Biodegradable Polymeric Materials in Degradable Electronic Devices

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ABSTRACT: Biodegradable electronics have great potential to reduce the environmental footprint of devices and enable advanced health monitoring and therapeutic technologies. Complex biodegradable electronics require biodegradable substrates, insulators, conductors, and semiconductors, all of which comprise the fundamental building blocks of devices. This review will survey recent trends in the strategies used to fabricate biodegradable forms of each of these components. Polymers that can disintegrate without full chemical breakdown (type I), as well as those that can be recycled into monomeric and oligomeric building blocks (type II), will be discussed. Type I degradation is typically achieved with engineering and material science based strategies, whereas type II degradation often requires deliberate synthetic approaches. Notably, unconventional degradable linkages capable of maintaining long-range conjugation have been relatively unexplored, yet may enable fully biodegradable conductors and semiconductors with uncompromised electrical properties. While substantial progress has been made in developing degradable device components, the electrical and mechanical properties of these materials must be improved before fully degradable complex electronics can be realized.

1. INTRODUCTION

As electronics become more integrated with our daily lives, there is an increasing demand for transience: the ability for technology to interact with nature without leaving a permanent mark. Conducting, semiconducting, dielectric, and substrate polymers are a natural bridge between electronics and soft matter, because the vast chemical design space for polymers allows tunability of electronic, mechanical, and transient properties (Figure 1A). The tunability of intrinsic polymer properties is beneficial for the development of advanced biodegradable electronics, since it circumvents the need to use complex architectures and patterns to achieve desired properties.

While the term “biodegradability” is not unanimously consistent across the literature, the minimum consensus is that biodegradable materials can be broken down into smaller constituent pieces at biologically benign or physiological conditions. For many applications, complete breakdown of polymers into their monomeric building blocks is unnecessary, and mere disintegration of devices is sufficient to alleviate the need for invasive and costly retrieval procedures. In this review, materials that display transient behavior will be referred to as type I (Figure 1B).

Disintegrable (type I) materials may have a major impact on the biomedical field, especially in basic research, therapeutics, and drug delivery. Even slightly conductive materials can be used to register and transmit biological electrical signals, a property that has been harnessed successfully for tissue engineering applications. Transience on the same time scale as healing or regeneration is critical for such in vivo applications, since nondegradable scaffolds risk causing a chronic inflammatory response. In the longer term, degradable complex implanted devices would avoid device removal surgeries, reducing the likelihood of infection. For any in vivo application, the material and its degradation products must be non-cytotoxic and capable of disposal by the body through processes like phagocytosis, metabolization, or bioabsorption.

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Outlook of their electronic properties, the biodegradable materials discussed in this review can be classified into one of two categories. Type I materials are disintegrable, though only the matrix, which holds together nondegradable active materials, can be fully broken down into small molecule building blocks. On the other hand, both the matrix and active materials comprising type II materials can be fully broken down into monomers or oligomers. Because type II materials are fully biodegradable, they can potentially also be recycled.

Figure 1. (A) Biodegradable electronics have numerous promising applications within the body and the environment. A typical electronic device, like the one depicted on this leaf, is built up from four main classes of materials: semiconductors (blue), conductors (silver), dielectrics (orange), and substrates (light green). (B) In general, biodegradable materials with desired electronic properties consist of an active material (dark blue) dispersed within a biodegradable matrix (light blue). For example, dielectric materials may use high dielectric constant fillers as active materials, whereas semiconductors and conductors use conjugated polymers as active materials that provide electronic conduction pathways within the matrix. Regardless of their electronic properties, the biodegradable materials discussed in this review can be classified into one of two categories. Type I materials are disintegrable, though only the matrix, which holds together nondegradable active materials, can be fully broken down into small molecule building blocks. On the other hand, both the matrix and active materials comprising type II materials can be fully broken down into monomers or oligomers. Because type II materials are fully biodegradable, they can potentially also be recycled.

Outside of the body, type I devices engineered to operate for a defined time scale may enable new sensing capabilities for mass-scale data acquisition without a permanent environmental footprint. Notably, the ICARUS (Inbound, Controlled, Air-Releasable, Unrecoverable Systems) program launched by the Defense Advanced Research Projects Agency (DARPA) aims to create vanishing systems that could be deployed via aircraft to hard-to-access territories where manual recovery would be prohibitively difficult and expensive. For such applications, biodegradability entails that the material must be fully converted by microorganisms into biomass and gases at time scales comparable to typical sewage and waste processing lifetimes.

Beyond macroscopic degradation, the molecular cleavage of the polymer backbone into oligomers and monomers enables further breakdown by microorganisms in the environment or via immunological mechanisms in the body. Ultimately, this more complete chemical degradation, which will be referred to as type II, is critical for creating sustainable devices comprising fully recyclable materials (Figure 1B).

Type II biodegradable electronics may help relieve the environmentally critical problem of discarded electronic waste, which has become exacerbated as electronics become more inexpensive and pervasive, resulting in cases of contaminated soil and water supplies. This trend is anticipated to worsen with the advent of technologies contributing to the Internet of Things. Furthermore, materials that can break down into bioderived or natural building blocks are highly desired due to their intrinsic biocompatibility, biodegradation, and recyclability. While significant work still needs to be done to fully understand the life cycles of new materials developed, both in the environment and within the body, type II materials that can break down into known biocompatible small molecules are less likely to elicit negative long-term responses.

