposition is an important prerequisite for the formation of a dense and pinhole-free gate dielectric. Usually, printing or other solution-based processes are followed [184, 185] for the deposition process. However, further improvements can be achieved by printing inorganic semiconducting nanowires or nano-ribbons [186].

An encapsulation layer should meet following criteria. For oxygen and water and other molecules, there should have low gas/fluid permeability. The organic semiconductor layer should have minimum damage effect during the deposition process. The volatility of the organic semiconductor molecules should be suppressed during temperature increase. The materials should be biocompatible and environment friendly. Parylene encapsulation of TFTs utilizes such characteristics for potential in diverse applications. Parylene is useful to encapsulate pentacene based transistors [162, 163]. However, the demonstration of parylene encapsulation for DNTT TFTs with SAM-based gate dielectrics was also found to be successful. Although in this case achieving high mobility ($1.2 \text{ cm}^2\text{V}^{-1}\text{s}^{-1}$) and high thermal stability ($150 \text{ }^\circ\text{C}$) were crucial to meet.

Solution processing methods are usually used for depositing thin films of soluble conjugated polymers. But, small molecules, because of their insolubility typically require deposition via vacuum sublimation. Both approaches yield amorphous films with variable degree of disorder. In wet-coating techniques polymers are dissolved in a volatile solvent, and then filtered and deposited onto a substrate. Drop casting, spin-coating, doctor-blading, inkjet printing and screen printing are common examples of solvent based coating techniques. Spin-coating is a favorable technique for small area thin film production. [179].

5. DISCUSSION (THEORETICAL PART)

Organic to biodegradable electronics are potential for both consumer and medical electronics. The present electronic technologies are in need of such approaches that can avoid the limitations of traditional silicon electronic technology. Cost [13, 14] and complex manufacturing processes [5, 13] are two main limitations of silicon electronic technology. However, existing and envisioned classes of implantable medical devices are also in need of much care. In the case of biomedical applications, rigid and hard structure, compatibility complexity in biological tissue, long term challenges are also adding to the limitations. Organic and biodegradable electronics are to outcast such limitations. However, There are currently two approaches existing towards organic electronics found from the review study which may offer solution to the issue of cost and manufacturing complexity and other stated limitations; conventional electronics used in biodegradable substrate material [5, 13] and another one is bioresorbable electronics [7, 13]. Both of the approaches of present path to biodegradable electronics, have their own ground of advantages and disadvantages and preferred application areas. Conventional electronics used in biodegradable substrate materials are efficient, reliable and robust in operation, but at the same time bioresorbable electronics possess potential for developing biocompatible, resorbable and even metabolizable devices [2, 5]. Basically, the latter approach is the advancement and future of the organic substrate based conventional electronics. Conventional electronics used in flexible and biodegradable are utilized in sensing applications where efficiency is required. Silicon electronics are still found to be much more efficient than organic materials and molecules. While on the other hand, bioresorbable electronic technology is under development to meet necessary performance criteria.

Different kinds of natural and synthetic polymers, protein and fibroin protein [1, 5], natural pigments [5] and even biodegradable metal and metal alloys [7, 15, 16] are studied and they found to be potential candidates for biodegradable electronics. Organic materials possess potential for flexible organic and biodegradable electronic devices. Significant progress and achievement have already left remarks of success. However, a fundamental study of the structural property relationship is still a prerequisite for the rationally modified and improved materials to achieve device performance parameters to a desired level.

Polymer plays a vital role in biomaterials. Several polymers have been investigated for biocompatible, biostable to biodegradable and bioresorbable biomaterials. Thus polymers as organic materials used in organic or biodegradable electronics are of great potential. Polymer provides flexible substrate for organic electronics. Moreover, the option of tailoring properties of polymer has also enables the desired modifications to meet the expectation. Polymer ensures the long term challenge for active implantable device with necessary biocompatibility.

Organic to biodegradable transistor, thin-film transistor yield potential in medical applications. Extremely flexible, bendable organic thin-film transistors possess

prospect in biomedical applications such as biosensors, detectors etc. Flexibility and bendability enables easy insertion of biosensors consisting microelectrode arrays, printable logic circuits etc. Such configurations can be inserted as rolled in catheter for spatial detection of biological events along its length. It also ensures minimum invasive process. The thermal stability, good air stability ensures the uninterrupted detection and durability for medical applications. Biodegradability avoids the removal surgery of the active medical implant device. However, achieving desired degrading rate and manner is often hard to achieve. Biodegradable electronics is utilizing degradable to non-degradable and organic to inorganic materials. However, the technological advancement is subjected to develop electronic system with degradability and elevated biocompatibility. Such approach is very much suitable for biosensor technology.

