

From Nature to Implant: Biodegradable Piezoelectric Materials for Transient Biosensors

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Abstract: Biodegradable piezoelectric materials are emerging as promising platforms for transient biosensors because they can mechanically interact with tissues, generate useful electrical signals, and degrade after a defined functional lifetime. Unlike conventional piezoelectric ceramics and fluorinated polymers, which raise concerns related to toxicity, persistence, or device retrieval, these materials aim to combine sensing performance with bioresorption and safer biological integration. This review distinguishes biodegradability from biocompatibility while examining how the two concepts intersect in the design of transient piezoelectric biosensors. It first discusses how the literature addresses degradation mechanisms, functional lifetime, byproduct safety, cytocompatibility, inflammatory response, and mechanical compatibility. It then surveys major material classes, including amino acid crystals, natural biopolymers, synthetic biodegradable polymers, and peptide-based self-assembling systems. Representative biosensing applications are considered, ranging from short-term implantable pressure monitoring to healing-related interfaces and therapy-adjacent transduction platforms. Finally, the review highlights key challenges, including the need for standardized degradation testing under physiologically relevant conditions, full-system biodegradable integration, and more rigorous evaluation of degradation products in realistic implant environments.

Keywords: biodegradable piezoelectrics; transient biosensors; implantable sensing; bioresorbable electronics; biomechanical energy harvesting

1. Introduction

Piezoelectric materials have long been used for sensing, actuation, and energy conversion as they are able to directly couple mechanical deformation to electrical response [1–15]. This electromechanical coupling enables self-powered operation by converting physiological motions, such as cardiac pulsation, joint movement, or tissue deformation, into detectable electrical signals, making these materials particularly attractive for implantable devices [16–20]. However, conventional high-performance piezoelectric materials face significant challenges to practical biomedical application [21–23]. Lead-based ceramics such as lead zirconate titanate (PZT) are brittle and raise cytotoxicity concerns, while ferroelectric polymers such as polyvinylidene fluoride (PVDF) are non-biodegradable, limiting their suitability for applications where temporary implantation is preferred [24–26]. Moreover, even when constituent materials are biocompatible, long-term device persistence remains a fundamental limitation for temporary implantable biomedical devices [27–29]. Many existing implantable materials are designed to maintain mechanical integrity and electrical function over extended periods, whereas numerous



diagnostic and monitoring tasks require operation only over a short and well-defined operational timeframe [16,27,30,31]. This mismatch between material lifetime and functional lifetime creates unnecessary constraints on device design and leaves residual structures in place beyond the period of required operation. From a materials perspective, this challenge motivates the development of transient systems whose operational stability is maintained only for the required period, followed by controlled degradation into benign by-products [32–34]. In this context, transient piezoelectric biosensors offer an attractive route toward devices that combine electromechanical functionality with controlled degradation after the required period of operation [20,30,31,34].

To address these limitations, a growing class of biodegradable piezoelectric materials offers an alternative design paradigm in which devices operate over a defined functional lifetime and then undergo controlled degradation, eliminating the need for secondary removal [35]. Importantly, biodegradability in these materials does not necessarily come at the expense of piezoelectric output [36,37]. For example, β -glycine remains intrinsically biodegradable yet shows a high piezoelectric voltage constant, $\sim 8.13 \text{ V}\cdot\text{m/N}$, indicating that strong electrical response and biodegradability can coexist [23,33,38,39]. Such requirements align closely with the broader development of transient electronics, which gained momentum after Rogers and co-workers demonstrated physically transient silicon electronics in 2012 [29]. Within this framework, devices are designed not for indefinite durability but for a defined operational lifetime followed by safe and controlled degradation [40]. In this sense, transient piezoelectric biosensors represent a particularly promising class of temporary implantable devices, because they combine programmed functional lifetime with self-powered electromechanical sensing of physiological activity [41].

Despite this promise, the development of biodegradable piezoelectric materials remains challenging. Achieving strong electromechanical performance often requires high crystallinity, aligned dipoles, and ordered molecular packing [42–44]. At the same time, these structural characteristics can reduce mechanical compliance, complicate processing, and slow hydrolytic or enzymatic degradation [45,46]. As a result, material designs that maximize piezoelectric output do not always align with the requirements for soft tissue integration and predictable transience [47,48]. This trade-off has emerged as one of the major challenges, making it difficult to compare material platforms using a single performance metric or a simplified definition of biodegradable suitability [49].

Biodegradable and non-biodegradable piezoelectric polymers should also be distinguished according to their intended use. PVDF and PVDF-TrFE offer high and stable electromechanical performance and remain important benchmarks for permanent wearable or implantable transducers, but their persistence limits their suitability for temporary devices that should disappear after use. Biodegradable polymers such as poly-L-lactic acid (PLLA), poly-3-hydroxybutyrate (PHB), and poly(3-hydroxybutyrate-co-3-hydroxyvalerate) (PHBV), and selected natural biopolymers generally provide lower or more processing-dependent piezoelectric output, yet they enable transient implantation, reduce the need for surgical retrieval, and permit functional lifetime to be coupled to tissue healing or monitoring requirements. In this review, non-biodegradable PVDF-based systems are therefore included only when they provide a mechanistic or performance benchmark relevant to the development of degradable platforms.

Accordingly, this review surveys biodegradable piezoelectric materials through a broader evaluative standard encompassing piezoelectric performance, degradation behavior, biocompatibility, processing strategies, and device-level relevance. This broader perspective is needed because piezoelectric coefficient alone does not determine whether a material is suitable for transient biosensing; practical utility also depends on manufacturability, operational stability, biocompatibility, and controlled degradation in the target biological environment [19,50]. From this standpoint, the review compares the main material classes, highlights recurring trade-offs across different studies, and identifies the considerations most critical for the design of transient piezoelectric biosensors.

2. Key Considerations in Biodegradability and Biocompatibility

2.1. Biodegradability in Transient Piezoelectric Biosensors

In transient piezoelectric biosensors, biodegradability is not defined solely by whether a material eventually disappears, but also by how long the device remains functional and what degradation products are released in the process [27,51]. These considerations vary across material classes and are therefore worth outlining before the materials themselves are surveyed.

Degradation mechanism: Different material classes used in biodegradable piezoelectric biosensors degrade by different mechanisms, and these differences influence both material selection and device design. Synthetic aliphatic polyesters such as PLLA are typically described as degrading through bulk hydrolysis [52–54]. The process begins in the amorphous regions, where water penetrates and cleaves ester bonds, and then gradually extends into the more resistant crystalline domains. Natural polymers, by contrast, are more often broken down through enzyme-mediated

processes, although the extent of this behavior depends strongly on the material class [55,56]. Silk fibroin and collagen undergo enzyme-assisted breakdown into amino acid products under physiological conditions, and chitin can likewise be hydrolyzed by lysozyme present in mammalian tissues [56,57]. Cellulose differs in this respect, as it is generally not readily resorbed in the human body because its degradation depends mainly on microbial or fungal enzymes that are absent in mammalian tissue [55].

These mechanistic differences are important because both degradation rate and behavior depend in part on material structure [23]. In enzyme-dependent systems, parameters such as crystallinity, molecular packing, surface area, and molecular weight influence the extent to which the material is accessible to enzymes, making these features relevant to both piezoelectric performance and degradation behavior [36]. Silk fibroin, for example, degrades negligibly in phosphate-buffered saline at physiological temperature, yet breaks down much more rapidly in the presence of proteolytic enzymes [57]. This shows that degradation results from static buffered conditions are useful for comparison, but do not necessarily reflect in vivo behavior [57].

Functional lifetime: A second point is the distinction between material lifetime and functional lifetime. For transient piezoelectric biosensors, the relevant timescale concerns both the persistence of the bulk material and the duration over which the device can maintain stable electrical output [27]. Electrical failure may occur well before substantial mass loss because of moisture ingress, electrode corrosion or interfacial delamination under cyclic strain [29]. This distinction matters because sensor failure is often governed by the weakest device components, such as electrodes, encapsulation layers, or interfaces, rather than by complete degradation of the piezoelectric material itself. For example, a reported implantable piezoelectric sensor based on PLLA maintained reliable electrical operation for only a few days in an aqueous physiological environment, whereas bulk PLLA implants have been documented to persist for years in vivo [16,52]. These observations highlight that biodegradability at the material level does not directly translate into transience at the device level. From a materials perspective, this means that crystallinity, molecular weight, encapsulation strategy, and composite architecture must be considered in relation to both eventual degradation and the earlier point at which electrical and mechanical integrity begin to decline. For design purposes, material lifetime should therefore be defined as the period over which the material or device remains physically present, whereas functional lifetime is the shorter or equal period over which the sensor retains its specified sensitivity, signal stability, and mechanical integrity. A transient implant should be engineered to remain functional throughout the intended diagnostic or therapeutic window and to lose function and resorb only after that window has closed.

Degradation products: The importance of degradation products has received increasing attention as biodegradable piezoelectric systems become compositionally more complex [28]. A biodegradable polymer that yields benign monomers does not necessarily guarantee equally benign behavior at the device level [29]. PLLA, for example, hydrolyzes to lactic acid and subsequently to water and carbon dioxide, which are generally well tolerated [58]. However, local accumulation of lactic acid during degradation can temporarily acidify the surrounding microenvironment. Recent work has shown that local acidification during PLLA degradation can reduce the osteogenic differentiation capacity of mesenchymal stem cells grown on PLLA nanofibers, indicating that the local consequences of breakdown depend on more than the identity of the final products alone [51]. In composite systems containing nanoparticle fillers, conductive additives, crosslinkers, or interfacial modifiers, the degradation products of these secondary components are often far less well characterized than those of the primary components [28]. From a materials perspective, this means that biodegradability must be considered for the full material system and its breakdown pathway over time, rather than only for the base polymer or crystal. Likewise, the cytocompatibility of a pristine material does not guarantee the safety of its degradation eluate, and this distinction becomes increasingly important as piezoelectric composites become more compositionally sophisticated.

Overall, these considerations suggest that biodegradability in transient piezoelectric biosensors is best interpreted not as a single material label, but as a materials property closely tied to degradation pathway, device-level functional persistence, and the nature of the resulting degradation products.

2.2. Biocompatibility in Transient Piezoelectric Biosensors

Similar to biodegradability, biocompatibility is a measurable property that can be assessed in several different ways, most commonly including in vitro cytocompatibility, in vivo inflammatory response, and mechanical compatibility with the surrounding tissue [21,22]. These properties are related to each other but are not equivalent. As a result, materials that are often grouped together as biocompatible may in fact differ substantially in the strength of the evidence supporting that claim.