This review will introduce common chemistries utilized in creating biodegradable polymers, and will highlight specific examples of polymers that not are only biodegradable but also are able to be used in electronic devices as either substrates, dielectrics, conductors, or semiconductors.

2. COMMON CHEMISTRIES USED FOR BIODEGRADABLE MATERIALS

Biodegradable polymers include naturally derived materials and synthetic polymers. Among naturally derived materials, plant-based polysaccharides (e.g., cellulose, alginate, dextran) and animal-derived polymers (e.g., collagen, silk, chitosan) have been employed for transient applications due to their intrinsic enzymatic degradability. However, these materials can exhibit high batch-to-batch variation and typically have inherent bioactivity, which can elicit immunogenic response when introduced into the body. Conversely, synthetic polymers typically display more predictable physical properties and degradation profiles that can be chemically engineered, and are typically biologically inert.

Widely used synthetic biodegradable polymers (e.g., polylactide, PLA; polycaprolactone, PCL; polyglycolide, PGL) contain an ester bond to impart hydrolytic degradation. Other chemically and enzymatically hydrolytic degradable moieties include amide, thioester, anhydride, carbonate, urea, urethane, imide, and imine bonds, which serve as sites on the polymer backbone for cleavage under biologically benign conditions (Figure 2A). While there have been reports of enzymatic cleavage of carbon—carbon bonds and potential of other moieties (e.g., sulfonamides, phosphonates, ethers) susceptible to hydrolysis with catalytic acid or base (Figure 2C), most of the literature related to electronic biodegradable polymers has thus far been limited to utilizing the aforementioned hydrolyzable linkages to degrade in physiological, aqueous conditions.

The rate of hydrolysis depends on the chemical architecture and morphology of the polymer, as well as the composition and temperature of the surrounding environment. Degradation rate...
typically increases with the frequency of hydrolyzable groups, hydrophilicity, and accessible surface area (i.e., bulk degradation is faster than surface erosion). Degradation rate typically decreases with increased crystallinity and cross-linking density, which both limit the rate of water uptake. Moreover, enzyme-catalyzed degradation tends to occur via surface erosion, since enzymes are often too large to access degradation surfaces within the bulk of a polymer. Collectively considering these parameters, degradation times of common synthetic biodegradable materials can be tuned from a few days to multiple years.

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Complementary to hydrolysis, oxidation is a biologically relevant mechanism by which polymers can be broken down chemically and enzymatically. Activated phagocytes like macrophages, which play a large role in wound healing, release free radicals in the form of reactive oxygen or nitrogen species that can initiate the depolymerization of polymers by oxidation. Degradation is triggered by oxidation of 1,3-diols in the backbone, which can be catalyzed by either secondary alcohol oxidase (SAO) or periplasmic PVA dehydrogenase (PDH). Iterative oxidation and further degradation by aldolase and β-diketone hydrolyase along the PVA backbone lead to simple byproducts, such as acetic acid. Image adapted with permission from refs 10 and 11. Copyright 2008 Woodhead Publishing and 2014 Wiley.

Figure 2. Chemical structures of moieties susceptible to hydrolysis (A) and oxidation (B) are shown. Hydrolyzable bonds and sites of oxidative attack are highlighted in red and marked with an asterisk. (C) Ester hydrolysis may occur chemically (acid or base) or enzymatically. The mechanism for acid-catalyzed hydrolysis is shown, where the ester bond is cleaved to yield a carboxylic acid and alcohol byproducts. (D) PVA degradation is triggered by oxidation of 1,3-diols in the backbone, which can be catalyzed by either SAO or PDH. Iterative oxidation and further degradation by aldolase and β-diketone hydrolyase along the PVA backbone lead to simple byproducts, such as acetic acid. Image adapted with permission from refs 10 and 11. Copyright 2008 Woodhead Publishing and 2014 Wiley.

### 3. BIODEGRADABLE POLYMERIC COMPONENTS FOR ORGANIC ELECTRONICS

Polymers used in organic electronics can be divided into two broad categories: (i) insulators and (ii) conjugated, conducting polymers. Insulators function as the substrates or dielectrics in electronic devices, whereas conjugated polymers function as the semiconductors or conductors. The choice of polymer for the substrate is constrained primarily by compatibility with device processing, whereas dielectric insulators must also be polarizable by an electric field. Conjugated polymers can be either semiconducting or conducting, depending on their Fermi level. The following sections will discuss the chemical and engineering strategies utilized to overcome challenges associated with creating the biodegradable counterparts of these four material types.
3.1. Biodegradable Substrates. Substrates typically constitute the majority of the weight in a device, with micrometer-scale thicknesses compared to other components that can be hundreds of nanometers thick. Therefore, substrates largely dictate the overall degradation behavior of a device. Consequently, transient devices have been demonstrated that incorporate thin, dissolvable layers of inorganic semiconducting (e.g., Si), dielectric (e.g., SiO2, MgO), and conducting components (e.g., Mg, Fe) on fully degradable substrates. Clearly, selecting substrates with desired degradation profiles is essential to designing biodegradable devices.