With immense potential, biodegradable electronic technology is becoming an emerging technology not only for medical electronic applications but also for consumer electronics. This is because of the low manufacturing cost and less complex manufacturing techniques offered by biodegradable electronics. However, because of the need for a universal manufacturing process, they still remain costly to some extent. Moreover, strongest challenge would be achieving high and reliable performance in contrast to silicon based electronics. If the challenges regarding biodegradable electronics can be overcome, that would be advantageous and widely applicable in implantable medical device to consumer electronics. Steady advancement in the quality and variety of available and tailored organic conductors to semiconductors, as well as fundamental study of materials physics, organic chemistry and device engineering may enable the future of biodegradable electronics.

EXPERIMENTAL PART

Contribution to the writer:

The experiment part was done along with my colleague M.Sc. Timo Salpavaara. The handmade LC resonator circuits and the biodegradable encapsulation were prepared by the writer. Mr. Salpavaara made the experimental setup, necessary signal processing work and recorded the characteristic curves for feature extraction.

6. Biodegradable Encapsulation for inductively measured resonance circuit

This experiment comprises the study of the feasibility of biodegradable encapsulation of the LC resonance circuit. Existing LC resonance circuit based biosensors are mainly encapsulated or embedded on biostable polymers or substrate materials for demonstration and research purposes [191- 193]. The reason behind using biostable material could be the repeatable use of the sensor. These resonance circuits are commonly used for wearable or even implantable sensors. However, this study was to encapsulate LC resonance circuit by biodegradable substrate material to observe its behavioral response after immersion in fluid. The main objective of this experiment includes:

1. Inspecting feasibility of the biodegradable polymeric encapsulation for a LC resonance circuit and the reliability of measurement method
2. Study the extracted features to monitor the water absorption.

Polycaprolactone (PCL) and 70/30 poly-L-lactide/caprolactone (PLCL) were used in this experiment. The encapsulated circuits or sensors were immersed into phosphate buffer solution and observed for an 80days span of testing. The phase and magnitude responses were observed using an inductive link.

6.1. Background

An LC circuit is an electrical analogue of a tuning fork; hence it is also known as tuned circuit. When an inductor (L) and a capacitor (C) are connected together, the combination may work as an electrical resonator, so they are also known as resonant circuit. Due to their resonance behavior, they have a potential in sensor technology e.g. measurement of different biological variables. In sensor technology, they are commonly known as passive resonance sensors. It is called 'passive' because, the responses are measured wirelessly via an inductive link by a reader coil held externally. The passive resonance sensors have been widely used for measuring pressure [192], chemical signals [195] and biopotential signals [193]. The working principle is based on near field wireless transmission of electrical energy between two coils held by

mutual inductance (Figure 20). An LC circuit can store electrical energy oscillating at its resonant frequency. An available voltage across the two plates of a capacitor allows it to store energy in the electric field between the plates. An inductor stores energy in its magnetic field, depending on the available current that passes through it. So, if a charged capacitor is connected across an inductor, an LC circuit should oscillate at its resonant frequency. Ideally, an LC circuit is assumed to be free from resistive loss thereby no dissipation of energy throughout oscillation is seen. However, a practical LC circuit will always include very small but non-zero resistance in the wires connecting the circuit elements, series and shunt resistances associated within the elements themselves.

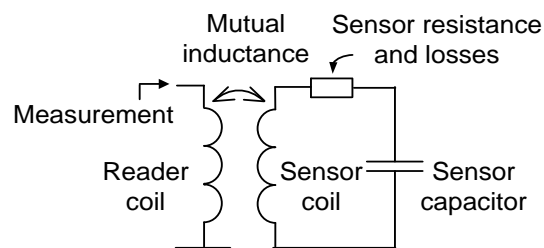


Figure 20: Working principal of passive resonance measurement

There are mainly two distinguishing advantages of using such sensors. For one the simplified and structurally small sensor enables developing new sensors utilizing different substrate materials for demonstration. And second, the making of wireless measurements through the nonconductive medium is enabled. These advantages of passive sensors are making vistas to develop an entirely biodegradable sensor. Entirely biodegradable resonance sensors are demonstrated experimentally made of biodegradable metal and polymers. [196] However, it still remains a challenge to have them functioning reliably, especially in aqueous medium.