Cytocompatibility: Cytocompatibility is usually evaluated as one aspect of biocompatibility by measuring cell viability or proliferation, or by using live/dead tests, either on the material surface or in cells exposed to

substances released from the material [59,60]. Based on short-term in vitro cytocompatibility alone, many biodegradable piezoelectric materials appear promising [59]. In reality, however, this evidence alone is not sufficient to establish longer-term implant biocompatibility. For example, glycine-based composites have generally shown high cell viability in direct-contact studies, and chitosan is widely regarded as non-cytotoxic and is frequently noted for additional antibacterial properties [59,61]. Such results are nevertheless better understood as preliminary evidence of biological tolerance under simplified in vitro conditions, rather than as confirmation of biocompatibility after implantation. Cytocompatibility by itself does not capture the effects of prolonged implantation, dynamic mechanical loading, host immune response, or changes associated with material degradation over time [49,62].

In vivo inflammatory and tissue response: Beyond cytocompatibility, in vivo inflammatory and tissue response are considered a more demanding criterion of biocompatibility. This includes inflammatory reactions and the broader tissue response associated with implantation and degradation. Across studies, the absence of acute cytotoxicity does not preclude these longer-term responses, which is a particular concern for degradable piezoelectric materials, as the biological environment during implantation, including local chemistry and degradation products, changes over time [28,58]. For example, PLLA is widely regarded as biocompatible and clinically acceptable, but that should not be taken to mean that it is biologically inert [52]. Although many studies report minimal inflammatory response, later-stage tissue interactions can still appear as degradation proceeds and residual fragments remain [58]. By comparison, for glycine-based composites and especially peptide-derived piezoelectric materials, in vivo evidence remains much more limited [21]. In these cases, encouraging in vitro findings are not yet matched by similarly developed evidence on longer-term inflammatory and tissue response.

Mechanical compatibility: Mechanical compatibility has emerged as an additional dimension of biocompatibility in implantable piezoelectric biosensors. The device chemically and mechanically interacts with surrounding tissue, and this relationship can affect both biological response and sensing stability [16,28]. A material may show acceptable cytocompatibility yet still be poorly suited for implantation if its stiffness differs markedly from that of the host tissue. Such mismatch can contribute to chronic irritation, unstable tissue-device interfacing, and variability in electrical output during use. In piezoelectric materials, strategies used to improve electromechanical performance often also increase stiffness, meaning that better piezoelectric performance may come at the cost of tissue-level mechanical compliance [36,38,39]. Flexible biodegradable polymers are relatively a better match for soft biological tissues. However, highly crystalline PLLA and glycine-containing composites may still be much stiffer than skin or other soft tissue environments [16,36]. Similarly, self-assembled peptide such as diphenylalanine nanotubes shows a high Young's modulus despite its favorable molecular biodegradability [63]. Mechanical compatibility therefore reasonably needs to be treated as part of biocompatibility in implantable biosensors.

These points indicate that biocompatibility in transient piezoelectric biosensors is best understood across three distinct but related dimensions. Cytocompatibility provides an initial indication of whether a material is tolerated under simplified in vitro conditions. In vivo inflammatory and tissue-response data offer a stronger basis for assessing whether that tolerance is maintained during implantation and degradation. Mechanical compatibility adds a further device-level consideration by determining whether the material can sustain a stable and biologically acceptable interface with soft, dynamic tissue. Table 1 summarizes these differences by bringing together the available biodegradability and biocompatibility across the principal biodegradable piezoelectric materials discussed in this review. Although biodegradability and biocompatibility are closely connected, they are not always discussed with the same depth or emphasis across material classes [22,23]. In practice, material suitability is typically presented as a balance among piezoelectric output, degradation profile, biological response, and processability rather than as a single optimizable property [21,28]. For this reason, the following Materials section examines these aspects together in order to provide a more comprehensive assessment of each material class, reflecting the way piezoelectric performance, degradation behavior, and biological compatibility are interrelated in practice.

Table 1. Comparative biocompatibility and degradation profile of biodegradable piezoelectric materials.

Materials	Degradation Mechanism	Device-Level Functional Lifetime	Degradation Products	Cytocompatibility	Inflammatory Response	Mechanical Modulus
β -Glycine composites (e.g., chitosan)	Matrix-dependent hydrolysis; glycine dissolves rapidly without polymer stabilization	Limited device data; Glycine (essential amino acid; metabolized); matrix governs encapsulation lifetime	Glycine (essential amino acid; metabolized); matrix products polymer-dependent	Confirmed in vitro; high stem cell viability in direct contact	Chitosan matrix generally low-immunogenic; limited in vivo composite data	MPa range (polymer-dependent)
PLLA	Bulk hydrolysis; amorphous regions first, then crystalline; enzyme-independent	Approx. 4 days reliable electrical operation reported in aqueous physiological environment; bulk material persists years in vivo	Lactic acid; ultimately metabolized to CO ₂ and H ₂ O; local pH reduction possible during degradation	FDA-approved injectable PLLA formulation provides clinical-use precedent; extensive cytocompatibility and clinical-use record	Generally mild inflammatory response reported; transient early reaction and late-stage macrophage-mediated clearance may occur	$\approx 1\text{--}4$ GPa in bulk; lower and architecture-dependent in electrospun nanofiber form
Silk fibroin	Enzyme-assisted (protease-dependent); negligible in PBS alone; β -sheet content governs rate	Up to 6 weeks structural and piezoelectric stability in aqueous environments reported; device-level data limited	Amino acids (absorbed or excreted)	Well established in biomedical scaffolds; extensive in vitro data	Low immunogenicity; animal implantation literature available	$\approx 2\text{--}500$ MPa; strongly dependent on processing, β -sheet content, and hydration
Chitosan	Enzymatic (lysozyme); physiologically relevant lysozyme-mediated degradation; rate depends on crystallinity and deacetylation degree	Device-level data limited; matrix used mainly in composites	Glucosamine and N-acetyl-D-glucosamine oligomers/monomers; generally considered biocompatible	Non-cytotoxic; antibacterial properties documented	Generally low immunogenicity; response depends on purity, deacetylation degree, and formulation	1–10 MPa
FF peptide systems	Expected peptide/protease-mediated breakdown; physiological degradation and loading stability remain insufficiently established	No device-level operational stability data; in vivo stability remains uncharacterized	Phenylalanine and related peptide fragments; expected to be metabolizable	Limited; early in vitro data are generally favorable	Largely unexplored in vivo	approx. 19 GPa (assembled nanotube)
PHB/PHBV	Hydrolytic and enzyme-assisted degradation; rate depends on crystallinity, copolymer composition, molecular weight, and scaffold architecture	Emerging device data; complete in vivo degradation over ≈ 12 weeks reported for a PHBV-based PENG composite; functional lifetime remains architecture-dependent	3-hydroxybutyric acid and, for PHBV, 3-hydroxyvaleric acid; generally regarded as biocompatible metabolites	Confirmed in vitro; favorable cell attachment, chondrocyte response, and rabbit cartilage-model results reported	Generally low immunogenicity; in vivo evidence is growing but remains less extensive than for clinically established PLLA	Generally lower and more tunable than PLLA; copolymer composition, porosity, and fiber architecture strongly affect stiffness

PENG: Piezoelectric nanogenerator.

3. Material Classes

Biodegradable piezoelectric materials are often discussed primarily as natural or synthetic polymers, but in a broader context the category also includes amino acids, peptides, proteins, polysaccharides, and related bio-derived assemblies. For the purposes of this review, the materials are compared along four aspects: the origin of the piezoelectric response, the way degradation proceeds, the extent to which biocompatibility has been demonstrated, and the level of device development achieved so far.

Although all piezoelectric polymers require a non-centrosymmetric organization that allows mechanical deformation to change net polarization, the molecular origin of this response is not identical across material classes. In PLLA, shear piezoelectricity arises primarily from deformation of oriented helical chains containing aligned carbonyl dipoles, whereas PHB and PHBV rely on polar ester groups, crystalline chain packing, and processing-induced orientation. PVDF and PVDF-TrFE differ because their strong response is associated with polar all-trans chain conformations, stabilization of the ferroelectric phase, and domain polarization. In natural polymers, the relevant asymmetry is hierarchical, with oriented β -sheet crystallites dominating in silk fibroin, triple-helical peptide-bond dipoles contributing in collagen, and polar functional groups and hydrogen-bond networks contributing in chitosan. In contrast, amino-acid and peptide systems derive their piezoelectric response from non-

centrosymmetric molecular or supramolecular packing. Thus, molecular dipoles and structural asymmetry provide a common physical basis, but chain conformation, crystal symmetry, hydrogen bonding, and domain behavior produce material-specific deviations in the detailed mechanism.

3.1. Amino Acids and Small-Molecule Crystals

Amino acid crystals are a class of biodegradable piezoelectrics in which strong electromechanical response arises from simple, water-soluble biomolecules. Glycine, as a representative example, shows that its piezoelectric response varies dramatically depending on crystalline phase and molecular packing (Figure 1a) [39,64]. α -glycine is centrosymmetric and therefore non-piezoelectric, whereas β - and γ -glycine are non-centrosymmetric and thus piezoelectric. The β -phase exhibits a large shear piezoelectric coefficient d_{16} of approximately 174–195 pm/V, while γ -glycine is more often discussed in terms of voltage output and structural stability [65]. Other small molecules in this category include DL-alanine and several dipeptides, although these have generally been studied less extensively (Figure 1b,c) [66,67].