The range of biodegradable, insulating materials that can be used as substrates is limited by compatibility with the device fabrication processing steps, necessitating considerations around thermal stability, solvent compatibility, and mechanical robustness. Device fabrication often involves photolithography and etching processes, which can expose materials to high temperatures or harsh chemical solvents. To circumvent these conditions, the target substrate can be decoupled from the processing steps by transferring devices to the substrate after fabrication. As an example of this strategy, Hwang and co-workers demonstrated a general transfer printing method to fabricate a complementary metal–oxide–semiconductor (CMOS) array on various synthetic biodegradable substrates, such as polylactic-co-glycolic acid (PLGA), PCL, and rice paper. The process involved patterning devices on a sacrificial layer of poly(methyl methacrylate) (PMMA) on silicon, and then depositing a layer of diluted polyimide (D-PI) on top. By etching openings in the top D-PI layer, the PMMA layer could be exposed for dissolution, thus releasing the devices to be retrieved by a PDMS stamp for transfer to the desired degradable substrate. The authors used this technique to fabricate a transient hydration sensor made with dissolvable Si, SiO2, and Mg components on PLGA that could be used to monitor wound healing, for which adequate hydration is critical. While the dissolvable inorganic components degraded on an order of days at physiological conditions (PBS, 37 °C), the PLGA substrate degraded on the order of months. The authors harnessed this difference in degradation times to create a robust yet transient sensor that used the degradation of inorganic elements as the sensing mechanism. Critically, the authors demonstrated that device performance before and after transfer to degradable substrates was comparable. Similar transfer-based strategies have also been reported for transient silicon-based devices on PVA (Figure 3B), silk, and cellulose. The generalizable nature of transfer-based strategies enables substrate degradation rates to be tuned with relative ease.

Silkworm silk has been extensively explored as an enzymatically degradable biomaterial because its well-characterized degradation rate in water can be readily tuned by several orders of magnitude by controlling its degree of crystallization via β sheet formation. Highly crystalline, slowly degrading silk tends to be brittle and difficult to handle, while less crystalline silk tends to be more flexible, but also incompatible with aqueous processing steps due to the fast degradation rate. This trade-off typically limits device fabrication on silk substrates to be performed using transfer printing methods. Hwang and co-workers used a transfer printing method to fabricate Si-based microheaters on silk that degrade after 15 days for transient thermal therapy to prevent infections after surgery. Papers composed of cellulose nanofibers (CNF) have also been explored as bioderived, biodegradable substrates. Cellulose is derived from wood and has the advantages of being flexible, transparent, and stable at high temperatures (Figure 3C).

Additionally, cellulose substrates have been shown to degrade slowly, on the order of months, in the presence of naturally occurring fungi, which suggests that they can be used in consumer electronics with reduced environmental footprint. While transfer printing methods have been used to fabricate biodegradable and flexible devices on CNF substrates, direct fabrication onto substrates is preferred for scalability. The thermal stability of CNF papers enabled Hsieh and co-workers to directly print and anneal conductive silver lines onto these substrates, demonstrating its potential for roll-to-roll fabrication.
We used trimethylsilyl-functionalized cellulose, which may be hydrolytically depolymerized to reduce the film thickness by one-third (Figure 3C). The hydrolyzed cellulose substrates exhibited high thermal and organic solvent stability, enabling direct fabrication of devices on cellulose.17

While the aforementioned biodegradable substrates may possess flexibility when they are sufficiently thin, improved integration with dynamic surfaces necessitates the development of substrates that are stretchable and elastic.20,21 Such considerations are particularly significant for wearable and implantable electronics, which may need to adhere to dynamic surfaces like the heart and brain. For these purposes, polyester-based elastomers cross-linked with ester bonds, such as poly(diol citrates) and poly(glycerol sebacate) (PGS), are attractive synthetic biodegradable substrates derived from natural materials such as citric acid.22,23 Stretchable, transient Si-based pH and electro-physiological sensors were fabricated from poly(1,8-octanediol-citrate) (POC) using transfer printing, and complete dissolution was observed upon immersion in PBS (pH 10) at room temperature after 12 h.24 To obviate the need for long thermal condensation curing, these elastomers can additionally be made photo-cross-linkable by introducing maleic anhydride, yielding poly(octamethylene maleate (anhydride) citrate) (POMaC) (Figure 3D).23 Similar strategies can be utilized with other synthetic degradable polymers to broaden the range of materials available to make stretchable and degradable substrates.25,26

3.2. Biodegradable Dielectrics. Dielectric polymers are insulators that can be polarized by an electric field. Key figures of merit are dielectric constant (κ), which should be high or low depending on the application; low dielectric loss for minimal dissipation of electromagnetic energy; and high breakdown voltage for stability. Dielectrics are used to fabricate capacitors, and therefore have important uses in capacitive sensing and field effect transistors (FETs).