The resonance response of LC circuits which are not isolated from environment by a dielectric mean is prone to be deteriorated by the permittivity and conductivity of the environment. The parasitic capacitance allows the permittivity to shift the resonance frequency and the conductivity leads to resistive loss which reduces the Q-factor. Thus the desired frame is reduced to detect the resonance frequency from the response. However, a dielectric encapsulation is needed to reduce the effect of environment. Resonance circuits, especially for biopotential applications, are usually encapsulated by polymeric material. In this study we demonstrated biodegradable polymeric materials to study biodegradable passive resonance sensors.

6.2. Materials and methods

This section presents the description of handmade resonance circuit and the encapsulation process. The experimental setup for the demonstration of the circuits is also documented.

6.2.1. Resonance circuit

The LC circuits were made of non-degradable materials. The sensor has three main parts; a 3-turn coil made of insulated copper wire with a round cross-section thickness of 0.17mm. A 22pF surface mounted capacitor (0603 SMD casing) is soldered with the free ends of coil to yield LC circuit. Parallel planner capacitors are commonly used in sensors, but they have much influence of environmental changes compared to bulk capacitor. Bulk capacitor 0603 SMD was used instead of parallel plane configuration to achieve better stability in performance and controlling the dimension during manufacturing. The bulk capacitor was soldered on the two open left ends of the wounded coil.



Figure 21: Handmade resonance sensors before biodegradable encapsulation

6.2.2. Circuit encapsulation

The encapsulation procedure is based on compression molding. The polymer granules Poly(lactide-caprolactone) copolymer (PLCL) and Polycaprolactone (PCL) (Purac biochem bv, Gorinchem, The Netherlands) were vacuum-dried in vacuum chamber prior the compression and then compressed to polymer sheets of specific thickness by applying pressure and temperature. The sensor circuit was then covered by two polymer sheets on the either sides to encapsulate the circuit into predefined thickness. Heat and pressure was applied when embedding the component into the polymer. Due to the limitations of compression molding process some air bubbles were formed. However, they were removed by melting some more granules or threads to fill the air bubbles and apply pressure to enforce the packing (Figure 23). Later the embedded part of polymers sheet were cut into disk shape. After they were cut to disc shape the dimensions were measured. The final thickness of the encapsulated samples varied from 2.24 mm to 2.40mm.

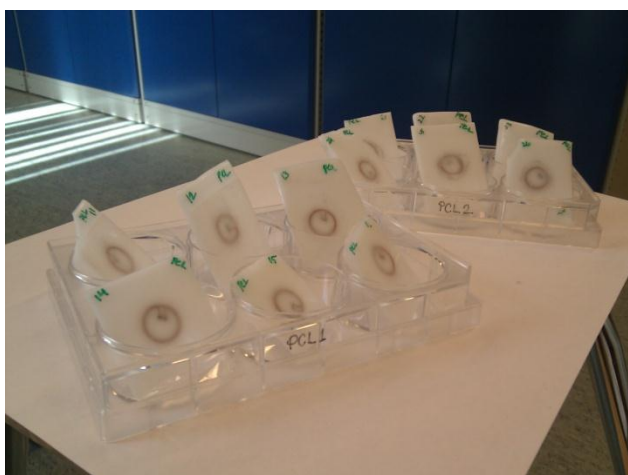


Figure 23: Resonance sensors after biodegradable encapsulation kept in 6-well plate (before cutting into disc shape)

6.2.3. Measurement setup

The behavioral responses were measured wirelessly through the inductive link. The circuit was kept in Sørensen phosphate buffer solution (PBS) inside a closed cell well plate (Figure 24). The measurements were observed with a hand held reader device [198]. The frequency resolution for the measured data points was 100 kHz. . In this experiment the encapsulated resonance circuit was submerged into 10 ml of the buffer solution in 6-well plate. The temperature was maintained 37°C. A flat reader coil (diameter of 40mm) was used to observe phase and magnitude responses. Each sensor on the well plate was measured underneath the well plate for a span of 80 days of observation.