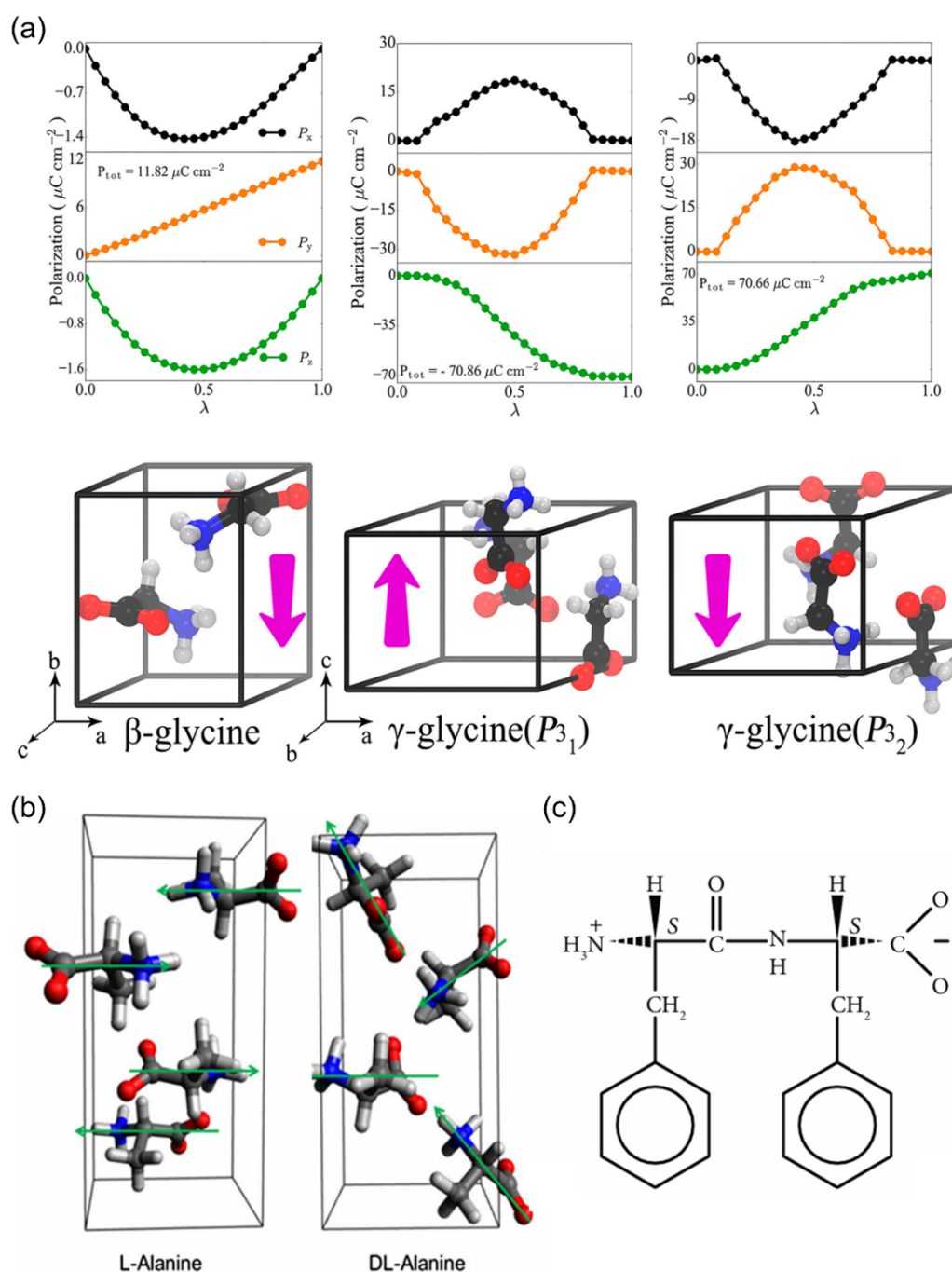


Figure 1. Molecular origins of piezoelectricity in amino acids and small-molecule crystals. (a) Phase-dependent polarization and crystal packing of β - and γ -glycine polymorphs, illustrating how molecular arrangement governs

the piezoelectric response of glycine crystals [64]. (b) Crystal packing of L-alanine and DL-alanine, showing the racemic packing arrangement that produces a non-zero net polarization in DL-alanine [67]. (c) Molecular structure of diphenylalanine (FF), a representative building block for piezoelectric self-assembled peptide systems [66]. Adapted with permission from Ref. [64]. Copyright 2019, American Chemical Society. Reprinted with permission from Ref. [67]. Copyright 2019, American Physical Society. Adapted with permission from Ref. [66]. Copyright 2019, American Association for the Advancement of Science.

The challenge, however, lies in stabilizing the piezoelectric phase under physiologically relevant conditions, which has led to the development of matrix-assisted processing approaches (Figure 2a–c) [33,60]. A representative example is the β -glycine/chitosan composite film, in which chitosan acts as a mechanical support and participates in polymorph selection by controlling crystallization kinetics during solvent casting, suppressing the conversion to the non-piezoelectric α -phase (Figure 2a) [60]. Flexible pressure sensors based on this composite have been reported with sensitivities around $2.82 \pm 0.2 \text{ mV kPa}^{-1}$, a level of performance relevant to physiological pressure sensing at biointerfaces (Figure 2b) [60]. Glycine/alginate/glycerol films further demonstrate that polymer matrices can support monolithic β -glycine spherulite formation and flexible biodegradable force sensing (Figure 2c) [33].

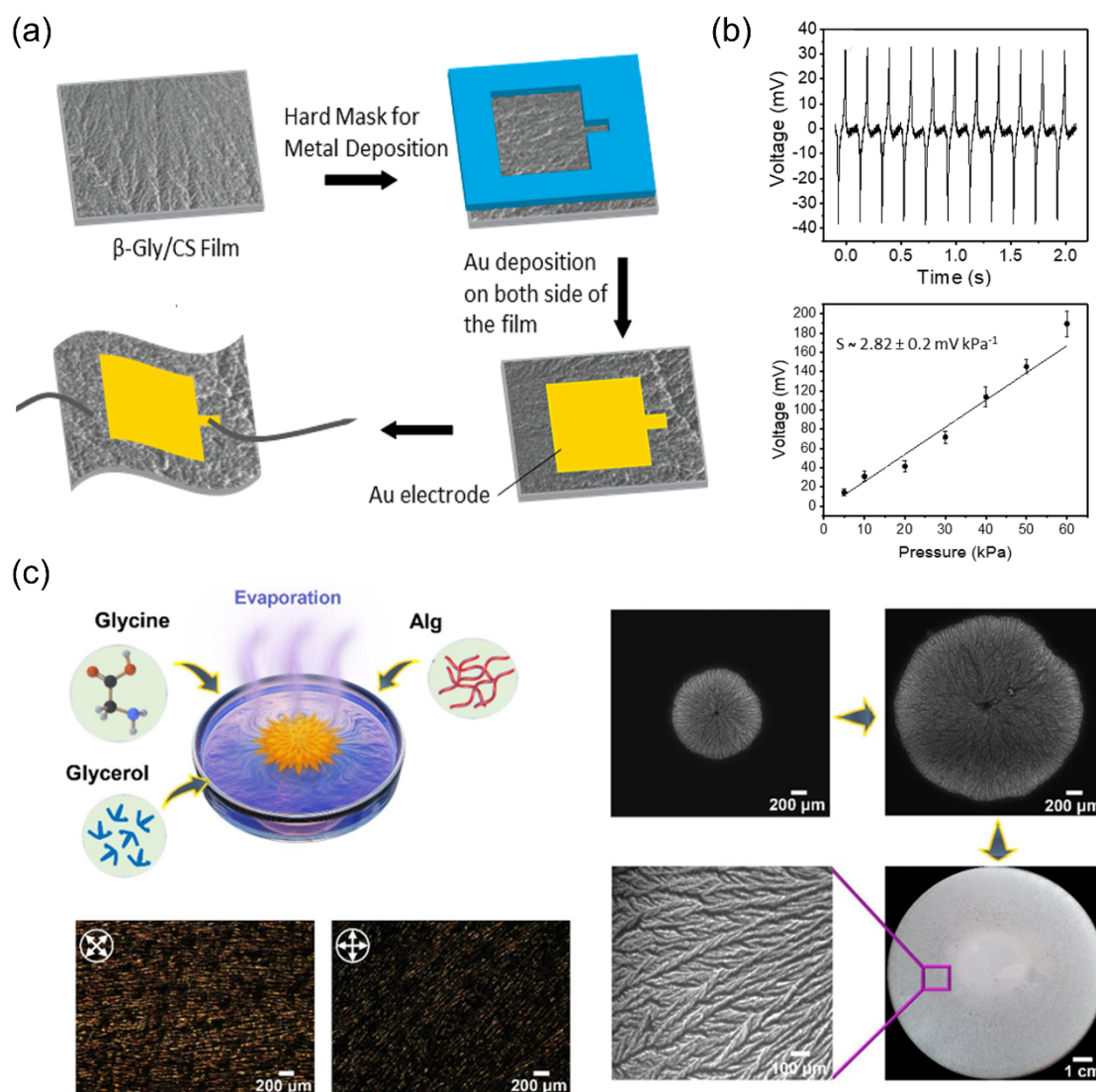


Figure 2. Matrix-assisted glycine-polymer piezoelectric systems for biodegradable sensing. (a) Fabrication schematic of a β -glycine/chitosan flexible piezoelectric pressure sensor. (b) Corresponding output-voltage response and pressure-voltage sensitivity of approximately $2.82 \pm 0.2 \text{ mV kPa}^{-1}$ [60]. (c) Matrix-assisted preparation of a glycine/alginate/glycerol piezoelectric film, including solvent evaporation and the resulting monolithic β -glycine spherulite morphology [33]. Adapted with permission from Ref. [60]. Copyright 2020, American Chemical Society. Adapted with permission from Ref. [33]. Copyright 2024, Oxford University Press and Chinese Society for Biomaterials.

Glycine can also function as a molecular and crystallization modifier in biodegradable polymers rather than only as an independent piezoelectric crystal. In electrospun PHB-glycine scaffolds, glycine crystallization within the fibrous matrix has been reported to alter surface topography, wettability, PHB crystallite dimensions, and overall crystallinity, while the electrospinning environment can promote the piezoelectrically active β -glycine form. This example illustrates that glycine loading can simultaneously modify polymer microstructure and contribute its own polar crystalline phase, although the resulting response remains dependent on glycine content, polymorph selection, dispersion, and processing conditions [68].

Another point is that the piezoelectric charge coefficient alone does not determine whether a material is well suited for biosensing. Amino-acid crystals often combine relatively low dielectric constants with favorable piezoelectric coefficients, which can lead to strong voltage output. Glycine is therefore important not only because of its large d -values in selected crystallographic modes, but also because it shows how this combination can be advantageous for sensing [39,64]. DL-alanine is often discussed alongside glycine, although its piezoelectric response is more modest [67].

From a biodegradation standpoint, amino acids are attractive because their final breakdown products are already familiar to biological metabolism [31]. The greater challenges lie in phase stability, sensitivity to water, and the ability to retain performance once the material is built into a device [33,36,65]. In practice, amino-acid crystals are best understood as a high-performance but stabilization-limited class of materials [69]. Recent biodegradable amino-acid-crystal tactile sensors further support the relevance of this material class for transient sensing applications [70]. They show some of the strongest intrinsic piezoelectric behavior among biodegradable systems, but that behavior usually has to be stabilized through matrix engineering, interfacial control, or both before it can be maintained under wet or physiological conditions.

3.2. Natural Biopolymers: Protein- and Polysaccharide-Based Piezoelectrics

Natural biopolymers offer rather different advantages. Although their intrinsic piezoelectric coefficients are often modest compared with amino-acid crystals or conventional ceramics, they benefit from biological familiarity, mechanical softness, and established relevance in biomedical applications [60]. In these materials, piezoelectricity is closely related to hierarchical structure, chain orientation, crystallinity, and hydrogen-bond organization [71,72]. As a result, their electromechanical response is highly sensitive to processing conditions, and the same structural features that influence output also tend to influence degradation.

