

Smart Electroactive Scaffolds for Next-Generation Regenerative Therapies: Materials, Mechanisms, and Applications

Zahra Barabadi^{1,2*} , Masoumeh Sepehri³, Marzieh Jalali Monfared⁴, Pejman Porouhan⁵

1.School of Medicine, Sabzevar University of Medical Sciences, Sabzevar, Iran.

2.Mehr Fertility Research Center, Mehr Outpatient Surgical and Infertility Center, Guilan University of Medical Sciences, Rasht, Iran.

3.Department of Tissue Engineering, School of Advanced Technologies in Medicine, Tehran University of Medical Sciences, Tehran, Iran

4.Biomaterials and Medicinal Chemistry Research Center, Aja University of Medical Sciences, Tehran, Iran

5.Non-Communicable Diseases Research Center, Sabzevar University of Medical Sciences, Sabzevar, Iran

*Corresponding Author: Zahra Barabadi, PhD in Tissue Engineering; Postal Address: Sabzevar University of Medical Sciences, Sabzevar, Iran; Postal code: 9617913112; Tel: +989155711965; Email: barabadiz@medsab.ac.ir

Received: 29 Aug. 2026, Revised: 27 Sep. 2026, Accepted: 4 Oct. 2026

Abstract

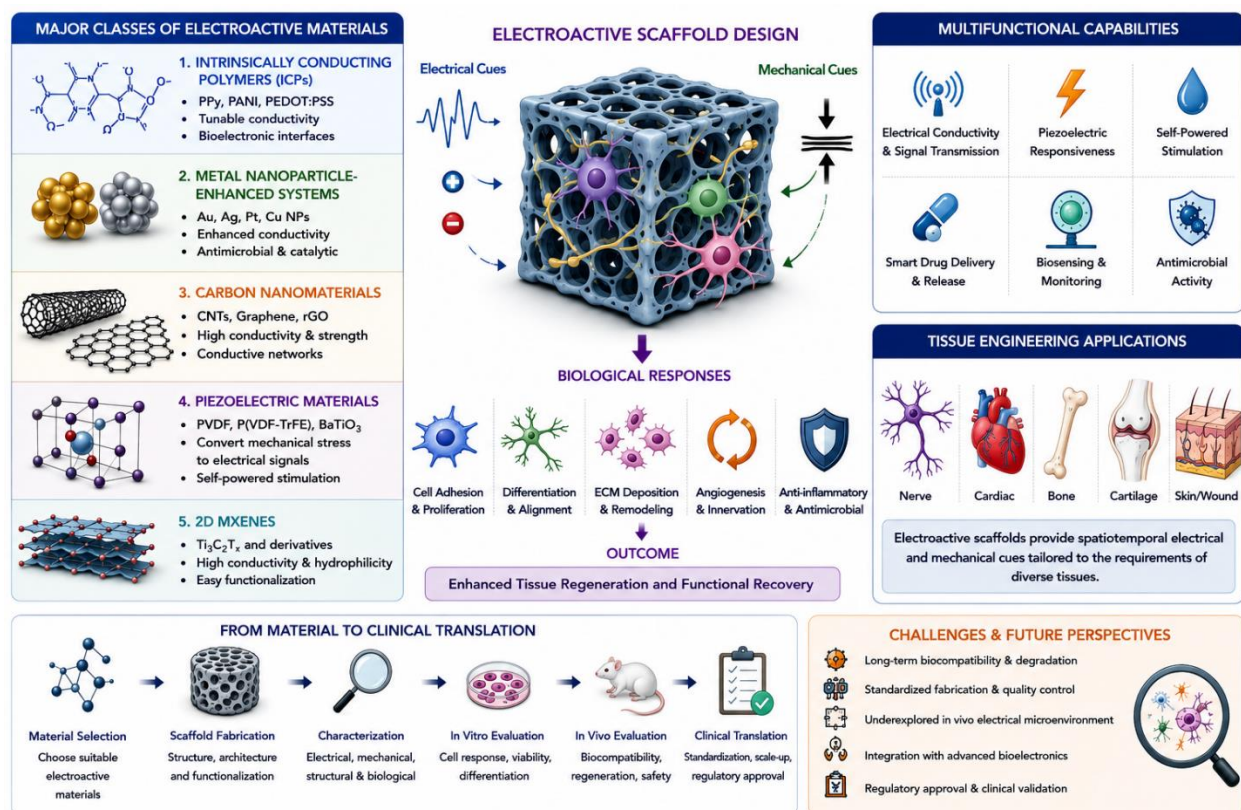
The extracellular microenvironment is far more than a passive structural framework; it represents a dynamic and electromechanically active niche that influences cellular behavior, tissue organization, and regenerative processes. Although conventional polymeric scaffolds have been successful in reproducing key structural and biochemical features of native tissues, they have generally ignored the critical role of endogenous bioelectric signals that regulate fundamental biological events, including wound repair, neural development, and cardiac electrical synchronization. In recent years, a fundamental shift has emerged in tissue engineering, moving away from the concept of scaffolds as inert structural supports toward the development of electroactive scaffolds.

This critical narrative review synthesizes literature from January 2010 to September 2026 across PubMed/MEDLINE, Web of Science, Scopus, and IEEE Xplore. It examines the major classes of electroactive materials, including intrinsically conductive polymers, metal-enhanced electroactive polymers, carbon-based nanomaterials, piezoelectric ceramics and polymers, and emerging two-dimensional materials such as MXenes, with a focus on their physicochemical characteristics, fabrication strategies, and biological integration. We provide head-to-head comparisons of material performance under physiological conditions, discuss how electrical conductivity, piezoelectric responses, and stimuli-responsive properties regulate cellular functions and enhance regeneration in neural, cardiac, musculoskeletal, and skin tissues. Particular attention is given to the relationship between material properties and electrical stimulation strategies, the development of self-powered and multifunctional scaffold systems, and the remaining challenges associated with clinical translation, including long-term material stability, manufacturing standardization, and regulatory considerations.

While preclinical models demonstrate excellent structural and functional restoration, clinical translation remains hindered by inconsistent electrical stimulation protocols, incompletely characterized long-term degradation and biocompatibility profiles, and complex regulatory pathways for combination products. Future directions emphasize closed-loop, self-powered bioelectronic platforms and sustainable bioderived conductors to bridge the gap between laboratory promise and clinical reality.

Keywords: Electroactive scaffolds; Conductive biomaterials; Piezoelectric biomaterials; MXenes; Electrical stimulation

Graphical Abstract



Introduction

Tissue regeneration is shaped not only by biochemical signals and extracellular-matrix architecture but also by biophysical cues such as endogenous electric fields, ionic gradients, and electromechanical signals. These factors are especially relevant in electrically active tissues, including the nervous system, myocardium, and bone, where bioelectric signaling contributes to cell migration, differentiation, intercellular communication, contraction, and tissue remodeling. Consequently, electrical stimulation has emerged as a promising strategy for modulating cellular behavior and supporting tissue regeneration (1).

Conventional tissue-engineering scaffolds mainly provide structural support, a three-dimensional environment for cell attachment, and a framework for extracellular-matrix deposition. However, many commonly used polymers and hydrogels are electrically insulating and therefore cannot fully reproduce the electromechanical microenvironment of native tissues. Electroactive scaffolds address this limitation by incorporating conductive, piezoelectric, ferroelectric, triboelectric, or other stimuli-responsive components into scaffolds. Depending on their composition, these materials can transmit applied electrical signals, generate electrical potentials in response to mechanical deformation, or regulate local ionic and redox conditions. Thus, electroactive scaffolds

combine structural support with biophysical cues that modulate cellular behavior during tissue regeneration (1,2).

The development of electroactive scaffolds has been supported by an expanding range of functional biomaterials. Intrinsically conducting polymers, such as polypyrrole, polyaniline, and poly(3,4-ethylenedioxythiophene) (PEDOT), offer tunable electrical and electrochemical properties and can be fabricated as coatings, fibers, hydrogels, or composite matrices (3). Among them, PEDOT: PSS is particularly promising because of its mixed ionic–electronic conductivity, relatively high electrochemical stability, and mechanical compliance, which facilitate interaction with the ionically conductive environment of biological tissues (4). Carbon-based nanomaterials, including carbon nanotubes, graphene derivatives, and graphene oxide, can form conductive networks while enhancing mechanical properties at relatively low concentrations; however, their dispersion, surface functionalization, degradation behavior, and long-term biocompatibility must be carefully considered (5,6). Piezoelectric polymers, such as poly(vinylidene fluoride) (PVDF) and poly(vinylidene fluoride-co-trifluoroethylene) [P(VDF-TrFE)], provide a distinct mechanism by converting physiological movements or externally applied mechanical forces into localized electrical signals (7,8). More recently, two-dimensional transition-metal carbides, nitrides, and carbonitrides, collectively known as MXenes, have gained

considerable attention because of their high electrical conductivity, hydrophilic surface chemistry, and suitability for incorporation into hydrogel-based composites (9).

These material classes have been investigated across several regenerative applications. In neural tissue engineering, conductive scaffolds can support neurite extension, Schwann-cell activity, axonal organization, and electrical stimulation delivery (3). In cardiac repair, conductive hydrogels and patches are being developed to improve electrical coupling across infarcted myocardium and to reduce conduction heterogeneity (10-12). In bone regeneration, conductive and piezoelectric scaffolds aim to reproduce aspects of the electromechanical behavior of bone and to promote osteogenic differentiation, mineralization, and osseointegration (13-15). Electroactive systems are also being explored for skeletal muscle, peripheral nerve, osteochondral tissue, skin, wound healing, tendon, and other mechanically or electrically responsive tissues (16-19). While the potential of these materials is widely recognized, critical reviews in the field have focused primarily on isolated components. For instance, Marsudi et al. concentrated on the processing and manufacturing aspects of polymer-based systems (1), Liu et al. focused on stem cell fate determination (2), and Senanayake & Sundararaghavan limited their scope to neural conduit applications (3).

This critical narrative review bridges these perspectives. We offer a mechanistic and comparative analysis that links material science and bioelectronics with translational design principles. We examine how different material classes perform head-to-head under physiological conditions. We also explore how their properties can be tuned to match native tissues, and outline the technical and regulatory pathways required to translate these advanced materials into clinical practice.

By integrating materials science, bioelectronics, tissue engineering, and translational considerations, this review aims to identify the design principles and standardization efforts needed to move electroactive scaffolds from experimental platforms toward reliable regenerative technologies.

1. Search Scope and Literature Selection

This critical narrative review is based on a structured search of PubMed/MEDLINE, Web of Science, Scopus, and IEEE Xplore for peer-reviewed experimental and translational studies published between 2010 and August 2026. Search terms combined material classes (“electroactive scaffold”, “conductive polymer”, “piezoelectric biomaterial”, “MXene”) with applications (“tissue engineering”, “neural regeneration”, “cardiac patch”, “bone regeneration”, “wound healing”). We prioritized studies reporting fabrication, physicochemical characterization, biological performance, or in vivo outcomes of scaffold-based electroactive systems. Purely computational studies, non-scaffold devices, and abstracts were excluded. Data were synthesized narratively by material class, design principle, and clinical context, acknowledging the heterogeneity of the field.

2. The Materials Spectrum: From Conducting Polymers to MXenes

No single material satisfies all requirements of conductivity, mechanical matching, biodegradability, and bioactivity. The selection of electroactive materials depends on balancing electrical performance, mechanical compatibility, biodegradability, and tissue-specific biological requirements. An overview of the major classes of electroactive materials and their biological functions is presented in Figure 1.

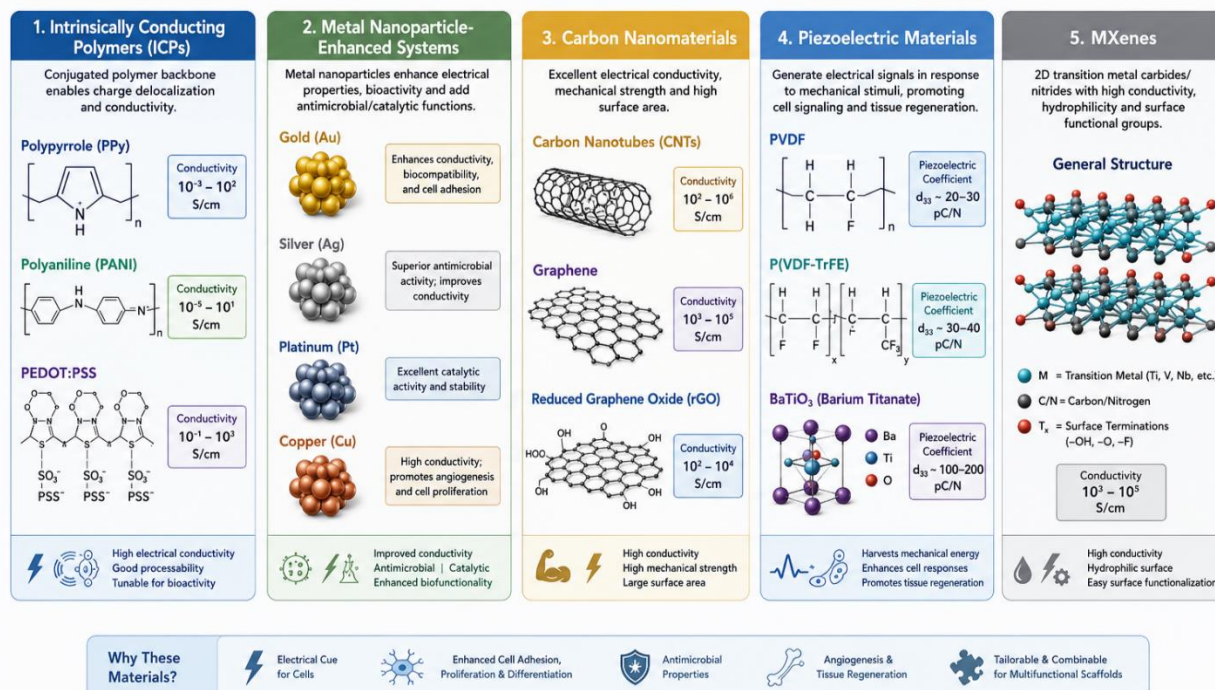


Figure 1. Structural classification and material selection spectrum of electroactive biomaterials used in tissue-engineering scaffolds. Schematic overview of the major classes of electroactive biomaterials, including (1) intrinsically conducting polymers (ICPs) such as polypyrrole (PPy), polyaniline (PANI), and PEDOT:PSS; (2) metal nanoparticle-enhanced systems incorporating gold (Au), silver (Ag), platinum (Pt), and copper (Cu); (3) carbon-based nanomaterials including carbon nanotubes (CNTs), graphene, and reduced graphene oxide (rGO); (4) piezoelectric materials such as poly(vinylidene fluoride) (PVDF), P(VDF-TrFE), and barium titanate (BaTiO₃); and (5) emerging two-dimensional MXene materials.