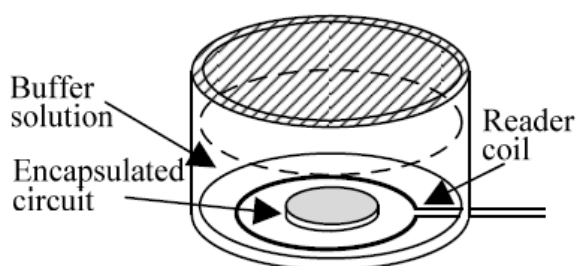


Figure 24: Experimental set-up

6.3. Results

6.3.1. Encapsulation observations

As PLCL needs higher temperature for melt-processing, the encapsulation process became somewhat unreliable due the limitations in processing method. Some of the testing circuits were damaged during the melt-processing under pressure in compression molding machine. Overall, encapsulation of PLCL was found to be irregular. However, both materials were found to be comparatively easy to encapsulate.

6.3.2. Characteristics of measured data

Figure 25 illustrate the impedance phase measurement of a PCL encapsulated resonance sensor. At day 0, when the sensor was submerged, a clear deflect in the resonance induced curve is seen from the dry condition. The phase response is seen to be shifted to lower frequencies and the peak to peak height of the pattern was decreased slightly. However, day 1 shows the peak to peak height of the curve getting notably smaller and pattern to be wider than the previous conditions. After the sensor was stabilized (day 1), it is hard to detect a significant change in the response curve during the 2 month follow-up.

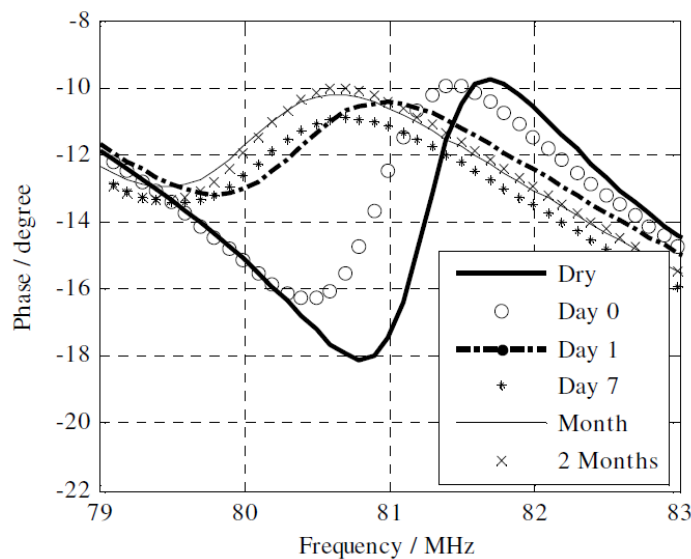


Figure 25: Impedance phase curves of a PCL encapsulated resonance circuit (when immersed in buffer solution)

The impedance phase measurements of the PLCL encapsulated resonance circuit was also studied and is illustrated in Figure 26. The impedance phase curve seen to deflect due to water absorption right after the immersion similarly to the PCL encapsulated resonance circuit.

But a continuous shifting towards lower frequencies and the reduction of the peak to peak height of the curve ended up in invalid level. After two months, it was hard to detect any information from the curve.

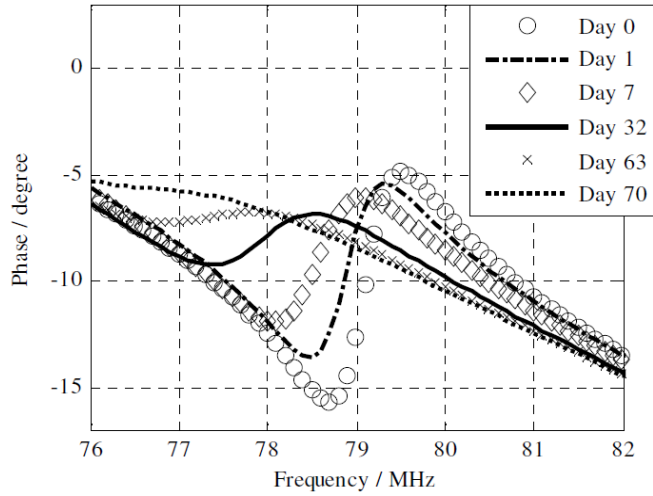


Figure26: Impedance phase curves of a PLCL encapsulated resonance sensor (when immersed in buffer solution)

The magnitude response curve of the PCL encapsulated resonance sensor was also studied. Figure 27 shows the measured magnitude response curve. Similar information as in impedance phase curve can be extracted from this curve also. The dip in the curve is seen to get wider and lower in frequency level.