Silk fibroin is one of the best-known natural biopolymers. Its piezoelectric response is generally linked to oriented β -sheet domains, and both electrical output and degradation rate can be modulated by controlling structural assembly during processing [57,71,72]. Recent work on electrospun silk fibroin shows a fabrication route from cocoon degumming and CaCl_2 /formic-acid dissolution to electrospinning, and reports an effective piezoelectric coefficient reaching 43 pC/N for the optimized material (Figure 3a,b) [72]. This feature makes silk fibroin attractive for transient biosensor applications because structural engineering can influence both function and lifetime.

Collagen is important for a somewhat different reason. It is not only a biomaterial candidate but also one of the sources of electromechanical coupling already present in native human tissue [73,74]. Piezoelectricity in collagen is usually discussed in relation to its triple-helical structure and its role in load-bearing tissues such as bone and tendon. Resonance-enhanced piezoresponse force microscopy has shown spatially heterogeneous piezoresponse in type I collagen fibrils, with gap regions exhibiting stronger response than overlap regions (Figure 3c,d) [75]. This provides a biologically intuitive link between endogenous mechanotransduction and engineered transient sensing.

Chitin and chitosan occupy an intermediate position between biological familiarity and practical processability. Chitosan offers solution processability and biodegradability, and has been reported to exhibit piezoelectricity in thin-film form [22,59,76]. Recent chitosan-film processing via solvent casting followed by NaOH treatment highlights how deprotonation and film formation can be used to obtain flexible, robust, and bioactive piezoelectric chitosan films (Figure 3e) [76]. Both chitin and chitosan are attractive because they degrade through lysozyme-mediated pathways that are physiologically relevant in mammals [56].

Although natural biopolymers are generally attractive because of their biocompatibility and relevance to soft tissue, their piezoelectric coefficients are usually lower than those of amino-acid crystals and far below those of conventional ceramics. Composite formation can improve output, but adding non-degradable fillers or additives can make the overall biodegradability less clear. Natural biopolymers are therefore often best understood as biologically favorable but performance-limited materials unless structure and processing are carefully optimized.

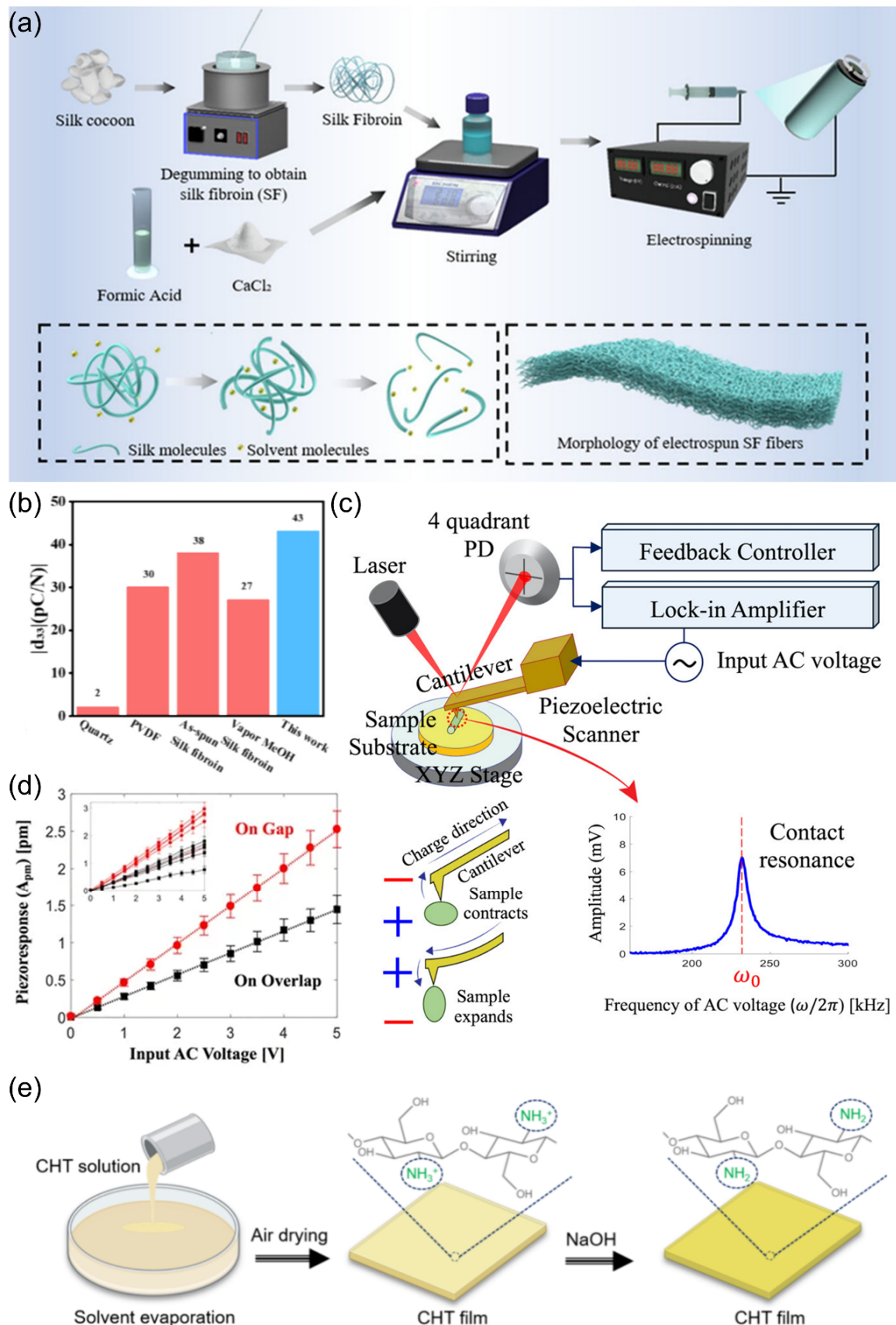


Figure 3. Natural biopolymer piezoelectrics based on silk fibroin, collagen, and chitosan. (a) Fabrication route for electrospun silk fibroin fibers, including cocoon degumming, CaCl_2 /formic-acid dissolution, stirring, electrospinning, and the resulting electrospun fiber morphology [72]. (b) Comparison of effective piezoelectric coefficient $|d_{33}|$ values, highlighting the optimized silk fibroin material with $|d_{33}| = 43$ pC/N [72]. (c) Resonance-enhanced piezoresponse force microscopy setup for quantifying nanoscale piezoresponse in collagen type I fibrils [75]. (d) Collagen fibril piezoresponse as a function of input AC voltage, showing higher response in gap regions than overlap regions [75].

(e) Solvent-casting and NaOH-treatment schematic for chitosan film fabrication, illustrating the conversion from protonated chitosan film to deprotonated chitosan film [76]. Adapted with permission from Ref. [72]. Copyright 2025, American Chemical Society. Adapted with permission from Ref. [75]. Copyright 2020, American Chemical Society. Adapted with permission from Ref. [76]. Copyright 2025, American Chemical Society.

3.3. Synthetic Biodegradable Polymers

Among synthetic biodegradable piezoelectric polymers, PLLA is one of the most translationally mature materials because it combines a longstanding history of biomedical use, a comparatively well-characterized hydrolytic degradation pathway, controllable molecular orientation, and multiple device-level demonstrations. Its piezoelectric response is associated with shear deformation of oriented helical chains containing aligned carbonyl dipoles and depends strongly on crystallinity, draw ratio, molecular orientation, and composite architecture [16,42,77]. Importantly, this maturity does not imply that PLLA has the highest intrinsic piezoelectric coefficient; rather, its processing window, mechanical behavior, degradation profile, and biomedical familiarity are more established than those of many emerging molecular and peptide systems.

Recent PLLA-based composite films show how this material class is being extended beyond neat oriented PLLA. Yttrium-doped Zinc Oxide (ZnO)/PLLA hybrid films were prepared by first synthesizing Yx-ZnO particles and then dispersing them in OH-PLLA-COOR solution to form spin-coated composite films (Figure 4a) [78]. Structural characterization by X-ray diffraction confirms the crystalline phase of ZnO and Y-doped ZnO particles (Figure 4b), while output measurements show composition-dependent open-circuit voltage and short-circuit current from ZnO/PLLA and Yx-ZnO/PLLA films (Figure 4c) [78]. This example illustrates that PLLA-based biodegradable piezoelectric polymers can be strengthened by inorganic piezoelectric fillers, although full-system biodegradability must then be considered carefully. Because some device components and inorganic fillers may not share the same degradation pathway as PLLA, this example is best viewed as a PLLA-based biodegradable active-layer strategy rather than a fully biodegradable device demonstration.

PLLA also shows that piezoelectric performance depends not only on generating molecular order, but on maintaining it for long enough to be useful [42,77]. In a different strategy, crystalline PLLA nanotubes have been used as soft piezoelectric interfaces for biological systems, where nanotube morphology and polymer crystallinity were used to regulate cell attachment (Figure 4d,e) [79]. The higher cell attachment observed on crystalline PLLA nanotubes compared with amorphous PLLA nanotubes suggests that electromechanical and topographical cues can be coupled in biodegradable polymer biointerfaces [79].

PHB and its copolymer PHBV constitute an important family of biosynthesized biodegradable polyesters for piezoelectric biomedical platforms. Their electromechanical response is generally associated with polar ester groups, non-centrosymmetric crystalline packing, and chain orientation generated during film formation, drawing, electrospinning, or additive manufacturing. PHB is attractive because of its microbial origin and bioresorbability, while incorporation of hydroxyvalerate in PHBV can reduce brittleness and improve processing and mechanical compliance. Biomedical demonstrations include nanofibrous cartilage scaffolds, piezoelectric bone-regeneration constructs, and composite systems containing graphene oxide or barium titanate. The glycine-loaded electrospun PHB scaffold discussed above further illustrates how molecular additives can tune PHB topography, crystallinity, and piezoelectric response [68]. However, neat PHB is relatively brittle, and the use of persistent inorganic fillers can complicate claims of complete device biodegradability. These materials should therefore be assessed through the combined effects of polymer composition, architecture, filler fate, and degradation products [80–82].

