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Review Article

Electro-conductive biomaterials: Bridging bioelectronics and tissue regeneration

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ABSTRACT

Electro-conductive biomaterials serve as a vital bridge between bioelectronics and regenerative medicine by merging electrical functionality with biocompatible structures. These materials facilitate essential cellular behaviors such as communication, migration, proliferation, and differentiation processes that are crucial for the repair and regeneration of neural, cardiac, musculoskeletal, and dermal tissues. Recent progress in conductive polymers, nanomaterials, and hydrogels has led to the development of smart scaffolds and implantable devices that guide cell organization and deliver electrical cues to support tissue growth. By combining electroconductive materials with electrical stimulation, these systems enhance regeneration and open new pathways for building functional tissues and bioelectronic interfaces. This study provides a comprehensive review of electro-conductive biomaterials, including their classifications, mechanisms of conductivity, biocompatibility, and biodegradation. It further explores their applications across various tissue engineering domains, recent innovations in fabrication methods, and the technical and clinical challenges that must be addressed. Ultimately, this work outlines the potential of these materials to transform the future of regenerative medicine and bioelectronic integration.
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Table of Contents:
1. Introduction....1
2. Fundamentals of Electro-conductive Biomaterials....2
  2.1. Types of Electro-conductive Materials....2
  2.2. Mechanisms of Electrical Conductivity....2
  2.3. Biocompatibility and Degradation....2
3. Applications in Tissue Regeneration....3
  3.1. Neural Tissue Engineering....3
  3.2. Cardiac Tissue Repair....3
  3.3. Bone and Musculoskeletal Regeneration....3
  3.4. Wound Healing....3
4. Challenges and Future Perspective....4
5. Conclusion....4
6. References....4

1. Introduction

Electro-conductive biomaterials have become a groundbreaking area in tissue engineering and regenerative medicine, opening new possibilities for linking bioelectronics with tissue repair [1, 2]. These materials are designed to mimic the electrical properties of natural tissues, which are crucial for restoring the function of electroactive tissues like heart, nerve, and muscle [3]. Adding electrical conductivity to biomimetic scaffolds enhances cellular communication, growth, and differentiation, addressing a key gap often seen in traditional tissue engineering approaches [4]. Combining electro-conductive biomaterials with bio-electronic devices enables the restoration of electrical communication in tissues while allowing for real-time monitoring and modulation of tissue functions [5-7]. This synergy is especially useful in cardiac and neural tissue engineering, where electrical stimulation can trigger molecular cascades that promote regeneration and recovery [7, 8].

Advances in conductive polymers, metal nanoparticles, and nanocomposites have resulted in the creation of scaffolds that are

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biocompatible, biodegradable, and capable of delivering electrical signals tailored to the specific needs of different tissues [5, 6, 9].

Electro-conductive biomaterials provide a significant benefit by connecting implanted cells with host tissues or across damaged areas, thereby restoring disrupted electrical signals. This bridging ability is essential for addressing issues caused by tissue injury and disease, where normal electrical communication is impaired [6, 7].

Additionally, these materials can be engineered to deliver biological molecules like antibodies and enzymes, enhancing their regenerative capabilities and enabling multifunctional therapeutic applications [6, 10]. Although significant progress has been made, challenges remain in fully understanding and optimizing how electrical stimuli interact with cellular behavior in engineered tissues. The specific ways in which conductive scaffolds influence cell signaling, metabolism, and gene expression are still under investigation, and long-term in vivo studies are needed to confirm their safety and effectiveness [11].

Additionally, developing fabrication methods that allow precise control over electrical, mechanical, and biochemical properties is crucial for advancing clinical applications [11, 12]. This review offers a comprehensive overview of electro-conductive biomaterials, their functional mechanisms, and applications in linking bioelectronics with tissue regeneration. It covers current challenges and future research directions, highlighting how these advanced materials can be improved for effective, durable tissue repair. The aim is to enhance the integration of bio-electronic interfaces with regenerative medicine.