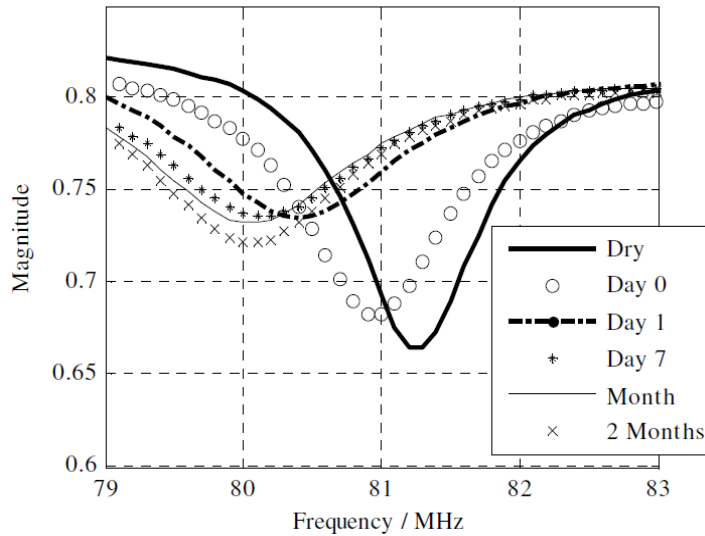


Figure 27: magnitude curves of the PCL encapsulated resonance circuit (when immersed in buffer solution)

6.3.3. Feature extraction

The PDMS encapsulated resonance circuit (provided by Mr. Salpavaara) was the control circuit and the features were estimated from the maxima of the impedance phase response curve. Figure 28 illustrates the frequency shift of the resonance circuits when they were immersed into aqueous medium.

In case of PCL, a clear shift in the frequency response is seen just after the immersion and it continued for five days. Another slight shift is also visible after 20 days

immersion. Initial frequency drop of PLCL encapsulated circuit is higher than that of the PCL one. After that, the frequency drift is seen to drop faster than in PCL encapsulated circuit. There is a significant drop in the frequency after 63 days, but the features could still be observed. It continues to drop further until the elimination of features is detected after 78 days of immersion. In case of PDMS control circuit, the frequency shift is rapid in the first days then it stables.

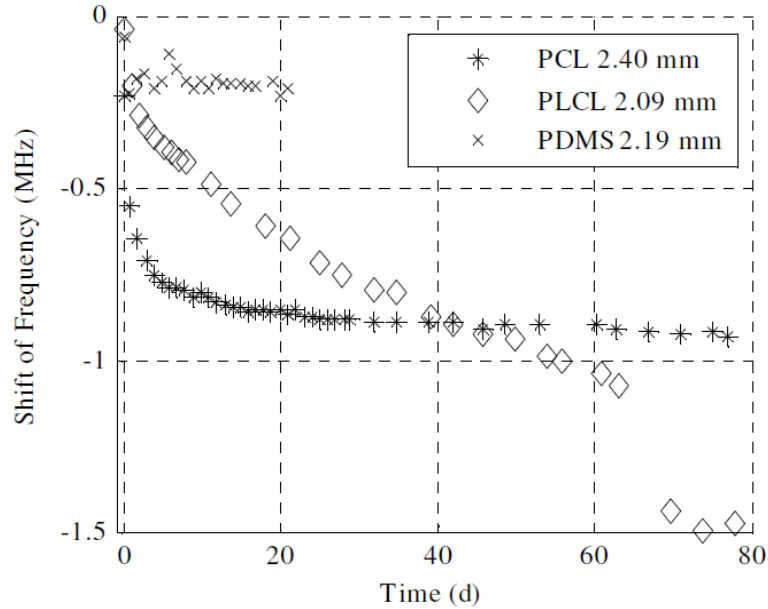


Figure 28: shift of phase maxima of PCL, PLCL, and PDMS encapsulated resonance circuits were observed (immersed in buffer solution)