Fabrication method provides another level of control over the performance of PLLA- and PHB-based systems. Electrospinning generates extracellular-matrix-like nanofibers with high surface area and can promote chain and fiber alignment, making it effective for enhancing piezoelectric response and cell-material interactions. Three-dimensional (3D) printing provides more direct control over macroscopic pore geometry, load paths, patient-specific shape, and spatially varying stiffness; 3D-printed PLLA scaffolds have consequently been investigated as biodegradable piezoelectric constructs for bone regeneration [83]. Four-dimensional (4D) printing extends this concept by introducing time-dependent or stimulus-responsive shape change, although its integration with reproducible piezoelectric output and programmed biodegradation remains less mature. Thus, electrospinning is advantageous for nanoscale alignment, whereas 3D and emerging 4D printing offer high architectural control and adaptability. These methods shall be selected according to whether molecular orientation, tissue-scale porosity, or dynamic shape evolution is the dominant design requirement [40,54,80,83].

Regulatory familiarity should be discussed at the level of specific products and indications rather than by labeling an entire polymer family as universally approved. For example, injectable PLLA formulations, such as Sculptra/Sculptra Aesthetic, have received FDA approval for specific dermal applications, providing a useful

clinical-use precedent for PLLA-based biomaterials without establishing universal approval for all PLLA compositions or piezoelectric PLLA devices [84]. Piezoelectricity adds a distinct biomedical function to this established biodegradable material platform by converting physiological deformation into electrical signals for self-powered sensing or into localized electrical cues for stimulation, potentially reducing reliance on implanted batteries and external wiring.

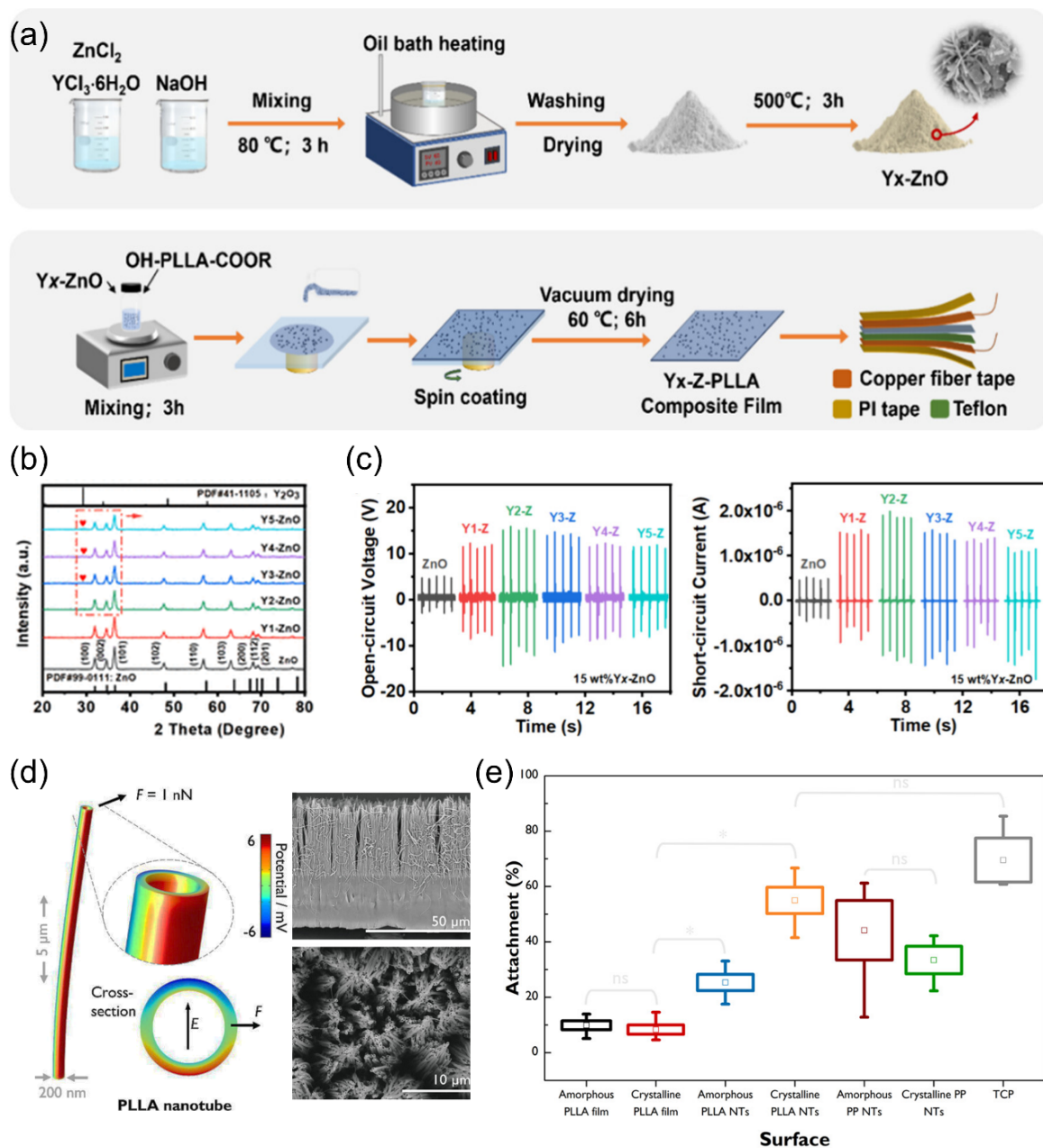


Figure 4. Synthetic biodegradable piezoelectric polymers based on PLLA composite films and PLLA nanotube biointerfaces. (a) Synthesis and device-fabrication scheme for degradable Yx-ZnO/PLLA piezoelectric composite films, including Yx-ZnO particle preparation, spin coating with OH-PLLA-COOR, vacuum drying, and device stacking with copper fiber tape, PI tape, and Teflon [78]. (b) X-ray diffraction patterns of ZnO and Y1-ZnO to Y5-ZnO, confirming the crystalline structure of the Y-doped ZnO fillers [78]. (c) Open-circuit voltage and short-circuit current outputs of ZnO/PLLA and Yx-ZnO/PLLA composite films, illustrating composition-dependent piezoelectric performance [78]. (d) Piezoelectric PLLA nanotube schematic and SEM morphology, including simulated potential distribution under a 1 nN force and vertically aligned nanotube morphology [79]. (e) Cell attachment on amorphous/crystalline PLLA films and nanotubes, PP nanotubes, and tissue-culture plastic, showing enhanced attachment on crystalline PLLA nanotube interfaces, with statistical significance symbols indicating ns = not significant and * = $p < 0.01$ [79]. Adapted with permission from Ref. [78]. Copyright 2024, American Chemical Society. Adapted with permission from Ref. [79]. Copyright 2020, American Chemical Society.

3.4. Peptide-Based and Self-Assembling Systems

Peptide-based materials are emerging as an important class because they bring molecular programmability into the design of biodegradable piezoelectric materials [66]. Their piezoelectric response can be tuned through amino-acid sequence, supramolecular packing, self-assembly pathway, and external-field-directed organization, which makes them conceptually distinct from both amino-acid crystals and conventional biodegradable polymers [85–87].

Diphenylalanine (FF) self-assembles into ordered nanostructures whose non-centrosymmetric packing gives rise to piezoelectricity, with comparatively strong responses among peptide-based systems (Figure 5a,b) [88,89]. Electric-field-assisted self-assembly provides one route to align FF microrods and improve energy conversion performance, illustrating how external fields can guide the assembly of peptide-based piezoelectric structures [89]. Despite this promising behavior, translating FF assemblies into stable transient devices under physiological conditions remains challenging. Incorporating hydrophobic porphyrin into FF nanotubes has been used to control biodegradability and structural stability (Figure 5c) [90].

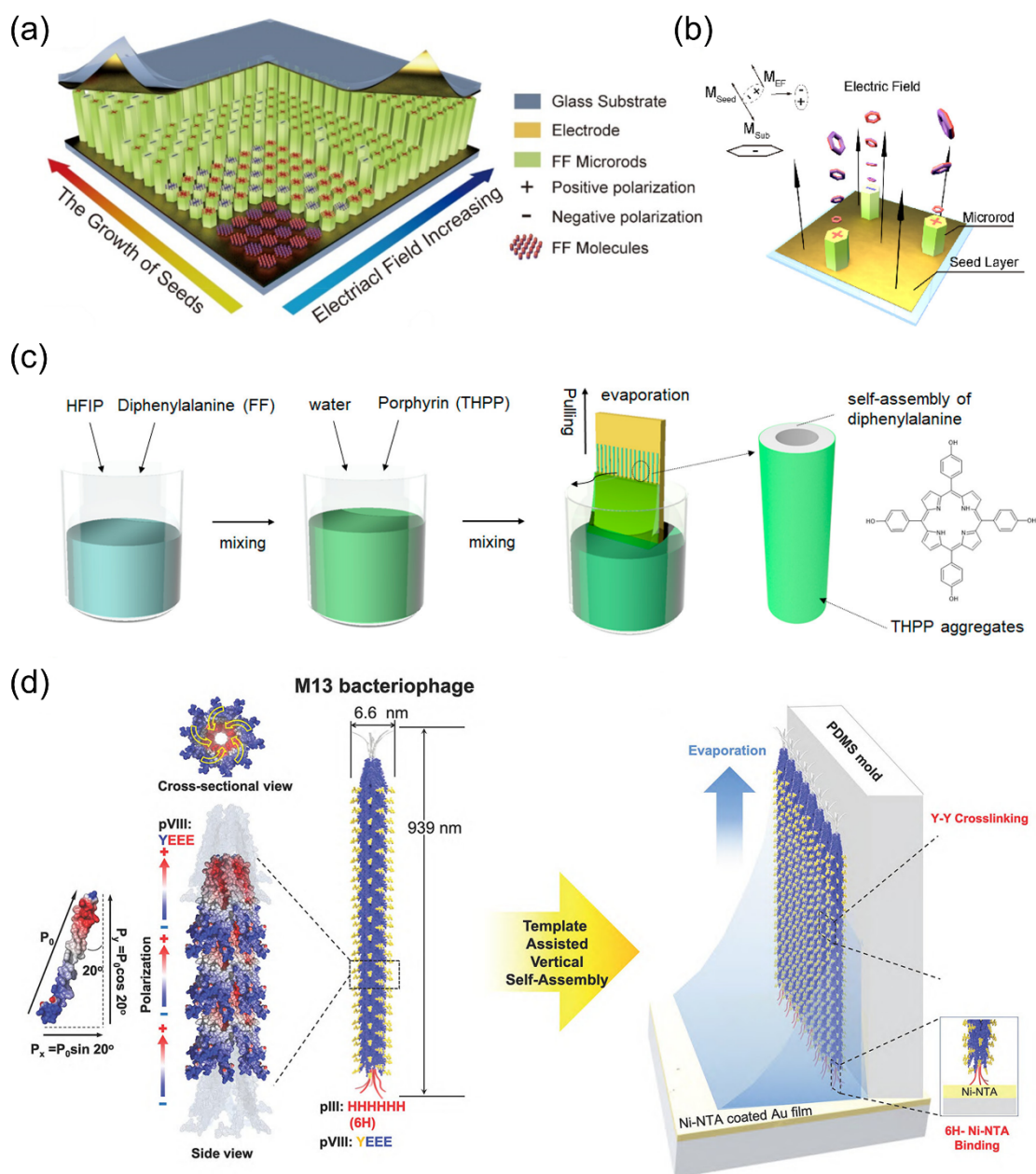


Figure 5. Peptide-based and self-assembling piezoelectric systems. (a) Electric-field-assisted growth of FF microrods in an FF-based piezoelectric nanogenerator, showing the relationship between seed growth, field direction, and positive/negative polarization in the assembled microrods [89]. (b) Schematic illustration of electric-field-induced twisting and alignment of FF rings during microrod self-assembly [89]. (c) Fabrication route for THPP-integrated diphenylalanine peptide nanotubes, including HFIP/FF solution, water/porphyrin solution, mixing, meniscus-driven

pulling/evaporation, FF self-assembly, and THPP aggregate incorporation [90]. (d) Vertically self-assembled M13 bacteriophage piezoelectric nanostructures, showing engineered pVIII YEEE and pIII 6H motifs, polarization orientation, and template-assisted vertical self-assembly on Ni-NTA-coated Au film using a PDMS mold [87]. Adapted with permission from Ref. [89]. Copyright 2023, American Chemical Society. Adapted with permission from Ref. [90]. Copyright 2022, American Chemical Society. Adapted with permission from Ref. [87]. Copyright 2019, American Chemical Society.