In transistors, a large capacitance per area is desired to enable lower voltage operation. Capacitance per area is directly proportional to κ and inversely proportional to the insulator thickness of a defect-free film. Thus, processing as well as intrinsic material property considerations are essential to select a proper dielectric. κ depends on the number of polarizable groups in a material, and has a frequency dependence in an oscillating electric field attributed to the time dependency of polarization mechanisms. Often, κ is reported for static fields, though most electronics actually operate in the high-frequency regime (GHz).27 While high-κ dielectrics help to prevent significant leakage current when scaling down FETs, they tend to also have lower switching speeds than low-κ materials. Additionally, since ac power dissipation is proportional to capacitance, low-κ dielectrics may be desired to reduce power consumption.27 There are a wide variety of biodegradable materials and engineering methods available to prepare dielectric materials with tailored properties for particular applications.

A general strategy to create biodegradable dielectrics is to incorporate high-κ fillers into a degradable polymer matrix. Common high-κ metal oxides include SiO2 (κ = 3.9), aluminum oxide (Al2O3, κ = 9) and hafnium oxide (HfO2, κ = 25). For example, Al2O3 additives were used to tune the dielectric constant of degradable cellulose acetate, resulting in a high κ value of 27.57 at low frequency (50 Hz) (Figure 4A).28 Besides metal oxides, carbon nanotubes also improved the κ at 1 kHz of a paper made from biodegradable CNFs to 3198 (Figure 4B).29 These composites exhibit general transience through matrix degradation while achieving tunable dielectric constants.

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Figure 4. (A, B) The dielectric constant of degradable composites can be increased by incorporating high-κ additives such as Al2O3 (A) and carbon nanotubes (CNTs) (B). (C) DNA can be solution-processed into thin films by complexing it with cationic surfactants like hexa-decyltrimethylammonium chloride (CTMA). (D) Structures of DNA nucleobases used as thin film dielectrics in OFETs. (E) Pyramidal micro-structures enhance the sensitivity of capacitive pressure sensors made with the elastomeric dielectric PGS. Pressure sensor arrays fabricated from these devices are capable of detecting the presence of a 5 mg grain of rice. Images adapted with permission from refs 28, 29, 32, 33, and 37. Copyright 2017 Springer, 2016 Royal Society of Chemistry, 2010 Wiley, 2010 Springer, and 2015 Wiley.
4.5 MV/cm, respectively, and low loss tangent on the order of $10^{-2}$ at 100 mHz. Moreover, sugars are effective at forming pinhole-free films when processed as aqueous and/or DMSO solutions. OFETs fabricated with sugar dielectrics and fullerene as the semiconductor displayed minimal hysteresis and had capacitances per area of 6.8 nF/cm² for lactose and 2.15 nF/cm² for glucose.32

DNA and its precursors have also been explored as gate dielectrics. To render DNA solution-processable for thin film processing, it can be complexed with the cationic surfactant hexadecyltrimethylammonium chloride (CTMA) (Figure 4C).33−36 However, OFETs with DNA-CTMA dielectrics have significant hysteresis due to the presence of mobile ion impurities.32−34 Yumusak and co-workers sought to limit ionic mobility by cross-linking DNA-CTMA with poly(phenylisocyanate)-co-formaldehyde, leading to reduced hysteresis and increased mechanical robustness, though with relatively low capacitance per area of 0.8 nF/cm².34 An alternative way to address hysteresis is to directly use DNA nucleobases, which can be purified and vacuum processed into films as thin as 2.5 nm since they are small molecules (Figure 4D). OFETs fabricated with vacuum processed thin films of guanine and cytosine demonstrated low losses in the range of $10^{-3}$ at 100 mHz, and dielectric constants and breakdown voltages comparable to those of glucose and lactose. Notably, high capacitances per area were achieved in OFETs: 9.25 nF/cm² for guanine and 13.8 nF/cm² for cytosine.32

Besides natural materials, synthetic biodegradable polymers like PGS also exhibit useful dielectric properties. Elastic materials like PGS are especially useful for capacitive sensors, since they can more reversibly withstand compression than more viscoelastic alternatives. We previously reported fully degradable capacitive pressure sensors consisting of pyramidal microstructures of PGS as the dielectric sandwiched between biocompatible electrodes made from corrodible metals Mg and Fe. Since un-cross-linked PGS is a viscous polymer solution, it can be readily patterned to form structured dielectrics by thermally curing after casting into a mold. The highly sensitive pressure sensors can detect a 5 mg grain of rice (Figure 4E), with an approximate in vivo degradation rate of 0.2−1.5 mm per month.57 Further ability to tune the mechanical properties of degradable dielectrics will help enable new sensor designs and stretchable devices that better conform to dynamic surfaces. Additionally, it should be noted that most of the aforementioned dielectrics were investigated at relatively low operational frequencies (<kHz). For eventual use in more complex electronic devices, additional study and optimization of the high-frequency performance of biodegradable dielectrics is required.