In Figure 29, the heights and widths information were extracted from the impedance phase response curve. Both of these extracted features are dependent on the Q-factor of the resonator. Also, the height is strongly dependent on the coupling factor between the inductor coils. It is assumed to be remained constant thought out the test. However, In PCL encapsulated resonance sensor, the height of phase curve is seen to drop and the width to be increased right after the immersion. After that it continues with a stabilized path. But in case of PLCL encapsulated resonance sensor, the curve is not seen to be stabilized. It drops quiet steadily after the initial water intake. The width in this case is seen to be widened steadily throughout the 63 days, after which it takes an irregular and rapid pattern. In case of PDMS encapsulated circuit, the width of the resonance curve is seen to get wider during the very first days of immersion. This explains the small frequency drift of the phase curve maxima in Figure 28.

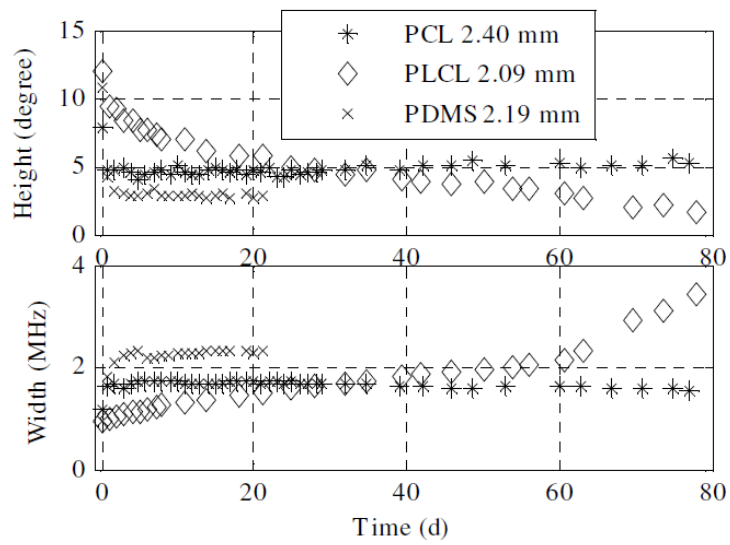


Figure 29: Heights and widths of measured impedance phase resonance curve

The stability of PCL encapsulation was also studied by the frequency minimum of the magnitude dip, illustrated in figure 30. It explains the similar result to that of the extracted features from the shift of maxima of the phase curves.

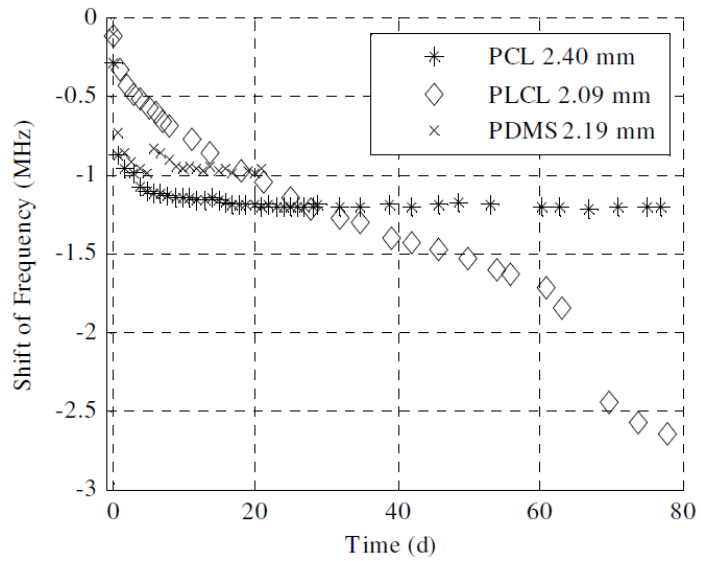


Figure 30: The shift of the frequency of the dip in the magnitude curve.