M13 bacteriophage-based systems highlight a different route to biodegradable piezoelectric design, one in which electromechanical behavior can be shaped through biological sequence design as well as processing (Figure 5d) [87,91]. Vertically aligned and genetically engineered M13 phage nanostructures can be assembled on Ni-NTA-coated substrates through template-assisted self-assembly, producing unidirectional polarization and improved piezoelectric output [87]. This coupling makes them particularly attractive as conceptual platforms, because piezoelectric response and degradation behavior could, in principle, be tuned together at the molecular level [92]. Table 2 summarizes the main biodegradable piezoelectric material classes discussed above, comparing their representative materials, structural origins of piezoelectricity, reported piezoelectric responses, degradation characteristics, strengths, and current limitations.

Overall, peptide-based systems are becoming an important, though still early-stage, class of piezoelectric materials for biosensor applications. Their significance lies less in present translational maturity than in the design possibilities they open up [85]. They point toward a future in which biodegradable piezoelectric materials may be tuned not only through post-processing and composite formulation, but also at the level of sequence, supramolecular assembly, and biologically programmable architecture.

Table 2. Comparative summary of the main biodegradable piezoelectric material classes.

Material Class	Representative Materials	Origin of Piezoelectricity/ Structural Basis	Typical Reported Piezoelectric Response *	Degradation/ Resorption Characteristics	Main Strengths	Main limitations/ Current Status
Amino acids and small-molecule crystals	β -glycine, γ -glycine, DL-alanine	Non-centrosymmetric packing and phase-dependent dipole alignment.	β -glycine: $d_{16} \approx 174\text{--}195 \text{ pm/V}$; γ -glycine often discussed in terms of voltage output and stability; DL-alanine lower	Biocompatible metabolites; limited by water sensitivity and phase instability.	High intrinsic response and low dielectric constant.	Requires matrix or interfacial stabilization in wet environments.
Natural biopolymers: protein- and polysaccharide-based piezoelectrics	Silk fibroin, collagen, chitin/chitosan	Oriented hierarchical structures and hydrogen-bonded dipoles: β -sheets in silk, triple helices in collagen, and polar chains in chitosan.	Generally modest and strongly dependent on orientation and processing.	Enzyme-assisted degradation; rate depends on molecular order and hydration.	Good biocompatibility, softness, and tissue relevance.	Lower output and greater processing variability than crystalline systems.
Synthetic biodegradable polymers	PLLA, PHB/PHBV	PLLA: oriented helical chains and carbonyl dipoles. PHB/PHBV: ester dipoles and non-centrosymmetric crystalline order.	PLLA: $d_{14} \approx 8\text{--}12 \text{ pC/N}$; PHB/PHBV generally lower.	PLLA degrades by bulk hydrolysis; PHB/PHBV by hydrolytic and enzyme-assisted pathways.	Established biomedical use; compatible with drawing, electrospinning, and 3D printing.	PLLA is device-mature; PHB/PHBV remain emerging. Crystallinity links output, stiffness, and degradation.
Peptide-based and biological self-assembling systems	FF, M13 bacteriophage, and related peptide-derived assemblies	Non-centrosymmetric supramolecular packing and sequence-dependent dipole organization.	Potentially strong, but highly architecture- and alignment-dependent.	Potentially biodegradable, but physiological stability and clearance remain uncertain.	Molecularly programmable through sequence and self-assembly.	Mostly proof-of-concept; limited device-level and in vivo evidence.

Note: Reported piezoelectric values are not directly comparable across all materials because different coefficients, modes, sample architectures, and measurement methods are used.

4. Applications as Biosensors

Recent studies in biodegradable piezoelectric biosensors fall into four application directions: non-invasive wearable monitoring, short-term implantable physiological sensing, temporary interfaces for healing and functional recovery, and systems that progress from sensing toward active therapy. These directions reflect the main application scenarios now emerging in the field and point to a broader shift beyond passive sensing, toward transient multifunctional biointerfaces that combine sensing, transduction, and, in some cases, stimulation within a single platform.

4.1. Non-Invasive Wearable Monitoring

Wearable biodegradable piezoelectric devices have attracted significant attention in recent years because they enable transient or environmentally benign monitoring without surgical placement [93,94]. They also provide a relatively accessible platform for evaluating signal quality, mechanical durability, and device stability under body-relevant deformation. In this context, bacterial-cellulose and wood-derived piezoelectric platforms are attractive because they combine renewable materials, porous architectures, and pressure-sensitive electromechanical output (Figure 6a–d) [95,96]. A molecular ferroelectric embedded in a bacterial cellulose hydrogel has been demonstrated as a biodegradable and recyclable piezoelectric sensor, while delignified wood sponge piezoelectric nanogenerators have been used for wearable sensing and mechanical energy harvesting [95,96]. Wearable systems are also useful for showing another advantage of biodegradable piezoelectrics. They are well suited for temporary or disposable monitoring devices, where the sensor only needs to work for a short time and does not have to remain in the environment afterward.

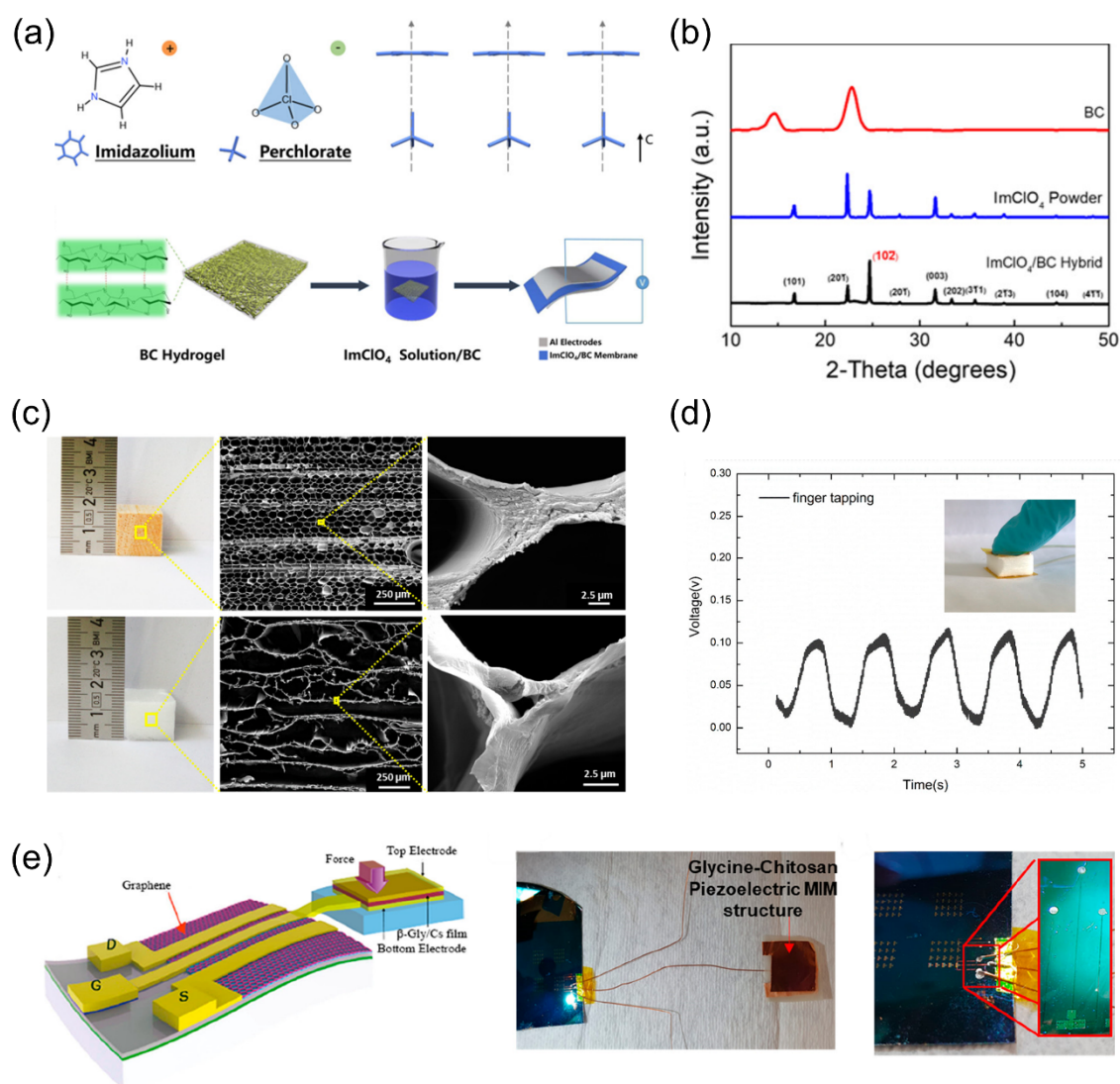


Figure 6. Wearable and short-term biodegradable piezoelectric biosensors. (a,b) Bacterial cellulose hydrogel sensor based on an embedded molecular ferroelectric, including ImClO₄ molecular components/packing, BC hydrogel-to-ImClO₄/BC membrane sensor fabrication with Al electrodes, and X-ray diffraction patterns of BC, ImClO₄ powder, and the ImClO₄/BC hybrid [95]. (c,d) Sustainable wood-sponge piezoelectric nanogenerator for wearable sensing, showing native balsa wood and delignified wood sponge photographs/SEM morphologies and finger-tapping voltage response as a representative wearable sensing demonstration [96]. (e) Graphene field-effect transistor coupled with a biodegradable β-glycine/chitosan piezoelectric MIM structure in an extended-gate configuration, including device schematic and optical images of the piezoelectric sensor connected to the GFET/contact pads [97]. Adapted with permission from Ref. [95]. Copyright 2022, American Chemical Society.