3.3. Biodegradable Conductors. Conjugated polymers that have been doped into a conducting state are used for device interconnects and contacts. They are typically characterized by their conductivity ($\sigma$). Besides connecting different components within an electronic circuit, they can also connect electrically responsive entities within the body, such as neurons and cardiac cells. Since doping is required to render conjugated polymers conducting, the biocompatibility of the doping process also needs to be considered. Common conjugated polymers that are stable in their doped, conducting states are polypyrrole (PPy), polyaniline (PANI), and poly(3,4-ethylenedioxythiophene) (PEDOT), which has conductivities up to $4.6 \times 10^{3}$ S/cm when doped with poly(styrenesulfonate) (PEDOT:PSS).38

Electronic conduction in conducting polymers occurs across rigid conjugated regions. As a result, highly conductive polymer films are often brittle and stiff. This inherent mechanical limitation of conjugated polymers can be overcome since excellent electrical properties can be achieved at low concentrations of the conjugated polymer within a composite.39−41 Analogous to dielectric composites, one strategy for biodegradable conducting polymers is to blend conjugated polymers with biodegradable, insulating polymers. Conductive composites made in this way exhibit type I degradation, and are able to disintegrate even if the polymers cannot be fully broken down into their monomeric constituents. Since the electronic component is non-degradable, the objective is to maximize electrical conductivity while minimizing the relative concentration of the nondegradable conjugated component.

Dispersing conjugated polymer nanoparticles within a biodegradable polymer matrix is an attractive blending approach, as doping of the conjugated polymer can be performed orthogonal.42−44 Distinctive from biodegradable dielectrics, the conductive filler must be above the percolation threshold to sufficiently form conduction pathways within the insulating host. Since minimizing the proportion of nanoparticles is important to achieve high degradability, this strategy is useful for applications where high conductivity is not required, such as moderate electrical stimulation to promote cell growth and tissue regeneration.45 Since tissue regeneration typically occurs on the order of 1 to 2 months, these types of materials ideally should disintegrate at similar time scales.42

An early example of conductive composites prepared by this method involved PPy nanoparticles, which are conductive when doped by oxidation (Figure 5E).46 In 2004, Shi and co-workers demonstrated upregulation of fibroblast growth on composites of PPy nanoparticles within poly(3,4-lactic acid) (PDLLA). The oxidized PPy nanoparticles were emulsion polymerized in the presence of FeCl₃. A conductive network was formed within the PDLLA matrix due to aggregation of the PPy nanoparticles, and the authors reported conductivities as high as $1 \times 10^{-8}$ S/cm with just 3 wt % PPy loading. The composite was able to sustain a detectable DC current at physiological conditions for 1000 h, approaching the requirements for tissue engineering.42

Similarly, Wang and co-workers enhanced the neural outgrowth of neuron-like pheochromocytoma (PC12) cells by culturing on a conductive composite of hyaluronic acid doped PEDOT nanoparticles (PEDOT-HA) within poly(3,4-lactic acid) (PLLA), which had conductivities as high as $4.7 \times 10^{-8}$ S/cm at 10% nanoparticle loading. The authors characterized the biodegradation of their composites by investigating both the degradation rate of the films and the cytotoxicity of degradation intermediate products. The presence of PEDOT-HA accelerated the degradation of PLLA by 10% after 8 weeks, which they postulated could be attributed to increased water penetration due to the hydrophilic domains of HA (Figure 5D). Additionally, they determined that PEDOT-HA/PLLA during degradation showed no significant cytotoxic impacts on PC12 cell growth and viability. In fact, cell viability was comparable to if not better than with PLLA alone, since PLLA hydrolyzes to lactic acid, which is somewhat toxic.42

Electrospinning is an effective method for creating 3D connected fibrous porous structures with fiber diameters ranging from hundreds of nanometers to several micrometers, which is particularly advantageous for applications involving cell growth.47,48 Biodegradable conducting scaffolds have been formed by electrospinning biodegradable polymers and subsequently polymerizing conducting monomers in situ.49,50 For example, in situ polymerization of pyrrole in the presence of

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biodegradable PLGA scaffold led to increased growth and differentiation of PC12 cells compared to noncoated PLGA controls (Figure 5A,B). Alternatively, conducting polymers can also be cospun with biodegradable polymers to form conductive fibers. For instance, PANI doped with camphorsulfonic acid (CPSA) was cospun with gelatin to yield fibrous sheets with conductivities up to $2.1 \times 10^{-2}$ S/cm. Similarly, CPSA-doped PANI cospun with poly(l-lactide-co-ε-caprolactone) (PLCL) exhibited conductivities as high as $1.38 \times 10^{-2}$ S/cm with 30 wt % PANI. Electrical stimulation of fibroblasts and myoblasts on these conducting fibrous scaffolds enhanced adhesion and proliferation.

Type II biodegradation may be achieved through conjugation breaking, where flexible but nonconjugated linkers are introduced along the polymer backbone. Conjugation breakers have been used to enhance the processability and mechanical properties of conducting and semiconducting polymers with minimal compromise to device performance. Analogously, type II polymers of short conjugated groups linked to biodegradable units show decent charge transport characteristics. Conjugated oligomers may be considered biocompatible degradation products, since they are small enough to be phagocytized by macrophages that naturally migrate to implantation sites as part of the body’s innate immune response. To date, type II conducting polymers do not exhibit conductivities as high as their type I counterparts (Table 1). Due to their low conductivities, type II conductors that have been developed thus far are primarily useful for registering and stimulating small bioelectronic signals. Better control over the chemistry, doping, and morphology of these materials should help close the gap with type I conductors and approach the conductivities required for fabricating high-performance electronics.