2.1 Intrinsically Conducting Polymers

Among organic electroactive materials, intrinsically conducting polymers (ICPs) remain extensively investigated for bioelectronic and tissue engineering applications. Polypyrrole (PPy), polyaniline (PANI; sometimes abbreviated PANi), and poly(3,4-ethylenedioxythiophene) (PEDOT) offer different combinations of electrical conductivity, synthesis and processing requirements, mechanical properties, electrochemical stability, and biological compatibility. Importantly, these properties are not determined solely by the polymer backbone; they are also influenced by the dopant, polymerization route, film morphology, thickness, substrate, and surrounding biological environment (20,21).

PPy has attracted considerable interest because pyrrole can be polymerized under relatively mild aqueous conditions and PPy coatings can provide low-impedance, electroactive interfaces for neural and cardiac cells. PPy has also been widely incorporated into hydrogels, electrospun fibers, nerve conduits, and extracellular-matrix-based scaffolds. However, neat PPy is difficult to process, poorly soluble, intrinsically resistant to biodegradation, and mechanically brittle when dehydrated. In addition, repeated redox cycling or overoxidation can reduce its conductivity and promote cracking or delamination. These limitations have encouraged

the development of PPy-based composite architectures incorporating hydrophilic or biodegradable components. For example, blending PPy with biodegradable polymers, including polylactide, polycaprolactone, gelatin, chitosan, collagen, or hyaluronic acid (HA), can improve water uptake, flexibility, cell interaction, and scaffold processability while reducing the fraction of the nondegradable conducting phase (22,23). HA-containing PPy systems provide specific examples of this design principle. HA-doped PPy films showed increased hydrophilicity as the molecular weight of HA increased. HA molecular weight strongly influenced the properties of electrochemically synthesized PPy/HA films (22). In another study, PPy-containing HA hydrogels formed soft and porous conductive scaffolds that supported cell adhesion and proliferation (23). More recently, gelatin/HA hydrogels containing PPy nanoparticles were 3D printed into porous scaffolds with conductivity in the order of 10^{-6} Scm⁻¹, mechanical properties relevant to spinal-cord tissue, and cytocompatibility toward mesenchymal and neural stem cells (24). Three-dimensional HA hydrogels containing PPy and carbon nanotubes also promoted neuronal differentiation and electrophysiological maturation of human neural stem/progenitor cells (25). These findings indicate that HA can improve the hydrophilicity, biological interface, and cell-

supportive properties of PPy-based scaffolds. However, they do not establish degradation of the PPy phase. Claims concerning degradation control should be supported by direct measurements of dry-mass loss, molecular-weight reduction, chemical changes in the polymer, dopant release, electrical-property retention, and enzymatic or hydrolytic degradation under defined physiological conditions.

Additional strategies for addressing PPy's limited processability and degradability include blending or copolymerization with biodegradable polymers and the use of degradable dopants or composite matrices (26). Such approaches have shown promise in neural and peripheral-nerve tissue engineering, although the resulting material properties depend strongly on the composition, dopant, synthesis method, and degradation environment.

PANI provides a different set of advantages and limitations. Its electrical properties can be tuned through changes in oxidation state and protonic doping, making PANI useful for pH-responsive and electrochemical systems. However, its conductivity is strongly pH-dependent: deprotonation at neutral or alkaline pH can markedly reduce electroactivity. This is particularly relevant to physiological applications, where PANI may not maintain the conductivity achieved under acidic doping conditions. PANI also has a rigid and poorly soluble backbone, and residual aniline monomer, acidic dopants, or low-molecular-weight degradation products may affect cytocompatibility (27,28). Consequently, although PANI can support cell adhesion and differentiation when appropriately formulated, its biological performance is often more sensitive to formulation and local pH than that of PEDOT-based systems.

PANI limitations can be mitigated through the use of biocompatible strong-acid dopants, polymeric dopants, blending with hydrophilic or biodegradable matrices, and incorporation of aniline oligomers into degradable polymers. For example, phytic-acid-doped PANI incorporated into a chitosan-based conductive scaffold retained electroactivity and relatively low surface resistivity after immersion in physiological medium and was investigated as a cardiac patch (29). In a complementary strategy, oligoaniline-containing polyesters and PCL- or PEG-based copolymers retain redox activity through the aniline segments while allowing hydrolysis of the surrounding biodegradable polymer domains. These systems may improve processability and reduce the amount of free PANI or residual dopant, but their performance must still be assessed under physiological pH and in relevant cardiac, neural, or muscle models (30-31).

PEDOT and its polyelectrolyte complex with poly(styrene sulfonate), PEDOT:PSS, are particularly attractive for bioelectronics because they combine comparatively high electrochemical stability, mechanical compliance, and mixed ionic-electronic conductivity (32-33). These properties facilitate coupling between electronic devices and ionically conductive biological tissues. Commercially available PEDOT:PSS aqueous dispersions can also be processed into films, coatings, hydrogels, fibers, and printable formulations, which has supported their integration into neural electrodes, bioelectronic interfaces, and tissue-engineering constructs (34). PEDOT:PSS-based interfaces have demonstrated utility for neural recording and stimulation, while PEDOT:PSS hydrogels have also been used in soft optoelectronic interfaces capable of stimulating hippocampal neurons and modulating the beating of cardiac myocytes (35-36). The principal limitation of PEDOT:PSS is not electrochemical performance but long-term biological and structural stability (37). PEDOT is not intrinsically biodegradable, and PSS may contribute to acidity, swelling, ion exchange, delamination, or biological effects if it is present in excess or released from the scaffold (38). Strategies to address these issues include using alternative counterions, crosslinking or partially removing excess PSS, blending PEDOT with biodegradable hydrogels or elastomers, and developing degradable PEDOT analogues or composites. Accordingly, PEDOT:PSS may be preferable for stable long-term electrical interfaces, whereas PPy or PANI may be advantageous when simpler synthesis, redox responsiveness, or integration with specific biodegradable matrices is prioritized (39,40).

2.2 Metal-Enhanced Electroactive Polymers Through Nanoparticle Incorporation

Incorporating metal nanoparticles into conductive polymer matrices is an effective strategy for enhancing the electrical, antimicrobial, catalytic, and, in some systems, electromechanical properties of electroactive scaffolds. Gold (Au), silver (Ag), platinum (Pt), palladium (Pd), and copper (Cu) nanoparticles have been widely investigated as nanofillers, with each metal providing distinct physicochemical characteristics (41). Their incorporation can increase electrical conductivity by forming percolating pathways, facilitate charge transfer across the polymer-nanoparticle interface, and, in piezoelectric or stimuli-responsive polymers, potentially improve electromechanical coupling (41,42).

Metal-polymer nanocomposites can generally be fabricated using three approaches. In situ chemical reduction involves introducing metal-ion precursors into the polymer matrix or

monomer solution and subsequently reducing them to metallic nanoparticles using agents such as sodium borohydride, ascorbic acid, or citrate (41,43). This approach can promote uniform nanoparticle formation and strong interfacial interactions, although the reduction kinetics must be carefully controlled to minimize particle growth and aggregation. Ex situ blending involves incorporating pre-synthesized and, when necessary, surface-functionalized nanoparticles into polymer solutions or melts (41,44). This method provides greater control over nanoparticle size and morphology but can present difficulties in achieving homogeneous dispersion and maintaining stability during processing and subsequent use (44). Electrochemical deposition provides another option, particularly for surface modification, by enabling metal ions to be reduced directly onto conductive polymer substrates under controlled electrochemical conditions (45).

Silver nanoparticles (AgNPs) are of particular interest because they combine electrical conductivity with broad-spectrum antimicrobial activity against both Gram-positive and Gram-negative bacteria, making them attractive for wound-healing applications in which infection control is essential (46). Their antimicrobial action arises from multiple, often synergistic mechanisms: (i) sustained release of Ag^+ ions that bind to thiol groups in bacterial enzymes and disrupt metabolic pathways; (ii) direct interaction of nanoparticles with the bacterial cell envelope, causing membrane depolarization, increased permeability, and leakage of cytoplasmic contents; (iii) generation of reactive oxygen species (ROS) that induce oxidative damage to lipids, proteins, and DNA; and (iv) interference with DNA replication and protein synthesis following nanoparticle internalization. Rod-shaped or sharply edged AgNPs can produce stronger membrane disruption and enhanced bactericidal activity compared with spherical particles due to more efficient membrane penetration (47). Nevertheless, the release of silver ions can produce cytotoxic effects at elevated concentrations, highlighting the need to optimize nanoparticle loading, and ion release to achieve an appropriate balance between antimicrobial activity and tissue compatibility (48).

Gold nanoparticles (AuNPs), in contrast, are generally regarded as highly biocompatible and have been investigated extensively in neural tissue engineering (42,49). While AuNPs themselves are not strongly antimicrobial, they can serve as platforms for functionalization with antimicrobial peptides or as catalysts that modulate local redox environments (50).

Nanoparticle size and shape critically influence cellular uptake, subcellular localization, and toxicity. Particles in the

20–50 nm range typically show optimal cellular internalization via endocytosis, whereas very small (<10 nm) or larger (>100 nm) particles may exhibit reduced uptake or altered trafficking pathways. Smaller nanoparticles possess higher surface-area-to-volume ratios, leading to increased reactivity, ROS generation, and potential cytotoxicity, but they may also be cleared more rapidly via renal filtration, reducing long-term accumulation (48). Spherical nanoparticles generally display more efficient and less disruptive cellular uptake compared with rod-shaped or angular particles, which can induce greater mechanical stress on the cell membrane and enhance cytotoxicity. In the context of antimicrobial activity, smaller AgNPs (2–5 nm) and anisotropic shapes often show enhanced bactericidal efficacy due to improved membrane interaction and penetration, albeit with correspondingly higher risk of off-target toxicity in host tissues (47,51).

The long-term biological fate of metal nanoparticles and released ions remains a key consideration for clinical translation. Metal ions such as Ag^+ can bind to proteins, accumulate in organs (e.g., liver, spleen, kidney), and induce chronic oxidative stress or inflammatory responses if clearance mechanisms are overwhelmed. Ultra-small nanoparticles (<10 nm) may undergo renal clearance, whereas larger particles tend to persist in the reticuloendothelial system and can slowly degrade, releasing ions over extended periods. Surface coatings (e.g., PEGylation, silica shells) and incorporation into biodegradable polymer matrices can modulate dissolution rates, reduce nonspecific protein adsorption, and direct biodistribution, thereby mitigating long-term toxicity risks (47,48,51).

Metal-containing polymer systems can also provide opportunities for remotely controlled stimulation. Recent studies of magnetoelectric composites have explored the incorporation of cobalt ferrite (CoFe_2O_4) nanoparticles into PEDOT matrices, where the magnetic component can enable wireless stimulation in response to externally applied alternating magnetic fields (52,53). Magnetoelectric nanoparticles composed of cobalt ferrite and barium titanate ($\text{CoFe}_2\text{O}_4\text{--BaTiO}_3$) have demonstrated wireless modulation of neuronal activity under low-frequency alternating magnetic fields. In these composite systems, magnetic-field-induced magnetostriction of CoFe_2O_4 is mechanically transferred to piezoelectric BaTiO_3 , generating local electrical potentials that can stimulate excitable cells. In cultured neurons and mouse models, magnetic activation of these nanoparticles increased calcium signaling and neuronal excitability, supporting their potential for minimally invasive neuromodulation (54). In parallel, iron oxide nanoparticle

containing aligned electrospun scaffolds have been investigated as magnetically responsive neural guidance substrates. When combined with magnetic field exposure, these fibers promoted neurite extension, illustrating how magnetic nanoparticle incorporation and anisotropic scaffold architecture can jointly provide physical guidance and remote stimulation cues (55). More broadly, magnetic stimulation of Fe_3O_4 -containing scaffolds may operate through magneto-mechanical forces or torques, magnetic-field-dependent changes in scaffold organization, and, in alternating-field systems, magnetothermal effects. However, the relative contribution of these mechanisms is highly dependent on particle composition, concentration, magnetic-field amplitude and frequency, polymer matrix, and cellular context; therefore, mechanistic claims should be made cautiously.

Such systems may be particularly useful for deep-tissue applications in which direct electrical connections are difficult to implement. However, translating magnetic stimulation to clinical practice faces several challenges: achieving sufficient magnetoelectric coupling at safe field strengths and frequencies to avoid tissue heating or off-target effects; ensuring uniform nanoparticle dispersion and stable integration within biodegradable scaffolds to prevent aggregation and embolization; controlling the long-term fate of magnetic nanoparticles, including potential accumulation in the liver and spleen; and designing external field generators that are compatible with clinical workflows and patient comfort (56,57).

2.3 Carbon-Based Nanomaterials

While intrinsically conducting polymers (ICPs) provide tunable electrical conductivity through a conjugated backbone and controllable doping, carbon nanomaterials can complement them by contributing high aspect-ratio reinforcement, excellent electrical conductivity, and efficient conductive-network formation within polymer matrices (5,37,58). The most widely studied carbon nanomaterials for electroactive tissue-engineering scaffolds include carbon nanotubes (CNTs), graphene, graphene oxide (GO), and reduced graphene oxide (rGO). Their performance is governed not only by their intrinsic electrical and mechanical properties, but also by dimensions, morphology, surface chemistry, purity, dispersion quality, and interactions with cells and the surrounding extracellular environment.