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4.2. Short-Term Implantable Physiological Monitoring

An early and still influential benchmark for biodegradable piezoelectric biosensing is the implantable PLLA force/pressure sensor reported by Curry and co-workers in 2018 [16]. The device was placed in the abdominal cavity of mice and used to track diaphragmatic contraction, operating across a physiological pressure range of 0–18 kPa while maintaining stable function for about four days under aqueous physiological conditions. This work marked a shift from piezoelectric material characterization toward genuinely functional implantable sensing.

More recent device concepts suggest that this application direction is expanding beyond passive force readout. For example, a graphene field-effect transistor coupled to a biodegradable β -glycine/chitosan piezoelectric metal-insulator-metal structure has been used as a low-voltage dynamic pressure sensor (Figure 6e) [97]. In this configuration, the biodegradable piezoelectric component converts pressure into a gate signal that is amplified by the graphene transistor, showing how bio-derived piezoelectric materials can be integrated with active electronic readout platforms [97]. Together with biodegradable hydrogel and wood-sponge sensors, this example broadens the discussion from implantable pressure readout toward biodegradable and environmentally benign piezoelectric sensing platforms.

This area is well aligned with transient electronics, where device operation is intended to match a limited therapeutic or diagnostic window. In many cases, clinically relevant measurements are needed only for a short period, such as after surgery, during functional recovery, or in early detection of organ dysfunction. For these situations, a self-powered device that operates only as long as needed and then safely degrades offers a clear advantage over a permanent implant. Viewed in this way, biodegradable piezoelectric sensors are particularly well suited to temporary, localized measurements that are closely linked to tissue motion.

4.3. Temporary Interfaces During Tissue Healing and Functional Recovery

Endogenous electrical potentials and fields contribute to cell migration, differentiation, wound closure, nerve growth, and tissue remodeling. Reported endogenous bioelectric cues and collagen-related piezoelectric potentials can fall within a comparable millivolt-scale range under selected mechanical conditions, suggesting that the output magnitude of some piezoelectric materials may be biologically relevant in specific settings [73,74,98]. Piezoelectric scaffolds can partially emulate or augment these cues by generating localized surface charge and electric fields during physiological loading or ultrasound excitation, and several studies report downstream effects involving calcium signaling, focal adhesion, cytoskeletal organization, and lineage-specific differentiation [98]. However, the open-circuit voltage or nominal power measured at a device terminal is not equivalent to the electric field experienced by cells. Ionic screening, tissue impedance, electrode geometry, device-cell distance, loading frequency, and stimulation duration all influence the effective biological dose. Current evidence therefore supports the ability of selected platforms to induce functional biological responses in vitro and in vivo, but it does not yet establish a universal output threshold sufficient to modulate endogenous potentials. Standardized reporting of local electric field, charge density, current density, waveform, and exposure duration is required for quantitative comparison.

Another important application direction involves temporary piezoelectric interfaces used during healing and functional recovery. In this setting, sensing and stimulation are often closely intertwined rather than fully separable. Bone repair, cartilage remodeling, peripheral nerve regeneration, and wound healing all fall into this category because the useful lifetime of the device is tied to a biological process that typically unfolds over weeks or months rather than years [62,81]. At these mechanically active healing sites, the piezoelectric element can respond to local deformation while also generating electrical cues that influence tissue repair [99,100].

For cartilage-related examples, graphene oxide-reinforced PHBV nanofibrous scaffolds have been developed to enhance mechanical and piezoelectric properties while improving chondrocyte proliferation and extracellular-matrix production (Figure 7a,b) [82]. In the system, reinforcement increased the piezoelectric coefficient and generated voltage, and the GO-reinforced scaffolds promoted cell attachment, viability, ECM production, and collagen type-II expression [82]. This illustrates how biodegradable piezoelectric scaffolds can be designed not only as passive materials but as mechanically responsive interfaces for cartilage-oriented tissue regeneration.

Piezoelectric stimulation has also been investigated as a physical cue for osteogenic differentiation. PVDF and PVDF-CFO electroactive films crystallized in the β -phase were used as two-dimensional substrates for mesenchymal stem cells, where electromechanical stimulation of PVDF-CFO induced focal adhesion changes, vimentin reorganization, and metabolomic shifts toward an osteogenic phenotype (Figure 7c,d) [101]. Although PVDF itself is not biodegradable, the study clarifies how piezoelectric or electromechanical stimulation can

influence early osteogenic commitment, a mechanism relevant to the design of future degradable stimulation-responsive scaffolds. Because PVDF and PVDF-CFO are non-biodegradable, this example is included as a mechanistic benchmark for how electromechanical stimulation can influence osteogenic commitment, rather than as a transient-device demonstration.

Peripheral nerve repair provides another example of an active regenerative interface. Ultrasound can activate piezoelectric materials within the scaffold, generating local electrical cues without implanted wires [20,102,103]. Recently, barium titanate (BTO)-loaded chitosan microporous scaffolds were shown to promote Schwann-cell migration and neurotrophin production under ultrasound stimulation, highlighting their potential as degradable, stimulation-responsive scaffolds for nerve-regenerative biointerfaces (Figure 7e,f) [103].

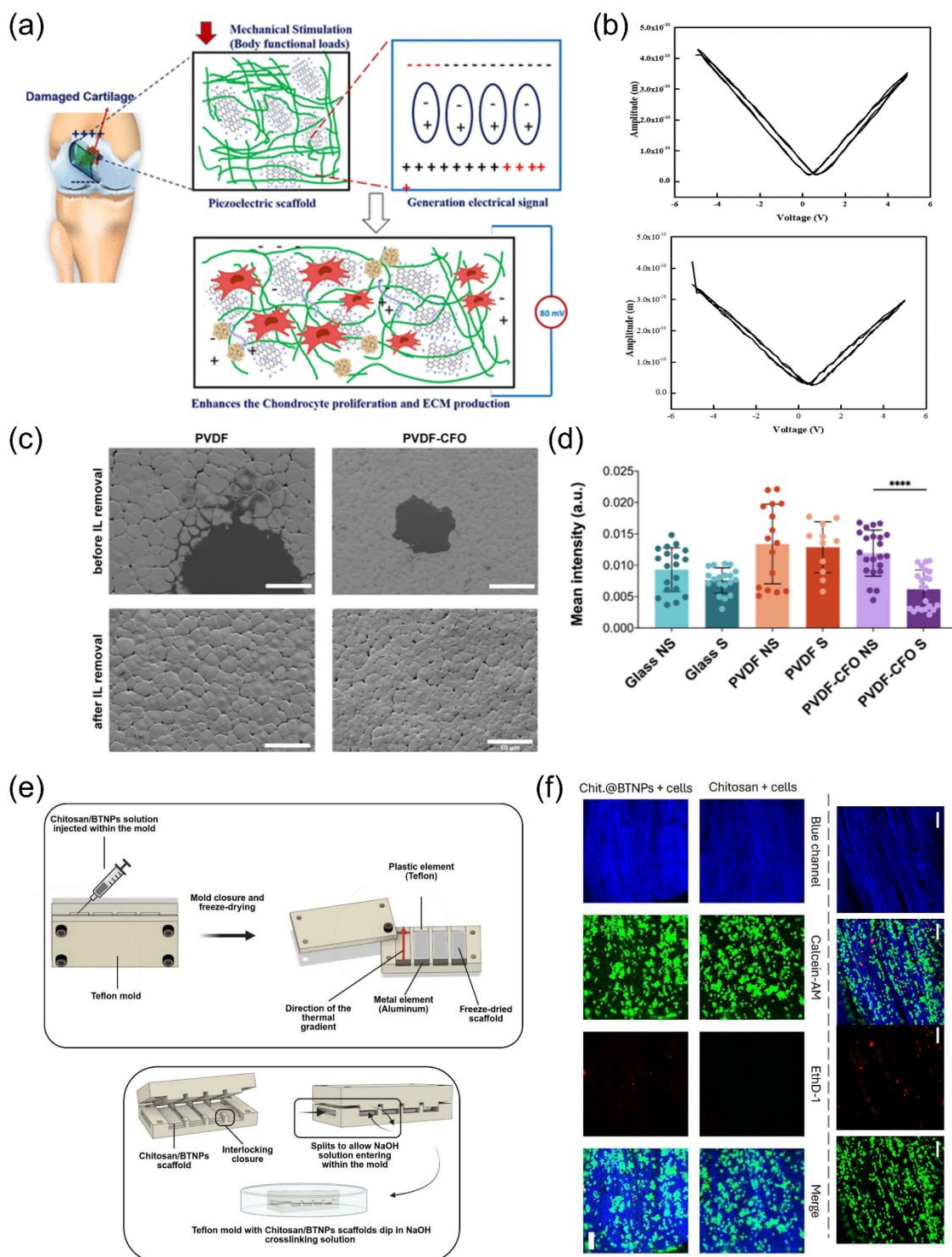


Figure 7. Therapy-adjacent piezoelectric biointerfaces and biodegradable scaffold platforms for tissue regeneration and stimulation. **(a,b)** GO-reinforced PHBV nanofibrous scaffold for cartilage-oriented regeneration, including a

concept schematic in which body-load-induced mechanical stimulation generates electrical cues that enhance chondrocyte proliferation and ECM production, and PFM displacement-amplitude loops confirming piezoresponse behavior in PB and PB-GO scaffolds [82]. (c,d) Electroactive PVDF/PVDF-CFO substrates for piezoelectric stimulation of mesenchymal stem cells, including FESEM images before and after ionic-liquid removal and vimentin mean-intensity quantification showing decreased vimentin intensity in stimulated PVDF-CFO samples as an early osteogenic cytoskeletal response [101]. (e,f) Piezoelectric chitosan/BTNP microporous scaffolds for ultrasound-driven Schwann-cell biointerfaces, including the custom mold/freeze-drying/NaOH-crosslinking fabrication scheme and LIVE/DEAD fluorescence images showing cell viability and alignment along anisotropic scaffold pores [103]. Adapted with permission from Ref. [82]. Copyright 2020, American Chemical Society. Adapted with permission from Ref. [101]. Copyright 2024, American Chemical Society. Adapted with permission from Ref. [103]. Copyright 2026, American Chemical Society.