Rivers and co-workers reported a biodegradable polymer consisting of pyrrole-thiophene-pyrrole trimers and aliphatic chains linked with ester bonds. Conductivities of $10^{-4}$ S/cm with iodine doping were reported, and degradation products were detected after 2 weeks in PBS at body temperature ($37^\circ$C) in the presence of the enzyme esterase. In vivo biocompatibility studies confirmed that both the films and their degradation products were nontoxic, though the iodine dopant was found to be cytotoxic. To avoid using iodine, Guimard and co-workers doped a thiophene oligomer-based copolymer with nontoxic ions FeCl$_3$ and Fe(ClO$_4$)$_3$. While conductivity measurements were not performed, successful doping was inferred from redox activity using cyclic voltammetry and polaron states observed from UV–vis spectroscopy. Crucially, in vitro compatibility studies using Schwann cells demonstrated nearly 100% cell viability relative to controls.

Aniline oligomers are also attractive due to their relatively simple synthesis. Although aniline oligomers exhibit lower conductivities than their PPy and PEDOT counterparts, aniline-based materials doped with CPSA have sufficient conductivities
Table 1. Conductivities of Various Biodegradable Conducting Polymeric Materials

| Material System                  | Type I: Conductive Blends | Type II: Conjugation Breaking |
|----------------------------------|---------------------------|------------------------------|
| PANI gelatin nanobrushes         | camphorsulfonic acid (CPSA) | 2.1 × 10⁻² S/cm | 4.5 × 10⁻⁴ S/cm |
| PANI electrospun with PLLCL      | CPSA                      | 1.4 × 10⁻² S/cm | 6 S/cm |
| PPy with PCLL (polycaprolactone fumarate) | anionic dopants: naphthalene-2-sulfonic acid sodium salt and dodecyl benzene sulfonyl acid sodium salt | 6 × 10⁻³ S/cm | 2.4 × 10⁻³ S/cm |
| PEDOT particles in PLLA          | hyaluronic acid           | 4.7 × 10⁻³ S/cm | 4.7 × 10⁻⁴ S/cm |
| PPy nanoparticles in PDLLA        | oxidation with FeCl₃      | 1 × 10⁻⁵ S/cm | 5 S/cm |
| PPy-coated PLGA fibers           | oxidation with FeCl₃      | 1 × 10⁻² S/cm | 5 × 10⁻⁶ S/cm |

Conducting Polymeric Materials

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Outlook

To serve as conductive scaffolds for tissue engineering applications, biodegradable-electroconductive hydrogels have been fabricated by grafting polyaniline to gelatin and doping with CPSA, resulting in conductivities around 10⁻⁴ S/cm (Figure 5C). While hydrogels are appropriate as scaffolds, preparation of thin films is important for integration with standard device fabrication. Pure aniline pentamer (AP) thin films doped with HCl exhibit conductivity 2 orders of magnitude higher (10⁻² S/cm), but have limited use due to their mechanical rigidity. Combining AP with flexible PLA segments improved mechanical properties but reduced film conductivities to 5 × 10⁻⁶ S/cm², though this value can potentially be enhanced by tuning the macromolecular architecture. For example, Guo and co-workers demonstrated a 4-fold improvement in conductivity (2 × 10⁻⁵ S/cm from 5 × 10⁻⁶ S/cm) when copolymers of AP and PCL were fabricated with a hyperbranched, rather than linear, design. Similarly, aniline tetramer (TA) side chains grafted onto a biodegradable poly(ester amide) backbone achieved conductivities of 8.0 × 10⁻⁶ S/cm².

Besides biocompatibility issues, the mobility of dopants is potentially problematic for applications that require relatively long-term stability, since conductivity dramatically decreases when dopants leach out. To address this issue, Xu and co-workers synthesized a multisegment dopant-free conductive polyurethane (DCPU) elastomer (Figure 5F). DCPU consists of aniline trimers linked to biodegradable PCL and the dopant dimethyloproionic acid (DMPA) (Figure 5G). The DCPU conductivities ranged from 10⁻⁸ to 10⁻⁵ S/cm in the dry state, increasing with higher dopant content. Soaking in PBS further increased conductivity up to 4.7 × 10⁻⁴ S/cm. Degradation rate in aqueous PBS solution increased with DMCA, since its hydrophilic carboxyl groups rendered the polymer more hydrophilic. Crucially, while their polymer degraded to 75.8% of its original mass in PBS after 14 days in the presence of lipase, the conductivity did not decrease by over an order of magnitude. This improvement in electronic stability was attributed to reduced dopant removal due to it being covalently linked to the conducting polymer.

To date, there is a demand for biodegradable conductors with sufficiently high conductivities (>10⁻¹ S/cm) to be used as electrodes and interconnects in devices. The use of corrodbile Mg and Fe electrodes has been invaluable in the initial demonstration of biodegradable devices, though the range of mechanical properties achievable with these metals is limited. Advances in the development of intrinsically stretchable/elastic, highly conductive biodegradable polymeric materials will greatly contribute to the progress of complex electronics interfaced with dynamic surfaces, such as human skin.