Carbon nanotubes (CNTs), including single-walled CNTs (SWCNTs) and multi-walled CNTs (MWCNTs), have been incorporated into polymeric matrices at relatively low loadings to improve electrical conductivity, mechanical strength, and electroactive behavior while preserving scaffold porosity and

biodegradability (59-61). For example, CNT–GelMA hydrogels containing MWCNTs exhibited enhanced mechanical and electrophysiological properties while retaining the porous, biodegradable characteristics required for tissue-engineering applications (5). Carboxyl-modified multi-walled CNTs blended into alginate/gelatin scaffolds, for instance, have yielded scaffolds with increased hydrophilicity, conductivity, and compressive modulus, and also, showed a favorable PC12-cell proliferation and neurite outgrowth (62).

The biological behavior of CNTs depends strongly on their structural parameters. In SWCNTs, chirality, determines whether nanotubes are metallic or semiconducting and thereby influences their electrical transport, optical properties, and interaction with biological systems. Diameter is closely linked to chirality and affects nanotube curvature, accessible surface area, protein adsorption, mechanical rigidity, and membrane interactions. Chirality- and diameter-dependent differences have been observed in CNT transport behavior, while computational studies further indicate that CNT chirality, aspect ratio, and length can influence membrane adhesion, penetration, and endocytic uptake pathways. In general, smaller-diameter CNTs have higher surface curvature and specific surface area, which can increase chemical reactivity and cellular interaction; however, these same characteristics can increase oxidative stress and cytotoxicity when the nanotubes are poorly dispersed, insufficiently purified, or used at excessive concentrations (63).

CNT length and aspect ratio are also important determinants of biological response. Shorter and more entangled CNTs are generally more readily internalized or cleared by phagocytic cells than long, rigid, needle-like nanotubes. In contrast, long, straight MWCNTs may resist complete macrophage engulfment, resulting in frustrated phagocytosis, persistent inflammatory signaling, oxidative stress, and, in exposure models involving free CNTs, fibrotic responses (63-64).

Surface functionalization is central to the safe use of CNTs in biomedical composites. Pristine CNTs are highly hydrophobic and tend to aggregate through strong van der Waals interactions, which may impair reproducible processing and increase local cellular exposure. Covalent functionalization with carboxyl, hydroxyl, amine, or polyethylene glycol (PEG) groups can improve wettability, colloidal stability, and interfacial adhesion to hydrophilic polymer matrices. Non-covalent approaches, including coating with proteins, polysaccharides, surfactants, or aromatic polymers, can also improve dispersion while preserving more of the CNT π -conjugated network and electrical conductivity (65).

Graphene, graphene oxide (GO), and reduced graphene oxide (rGO) provide electrically conductive, mechanically reinforcing two-dimensional interfaces that can be incorporated into polymeric scaffolds for bone and neural tissue engineering. GO is generally more readily dispersed and chemically functionalized because of its oxygen-containing groups, whereas rGO and graphene typically provide greater electrical conductivity. Graphene-based materials may promote osteogenic differentiation by enhancing adsorption of serum and extracellular-matrix proteins and facilitating integrin-mediated cell adhesion. This can increase focal-adhesion formation and activate focal adhesion kinase (FAK)-dependent mechanotransduction, with downstream cytoskeletal and osteogenic signaling pathways that increase markers such as alkaline phosphatase, RUNX2, osteopontin, and osteocalcin (66-68). The integration of graphene with hydroxyapatite or bioactive glass has produced composite scaffolds with enhanced compressive strengths, suitable for load-bearing bone applications, while retaining the bioactivity necessary for osseointegration (69,70).

A major practical challenge is obtaining stable, reproducible dispersion of graphene-family nanomaterials in polymer matrices. Graphene and rGO sheets readily restack through π - π interactions, whereas GO may aggregate in the presence of salts, proteins, or changes in pH. Inadequate dispersion creates nonuniform conductive pathways and local mechanical heterogeneity, can increase the apparent percolation threshold, and may compromise porosity, printability, and batch-to-batch reproducibility. Aggregates can also act as stress concentrators and lead to uneven local cellular exposure. Surface functionalization, covalent incorporation into polymer networks, controlled ultrasonication, high-shear mixing, and polymer-compatible dispersants can improve dispersion; nevertheless, the dispersion method should be standardized because excessive processing can damage graphene sheets or alter their lateral size and electrical performance (71).

Long-term safety depends on graphene chemistry, lateral size, thickness, oxidation state, dose, aggregation state, impurity content, and whether the material remains immobilized or is released as the scaffold degrades. Persistent or poorly dispersed graphene-family materials may induce oxidative stress, membrane damage, inflammatory-cell activation, and accumulation in the liver, spleen, or other reticuloendothelial organs after systemic exposure. Conversely, oxidized and defect-rich graphene materials can undergo oxidative enzymatic degradation: graphene oxide

has been shown to be degraded by human peroxidases, and its dispersibility strongly affects the rate of this process (72).

2.4 Piezoelectric Materials

Not all electroactivity needs to be static. Piezoelectric scaffolds convert mechanical energy, whether from physiological motion, ultrasound, or deliberate loading, into bioactive electrical signals, mimicking the natural electromechanical coupling of bone, tendon, and cartilage (15,73).

Poly (vinylidene fluoride) (PVDF) and its copolymer poly (vinylidene fluoride-co-trifluoroethylene) [P(VDF-TrFE)] remain on the top list of polymeric piezoelectricity. The β -phase crystalline content, which confers the highest piezoelectric coefficients, can be enhanced through electrospinning, mechanical stretching, or electrical poling; higher β -phase fractions consistently correlate with larger piezoelectric coefficients (e.g., d_{33}) and greater electrical output in PVDF-based scaffolds (7,74). Recent systematic reviews of preclinical studies have confirmed that PVDF-based scaffolds significantly improve bone healing compared to standard non-piezoelectric materials in preclinical models (75). Interestingly, the combination of piezoelectric scaffolds with external low-intensity pulsed ultrasound (LIPUS) appears to produce synergistic effects, activating PI3K-AKT and MAPK signaling pathways while enhancing Ca^{2+} influx (16,76).

At the cellular level, piezoelectric stimulation depolarizes membranes and activates voltage-gated and mechanosensitive Ca^{2+} channels (e.g., Cav1.2, PIEZO1, TRPV4), triggering Ca^{2+} influx that drives calmodulin/calcineurin-NFAT, PI3K-AKT, and MAPK/ERK pathways, upregulating Runx2 and other osteogenic genes. However, quantifying piezoelectric output in vivo remains challenging: local electric fields are small, transient, and load-dependent; measurement setups, loading conditions, and ultrasound parameters are not standardized; and correlating these signals with downstream biological responses is complicated by tissue heterogeneity and motion artifacts (77).

Ceramic piezoelectrics, particularly barium titanate (BaTiO_3), offer higher piezoelectric coefficients and superior stiffness for load-bearing applications. BaTiO_3 -coated titanium scaffolds fabricated via electron beam melting have demonstrated compressive strengths comparable to cortical bone, together with significantly enhanced osteogenesis and osseointegration in rabbit radial segmental defects (78). The toxicity of free BaTiO_3 nanoparticles remains a concern, but when incorporated as surface coatings or within stable

composite matrices, leaching appears minimal; nonetheless, long-term biodistribution, clearance, and potential chronic inflammatory responses of BaTiO₃ nanoparticles in vivo require further systematic evaluation (79,80). Recent work on decalcified bone matrix/BaTiO₃ composites and periosteum-bone inspired hierarchical scaffolds suggests that bioinspired architectural design can further amplify the osteogenic response to piezoelectric stimulation (8,13,14).

2.5 MXenes and Emerging Conductive Ceramics

MXenes are advanced two-dimensional nanomaterials that improve electroactive scaffolds for tissue engineering and regenerative medicine. They are ultra-thin sheets made of transition metal carbides, nitrides, or carbonitrides (81), typically synthesized by selective etching of the A layer from MAX phases (e.g., with HF or LiF/HCl) followed by intercalation and delamination (e.g., with TMAOH or organic bases) to yield few-layer or monolayer dispersion (82).

MXenes combine metallic conductivity with hydrophilic surfaces terminated by –O, –F, or –OH groups, permitting straightforward dispersion in hydrogel matrices without the aggressive functionalization required for CNTs (83). A conductive cardiac patch composed of MXene nanoflakes and gelatin, applied as a paintable layer onto infarcted rat myocardium, promoted connexin-43 expression, enhanced electromechanical coupling, and induced macrophage polarization toward the reparative M2 phenotype (84). Beyond cardiac repair, MXenes have shown considerable promise in wound healing applications, where their conductivity facilitates electrical stimulation delivery while their surface chemistry supports antimicrobial activity (9,85). Their antimicrobial activity arises from sharp-edge-mediated membrane disruption (nanoknife effect) and ROS generation (with additional photothermal/photodynamic contributions under light). MXenes show generally favorable short-term biocompatibility, but undergo gradual oxidative/hydrolytic degradation in physiological media (pH-, temperature-, and O₂-dependent), forming metal oxides and soluble ions; long-term in vivo fate and clearance remain incompletely defined and composition-dependent (86). Incorporating MXenes into hydrogels can enhance conductivity and sometimes

mechanical stiffness (via physical crosslinking), yet challenges include restacking/aggregation, maintaining uniform dispersion, and avoiding brittleness or loss of toughness without careful polymer selection and crosslinking strategies. Although early studies demonstrate favorable biological responses, comprehensive long-term degradation, biodistribution, and safety evaluations remain necessary before clinical translation.

2.6 Composite and Hybrid Systems

No single material satisfies the multifarious demands of regenerative scaffolds: conductivity, mechanical properties, biodegradability, and biological activity. Consequently, the field has increasingly moved toward hybrid architectures. Polymer-carbon composites combine easy-to-shape polymers with carbon nanofillers like carbon nanotubes or graphene to conduct electricity, promote tissue repair and regeneration (87). Polymer-ceramic piezoelectric composites convert natural body movements or external ultrasound into localized electrical signals, merging structural flexibility with high electromechanical performance for tissue engineering (88). Perhaps most advanced are the multi-component systems that integrate conductivity, piezoelectricity, and drug delivery within a single scaffold. For example, conductive polymer (e.g., PPy or PANI) combined with piezoelectric PVDF/P(VDF-TrFE) and piezoceramic nanoparticles (e.g., BaTiO₃ or ZnO) has been used to form electrospun or 3D-printed scaffolds that provide both electrical conduction and ultrasound-responsive piezoelectricity, while microcapsules or mesoporous carriers embedded in the matrix enable controlled release of antibiotics or osteogenic drugs (89-91). Similarly, piezoelectric P(VDF-TrFE)/BaTiO₃ or PVDF/BaTiO₃ composites have been coupled with conductive networks (e.g., rGO or MXene) (92,93), and with growth-factor-loaded hydrogels to create scaffolds that simultaneously deliver bioelectric cues and sustained biochemical signals for bone, neural, and cardiac regeneration (94-95).

The major electroactive material classes, their representative properties, advantages, limitations, and principal tissue engineering applications are summarized in Table 1.

Table 1. Comparison of major electroactive material classes used in tissue-engineering scaffolds

Material class	Representative materials	Representative electrical / functional property	Key advantages	Major limitations	Main tissue-engineering applications
Intrinsically conducting polymers (ICPs)	PPy; PANI; PEDOT:PSS	Conductivity (S/cm): PPy $\sim 10^{-3}$ – 10^2 PANI $\sim 10^{-2}$ – 10^1 PEDOT:PSS $\sim 10^{-4}$ – 10^3 (96)	High and tunable electrical conductivity; relatively versatile processing; useful for electrical stimulation and bioelectronic interfaces	Limited intrinsic biodegradability; poor processability/ solubility for some polymers; possible effects of residual monomers, dopants, and PSS; long-term stability concerns	Neural and peripheral nerve; cardiac; electrically responsive drug delivery; bioelectronic interfaces
Metal nanoparticle-enhanced systems	Au; Ag; Pt; Cu nanoparticles in polymer matrices	Conductivity enhancement depends on metal type, loading, particle size, dispersion, and matrix; can also enhance charge transfer and provide antimicrobial/catalytic functions	Improved electrical conductivity; antimicrobial activity (especially Ag); catalytic activity (Pt); potential enhancement of interfacial/ electromechanical properties; multifunctionality	Particle aggregation; uncontrolled ion release; oxidative stress and cytotoxicity at high exposure; inflammation; uncertain long-term fate of persistent metals	Wound healing; neural tissue engineering; cardiac and other electroactive interfaces; multifunctional scaffolds
Carbon nanomaterials	CNTs; graphene; rGO	Conductivity (S/cm): CNTs $\sim 10^2$ – 10^6 graphene $\sim 10^3$ – 10^4 rGO $\sim 10^{-2}$ – 10^4 (97–98)	Excellent electrical conductivity; high aspect ratio and surface area; mechanical reinforcement; efficient conductive-network formation at relatively low loading	Dispersion and re-agglomeration; hydrophobicity of pristine CNTs; potential toxicity; functionalization-dependent biocompatibility; degradation and long-term safety require evaluation	Neural/peripheral nerve; bone; cardiac and muscle-related applications; composite scaffolds
Piezoelectric materials	PVDF; P(VDF-TrFE); BaTiO ₃	Piezoelectric coefficient (pC/N): PVDF $d_{33} \sim 20$ – 30 P(VDF-TrFE) ~ 30 – 40 BaTiO ₃ ~ 100 – 200 (99–100)	Convert mechanical deformation into electrical signals; enable self-powered or mechanically activated stimulation; suitable for bone, tendon, and cartilage-related applications	Piezoelectric performance depends on phase/crystallinity, poling, architecture, and loading; in vivo generated fields are difficult to quantify; ceramic nanoparticles require safety assessment	Bone and osteochondral regeneration; tendon/ligament; neural regeneration; wound healing
MXenes	Transition-metal carbides, nitrides, and carbonitrides (e.g., Ti-based MXenes)	Conductivity (S/cm): $\sim 10^3$ – 10^5 (101); hydrophilic surfaces with –O, –F, and –OH terminations	High electrical conductivity; hydrophilic surface chemistry; readily dispersed in hydrogel matrices; surface functionalization; multifunctional biointerfaces	Limited long-term biocompatibility/degradation data; potential oxidative and inflammatory responses; long-term biological fate remains incompletely defined	Cardiac repair; wound healing; conductive hydrogel composites; emerging neural and regenerative applications

Material class	Representative materials	Representative electrical / functional property	Key advantages	Major limitations	Main tissue-engineering applications
Composite and hybrid systems	Polymer–carbon; polymer–ceramic; multi-component conductive/piezoelectric/drug-delivery systems	Properties are composition- and architecture-dependent; designed to combine conductivity, piezoelectricity, mechanics, degradation, and/or drug delivery	Combines complementary properties; tunable mechanics and electroactivity; enables multifunctional and stimuli-responsive scaffolds	Greater compositional and manufacturing complexity; difficult standardization; potential interactions among components; more demanding safety and regulatory evaluation	Neural, cardiac, bone, osteochondral, skin/wound healing, and other multifunctional regenerative applications

3. Design Principles: Engineering the Electromechanical Niche

3.1 Physicochemical Parameters

Designing an electroactive scaffold requires balancing electrical signals with structural, chemical, and biological properties that living cells need to thrive. Native tissues exhibit a wide range of conductivities based on their fluid, electrolyte, and water content.