2. Fundamentals of Electro-conductive Biomaterials

Electro-conductive biomaterials are materials designed to combine biocompatibility with electrical conductivity. This enables them to interact effectively with biological tissues and cells [13]. They represent a multidisciplinary combination of biology, materials science, and electronics, playing a crucial role in fields like tissue engineering, bioelectronics, and regenerative medicine [14].

2.1. Types of Electro-conductive Materials

Electro-conductive materials are substances that allow electric current to flow due to the presence and movement of free electrons or charged particles. They are typically classified based on their electrical conductivity and the type of charge carriers. Various types of electro-conductive materials are shown in Table 1 and Fig. 1.

2.2. Mechanisms of Electrical Conductivity

Electrical conductivity in biomaterials results from various mechanisms that enable the transfer of electrical charge, which is vital for applications like tissue engineering and bio-electronic devices [28]. A primary method involves incorporating intrinsically conductive polymers, which have π-conjugated systems that allow π-electrons to move freely along the polymer chain. This electron delocalization creates pathways for charge carriers, providing electrical conduction similar to synthetic metals while maintaining biocompatibility and biodegradability [7].

Another method to achieve conductivity is by creating composites that disperse conductive fillers such as metals, carbon nanotubes, or conductive ceramics within nonconductive polymer matrices [29]. This approach balances electrical performance with mechanical strength, as the filler-based conductive network allows charge flow, while the polymer matrix provides structural support and biocompatibility [30]. Furthermore, conductive biomaterials can harness bioelectric phenomena, such as endogenous electrical signals created by transmembrane potentials in cells [31, 32]. The interaction between cells and conductive surfaces can influence cell adhesion, growth, and differentiation by controlling ionic currents and interactions with the extracellular matrix [32, 33].

2.3. Biocompatibility and Degradation

Electro-conductive biomaterials are a promising area in regenerative medicine, where biocompatibility depends on surface properties, electrical stimulation, and immune responses. Their degradation occurs through chemical, physical, and biological processes that must be carefully controlled to maintain functionality while ensuring safe resorption [34, 35]. Innovations like bio-erodible PEDOT derivatives show potential in creating electro-conductive biomaterials that are both biocompatible and degradable, opening new possibilities for temporary implants such as cardiac tissue scaffolds and bioelectronics [9, 34].

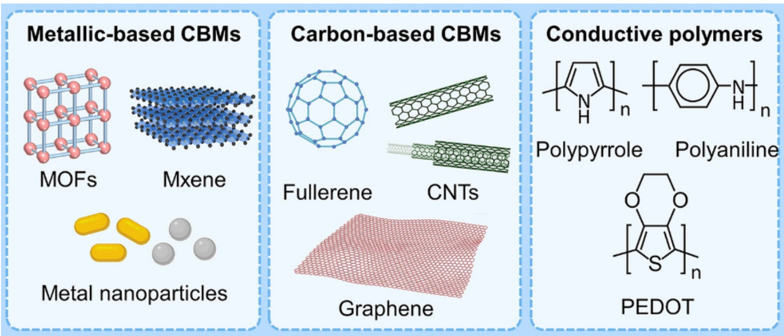

Fig. 1. Some of different Types of Electro-conductive Materials [15].

Table 1. Properties of different Types of Electro-conductive Materials

Type	Description	Properties	Examples	References
Metallic Conductors	Conduct electricity via free electrons moving through the metal lattice	High electrical conductivity, good mechanical strength, widely used in wiring and electronics.	Silver, Copper, Gold, Aluminum, Iron, Steel, Bronze	[16, 17]
Nonmetallic Conductors	Materials that are not metals but can conduct electricity due to special structures or additives.	Moderate conductivity; used in electrodes, flexible electronics, and composites.	Graphite, conductive polymers	[18-20]
Electrolytic Conductors	Conduct electricity through ion movement in a chemical reaction, often in liquid or gel form	Electrical conduction by ion displacement, used in batteries and electrochemical cells	Saltwater, acids, bases	[21-23]
Semiconductors	Materials with conductivity between conductors and insulators; conductivity can be modified	Used in electronic devices; conductivity controlled by doping and external conditions	Silicon, Germanium	[24, 25]
Superconductors	Materials that conduct electricity with zero resistance below a critical temperature	Perfect conductivity at low temperatures; used in MRI machines, particle accelerators	Niobium-tin, YBCO (ceramics)	[26, 27]