4.4. Sensing Platforms That Border on Active Therapy

A further application direction is the evolution from passive signal monitoring toward therapy-adjacent and actively therapeutic transient biointerfaces. In passive sensing, physiological deformation is converted into a readable electrical signal. In more advanced systems, the same electromechanical conversion can generate localized electrical or acoustic stimulation that modifies cell behavior, supports tissue regeneration, or facilitates drug delivery. Thus, their role extends beyond biosensing toward transient biointerfaces that can both detect physiological signals and deliver therapeutic cues [104,105].

For example, Chorsi et al. reported the glycine/PCL (glycine/polycaprolactone) biodegradable ultrasound transducer in 2023. The device was based on highly piezoelectric amino acid nanofibers and generated an ultrasonic output of 334 kPa at 0.15 V_{rms}. In orthotopic glioblastoma models, it was used to facilitate chemotherapeutic delivery to the brain and reportedly doubled animal survival time. The study demonstrates that a fully biodegradable piezoelectric platform can support stable implantable acoustic transduction [36]. In addition, Zhao et al. reported a biodegradable PLLA piezoelectric implant for wirelessly delivering electrical stimulation to the heart under ultrasound stress. The study pushed biodegradable piezoelectric interfaces into the area of cardiac modulation rather than passive recording alone [106]. Together with recent wireless intestinal motility monitoring platforms, these studies suggest that biodegradable piezoelectric devices are increasingly being designed as hybrid systems in which sensing, signal transmission, and therapeutic actuation can coexist within a single transient architecture. These studies show that the concept of a biosensor in this field is expanding. When a device produces electrical or acoustic output in response to mechanical input or external ultrasound, it can function not only as a sensor, but as a broader transient biointerface.

Current applications of biodegradable piezoelectric biosensors are centered on situations where device function is needed only for a limited period. These include non-invasive wearable monitoring, short-term implantable physiological sensing, healing-related interfaces, and systems that begin with sensing but extend toward stimulation or therapy. Across these areas, the recurring advantages are mechanical compliance, self-powered operation, and the ability to disappear after the useful monitoring or treatment window has passed. In practice, this makes biodegradable piezoelectric platforms especially well suited to temporary, localized applications such as abdominal pressure sensing, intestinal motility monitoring, wound healing, cartilage remodeling, and peripheral nerve recovery.

5. Challenges and Future Perspectives

The development of biodegradable piezoelectric biosensors has advanced to a stage where the main challenge is no longer simply finding materials that exhibit piezoelectricity. Several biodegradable material systems can already generate electromechanical outputs suitable for sensing, while also showing at least partial evidence of degradation or bioresorption. The more urgent challenge is now to integrate piezoelectric performance, degradation behavior, mechanical compatibility, and biological response into device architectures in a predictable and controllable way. In this sense, the field is shifting from material discovery toward quantitative system-level design [27,28].

A first challenge is the persistent trade-off among piezoelectric performance, degradation behavior, and mechanical compliance. In many biodegradable systems, the structural features that improve electromechanical response, such as higher crystallinity, stronger molecular alignment, or tighter supramolecular packing, also tend to increase stiffness and slow degradation. This is evident in semicrystalline polymers such as PLLA, as well as in ordered natural and small-molecule systems such as silk fibroin and amino-acid-based composites. As a result, materials cannot be optimized along a single axis. A design that improves piezoelectric output may simultaneously

move the system away from the softness, degradation rate, or lifetime control needed for transient biomedical use [39,107]. Taking PLLA as a representative example, drawing or annealing can increase chain orientation and crystallinity, thereby enhancing the shear piezoelectric response. However, the same increase in molecular ordering can also increase stiffness, reduce the fraction of water-accessible amorphous domains, and slow hydrolytic degradation. Similarly, increasing the β -sheet content in silk fibroin can improve structural stability and modulate the electromechanical response, while reducing enzymatic accessibility. Although these relationships should not be interpreted as universal quantitative laws, they illustrate an important design trade-off, where maximizing molecular order may conflict with soft-tissue conformity and programmed resorption.

A second challenge is functional stability under physiological loading and progressive degradation. Human motion is irregular in amplitude, frequency, direction, and contact condition, while moisture uptake, interfacial degradation, cyclic deformation, and local chemical changes can alter sensitivity before substantial mass loss occurs. Sensor reliability should therefore be evaluated through sensitivity retention, baseline and output drift, hysteresis, signal-to-noise ratio, frequency dependence, wet-state cyclic durability, and calibration under nonuniform loading. These electrical metrics should be correlated over time with molecular-weight reduction, mass loss, crystallinity, modulus, and dimensional change. Reference channels, signal normalization, waveform analysis, controlled encapsulation, and degradation-aware calibration may improve reliability, but common durability protocols for biodegradable piezoelectric sensors remain unavailable. More realistic long-term testing under physiologically relevant loading conditions is therefore required [50,108].

A third challenge is full-system biodegradability and synchronization of component lifetimes. A practical transient biosensor requires not only a degradable active layer, but also electrodes with adequate conductivity and controlled corrosion, interconnects that tolerate bending and fatigue, encapsulation that blocks moisture throughout the required functional window, and adhesives that prevent premature delamination. Rectification, signal conditioning, temporary energy storage, and wireless communication may further require transient semiconductors and circuit elements. If one component degrades too rapidly, the device fails before the intended endpoint; if another persists too long, residual material remains after the clinical need has passed. Future systems must therefore coordinate the functional and degradation lifetimes of the active layer, electrodes, interconnects, substrate, encapsulation, adhesives, and readout architecture, while also evaluating local pH change, inflammatory response, clearance of degradation products, sterilization tolerance, and shelf stability [27,29].

A fourth challenge is the absence of standardized degradation testing methods that are directly relevant to piezoelectric biosensors. At present, no widely accepted protocol can reliably relate *in vitro* degradation results to *in vivo* device lifetime. Buffer composition, temperature, enzymes, mechanical loading, and device geometry all influence degradation behavior, and these factors interact collectively. In addition, mass loss alone is not an adequate metric. A device may retain most of its bulk while already losing piezoelectric response, interfacial integrity, or signal stability. For this field, degradation testing must therefore follow functional output throughout the degradation process, not only morphology or weight change. Standardized evaluation frameworks that couple degradation with electromechanical performance would greatly improve comparability across studies [27,28].

A further opportunity is the use of piezoelectric metamaterials and topology optimization to improve effective electromechanical response without relying exclusively on higher intrinsic material coefficients. Auxetic lattices, kirigami or origami patterns, gradient porosity, and anisotropic load paths can concentrate or redistribute strain within a soft biodegradable architecture, potentially improving electrical output while preserving tissue-level compliance. Computational topology and shape optimization can identify unit-cell geometries that balance electromechanical coupling, stiffness, durability, and manufacturability [109]. For transient biomedical devices, however, the optimized geometry must remain effective as hydrolysis, swelling, fatigue, tissue ingrowth, and local mass loss alter the boundary conditions. Degradation-induced morphological evolution and signal drift should therefore be incorporated into future multiscale optimization frameworks.

A fifth challenge, but also a major future opportunity, is predictive materials design. Recent computational screening studies suggest that organic molecular crystals and related soft materials can be evaluated at scale for piezoelectric performance, opening the possibility of more rational discovery pipelines. For biodegradable piezoelectrics, however, the real opportunity is broader than screening for large coefficients alone. What is needed is a design framework that can connect electromechanical response, degradation susceptibility, stiffness, and device lifetime within the same workflow. That capability is still emerging, but it points toward a future in which material selection becomes less empirical and more predictive [40,43,44,108,110,111].

Natural and synthetic biodegradable piezoelectric materials also present different translational advantages. Synthetic polymers such as PLLA currently offer greater manufacturing reproducibility, control over molecular weight, crystallinity, mechanical properties, and degradation rate, and a more established route toward quality control. Natural biopolymers offer stronger biological familiarity, extracellular-matrix-like chemistry, and

opportunities for cell adhesion and tissue integration, but may exhibit batch variability, purification challenges, and less reproducible electromechanical properties. Accordingly, synthetic biodegradable polymers are presently more mature for standardized device translation, whereas natural-synthetic hybrid systems may provide the most balanced long-term strategy by combining reproducible processing with biological activity. This direction is supported by existing composite designs, including glycine/chitosan, chitosan-cellulose, and PHB/PHBV-based hybrid scaffolds, where matrix selection, filler incorporation, and architecture are used to combine bioactivity, processability, and electromechanical function [59,60,81,82].

These challenges suggest that the next stage of the field will depend less on identifying a single best biodegradable piezoelectric material and more on establishing design rules that link material structure with device architecture, biological environment, and intended functional lifetime. Progress will likely require advances on several fronts at once, including better control of processing and structural ordering, more realistic degradation and fatigue testing at the device level, and computational methods that can guide material selection before fabrication. These developments should help move biodegradable piezoelectric biosensors from promising demonstrations toward more reliable and rationally designed transient biointerfaces.

6. Conclusions

Biodegradable piezoelectric materials are expanding the design space of biosensors toward temporary, self-powered interfaces that function over a defined clinical period and then degrade without requiring removal. Their significance lies not only in piezoelectric output, but in the ability to combine electromechanical function with controlled degradation, biocompatibility, and device-level relevance. Current progress shows that different material classes contribute in different ways: amino acid-polymer composites offer strong bio-based piezoelectric performance; PLLA-based systems are among the most mature at the device level; PHB/PHBV provide biosynthesized scaffold-forming alternatives; natural biopolymers provide biological familiarity and soft-tissue relevance; and peptide-based systems point toward molecularly programmable designs. The field is also moving beyond passive sensing toward multifunctional transient biointerfaces that integrate sensing, transduction, and, in selected cases, therapy. Future advances will depend on matching material and functional lifetimes, correlating degradation with signal stability, exploiting topology-aware manufacturing, and developing fully integrated biodegradable device architectures. Synthetic polymers currently provide stronger standardization and translational readiness, while natural-synthetic hybrids may ultimately offer the best balance of reproducibility and biological integration.

Author Contributions

M.K.K.: Resources, Data Curation, Visualization, Writing—Original Draft; J.X.: Writing—Review & Editing; H.X.: Writing—Review & Editing; Z.J.: Writing—Review & Editing; J.H.: Writing—Review & Editing, Supervision, Funding acquisition; Y.C.: Conceptualization, Writing—Original Draft, Writing—Review & Editing, Supervision, Funding acquisition. All authors have read and agreed to the published version of the manuscript.

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Conflicts of Interest

The authors declare no conflict of interest.

Use of AI and AI-Assisted Technologies

The authors used AI (ChatGPT, Claude, and Deepseek) only to revise and improve English expressions in this work. All scientific content was reviewed and approved by the authors.

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