Conductive scaffolds for tissue engineering need a conductivity level within an order of magnitude of native tissue to successfully transmit electrical signals and promote cell growth. Equally important are mechanical matching and porosity. Mechanical mismatch between a stiff scaffold and soft neural tissue can increase foreign-body reactions and glial scarring. Similarly, pore interconnectivity, rather than porosity alone, determines cell infiltration, nutrient diffusion, and vascularization.

3.2 Stimuli-Responsive Functionalities

Smart scaffolds are defined as being able to change between different states on a reversible basis in response to external stimuli. Electrically responsive systems, typically ICP-based, can switch surface charge, or drug release profiles upon application of an electrical signal (102).

Other examples include mechanically responsive scaffolds (piezoelectric) that can generate an electrical signal in response to physical changes in the scaffold, such as contraction, without the need for external wiring. Recent interest has also focused upon magnetoelectric composites which are advanced materials that convert magnetic fields into electric energy, enabling wireless stimulation of deep body tissues like the brain or nerves, , though their complexity and the thermal effects of alternating magnetic fields require careful evaluation (53). Photothermal and photoelectric systems, responsive to near-infrared light, have shown utility in wound healing and on-demand drug release, though tissue

penetration depths limit their applicability in bulk organ regeneration (103,104).

3.3 Biodegradability and Biocompatibility

The non-degradability of traditional ICPs has long been considered their primary limitation. While permanent neural electrodes or cardiac patches may be clinically acceptable in certain contexts, most regenerative applications require scaffold resorption concurrent with tissue ingrowth. Degradable conducting polymers based on aniline or pyrrole oligomers, conductive polyester-urethane copolymers, and enzymatically degradable PEDOT derivatives have begun to address this need (105). The degradation kinetics must be carefully tuned: too rapid, and electrical functionality is lost before tissue maturation; too slow, and the scaffold persists as a foreign body (106). In parallel, the immunological response to electroactive nanomaterials, including inflammatory profiling needs careful examination. Carbon nanomaterials and MXenes, in particular, can generate reactive oxygen species or trigger inflammasome activation if not properly surface-modified (107,108).

4. Fabrication and Characterization

4.1 Fabrication Strategies

Fabrication techniques strongly influence the microarchitecture, electrical connectivity, and mechanical performance of electroactive scaffolds (Table 2). Electrospinning remains the most popular method for producing fibrous conductive scaffolds. Electrical signals combined with aligned structures greatly speed up the repair of complex tissues like nerves and heart muscle (109). This technique uses a strong electric field to stretch polymer jets and naturally form piezoelectric beta-phase PVDF nanofibers with aligned dipoles (110). Three-dimensional printing and bioprinting have advanced considerably, enabling the fabrication of anatomically shaped constructs with spatially graded conductivity (111). Two-photon polymerization of gelatin methacrylate loaded with multi-walled carbon

nanotubes creates precise, electrically conductive microstructures that help heart muscle cells grow and beat synchronously (112). Self-assembly approaches, including conductive peptide amphiphile hydrogels and supramolecular

networks, may offer the most biomimetic way, but they remain difficult and expensive to manufacture in large quantities (113).

Table 2. Comparison of scaffold fabrication techniques for electroactive tissue engineering

Fabrication Method	Dimensional Resolution	Electrical Connectivity Impact	Mechanical Properties	Major Limitations
Electrospinning	Fiber diameter: ~100 nm to 10 μ m	Excellent along fiber axes; aligned dipoles maximize piezoelectric properties.	High tensile strength; anisotropic; mimics fibrous ECM structures.	Low throughput; small pore sizes can restrict deep cell infiltration.
3D Printing / Bioprinting	Resolution: ~50 to 200 μ m	Creates structured 3D percolation pathways and conductive patterns.	Highly customizable; depends on bioink choice and crosslinking.	High shear forces can damage encapsulated cells during extrusion.
Two-Photon Polymerization (2PP)	Sub-micron: down to ~100 nm	Extremely precise; enables sub-micron conductive pathways.	Excellent for microscopic, highly detailed cell-guiding patterns.	High equipment costs; slow processing speeds; limited to small scales.
Self-Assembly	Nanometer scale: ~1 to 100 nm	Excellent localized networks via molecular-level self-organization.	Soft, highly hydrated hydrogels; mechanically delicate.	Difficult to scale up; challenging to control large-scale structure.

4.2 Characterization

A rigorous characterization workflow is essential. Four-point probe measurements provide bulk conductivity, while electrochemical impedance spectroscopy (EIS) and cyclic voltammetry (CV) reveal interfacial charge transfer kinetics and electrochemical stability under physiological conditions (114,115). For piezoelectric scaffolds, piezoresponse force microscopy (PFM) and direct d_{33} measurements quantify the piezoelectric coefficient, though the relationship between measured coefficients and *in vivo* generated fields remains poorly characterized (116). There are several well-known challenges in translating electroactive (piezoelectric/triboelectric/conductive) scaffolds from the lab to in-vivo use. Body fluids contain high concentrations of salts and charged ions, which can rapidly screen the electric fields generated by charged materials. In addition, unlike laboratory experiments that often involve simple and controlled mechanical loading, scaffolds in the body are exposed to complex forces, including stretching, bending, twisting, and compression from different directions. Directly measuring the small electric potential changes within living tissues is also challenging because conventional measurement techniques may disturb the surrounding cells and tissue. Furthermore, the scaffold may gradually degrade or become coated with biological materials in the body, which can alter its mechanical and electrical responses over time (117, 121).

5. Tissue-Specific Applications

5.1 Neural Tissue Engineering

Electroactive scaffolds offer a powerful way to repair damaged peripheral and central nervous tissue by combining physical support with electrical signals. Neural tissue is highly sensitive to electrical signals because neurons maintain an electrical charge through specialized ion gradients across their cell membranes (122). Growth cones, which are the tip of a growing axon, navigate along internal electric fields, and Schwann cells (nerve-supporting cells) align along conductive pathways to guide nerve repair and growth (123,124). Conductive nerve guidance conduits based on aligned CNT-composite hydrogels and piezoelectric nanofiber conduits have demonstrated enhanced neurite outgrowth, axon myelination, and functional recovery in rodent sciatic nerve injury models (125-127). The integration of electrical stimulation with conductive conduits appears particularly powerful. Aligned piezoelectric nanofiber-derived hydrogel conduits combined with ultrasound (US) stimulation generate localized electrical and mechanical signals that significantly improve peripheral nerve regeneration (128).

For spinal cord injury, where the inhibitory microenvironment and cystic cavitation present substantial obstacles to regeneration, electroactive hydrogel conduits offer both physical bridging and electrical platform to promote neural recovery (129). Recent studies utilizing conductive peptide-based hydrogels and aligned piezoelectric nanofiber conduits have reported improved nerve repair by mimicking native extracellular matrix architecture and delivering localized electrical or mechanical cues to promote cell alignment and

inhibit scar-forming cell proliferation (130), though functional motor recovery in large-animal models remains limited.

5.2 Cardiac Tissue Engineering

Myocardial infarction results in the loss of electrically coupled cardiomyocytes and their replacement by electrically inactive fibrotic scar, thereby increasing the risk of arrhythmias and heart failure (131). Conductive scaffolds are designed to restore electromechanical continuity across the infarct border zone. Injectable conductive hydrogels, based on polyaniline, polypyrrole, or MXene nanoflakes, have been delivered directly into the infarcted rat myocardium, where they promote connexin-43 expression, improve ejection fraction, and attenuate adverse remodeling (132-134).

Paintable cardiac patches represent a great delivery modality. A recent MXene-gelatin patch adhered to the epicardium without sutures, restored electrical signal propagation between cardiomyocytes, addressing conduction block (84). Janus hydrogel patches, with an adhesive, conductive cardiac-facing layer and an anti-adhesive pericardial-facing layer, have further refined this approach, permitting on-demand detachment and reducing postoperative adhesion formation (135). For end-stage heart failure, engineered cardiac patches must ultimately achieve vascularization and functional integration with the host cardiac conduction system. Although no electroactive scaffold has yet demonstrated these capabilities in humans, the preclinical progress remains promising.

5.3 Bone and Osteochondral Regeneration

Bone exhibits inherent piezoelectric properties, producing negative surface potentials in response to compressive forces that promote osteoblast activity, while generating positive potentials associated with osteoclast-mediated resorption (136). This electromechanical coupling makes piezoelectric scaffolds a promising strategy for bone tissue engineering. Preclinical evidence has increasingly demonstrated, with recent *in vivo* studies demonstrating superior bone regeneration outcomes for piezoelectric scaffolds compared with non-piezoelectric controls in critical-sized calvarial and femoral defect models (75). BV/TV values of 35–36% at 8 weeks, approaching native bone levels, have been reported for PVDF- and BaTiO₃-based systems (75).

Conductive scaffolds also play a role in modulating the osteoblast-osteoclast balance. Graphene-enhanced and conductive cryogel scaffolds have been shown to upregulate alkaline phosphatase activity, collagen type I expression, and RUNX2 signaling in mesenchymal stem cells (137,138). The combination of electrical stimulation with conductive scaffolds

further amplifies these effects, accelerating calcium ion transport and mitochondrial activity (139). For osteochondral defects, dual-gradient scaffolds that transition from piezoelectric/ceramic-rich (osseous) to hydrogel/cartilage-like (chondral) compartments represent an advanced approach to interface regeneration, though clinical translation remains challenging (17).

5.4 Skin and Wound Healing

Chronic wounds, particularly diabetic ulcers, suffer from disrupted endogenous electrical fields and persistent inflammation (140). Electroactive dressings address both pathologies. Conductive hydrogels and electrospun nanofibers containing piezoelectric polymers or MXenes have been reported to reproduce or enhance electrical cues associated with the wound environment (18, 141). Self-powered systems, such as piezoelectric PVDF dressings and triboelectric nanogenerators, harvest energy from patient movement or respiration to provide continuous, battery-free electrical stimulation (142,143). Magnetoelectric dressings composed of CoFe₂O₄@CTAB/PVDF nanofibers have demonstrated accelerated healing in chronic wound models through wearable magnetoelectric stimulation, representing a convergence of energy harvesting and therapeutic delivery (62).

5.5 Emerging Applications

Beyond these established applications, electroactive scaffolds are increasingly being explored for tendon and ligament regeneration, where piezoelectric collagen-mimetic scaffolds may reproduce the mechanoelectrical signaling mechanisms present in native entheses (19,144). In retinal tissue engineering, PEDOT-based biointerfaces are being investigated to facilitate the restoration of photoreceptor connectivity (145); while in intervertebral disc regeneration, conductive nucleus pulposus analogs aim to reestablish the electrochemical microenvironment of the avascular disc (146).

6. Electrical Stimulation Protocols

It is important to emphasize that a conductive scaffold, in the absence of a well-designed stimulation protocol, functions almost as a passive conductor. The parameters of electrical stimulation, waveform (DC, AC, pulsed), frequency, amplitude, and duty cycle, can profoundly influence cellular responses; however, these parameters remain highly heterogeneous and insufficiently standardized across studies (147). Representative stimulation protocols for different tissue types, including waveform, frequency, intensity, proposed mechanisms, and targeted outcomes, are summarized in

Table 3. In bone tissue engineering, direct current appears to induce early osteogenesis via intracellular ROS generation (148), whereas alternating or pulsed square waves maintain lower, safer baseline ROS levels while providing cyclical electrical field changes. These dynamics favor late-stage maturation, maximizing extracellular matrix (ECM) protein deposition and calcium phosphate mineralization without inducing oxidative cellular stress (15). For neural regeneration, pulsed stimulation at frequencies of 20–100 Hz generally enhances neurite outgrowth, though optimal parameters vary by cell type and scaffold conductivity (149).

The development of implantable, wireless, and biodegradable stimulation devices represents a critical foundational

technology. Biodegradable transient electronics, silicon-based or organic devices that dissolve after a defined functional period, offer a pathway to temporary electrical support without secondary surgical retrieval. Self-powered platforms, including piezoelectric and triboelectric nanogenerators integrated directly into scaffolds, eliminate the need for external power supplies altogether (139,143). A 3D-printed shape-memory piezoelectric scaffold combining PVDF with shape-memory polyurethane recently demonstrated in-situ self-powering under physiological mechanical stimulation, achieving enhanced bone regeneration while permitting minimally invasive implantation (150).