6.3.4. Stability of PCL encapsulation

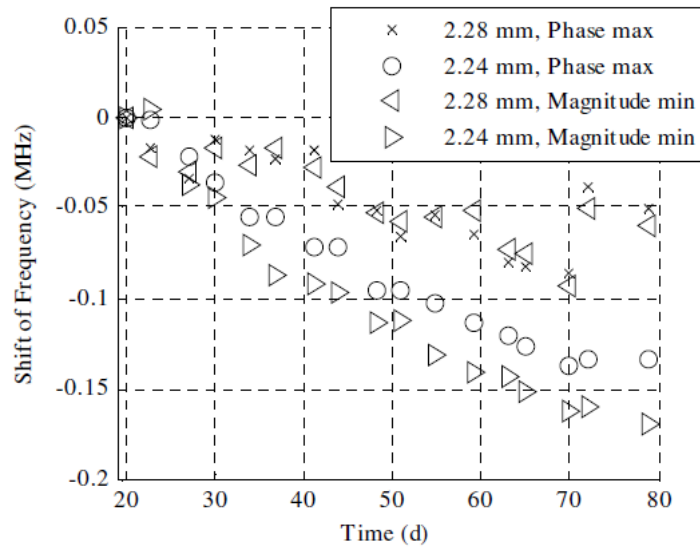


Figure 31: The stability of the phase maximum and the magnitude minimum features of two tested samples in PCL after twenty days of immersion.

The frequency shifts after 20 days of immersion were studied to validate the stability of the PCL encapsulation. This time frame was chosen as the PCL encapsulation water intake maxima was reached. Two samples of different thicknesses were studied to facilitate the repeatability of the experiment. Figure 31 shows the stability of the phase maximum and the magnitude minimum features of two sample circuits encapsulated by PCL. Similar shifts in the phase maximum and magnitude minimum features for both samples can be observed.

6.4. Discussion of the experimental part

The biodegradable polymer encapsulated LC resonance circuits were studied. The dielectric encapsulation reduced the environmental impact on the operation of resonance circuit. It has also enabled the wireless inductive measurement of the resonance circuit while submerged into a phosphate buffer solution. However, the environmental effect of the aqueous medium was still detectable despite the encapsulation. This can be controlled by using a thicker encapsulation. This should reduce the initial frequency shift of the resonance curve because it reduces the change of parasitic capacitances. The resonance was clearly detectable and the resonance dependent features were easily extracted immediately after immersion and during in vitro immersion.

The most significant changes were observed from the extracted features during the first few days of immersion. This is probably due to the water diffusion into chemical structure of the polymers. The thickness of the encapsulation and the temperature of the solution govern the speed and magnitude of the change. However, after few days of immersion, the polymer is saturated with water and thus is unable to intake more water into structure. The absorption of the water decreased the resonance frequency of the resonator as water increases the parasitic capacitances. The decrease in height and increased in width of the phase and magnitude curves indicates the resistive losses of the resonator circuits. The obvious reason for the losses is the increased quantity of the water in the proximity of the circuit but the exact origins of these losses is somewhat unclear.

PCL possesses good potential for biodegradable encapsulation for resonance sensor. The low processing temperature and the fast stabilization in taking up water into the structures are the main distinguishable characteristics. It also provides a good flexible structure to facilitate wearable and implantable sensing devices. However, the circuits encapsulated in PLCL might be a good candidate for further studies to show the reliability of the concept due to their faster degradation time. The concept was found to be useful tool when investigating the diffusion of water into the polymer chemical structure.

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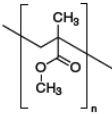
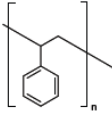
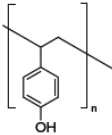
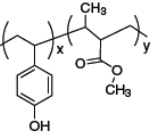
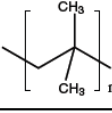
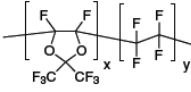

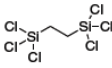
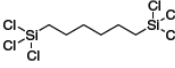
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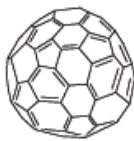
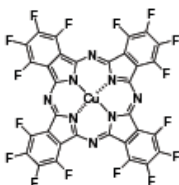
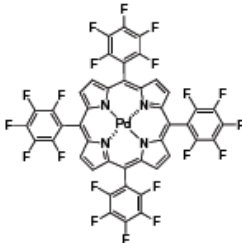
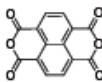