3.4. Biodegradable Semiconductors. Semiconductors are essential to the switching mechanism of organic transistors, and thus are critical to complex electronic circuitry. They are typically characterized by their carrier charge mobility (μ), which represents how quickly a free charge can move through the material when pulled by an electric field. Mobility and conductivity (σ) are related by the equation σ = ε(μₑμₚ + μₚμₑ), where n is the concentration of electrons with mobility μₑ and p is the concentration of holes with mobility μₚ. Mobility is normally expressed in cm²/V·s and can be calculated directly from working devices like thin film transistors. Typical semiconducting polymers are polythiophenes (e.g., poly(3-hexylthiophene), P3HT) and donor—acceptor copolymers developed originally for organic photovoltaics (e.g., diketopyrrolopyrroles, DPP).

There are fewer reports of biodegradable semiconductors because the primary target for developing biodegradable electronconducting polymers has focused on the detection of electrical signals in the body. However, degradable semiconductors are required to fabricate more complex biodegradable device architectures. Many of the strategies discussed above for making conducting polymers biodegradable are applicable to semiconducting polymers as well, since both have similar challenges arising from their conjugated structures. As with conducting polymers, blending has been utilized to generate semiconductors that exhibit type I degradation. To enhance miscibility with more polar biodegradable matrices, poly(3-thiophene methyl acrylate) (P3TMA), a derivative of P3HT with carbonyl substituents, was selected for blending with poly(tetramethylene succinate), PLA, poly(ester urea), and thermoplastic polyurethane (TPU). Stable, freestanding composite films supported cell adhesion and proliferation. Madrigal and co-workers observed semiconducting behavior in TPU:P3TMA nanomembranes and further elucidated the inhomogeneity of conductivities within spin-coated membranes with conductive AFM. A range of conductivities from 2.2 × 10⁻³ to 5.2 × 10⁻⁸ S/cm is achievable with these materials.
was measured, which they attributed to the presence of insulating TPU. Interestingly, while the TPU:P3TMA mixture had a higher band gap than P3TMA in solution, the spin-coated polymers had very similar band gaps (2.35 and 2.32 eV, respectively) due to changes in P3TMA conformation during spin coating.71

Electrospinning semiconducting polymers with an insulating, biodegradable polymer have been thoroughly reported. Degradable fibers of P3HT cospun with PCL72 and PLGA73 have been demonstrated, albeit with lower mobilities due to grain boundaries arising from macroscopic phase segregation. Electrospun P3HT nanofibers had a mobility of $1.7 \times 10^{-3}$ cm$^2$/V·s, whereas blended fibers with 20 wt % PCL had 1 order of magnitude lower mobility and 50 wt % PCL blends had 2 orders of magnitude lower mobility. As with blended transient conductors, these semiconducting polymer blends are type I since the semiconducting component is nondegradable, and the degradation behavior depends primarily on the matrix material.

Recent breakthroughs in understanding charge transport in semiconducting polymers may serve as inspiration for future designs of biodegradable semiconducting polymers. Overcoming the inherent rigidity and stiffness of conjugated semiconducting molecules and their crystalline, charge-transporting aggregates has been a persistent challenge for utilizing traditional semiconducting polymers in stretchable and flexible electronics. In 2013, Noriega, Rivnay, and co-workers demonstrated that high mobility could be achieved in macroscopically disordered semiconducting polymers with interconnected aggregates and efficient local intra- and intermolecular charge transport.74 In 2015, Wang and co-workers demonstrated that semiconducting polymers could retain high charge carrier mobility even when mixed with an insulating polymer matrix.75 The key to their result was a high resistance to disorder designed by tuning the semiconductor to form interconnected aggregates with locally efficient intermolecular charge transport.74 In principle, the strategy of blending rigid semiconducting polymers with inert polymers that have favorable properties can be extended to design materials consisting primarily of an insulating, biodegradable matrix. Such an approach would entail tuning both the semiconducting and inert polymer components to achieve the required interconnected morphology.

In the aforementioned examples, biodegradability is introduced via commonly hydrolyzable linkages like ester bonds. These linkages can be incorporated within a second component in a blend, which prevents the semiconductor from being completely degradable, or they can be directly incorporated into the semiconducting polymer backbone, which disrupts the conjugation responsible for higher mobilities. To enable type II biodegradable semiconductors, our group recently reported the seminal use of reversible imine bonds as conjugated linkages between DPP and p-phenylenediamine. The DPP-based semiconducting polymer retains conjugation along the backbone, allowing for hole mobilities as high as 0.34 cm$^2$/V·s when spin-coated onto octadecyltrimethoxysilane (OTS) treated SiO$_2$/Si substrates.17 The imine bonds degrade under acidic conditions (pH = 4.6), where the byproducts are the aldehyde and amine precursors (Figure 6A,B). Devices fully disintegrated after 30 days, by using cellulose as a substrate, Al$_2$O$_3$ as dielectric, and Fe electrodes. The pH of 4.6 is notably milder than that of gastric acid in the stomach (pH = 1.5–3.5). Therefore, imine-linked semiconductors are an innovative strategy to generate recyclable semiconductors or electronics intended to pass through and degrade within the digestive system.77