Table 3. Representative electrical stimulation protocols for different tissue types

Tissue type	Waveform type	Frequency / pulse rate	Intensity descriptor	Biological mechanisms	Targeted cellular outcomes
Neural / peripheral nerve	Pulsed or alternating electric field	Often ~20 Hz in selected neural-scaffold studies	~100 mV/mm in selected in-vitro studies	May modulate depolarization, calcium signaling, regenerative pathways, and neurotrophic-factor expression	Neurite extension, directional axonal growth, Schwann-cell activity, axonal regeneration/reinnervation
Cardiac	Charge-balanced biphasic pulsed stimulation; selected monophasic protocols	Commonly 1–3 Hz	~1–5 V/cm in selected engineered-tissue studies	Excitation–contraction coupling, electrical entrainment, calcium cycling, and gap-junction/sarcomeric maturation	Cardiomyocyte alignment, connexin-43 expression, synchronized beating, contractile maturation
Bone	DC, pulsed DC, or AC/sinusoidal; PEMF separately	N/A for continuous DC; specify for pulsed/AC protocols	Report current density/current field plus electrode geometry	May modulate calcium, ROS/redox, MAPK/ERK, and osteogenic transcriptional pathways	Osteogenic differentiation, RUNX2 and ALP expression, matrix mineralization
Skin / wound healing	Low-intensity DC or pulsed stimulation; HVPC separately	N/A for continuous DC; specify pulse rate for pulsed modalities	~10–100 mV/mm in selected in-vitro field studies	May mimic endogenous wound-field cues and direct cell migration	Keratinocyte/fibroblast migration, re-epithelialization, angiogenic responses, wound closure

7. Smart and Multifunctional Scaffold Systems

7.1 Integrated Drug and Growth Factor Delivery

The most advanced electroactive scaffolds provide functions beyond electrical conduction; they serve as programmable drug depots. Conducting polymer-based matrices can serve as electrically responsive drug delivery platforms. Electrical modulation of their redox state changes polymer charge and ion exchange; in polypyrrole systems, reduction commonly promotes release of incorporated anionic cargos. These platforms have demonstrated electrically enhanced release of neurotrophic proteins such as BDNF(151,152). Spatially resolved electrochemical control has been demonstrated in continuous conductive hydrogel structures. Bipolar electrochemistry generated reversible oxidized and reduced

regions within a PEDOT/alginate hybrid hydrogel, producing spatial gradients in anionic cargo loading and electrically triggered release (153).

7.2 Biosensing and Diagnostic Capabilities

The same electrical properties that make scaffolds therapeutic also make them diagnostic. Impedance spectroscopy is being investigated as a potential method for monitoring changes associated with tissue ingrowth, scaffold degradation, and inflammation. Strain and pressure sensing capabilities, particularly in cardiac patches, offer a means to monitor contractile function post-implantation (10). The integration of metabolite-sensitive electrodes could potentially transform regenerative scaffolds into continuous, real-time monitoring platforms, thereby creating a functional interface

between tissue engineering and implantable bioelectronics (154).

7.3 Self-Powered Electroactive Scaffolds

A further step toward smart scaffolds is the development of energy-independent systems. Triboelectric nanogenerators integrated with wound dressings or bioresorbable bone-fracture implants can harvest biomechanical energy from body motion and convert it into therapeutic electrical pulses for promoting wound repair or bone regeneration (155,156). Biofuel cells offer an alternative approach for powering regenerative and implantable bioelectronic systems. Enzymatic bioanodes can oxidize endogenous glucose or lactate at the implantation site, while the reduction of oxygen at the cathode completes the electrochemical circuit and generates electrical power (157,158). Although the energy output of these systems remains relatively low, rapid advances in the field may enable self-powered scaffolds to reduce or even eliminate the dependence of scaffolds on external power sources.

8. Challenges, Limitations, and the Translation Gap

Despite the considerable innovation demonstrated in preclinical studies, the translation of electroactive scaffolds into clinical practice remains challenging. Several critical barriers must be carefully addressed before these technologies can achieve broader clinical application.

Fundamental materials and manufacturing challenges remain for electroactive scaffolds. Achieving homogeneous dispersion of carbon nanomaterials during composite processing is difficult because of their strong interparticle interactions and tendency to re-agglomerate (61). In biodegradable conductive systems, degradation can disrupt conductive pathways and reduce electrical performance over time (1). Sterilization must also be validated for each formulation: gamma irradiation can induce polymer-chain scission, crosslinking, and oxidation, potentially altering mechanical, chemical, and electrical properties (159).

Biological and safety concerns remain central to the clinical translation of conductive nanomaterial-containing scaffolds. Although many studies report favorable short-term in vitro cytocompatibility, long-term in vivo safety, including biodistribution, persistence or clearance, degradation-product fate, and immunological response, remains incompletely characterized and is strongly material- and formulation-dependent (6,160). For permanent conductive implants, the foreign body response can produce fibrotic encapsulation, increase electrode–tissue impedance, electrically isolate the implant, and progressively impair device performance (161).

Electroactive regenerative scaffolds face substantial translational and regulatory barriers. Constructs combining an electroactive device component with cells, tissues, growth factors, or drugs may require a combination-product assessment. Translation is further complicated by limited standardization of electrical-stimulation protocols, material characterization, degradation testing, and long-term functional assessment. While FDA-regulated electrical and electromagnetic bone-growth stimulators and the broader clinical bioelectronics field offer relevant precedents, they do not directly establish a regulatory pathway for degradable, multifunctional electroactive tissue-engineering scaffolds.

9. Clinical Landscape and Translational Progress

The clinical translation of electroactive scaffolds remains limited, although related technologies based on electrical stimulation and conductive biomaterials have demonstrated clinical feasibility. Electrical stimulation devices have been clinically established for applications such as fracture nonunion and spinal fusion, but these systems generally rely on external stimulators or dedicated implanted electrical components rather than fully integrated conductive scaffold implants (162,163). In the cardiac space, conductive hydrogels and epicardial patches remain largely in preclinical or early-phase safety studies, with only limited human feasibility data for injectable hydrogels rather than scaffold-based implants (12,164). In neural applications, the translational pathway is comparatively more advanced. PEDOT neural electrodes have been used for intraoperative cortical recording in patients undergoing epilepsy and brain tumor surgery, demonstrating the feasibility of conducting-polymer-based interfaces in humans (165). Specific PEDOT-based coatings have received FDA and CE-mark approval for invasive neural devices (166). Collectively, these advances provide an important technological and materials foundation for the future development of regenerative scaffolds that integrate electrical stimulation, sensing, and tissue repair.

Commercially, the field is dominated by auxiliary technologies rather than scaffold products themselves. Piezoelectric bone growth stimulators are marketed for fracture healing, and conductive wound dressings have received FDA clearance for wound management. True electroactive regenerative scaffolds, implants that both structurally support tissue and actively participate in its electrical environment, have not yet reached the clinic. The regulatory classification of such products necessitates extensive safety and efficacy data that the field has only begun to generate.

10. Future Perspectives

Looking ahead, several research directions appear particularly promising. Organic bioelectronic materials based on mixed ionic–electronic conductors, which transmit signals through both electronic and ionic carriers, may provide a more biomimetic interface with biological tissues than conventional electronic conductors. MXene-based conductive composites are another emerging class of materials that may combine the processability and flexibility of polymers with the high electrical conductivity of two-dimensional materials, while their surface chemistry offers opportunities for further modification to improve biological compatibility. Although still at an early stage of development, genetically engineered electroactive proteins could potentially enable living cells to contribute directly to the formation or regulation of conductive networks (167).

Integrating electroactive scaffolds with synthetic biology may further expand the functional capabilities of scaffolds. Emerging approaches involving DNA-based conductive nanostructures, engineered bacterial biofilms capable of producing electrically conductive pili, and genetically programmed cell–electrode interfaces point toward increasingly intimate integration between living systems and synthetic materials. At the same time, sustainability is becoming an increasingly important consideration in biomaterial development. Bio-derived conductive materials, including melanin-inspired polymers and lignin-derived conductive materials, may offer opportunities to reduce the environmental burden associated with conventional scaffold manufacturing.

Conclusion

Electroactive scaffolds have progressed well beyond their traditional role as passive structural supports. They are now being developed as dynamic, bio-interactive platforms that can actively influence tissue regeneration through conductive, piezoelectric, and hybrid mechanisms. This progress has been supported by a broad range of materials, including intrinsically conducting polymers, carbon nanomaterials, piezoelectric ceramics and polymers, MXenes, and multifunctional composites. Together, these materials offer considerable flexibility in designing scaffolds for neural, cardiac, bone, and skin regeneration. Preclinical findings are encouraging: conductive and piezoelectric biomaterials have enhanced neurite outgrowth, helped restore electromechanical coupling in infarcted myocardium, accelerated bone mineralization, and promoted wound re-epithelialization. Despite these advances, there remains a significant gap between promising laboratory results and

clinical application. Inconsistent electrical stimulation protocols, limited understanding of long-term biocompatibility and degradation, difficulties in achieving uniform nanomaterial dispersion, and the complex regulatory requirements associated with combination products continue to hinder translation.

The development of biodegradable conducting polymers, self-powered systems that harvest biomechanical energy, and multifunctional platforms integrating biosensing with therapeutic delivery represent promising research strategies. Future work should prioritize standardizing scaffold fabrication, material characterization, and stimulation parameters to enable reproducible comparison across studies.

Statement of Ethics: No ethical approval was required because this article is a literature-based review and involved no human participants, animals, or identifiable data.

Funding: The authors declare that no financial support was received for the research, authorship, or publication of this article.

Conflict of Interest: The authors declare that they have no conflicts of interest.

Acknowledgments: The authors thank the researchers whose work has advanced the development of electroactive biomaterials and regenerative medicine.

References

1. Marsudi MA, Ariski RT, Wibowo A, Cooper G, Barlian A, Rachmantyo R, et al. Conductive Polymeric-Based Electroactive Scaffolds for Tissue Engineering Applications: Current Progress and Challenges from Biomaterials and Manufacturing Perspectives. *Int J Mol Sci.* 2021;22(21):11543. doi:10.3390/IJMS222111543.
2. Liu Z, Wan X, Wang ZL, Li L. Electroactive Biomaterials and Systems for Cell Fate Determination and Tissue Regeneration: Design and Applications. *Adv Mater.* 2021;33(32). doi:10.1002/ADMA.202007429.
3. Senanayake J, Sundararaghavan HG. Bioengineered Conductive Scaffolds for Neural Tissue Engineering. *Bioelectricity.* 2024;6(1):13–25. doi:10.1089/BIOE.2023.0023.
4. Ávila Ramírez AE, van der Laan DP, Shah MB, Wang L, Zeglio E, Savva A. PEDOT:PSS—A Key Material for Bioelectronics. *Adv Sci.* 2026;13(11):e13480. doi:10.1002/ADVS.202513480.
5. Shin SR, Jung SM, Zalabany M, Kim K, Zorlutuna P, Kim SB, et al. Carbon-nanotube-embedded hydrogel sheets for engineering cardiac constructs and bioactuators. *ACS Nano.* 2013;7(3):2369–80. doi:10.1021/NN305559J.
6. Zhang Y, Petibone D, Xu Y, Mahmood M, Karmakar A, Casciano D, et al. Toxicity and efficacy of carbon nanotubes and