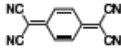
Appendix A

Description	Structure	Property/Purity
Poly(methyl methacrylate) (PMMA)		Avg. $M_w \sim 93,000$ Avg. $M_w \sim 996,000$
Polystyrene (PS)		Avg. $M_w \sim 280,000$
Poly(4-vinylphenol) (PVP)		Avg. $M_w \sim 20,000$
Poly(4-vinylphenol-co-methyl methacrylate) (PVP-co-PMMA)		$x:y = 1.8:1$ Avg. $M_w \sim 10,000$
Polyisobutylene		Avg. $M_w \sim 500,000$
Poly[4,5-difluoro-2,2-bis(trifluoromethyl)-1,3-dioxole-co-tetrafluoroethylene]		65 mol % dioxole 87 mol % dioxole
Hexachlorodisiloxane		96%
1,2-Bis(trichlorosilyl)ethane		97%
1,6-Bis(trichlorosilyl)hexane		97%

Appendix B

Description	Structure	*Mobility (cm ² /Vs) On/Off ratio
Benz[<i>b</i>]anthracene, (tetracene) 98%		0.4 cm ² /Vs
Pentacene		0.4–3 cm ² /Vs
Pentacene, sublimed, > 99.9%		10 ⁵ –10 ⁸
Also see p. 10 for Soluble Pentacene Precursors.		
5,5'-Dihexyl-2,2'-bithiophene, (DH-2T), 96%		
α -Quaterthiophene, (4T), 96%		0.006 cm ² /Vs 10 ⁴
α -Sexithiophene, (6T)		0.075 cm ² /Vs 10 ⁴
α,ω -Dihexylsexithiophene, (DH-6T)		0.13 cm ² /Vs 10 ⁴
Bis(ethylenedithio)tetrathiafulvalene, (BEDT-TTF), 98%		
Bis(4,5-dihydronaphtho[1,2- <i>d</i>])tetrathiafulvalene, 98%		
Copper (II) phthalocyanine, sublimed, 99%		0.01–0.02 cm ² /Vs 4x10 ⁵
Platinum octaethylporphyrin, 98%		2.2x10 ⁻⁴ cm ² /Vs 10 ⁴ –10 ⁵
Poly(3-hexylthiophene-2,5-diyl), (P3HT), regioregular, electronic grade, 99.995%		10 ⁻⁴ –10 ⁻¹ cm ² /Vs 10 ⁴
Poly(3-octylthiophene-2,5-diyl), (P3OT), regioregular, electronic grade, 99.995%		10 ⁻⁴ –10 ⁻¹ cm ² /Vs 10 ⁴
Poly(3-dodecylthiophene-2,5-diyl), (P3DDT), regioregular, electronic grade, 99.995%		10 ⁻⁴ –10 ⁻¹ cm ² /Vs 10 ⁴

Appendix C

Description	Structure	*Mobility (cm ² /Vs) On/Off ratio
Fullerene-C ₆₀ , sublimed, 99.9%		0.3 cm ² /Vs 10 ⁶
Fullerene-C ₇₀ , 99%		
Fullerene-C ₈₄ , 98%		1.1 X 10 ⁻³ cm ² /Vs
Hexadecafluoro copper phthalocyanine, (F ₁₆ CuPc), 80% dye content		0.03 cm ² /Vs 10 ⁴
Pd(II) <i>meso</i> -Tetra(pentafluorophenyl)porphine, 95% dye content		
1,4,5,8-Naphthalenetetracarboxylic dianhydride, (NTCDA)		0.003 cm ² /Vs
Perylene-3,4,9,10-tetracarboxylic dianhydride, (PTCDA), 97%		10 ⁻⁴ cm ² /Vs
<i>N,N'</i> -Dipentyl-3,4,9,10-perylenedicarboximide, (PTCDI-C5), 98%		
<i>N,N'</i> -Dioctyl-3,4,9,10-perylenedicarboximide, (PTCDI-C8), 98%		1.7 cm ² /Vs 10 ⁶
<i>N,N'</i> -Diphenyl-3,4,9,10-perylenedicarboximide, (PDCDI-Ph), 98%		10 ⁻⁵ cm ² /Vs
7,7,8,8-Tetracyanoquinodimethane, (TCNQ), 98%		10 ⁻⁵ cm ² /Vs 10 ³