Conjugated molecules found in nature could also serve as future building blocks for biocompatible electronics. Certain conjugated molecules found in foods and dyes have low toxicity and naturally defined degradation pathways, which helps ensure the biocompatibility of degradable devices over their broader life cycle. One of the earliest reported molecules was the natural dye indigo, which is produced from the plants Indigofera tinctoria and Isatis tinctoria. Indigo is a semiconductor with a band gap of 1.7 eV and balanced electron and hole mobilities on the order of 10$^{-2}$ cm$^2$/V·s. OFETs with fully natural materials have been fabricated by evaporating thin, crystalline films of indigo onto natural resin shellac substrate, using aluminum as a gate and Al$_2$O$_3$ as the dielectric (Figure 6C).76

**Figure 6.** (A) Highly flexible devices made with imine-degradable semiconductor PDPP-DP on ultrathin cellulose substrates can be transferred to target surfaces after dissolution of an underlying sacrificial dextran layer. (B) PDPP-DP contains imine bonds that can hydrolyze under acidic conditions to corresponding aldehydes and amines. (C) Chemical structure of indigo, along with a photo of degradable indigo-based transistors on shellac. (D, E) The comproportionation reaction between melanin and water has been proposed to explain the doping effect of water on melanin (D), as evidenced by the observed increase in melanin conductivity with hydration (E). Images adapted with permission from refs 17, 76, and 77.

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For future work, it would be interesting to consider different physiological environments within the body and elsewhere in nature that are conducive to breakdown mechanisms beyond simple hydrolysis.

The natural pigment melanin has also been shown to exhibit electronic behavior. Eumelanins, a subclass of melamins that constitute the primary component of skin pigment, are 2D sheet-like structures consisting of randomly cross-linked \( \pi-\pi \) stacked aggregated oligomers and polymer species formed from monomers 5,6-dihydroxyindole and 5,6-dihydroxyindole-2-carboxylic acid. Melanin conductivity can vary significantly depending on temperature, physical form, and hydration state, with fully hydrated melanin exhibiting conductivities as high as \( 10^{-3} \) S/cm, compared to \( 10^{-9} \) S/cm to \( 10^{-8} \) S/cm in the dehydrated state. The charge transport characteristics of eumelanin were explored in 2012 by Mostert and co-workers, who demonstrated that eumelanin is self-doped upon absorption of water, which causes a comproportionation reaction that produces free electrons and protons to impart dual ionic and electronic conductivity (Figure 6D,E). Due to the importance of hydration on melanin conductivity, it is a promising candidate for tissue engineering applications in the body. Bettinger and co-workers demonstrated fully hydrated melanin thin films with conductivities of \( 7 \times 10^{-3} \) S/cm that enhanced Schwann cell proliferation and PC12 neurite extension in vitro. In vivo observation confirmed that the melanin implants were nearly fully eroded and resorbed after 8 weeks, which is an appropriate time frame for a regenerative medicine scaffold.

Other notable molecules include \( \beta \) -carotene, a molecule responsible for the red-orange color of carrots, and derivatives of anthraquinone, a natural laxative. \( \beta \) -Carotene has been investigated as a molecular wire with p-type mobility up to \( 4 \times 10^{-4} \) cm\(^2\)/V⋅s. Anthraquinone derivatives, indanthrene yellow G and indanthrene brilliant orange RF, registered mobilities of \( 1.2 \times 10^{-2} \) cm\(^2\)/V⋅s when used in FETs made entirely of natural materials, with guanine and adenine as the gate dielectric and caramelized glucose as the substrate. When \( \text{Al}_2\text{O}_3 \) was incorporated into the gate dielectric, the mobility was further increased to 0.015 cm\(^2\)/V⋅s. To better ensure biocompatibility throughout the degradation life cycle, future work might consider designing synthetic polymers that incorporate conjugated biomolecules like \( \beta \) -carotene and anthraquinone into the polymer chain.

4. CONCLUSION

Innovative chemistries and processing techniques have enabled a wide selection of both natural and synthetic polymers for use as biodegradable device components. While numerous biodegradable polymers are substrates, dielectrics, and semiconductors, processing improvements are still needed to enhance said properties and introduce new functionality like stretchability. Synthetic materials afford greater control over mechanical properties, and therefore may be preferable to fabricate flexible and stretchable degradable devices. With synthetic conjugated polymers, materials design strategies like conjugation-breaking have been employed to create semiconductors and conductors with promising mobilities and conductivities, respectively, though progress remains to make these properties comparable to their non-degradable counterparts. Finally, new possibilities exist that utilize unconventional degradable linkages, as evidenced by the seminal demonstration of a fully conjugated, degradable semiconductor polymer earlier this year. For future work, it would be interesting to consider different physiological environments within the body and elsewhere in nature that are conducive to breakdown mechanisms beyond simple hydrolysis. For instance, to our knowledge, there have not been biodegradable electronic polymers created that utilize degradation mechanisms through the highly reactive oxygen and nitrogen radical species generated by macrophages upon encountering foreign bodies. Better understanding the chemistries of different natural and physiological environments could open the door for biodegradable chemistries that have yet to be explored with substrate, dielectric, semiconducting, and conducting polymer systems.
TPU, thermoplastic polyurethane; $\kappa$, dielectric constant; $\mu_c$, charge carrier mobility; $\sigma$, conductivity

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