- graphene: the utility of carbon-based nanoparticles in nanomedicine. *Drug Metab Rev.* 2014;46(2):232–46. doi:10.3109/03602532.2014.883406.
7. Bhadwal N, Ben Mrad R, Behdinin K. Review of Piezoelectric Properties and Power Output of PVDF and Copolymer-Based Piezoelectric Nanogenerators. *Nanomaterials.* 2023;13(24). doi:10.3390/NANO13243170.
 8. Dong Y, Zhang S, Xu T, Sun W, Liu X. Advances of piezoelectric biomaterials in bone defect repair: The role of direct and inverse piezoelectric effect. *J Orthop Translat.* 2026;58:101106. doi:10.1016/J.JOT.2026.101106.
 9. Mengru Z, Qinyi W, Zimo Y, Bingqing G, Zhongyu X, Xu J. MXenes in the application of diabetic foot: mechanisms, therapeutic implications and future perspectives. *J Mater Sci Mater Med.* 2025;36(1):42. doi:10.1007/S10856-025-06895-2.
 10. Qiu R, Zhang X, Song C, Xu K, Nong H, Li Y, et al. E-cardiac patch to sense and repair infarcted myocardium. *Nat Commun.* 2024;15(1):4133. doi:10.1038/s41467-024-48468-x.
 11. Lee M, Kim MC, Lee JY. Nanomaterial-Based Electrically Conductive Hydrogels for Cardiac Tissue Repair. *Int J Nanomedicine.* 2022;17:6181. doi:10.2147/IJN.S386763.
 12. Song X, Zhang J, Shen S, Liu D, Zhang J, Yin W, et al. Cardiac-Adaptive Conductive Hydrogel Patch Enabling Construction of Mechanical-Electrical Anisotropic Microenvironment for Heart Repair. *Research (Wash D C).* 2023;6. doi:10.34133/RESEARCH.0161.
 13. Yong S, Tian L, Huang D, Xi Y, Chen H, Jiao Z, et al. Engineered decalcified bone matrix/barium titanate piezoelectric composite scaffolds for bone regeneration. *J Mater Chem B.* 2025;13(29):8789–807. doi:10.1039/D5TB00321K.
 14. Zhao Y, Cai Y, Wang W, Bai Y, Liu M, Wang Y, et al. Periosteum-bone inspired hierarchical scaffold with endogenous piezoelectricity for neuro-vascularized bone regeneration. *Bioact Mater.* 2025;44:339–53. doi:10.1016/j.bioactmat.2024.10.020.
 15. Zaszczynska A, Zabielski K, Gradys A, Kowalczyk T, Sajkiewicz P. Piezoelectric Scaffolds as Smart Materials for Bone Tissue Engineering. *Polymers (Basel).* 2024;16(19):2797. doi:10.3390/POLYM16192797.
 16. Jia W, Zhou Z, Zhan W. Musculoskeletal Biomaterials: Stimulated and Synergized with Low Intensity Pulsed Ultrasound. *J Funct Biomater.* 2023;14(10):504. doi:10.3390/JFB14100504.
 17. Wang H, Li Y. Piezoelectric Biomaterials for Osteochondral Tissue Engineering: Advances, Mechanisms, and Translational Prospects. *J Funct Biomater.* 2026;17(4):173. doi:10.3390/JFB17040173.
 18. Yu R, Zhang H, Guo B. Conductive Biomaterials as Bioactive Wound Dressing for Wound Healing and Skin Tissue Engineering. *Nano Micro Lett.* 2021;14(1):1. doi:10.1007/S40820-021-00751-Y.
 19. Fernandez-Yague MA, Trotier A, Demir S, Abbah SA, Larrañaga A, Thirumaran A, et al. A Self-Powered Piezo-Bioelectric Device Regulates Tendon Repair-Associated Signaling Pathways through Modulation of Mechanosensitive Ion Channels. *Adv Mater.* 2021;33(40):2008788. doi:10.1002/ADMA.202008788.
 20. Hardy JG, Mouser DJ, Arroyo-Currás N, Geissler S, Chow JK, Nguy L, et al. Biodegradable electroactive polymers for electrochemically-triggered drug delivery. *J Mater Chem B.* 2014;2(39):6809–22. doi:10.1039/C4TB00355A.
 21. Qazi TH, Rai R, Boccaccini AR. Tissue engineering of electrically responsive tissues using polyaniline based polymers: A review. *Biomaterials.* 2014;35(33):9068–86. doi:10.1016/j.biomaterials.2014.07.020.
 22. Kim S, Jang Y, Jang M, Lim A, Hardy JG, Park HS, et al. Versatile biomimetic conductive polypyrrole films doped with hyaluronic acid of different molecular weights. *Acta Biomater.* 2018;80:258–68. doi:10.1016/J.ACTBIO.2018.09.035.
 23. Yang J, Choe G, Yang S, Jo H, Lee JY. Polypyrrole-incorporated conductive hyaluronic acid hydrogels. *Biomater Res.* 2016;20(1):31. doi:10.1186/S40824-016-0078-Y.
 24. Serafin A, Culebras M, Oliveira JM, Koffler J, Collins MN. 3D printable electroconductive gelatin-hyaluronic acid materials containing polypyrrole nanoparticles for electroactive tissue engineering. *Adv Compos Hybrid Mater.* 2023;6(3):109. doi:10.1007/S42114-023-00665-W.
 25. Shin J, Choi EJ, Cho JH, Cho AN, Jin Y, Yang K, et al. Three-Dimensional Electroconductive Hyaluronic Acid Hydrogels Incorporated with Carbon Nanotubes and Polypyrrole by Catechol-Mediated Dispersion Enhance Neurogenesis of Human Neural Stem Cells. *Biomacromolecules.* 2017;18(10):3060–72. doi:10.1021/ACS.BIOMAC.7B00568.
 26. Shi G, Rouabhia M, Wang Z, Dao LH, Zhang Z. A novel electrically conductive and biodegradable composite made of polypyrrole nanoparticles and polylactide. *Biomaterials.* 2004;25(13):2477–88. doi:10.1016/J.BIOMATERIALS.2003.09.032.
 27. Zhang X, Qi H, Wang S, Feng L, Ji Y, Tao L, et al. Cellular responses of aniline oligomers: a preliminary study. *Toxicol Res (Camb).* 2012;1(3):201–5. doi:10.1039/C2TX20035J.
 28. Guo B, Finne-Wistrand A, Albertsson AC. Molecular Architecture of Electroactive and Biodegradable Copolymers Composed of Polylactide and Carboxyl-Capped Aniline Trimer. *Biomacromolecules.* 2010;11(4):855–63. doi:10.1021/BM9011248.
 29. Mawad D, Mansfield C, Lauto A, Perbellini F, Nelson GW, Tonkin J, et al. A Conducting polymer with enhanced electronic stability applied in cardiac models. *Sci Adv.* 2016;2(11). doi:10.1126/SCIADV.1601007.
 30. Guo B, Finne-Wistrand A, Albertsson AC. Enhanced Electrical Conductivity by Macromolecular Architecture: Hyperbranched Electroactive and Degradable Block Copolymers Based on Poly(ϵ -caprolactone) and Aniline Pentamer. *Macromolecules.* 2010;43(10):4472–80. doi:10.1021/MA100530K.
 31. Guo B, Finne-Wistrand A, Albertsson AC. Versatile functionalization of polyester hydrogels with electroactive

- aniline oligomers. *J Polym Sci A Polym Chem*. 2011;49(9):2097–105. doi:10.1002/POLA.24643.
32. Lo CY, Wu Y, Awuyah E, Meli D, Nguyen DM, Wu R, et al. Influence of the molecular weight and size distribution of PSS on mixed ionic-electronic transport in PEDOT:PSS. *Polym Chem*. 2022;13(19):2764. doi:10.1039/D2PY00271J.
 33. Liang Y, Offenhäuser A, Ingebrandt S, Mayer D. PEDOT:PSS-Based Bioelectronic Devices for Recording and Modulation of Electrophysiological and Biochemical Cell Signals. *Adv Healthc Mater*. 2021;10(11):2100061. doi:10.1002/ADHM.202100061.
 34. Abidian MR, Corey JM, Kipke DR, Martin DC. Conducting-Polymer Nanotubes Improve Electrical Properties, Mechanical Adhesion, Neural Attachment, and Neurite Outgrowth of Neural Electrodes. *Small*. 2010;6(3):421. doi:10.1002/SMLL.200901868.
 35. Kim N, Kee S, Lee SH, Lee BH, Kahng YH, Jo YR, et al. Highly conductive PEDOT:PSS nanofibrils induced by solution-processed crystallization. *Adv Mater*. 2014;26(14):2268–72. doi:10.1002/ADMA.201304611.
 36. Zhang S, Chen Y, Liu H, Wang Z, Ling H, Wang C, et al. Room-temperature Formed PEDOT:PSS Hydrogels Enable Injectable, Soft, and Healable Organic Bioelectronics. *Adv Mater*. 2019;32(1):e1904752. doi:10.1002/ADMA.201904752.
 37. Green RA, Lovell NH, Wallace GG, Poole-Warren LA. Conducting polymers for neural interfaces: Challenges in developing an effective long-term implant. *Biomaterials*. 2008;29(24–25):3393–9. doi:10.1016/j.biomaterials.2008.04.047.
 38. Li J, Mo D, Hu J, Wang S, Gong J, Huang Y, et al. PEDOT:PSS-based bioelectronics for brain monitoring and modulation. *Microsyst Nanoeng*. 2025;11(1):87. doi:10.1038/s41378-025-00948-w.
 39. Han M, Yildiz E, Kaleli HN, Karaz S, Eren GO, Dogru-Yuksel IB, et al. Tissue-Like Optoelectronic Neural Interface Enabled by PEDOT:PSS Hydrogel for Cardiac and Neural Stimulation. *Adv Healthc Mater*. 2022;11(8):2102160. doi:10.1002/ADHM.202102160.
 40. Cellot G, Lagonegro P, Tarabella G, Scaini D, Fabbri F, Iannotta S, et al. PEDOT:PSS Interfaces Support the Development of Neuronal Synaptic Networks with Reduced Neuroglia Response In vitro. *Front Neurosci*. 2016;9(JAN):521. doi:10.3389/FNINS.2015.00521.
 41. Acharya R, Dutta SD, Patil T V., Ganguly K, Randhawa A, Lim KT. A Review on Electroactive Polymer–Metal Composites: Development and Applications for Tissue Regeneration. *J Funct Biomater*. 2023;14(10):523. doi:10.3390/JFB14100523.
 42. Barabadi Z, Bahmani A, Jalalimonfared M, Ashrafizadeh M, Rashtbar M, Sharifi E, et al. Design and characterization of electroactive gelatin methacrylate hydrogel incorporated with gold nanoparticles empowered with parahydroxybenzaldehyde and curcumin for advanced tissue engineering applications. *J Mater Sci Mater Med*. 2024;35(1):45. doi:10.1007/S10856-024-06808-9.
 43. Kellarakis A. In Situ Generation of Nanoparticles on and within Polymeric Materials. *Polymers (Basel)*. 2024;16(11):1611. doi:10.3390/POLYM16111611.
 44. Stefanescu EA, Daranga C, Stefanescu C. Insight into the Broad Field of Polymer Nanocomposites: From Carbon Nanotubes to Clay Nanoplatelets, via Metal Nanoparticles. *Materials (Basel)*. 2009;2(4):2095–153. doi:10.3390/MA2042095.
 45. Augustyn P, Rytlewski P, Moraczewski K, Mazurkiewicz A. A review on the direct electroplating of polymeric materials. *J Mater Sci*. 2021;56(27):14881–99. doi:10.1007/S10853-021-06246-W.
 46. Xiao L, Hui F, Tian T, Yan R, Xin J, Zhao X, et al. A Novel Conductive Antibacterial Nanocomposite Hydrogel Dressing for Healing of Severely Infected Wounds. *Front Chem*. 2021;9:787886. doi:10.3389/FCHEM.2021.787886.
 47. Karataş H, Eker F, Akdaşçi E, Bechelany M, Karav S. Silver Nanoparticles in Antibacterial Research: Mechanisms, Applications, and Emerging Perspectives. *Int J Mol Sci*. 2026;27(2):927. doi:10.3390/IJMS27020927.
 48. Awashra M, Młynarz P. The toxicity of nanoparticles and their interaction with cells: an in vitro metabolomic perspective. *Nanoscale Adv*. 2023;5(10):2674. doi:10.1039/D2NA00534D.
 49. Baranes K, Shevach M, Shefi O, Dvir T. Gold Nanoparticle-Decorated Scaffolds Promote Neuronal Differentiation and Maturation. *Nano Lett*. 2016;16(5):2916–20. doi:10.1021/ACS.NANOLETT.5B04033.
 50. Pal S, Barat A, Saha R, Panigrahi S, Mandal D, Mohanty PS, et al. Glyco functionalized gold nanoparticles for mechanistic understanding antimicrobial efficacy and translational applications. *Discov Chem*. 2026;3(1):433. doi:10.1007/S44371-026-00896-Y.
 51. El-Sayed Ellakwa D, Ellakwa TE. Biocompatible nanoparticles in medicine: from design to clinical translation. *Discov Mater*. 2025;6(1):28. doi:10.1007/S43939-025-00489-Z.
 52. Ke Q, Zhang X, Yang Y, Chen Q, Su J, Tang Y, et al. Wearable Magnetoelectric Stimulation for Chronic Wound Healing by Electrospun CoFe₂O₄@CTAB/PVDF Dressings. *ACS Appl Mater Interfaces*. 2024;16(8):9839–53. doi:10.1021/ACSAMI.3C17963.
 53. Singer A, Dutta S, Lewis E, Chen Z, Chen JC, Verma N, et al. Magnetoelectric materials for miniature, wireless neural stimulation at therapeutic frequencies. *Neuron*. 2020;107(4):631. doi:10.1016/J.NEURON.2020.05.019.
 54. Nguyen T, Vriesman Z, Andrews P, Masood S, Stewart M, Khizroev S, et al. 4009 Magneto-electric nanoparticles (MENs) cobalt ferrite-barium titanate (CoFe₂O₄–BaTiO₃) for non-invasive neuromodulation. *J Clin Transl Sci*. 2020;4(Suppl 1):11. doi:10.1017/CTS.2020.78.
 55. Funnell JL, Ziemba AM, Nowak JF, Awada H, Prokopiou N, Samuel J, et al. Assessing the combination of magnetic field stimulation, iron oxide nanoparticles, and aligned electrospun fibers for promoting neurite outgrowth from dorsal root ganglia in vitro. *Acta Biomater*. 2021;131:302–13. doi:10.1016/J.ACTBIO.2021.06.049.

56. Summer M, Ashraf R, Ali S, Bach H, Noor S, Noor Q, et al. Inflammatory response of nanoparticles: Mechanisms, consequences, and strategies for mitigation. *Chemosphere*. 2024;363. doi:10.1016/j.chemosphere.2024.142826.
57. Wang YL, Lee YH, Chou CL, Chang YS, Liu WC, Chiu HW. Oxidative stress and potential effects of metal nanoparticles: A review of biocompatibility and toxicity concerns. *Environmental Pollution*. 2024;346:123617. doi:10.1016/J.ENVPOL.2024.123617.
58. Sun H, Zhou J, Huang Z, Qu L, Lin N, Liang C, et al. Carbon nanotube-incorporated collagen hydrogels improve cell alignment and the performance of cardiac constructs. *Int J Nanomedicine*. 2017;12:3109–20. doi:10.2147/IJN.S128030.
59. Ghaziof S, Mehdikhani-Nahrkhalaji M. Preparation, characterization, mechanical properties and electrical conductivity assessment of novel polycaprolactone/multi-wall carbon nanotubes nanocomposites for myocardial tissue engineering. *Acta Phys Pol A*. 2017;131(3):428–31. doi:10.12693/APHYSPOLA.131.428.
60. McCullen SD, Stevens DR, Roberts WA, Ojha SS, Clarke LI, Gorga RE. Morphological, Electrical, and Mechanical Characterization of Electrospun Nanofiber Mats Containing Multiwalled Carbon Nanotubes. *Macromolecules*. 2007;40(4):997–1003. doi:10.1021/MA061735C.
61. Huang B. Carbon nanotubes and their polymeric composites: the applications in tissue engineering. *Bio-manuf Rev*. 2020;5(1):3. doi:10.1007/S40898-020-00009-X.
62. Ma H, Yu K, Wang H, Liu J, Cheng YY, Kang Y, et al. Fabrication and detection of a novel hybrid conductive scaffold based on alginate/gelatin/carboxylated carbon nanotubes (Alg/Gel/mMWCNTs) for neural tissue engineering. *Tissue Cell*. 2023;80. doi:10.1016/j.tice.2022.101995.
63. Liu Z, Tabakman S, Welscher K, Dai H. Carbon Nanotubes in Biology and Medicine: In vitro and in vivo Detection, Imaging and Drug Delivery. *Nano Res*. 2009;2(2):85. doi:10.1007/S12274-009-9009-8.
64. Skandani AA, Zeineldin R, Al-Haik M. Effect of Chirality and Length on the Penetrability of Single-Walled Carbon Nanotubes into Lipid Bilayer Cell Membranes. *Langmuir*. 2012;28(20):7872–9. doi:10.1021/LA3011162.
65. Witkowska M, Florek E, Mrówczyński R. Assessment of Pristine Carbon Nanotubes Toxicity in Rodent Models. *Int J Mol Sci*. 2022;23(23):15343. doi:10.3390/IJMS232315343.
66. Bellet P, Gasparotto M, Pressi S, Fortunato A, Scapin G, Mba M, et al. Graphene-Based Scaffolds for Regenerative Medicine. *Nanomaterials*. 2021;11(2):404. doi:10.3390/NANO11020404.
67. Girão AF, Sousa J, Domínguez-Bajo A, González-Mayorga A, Bdiin I, Pujades-Otero E, et al. 3D Reduced Graphene Oxide Scaffolds with a Combinatorial Fibrous-Porous Architecture for Neural Tissue Engineering. *ACS Appl Mater Interfaces*. 2020;12(35):38962–75. doi:10.1021/ACSAMI.0C10599.
68. Kang MS, Jeong SJ, Lee SH, Kim B, Hong SW, Lee JH, et al. Reduced graphene oxide coating enhances osteogenic differentiation of human mesenchymal stem cells on Ti surfaces. *Biomater Res*. 2021;25(1). doi:10.1186/S40824-021-00205-X.
69. Simorgh S, Alasvand N, Khodadadi M, Ghobadi F, Malekzadeh Kebria M, Brouki Milan P, et al. Additive manufacturing of bioactive glass biomaterials. *Methods*. 2022;208:75–91. doi:10.1016/J.YMETH.2022.10.010.
70. Li C, Qin F, Zhao S, Meng Q, He Q, Fan H. Preparation and characterization of a natural composite scaffold composed of chitosan, hydroxyapatite, and graphene oxide for bone repair. *Sci Rep*. 2026;16(1):15101. doi:10.1038/S41598-026-44493-6.
71. Zhu Y, Murali S, Cai W, Li X, Suk JW, Potts JR, et al. Graphene and Graphene Oxide: Synthesis, Properties, and Applications. *Adv Mater*. 2010;22(35):3906–24. doi:10.1002/ADMA.201001068.
72. Kurapati R, Martin C, Palermo V, Nishina Y, Bianco A. Biodegradation of graphene materials catalyzed by human eosinophil peroxidase. *Faraday Discuss*. 2021;227:189–203. doi:10.1039/C9FD00094A.
73. Wang X, Stefanello ST, Shahin V, Qian Y. From Mechanoelectric Conversion to Tissue Regeneration: Translational Progress in Piezoelectric Materials. *Adv Mater*. 2025;37(33):2417564. doi:10.1002/ADMA.202417564.
74. Yin Z, Tian B, Zhu Q, Duan C. Characterization and Application of PVDF and Its Copolymer Films Prepared by Spin-Coating and Langmuir–Blodgett Method. *Polymers (Basel)*. 2019;11(12):2033. doi:10.3390/POLYM11122033.
75. Minelli M, Micalizzi S, Longobardi V, Kon E, Oliva P, Della Rocca F. Piezoelectric scaffolds for bone regeneration: a systematic review of preclinical studies. *Front Bioeng Biotechnol*. 2026;14:1848820. doi:10.3389/FBIOE.2026.1848820.
76. Li M, Hu X, Liu X, Zhao L, Zhao W, Li Y, et al. 3D bioprinted piezoelectric hydrogel synergized with LIPUS to promote bone regeneration. *Mater Today Bio*. 2025;31:101604. doi:10.1016/J.MTBIO.2025.101604.
77. Alvarez-Lorenzo C, Zarur M, Seijo-Rabina A, Blanco-Fernandez B, Rodríguez-Moldes I, Concheiro A. Physical stimuli-emitting scaffolds: The role of piezoelectricity in tissue regeneration. *Mater Today Bio*. 2023;22:100740. doi:10.1016/J.MTBIO.2023.100740.
78. Fan B, Guo Z, Li X, Li S, Gao P, Xiao X, et al. Electroactive barium titanate coated titanium scaffold improves osteogenesis and osseointegration with low-intensity pulsed ultrasound for large segmental bone defects. *Bioact Mater*. 2020;5(4):1087. doi:10.1016/J.BIOACTMAT.2020.07.001.
79. Kadhum RN, Hamad TI. Barium titanate synthesis, mechanism of action and its applications in dentistry: A literature review. *J Appl Biomater Funct Mater*.
80. Ćurčić M, Hadžić B, Gilić M, Lazarević Z, Ilić A. BaTiO₃ Nanocarriers: Advancing Targeted Therapies with Smart Drug Release. *Pharmaceutics*. 2025;17(9):1203. doi:10.3390/PHARMACEUTICS17091203.
81. Liu H, Xing X, Tan Y, Dong H. Two-dimensional transition metal carbides and nitrides (MXenes) based biosensing and

- molecular imaging. *Nanophotonics*. 2022;11(22):4977. doi:10.1515/NANOPH-2022-0550.
82. Kiran H, Ali ABM, Ashraf R, Tahir MB, Nasir M, Hasnain N, et al. Comparative Study of Ti3C2Tx MXene Synthesized via HF and LiF-HCl Etching: Structural, Optical, and Photocatalytic Insights. *J Inorg Organomet Polym Mater*. 2025;35(11):9565–78. doi:10.1007/S10904-025-03832-2.
 83. Suchorowiec K, Kasznik J, Stepura A, Omastová M, Pielichowska K. Polysaccharide Hydrogels Doped with MXenes for Possible Biomedical Applications. *Molecules*. 2026;31(1):148. doi:10.3390/MOLECULES31010148.
 84. Lee M, Park J, Choe G, Lee S, Kang BG, Jun JH, et al. A Conductive and Adhesive Hydrogel Composed of MXene Nanoflakes as a Paintable Cardiac Patch for Infarcted Heart Repair. *ACS Nano*. 2023;17(13):12290–304. doi:10.1021/ACS.NANO.3C00933.
 85. A critical review of MXene-derived bioactive materials for accelerated wound healing: Mechanisms, therapeutic strategies, and clinical prospects. *Next Mater*. 2026;13:102745. doi:10.1016/J.NXMATE.2026.102745.
 86. Zhang WJ, Li S, Yan YZ, Park SS, Mohan A, Chung I, et al. Dual (pH- and ROS-) Responsive Antibacterial MXene-Based Nanocarrier for Drug Delivery. *Int J Mol Sci*. 2022;23(23):14925. doi:10.3390/IJMS232314925.
 87. Fenta EW, Mebratie BA. Advancements in carbon nanotube-polymer composites: Enhancing properties and applications through advanced manufacturing techniques. *Heliyon*. 2024;10(16):e36490. doi:10.1016/J.HELİYON.2024.E36490.
 88. Wu Y, Zou J, Tang K, Xia Y, Wang X, Song L, et al. From electricity to vitality: the emerging use of piezoelectric materials in tissue regeneration. *Burns Trauma*. 2024;12:tkae013. doi:10.1093/BURNST/TKAE013.
 89. Peidavosi N, Azami M, Beheshtizadeh N, Ramazani Saadatabadi A. Piezoelectric conductive electrospun nanocomposite PCL/Polyaniline/Barium Titanate scaffold for tissue engineering applications. *Sci Rep*. 2022;12(1):20828. doi:10.1038/s41598-022-25332-w.
 90. Miar S, Ong JL, Bizios R, Guda T. Electrically Stimulated Tunable Drug Delivery From Polypyrrole-Coated Polyvinylidene Fluoride. *Front Chem*. 2021;9:599631. doi:10.3389/FCHEM.2021.599631.
 91. Fathollahzadeh V, Khodaei M, Emadi S, Hajjisharifi K. Plasma activated PVDF-BaTiO3 composite nanofiber scaffolds loaded with vancomycin for enhancing biocompatibility and piezoelectric response. *Sci Rep*. 2025;15(1):28515. doi:10.1038/s41598-025-14391-4.
 92. Liu X, Tong J, Wang J, Lu S, Yang D, Li H, et al. BaTiO3/MXene/PVDF-TrFE composite films via an electrospinning method for flexible piezoelectric pressure sensors. *J Mater Chem C Mater*. 2023;11(14):4614–22. doi:10.1039/D2TC05291A.
 93. Kulkarni ND, Kumari P. Role of rGO on mechanical, thermal, and piezoelectric behaviour of PVDF-BTO nanocomposites for energy harvesting applications. *J Polym Res*. 2023;30(2):79. doi:10.1007/S10965-023-03449-4.
 94. Segneanu AE, Bejenaru LE, Bejenaru C, Blendea A, Mogoşanu GD, Biţă A, et al. Advancements in Hydrogels: A Comprehensive Review of Natural and Synthetic Innovations for Biomedical Applications. *Polymers (Basel)*. 2025;17(15):2026. doi:10.3390/POLYM17152026.
 95. Shan BH, Wu FG. Hydrogel-Based Growth Factor Delivery Platforms: Strategies and Recent Advances. *Adv Mater*. 2024;36(5):2210707. doi:10.1002/ADMA.202210707.
 96. Evaluating and Improving Biocompatibility of Conductive Polymers for Cardiac Tissue Engineering [Internet]. [cited 2026 Sep 23]. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC12831229/>
 97. Qiu C, Bennet KE, Khan T, Ciubuc JD, Manciu FS. Raman and Conductivity Analysis of Graphene for Biomedical Applications. *Materials (Basel)*. 2016;9(11):897. doi:10.3390/MA9110897.
 98. Xiang Y, Zhang L, Liu C. Electrical Properties of Carbon Nanotubes: From Individual to Assemblies. *Nanomaterials*. 2025;15(15). doi:10.3390/NANO15151165.
 99. Zhang L, Li S, Zhu Z, Rui G, Du B, Chen D, et al. Recent Progress on Structure Manipulation of Poly(vinylidene fluoride)-Based Ferroelectric Polymers for Enhanced Piezoelectricity and Applications. *Adv Funct Mater*. 2023;33(38):2301302. doi:10.1002/ADFM.202301302.
 100. Acosta M, Novak N, Rojas V, Patel S, Vaish R, Koruza J, et al. BaTiO3-based piezoelectrics: Fundamentals, current status, and perspectives. *Appl Phys Rev*. 2017;4(4). doi:10.1063/1.4990046.
 101. Amin I, Brekel H Van Den, Nemani K, Batyrev E, De Vooy A, Van Der Weijde H, et al. Ti3C2Tx MXene Polymer Composites for Anticorrosion: An Overview and Perspective. *ACS Appl Mater Interfaces*. 2022;14(38):43749–58. doi:10.1021/ACSAMI.2C11953.
 102. Ge J, Neofytou E, Cahill TJ, Beygui RE, Zare RN. Drug release from electric-field-responsive nanoparticles. *ACS Nano*. 2012;6(1):227–33. doi:10.1021/NN203430M.
 103. Sun S, Jiang G, Dong J, Xie X, Liao J, Tian Y. Photothermal hydrogels for infection control and tissue regeneration. *Front Bioeng Biotechnol*. 2024;12:1389327. doi:10.3389/FBIOE.2024.1389327.
 104. Chu Y, Liao S, Liao H, Lu Y, Geng X, Wu D, et al. Second Near-Infrared Photothermal Therapy with Superior Penetrability through Skin Tissues. *CCS Chemistry*. 2022;4(9):3002–13. doi:10.31635/CCSCHEM.021.202101539.
 105. Gayathri V, Khan T, Gowtham M, Balan R, Sebaey TA. Functionalized conductive polymer composites for tissue engineering and biomedical applications- a mini review. *Front Bioeng Biotechnol*. 2025;13:1533944. doi:10.3389/FBIOE.2025.1533944.
 106. Naeem A, Yu C, Zhou L, Xie Y, Weng Y, Huang Y, et al. Shape memory hydrogels in tissue engineering: Recent advances and

- challenges. *Bioact Mater.* 2025;54:215–47. doi:10.1016/J.BIOACTMAT.2025.08.009.
107. Alkaya D, Cagliani R, Summak GY, Giro L, Besbinar O, Alhosani M, et al. MXene Chemistries for Biomedicine: On-Body, In-Body, and Beyond. *ACS Nano.* doi:10.1021/ACS.NANO.6C05051.
 108. Liao X, Liu Y, Zheng J, Zhao X, Cui L, Hu S, et al. Diverse Pathways of Engineered Nanoparticle-Induced NLRP3 Inflammasome Activation. *Nanomaterials.* 2022;12(21):3908. doi:10.3390/NANO12213908.
 109. Shen H, Jia M, Zhu H, Shang Y, Wang L, Gao H, et al. Smart-responsive electrospun scaffolds (SRES) for neural repair: Recent advances and future prospects. *Bioact Mater.* 2026;66:234–72. doi:10.1016/J.BIOACTMAT.2026.06.048.
 110. Zhai D, Yin Z, Kang Z, Song X, Han Z. Improvement of piezoelectric properties of electrospun PVDF nanofiber membrane and its application. *J Ind Eng Chem.* 2026;160:161–217. doi:10.1016/J.JIEC.2026.03.036.
 111. Kim MS, Choi Y, Lee KY. Three-Dimensional Printing and Bioprinting Strategies for Cardiovascular Constructs: From Printing Inks to Vascularization. *Polymers (Basel).* 2025;17(17):2337. doi:10.3390/POLYM17172337.
 112. Sanjuan-Alberte P, Vaithilingam J, Moore JC, Wildman RD, Tuck CJ, Alexander MR, et al. Development of Conductive Gelatine-Methacrylate Inks for Two-Photon Polymerisation. *Polymers (Basel).* 2021;13(7). doi:10.3390/POLYM13071038.
 113. Chen J, Zou X. Self-assemble peptide biomaterials and their biomedical applications. *Bioact Mater.* 2019;4:120. doi:10.1016/J.BIOACTMAT.2019.01.002.
 114. Espinoza-Torres S, Choquehuanca-Azaña A, Azeredo NFB, Rufino M, Angnes L. Electropolymerized Molecularly Imprinted Polymers Supported on Carbon-Based Materials for (Bio)sensing: Direct and Indirect Detection Strategies. *Biosensors.* 2026;16(6):350. doi:10.3390/BIOS16060350.
 115. Özevin Ergür BÖ, Oktay B, Ciftci F, Ahlatcioğlu Özerol E. Production and Characterization of Conductive Scaffolds for Conducting Tissue Engineering. *ChemistrySelect.* 2025;10(24):e00790. doi:10.1002/SLCT.202500790.
 116. Khan B, Amara U, Khan B, Khan WU, Ahmad R u. S, Khan MS, et al. Next-Generation Piezoelectric Materials in Wearable and Implantable Devices for Continuous Physiological Monitoring. *Adv Sci.* 2025;12(41):e07853. doi:10.1002/ADVS.202507853.
 117. Duan X, Lieber CM. Nanoelectronics Meets Biology: From Novel Nanoscale Devices for Live Cell Recording to 3D Innervated Tissues. *Chem Asian J.* 2013;8(10):2304. doi:10.1002/ASIA.201300630.
 118. Kim S, Uroz M, Bays JL, Chen CS. Harnessing mechanobiology for tissue engineering. *Dev Cell.* 2021;56(2):180. doi:10.1016/J.DEVCEL.2020.12.017.
 119. Echeverria Molina MI, Malollari KG, Komvopoulos K. Design Challenges in Polymeric Scaffolds for Tissue Engineering. *Front Bioeng Biotechnol.* 2021;9:617141. doi:10.3389/FBIOE.2021.617141.
 120. Ryan CNM, Doulgeroglou MN, Zeugolis DI. Electric field stimulation for tissue engineering applications. *BMC Biomed Eng.* 2021;3(1):1. doi:10.1186/S42490-020-00046-0.
 121. Marx GH. The use of electric fields in tissue engineering: A review. *Organogenesis.* 2008;4(1):11. doi:10.4161/ORG.5799.
 122. Purves D, Augustine GJ, Fitzpatrick D, Katz LC, LaMantia AS, McNamara JO, et al. Electrical Signals of Nerve Cells [Internet]. 2001 [cited 2026 Aug 26]. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK11053/>
 123. Sun Q, Mu X, Gao Q, Wang J, Hu M, Liu H. Influences of physical stimulations on the migration and differentiation of Schwann cells involved in peripheral nerve repair. *Cell Adh Migr.* 2025;19(1). doi:10.1080/19336918.2025.2450311.
 124. Rajnicek AM, Foubister LE, McCaig CD. Growth cone steering by a physiological electric field requires dynamic microtubules, microfilaments and Rac-mediated filopodial asymmetry. *J Cell Sci.* 2006;119(9):1736–45. doi:10.1242/JCS.02897.
 125. Yin H, Hu Y, Cheng H, Zhang B, Gao S, Ma X, et al. Viscoelastic and conductive nerve guidance conduits for peripheral nerve repair. *Nanoscale.* 2025;17(35):20169–77. doi:10.1039/D5NR00742A.
 126. Cheng H, Hu Y, Liao M, Pang X, Zhang H, Yu M, et al. Conductive Nerve Guidance Conduits Loaded With Adipose Mesenchymal Stem Cells for Peripheral Nerve Regeneration. *Smart Medicine.* 2025;4(4):e70025. doi:10.1002/SMMD.70025.
 127. Li X, Yang W, Xie H, Wang J, Zhang L, Wang Z, et al. CNT/Sericin Conductive Nerve Guidance Conduit Promotes Functional Recovery of Transected Peripheral Nerve Injury in a Rat Model. *ACS Appl Mater Interfaces.* 2020;12(33):36860–72. doi:10.1021/ACSAMI.0C08457.
 128. Xu D, Fu S, Zhang H, Lu W, Xie J, Li J, et al. Ultrasound-Responsive Aligned Piezoelectric Nanofibers Derived Hydrogel Conduits for Peripheral Nerve Regeneration. *Adv Mater.* 2024;36(28). doi:10.1002/ADMA.202307896.
 129. Olushanu M. Biomaterials: Advancements in Spinal Cord Injury Treatment. *Premier J Neurosci.* 2024 Nov 7. doi:10.70389/PJN.100001.
 130. Moghaddasi M, Oktay B, Bingol AB, Yanikoglu R, Muslu M, Ozbolat IT, et al. Conductive Nanocomposite Hydrogels for Neural Tissue Engineering: A Systematic Scoping Review of Recent Trends. *Adv Sci.* 2025;12(38):e16085. doi:10.1002/ADVS.202416085.
 131. Talman V, Ruskoaho H. Cardiac fibrosis in myocardial infarction—from repair and remodeling to regeneration. *Cell Tissue Res.* 2016;365(3):563. doi:10.1007/S00441-016-2431-9.
 132. Zhang Z, Lang X, Zhang Y, Dong X, Han X, Xu C, et al. The Application of Injectable Hydrogels in Myocardial Infarction Repair: Material Design, Biological Functions and Clinical Translation. *Int J Mol Sci.* 2026;27(14):6464. doi:10.3390/IJMS27146464.

133. Yu R, Zhao R, Guo D, Shi M, Wen H, Niu X, et al. Supramolecular antioxidant conductive injectable hydrogel encapsulating L-arginine for synergistic modulation of myocardial infarction. *J Control Release*. 2026;390. doi:10.1016/j.jconrel.2025.114552.
134. Zhang L, Li T, Yu Y, Shi K, Bei Z, Qian Y, et al. An injectable conductive hydrogel restores electrical transmission at myocardial infarct site to preserve cardiac function and enhance repair. *Bioact Mater*. 2022;20:339–54. doi:10.1016/J.BIOACTMAT.2022.06.001.
135. Hu Q, Hou X, Shi H, Song Y, Zhou B, Hu X, et al. Design of a Janus Composite Patch with Anti-Adhesive and Growth-Promoting Functions for Abdominal Wall Defect Repair. *Bioengineering (Basel)*. 2025;12(5):522. doi:10.3390/BIOENGINEERING12050522.
136. Kao FC, Chiu PY, Tsai TT, Lin ZH. The application of nanogenerators and piezoelectricity in osteogenesis. *Sci Technol Adv Mater*. 2019;20(1):1103. doi:10.1080/14686996.2019.1693880.
137. Guo J, Cao G, Wei S, Han Y, Xu P. Progress in the application of graphene and its derivatives to osteogenesis. *Heliyon*. 2023;9(11):e21872. doi:10.1016/J.HELİYON.2023.E21872.
138. Xie H, Cao T, Franco-Obregón A, Rosa V. Graphene-Induced Osteogenic Differentiation Is Mediated by the Integrin/FAK Axis. *Int J Mol Sci*. 2019;20(3):574. doi:10.3390/IJMS20030574.
139. Farjaminejad S, Dingle AM. The role of electrical stimulation in bone regeneration: mechanistic insights and therapeutic advances. *Bioelectron Med*. 2025;11(1):18. doi:10.1186/S42234-025-00180-X.
140. Xu L, Wang E, Ying M, Luo L, Ren Y, Zhu C, et al. Restoration of endogenous electric fields with a glucose-powered symbiotic bioabsorbable bandage for diabetic wound healing. *Sci Adv*. 2026;12(24):eaed9445. doi:10.1126/SCIADV.AED9445.
141. Liu Y, Li W, Ge L. Conductive biomaterials for chronic wound healing. *Adv Interv Mater*. 2026;1(1):100001. doi:10.1016/J.ADVIM.2025.100001.
142. Wearable self-powered systems: Energy harvesting technologies and applications in health regulation. *Wearable Electronics*. 2026 Aug 15. doi:10.1016/J.WEES.2026.07.001.
143. Varshney A, Chauhan S, Rawal S, Herrera OR, Sharma S. Nanogenerators in Biomedical Frontiers: Revolutionizing Self-Powered Healthcare Systems. *ACS Omega*. 2026;11(7):10921. doi:10.1021/ACSOMEGA.5C08225.
144. Liu L, Li Z, Zhu T, Sun Y, Xu J. Advances in applications of low-dimensional piezoelectric materials in musculoskeletal system. *Mater Today Bio*. 2025;33:102065. doi:10.1016/J.MTBIO.2025.102065.
145. Barriga-Rivera A, Bareket L, Goding J, Aregueta-Robles UA, Suaning GJ. Visual prosthesis: Interfacing stimulating electrodes with retinal neurons to restore vision. *Front Neurosci*. 2017;11(NOV):307497. doi:10.3389/FNINS.2017.00620.
146. Wang J, Huang L, Guo T, Liu Z, Xu H, Yang H, et al. A self-powered sandwich-structured scaffold with dual-electroactive properties to regenerate damaged intervertebral discs after discectomy. *J Mater Chem B*. 2025;13(18):5389–402. doi:10.1039/D5TB00100E.
147. Miller JP, Eldabe S, Buchser E, Johanek LM, Guan Y, Linderorth B. Parameters of Spinal Cord Stimulation and Their Role in Electrical Charge Delivery: A Review. *Neuromodulation*. 2016;19(4):373–84. doi:10.1111/ner.12438.
148. Srirussamee K, Mobini S, Cassidy NJ, Cartmell SH. Direct electrical stimulation enhances osteogenesis by inducing Bmp2 and Spp1 expressions from macrophages and preosteoblasts. *Biotechnol Bioeng*. 2019;116(12):3421. doi:10.1002/BIT.27142.
149. Park S, Koppes RA, Froriep UP, Jia X, Achyuta AKH, McLaughlin BL, et al. Optogenetic control of nerve growth. *Sci Rep*. 2015;5(1):9669. doi:10.1038/srep09669.
150. Li B, Ma Y, Fatima K, Zhou X, Gu X, Chen S, et al. 3D printed shape-memory piezoelectric scaffolds with in-situ self-power properties for bone defect repair. *J Nanobiotechnol*. 2025;23(1):244. doi:10.1186/S12951-025-03325-X.
151. Thompson BC, Richardson RT, Moulton SE, Evans AJ, O'Leary S, Clark GM, et al. Conducting polymers, dual neurotrophins and pulsed electrical stimulation — Dramatic effects on neurite outgrowth. *J Control Release*. 2010;141(2):161–7. doi:10.1016/J.JCONREL.2009.09.016.
152. Evans AJ, Thompson BC, Wallace GG, Millard R, O'Leary SJ, Clark GM, et al. Promoting neurite outgrowth from spiral ganglion neuron explants using polypyrrole/BDNF-coated electrodes. *J Biomed Mater Res A*. 2009;91(1):241–50. doi:10.1002/JBM.A.32228.
153. Da Silva AC, Hu X, Paschoal VH, Hagis N, Zajac AJ, Ribeiro MCC, et al. Bipolar electrochemistry-driven wireless drug loading and energy harvesting in conductive hybrid hydrogels. *Commun Mater*. 2025;6(1):28. doi:10.1038/s43246-025-00750-1.
154. Fernandes E, Ledo A, Barbosa RM. Implantable microelectrode biosensors for monitoring neurometabolic markers. *Bioelectrochemistry*. 2026;171. doi:10.1016/j.bioelechem.2026.109286.
155. Barman SR, Chan SW, Kao FC, Ho HY, Khan I, Pal A, et al. A self-powered multifunctional dressing for active infection prevention and accelerated wound healing. *Sci Adv*. 2023;9(4). doi:10.1126/SCIADV.ADC8758.
156. Kang M, Lee DM, Hyun I, Rubab N, Kim SH, Kim SW. Advances in Bioresorbable Triboelectric Nanogenerators. *Chem Rev*. 2023;123(19):11559–618. doi:10.1021/ACS.CHEMREV.3C00301.
157. Chakraborty I, Olsson RT, Andersson RL, Pandey A. Glucose-based biofuel cells and their applications in medical implants: A review. *Heliyon*. 2024;10(13):e33615. doi:10.1016/J.HELİYON.2024.E33615.

158. Cai J, Shen F, Zhao J, Xiao X. Enzymatic biofuel cell: A potential power source for self-sustained smart textiles. *iScience*. 2024;27(2). doi:10.1016/J.ISCI.2024.108998.
159. Naikwadi AT, Sharma BK, Bhatt KD, Mahanwar PA. Gamma Radiation Processed Polymeric Materials for High Performance Applications: A Review. *Front Chem*. 2022;10:837111. doi:10.3389/FCHEM.2022.837111.
160. Li Y, Li N, De Oliveira N, Wang S. Implantable bioelectronics toward long-term stability and sustainability. *Matter*. 2021;4(4):1125–41. doi:10.1016/j.matt.2021.02.001.
161. Gori M, Vadalà G, Giannitelli SM, Denaro V, Di Pino G. Biomedical and Tissue Engineering Strategies to Control Foreign Body Reaction to Invasive Neural Electrodes. *Front Bioeng Biotechnol*. 2021;9:659033. doi:10.3389/FBIOE.2021.659033.
162. Akhter S, Qureshi AR, Aleem I, El-Khechen HA, Khan S, Sikder O, et al. Efficacy of Electrical Stimulation for Spinal Fusion: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *Sci Rep*. 2020;10(1). doi:10.1038/S41598-020-61266-X.
163. Aleem IS, Aleem I, Evaniew N, Busse JW, Yaszemski M, Agarwal A, et al. Efficacy of Electrical Stimulators for Bone Healing: A Meta-Analysis of Randomized Sham-Controlled Trials. *Sci Rep*. 2016;6. doi:10.1038/SREP31724.
164. Holme S, Richardson SM, Bella J, Pinali C. Hydrogels for Cardiac Tissue Regeneration: Current and Future Developments. *Int J Mol Sci*. 2025;26(5). doi:10.3390/IJMS26052309.
165. Khodagholy D, Gelin JN, Thesen T, Doyle W, Devinsky O, Malliaras GG, et al. NeuroGrid: recording action potentials from the surface of the brain. *Nat Neurosci*. 2014;18(2):310–5. doi:10.1038/nn.3905.
166. Boehler C, Aqrave Z, Asplund M. Applications of PEDOT in Bioelectronic Medicine. *Bioelectron Med (Lond)*. 2019;2(2):89–99. doi:10.2217/BEM-2019-0014.
167. Lovley DR, Holmes DE. Protein nanowires: The electrification of the microbial world and maybe our own. *J Bacteriol*. 2020;202(20). doi:10.1128/JB.00331-20.