3. Applications in Tissue Regeneration

Electro-conductive biomaterials have emerged as a revolutionary class of materials in tissue regeneration because they can mimic the electrical properties of natural tissues and influence cell behaviors vital for healing. They are utilized across various tissue types, including cardiac, neural, bone, cartilage, muscle, and skin regeneration.

3.1. Neural Tissue Engineering

Using electro-conductive biomaterials in neural tissue engineering represents a significant advancement in regenerative medicine, particularly for repairing damaged central and peripheral nervous system tissues.

These materials establish a vital interface that replicates the natural electrical environment of neural tissues, enabling electrical stimulation (ES) to encourage neural stem/progenitor cell (NS/PC) differentiation into functional neuronal networks. Incorporating electrical cues into biomaterial scaffolds enhances the simulation of the physiological microenvironment of the central nervous system (CNS), which is essential for supporting neural differentiation, growth, and network formation [9].

Conductive biomaterials, such as electro-conductive polymers (ECPs) and nano-biomaterials, provide distinct advantages like biocompatibility, biodegradability, and the ability to deliver external electrical stimuli that encourage nerve regeneration. In peripheral nerve repair, these materials are incorporated into nerve guidance conduits (NGCs), which offer structural support and alter the bioelectrical environment to accelerate nerve growth and improve functional recovery [36].

Electrical stimulation through conductive scaffolds has been shown to activate molecular pathways that support axonal regeneration and remyelination, leading to better motor and sensory outcomes [36, 37].

Recent progress includes developing 3D conductive hydrogel systems and printed conductive polymer microelectrode arrays, enabling 3D electrical stimulation of neural tissues derived from human neural stem cells. These platforms promote extensive neuron maturation and the formation of functional neural networks, showing promise for creating clinically relevant neural tissue constructs for research and therapy [9, 38]. Additionally, these biomaterials are useful for modeling neural development, disease, and drug screening [38].

3.2. Cardiac Tissue Repair

Tissue engineering has appeared as a promising frontier in regenerative medicine, aiming to restore, maintain, or improve tissue functions [39]. Electroconductive biomaterials, including conductive nanomaterials such as gold nanoparticles, carbon-based nanomaterials such as carbon nanotubes, graphene oxide, silicon-derived nanomaterials, and electroconductive polymers like polyaniline and polypyrrole, have been integrated into cardiac patches and injectable hydrogels. These materials enable the transmission of electrical signals essential for synchronized cardiac muscle contraction, which is often impaired after MI due to tissue damage and fibrosis [34, 40]. By restoring electrical conductivity, these biomaterials enhance cell-to-cell communication among cardiomyocytes, promote tissue maturation, and improve contractile function [34].

Two main strategies have emerged for using electro-conductive biomaterials in cardiac repair. The first strategy involves fabricating electro-conductive patches or scaffolds in the lab, which are then implanted onto damaged heart tissue to provide mechanical support and electrical connection with the surrounding tissue. The second strategy employs injectable conductive hydrogels that can be directly delivered into the myocardium, offering a less invasive treatment option [40, 41]. These hydrogels not only help reestablish electrical coupling but also serve as delivery systems for therapeutic agents, genes, and growth factors to promote new blood vessel formation and tissue regeneration [40].

Fig. 2 shows injectable conductive hydrogels used in cardiac tissue engineering to restore electrical function and deliver therapeutic agents. These biomaterials' unique electrical properties help minimize adverse remodeling, such as myocardial cell death and fibrosis, which lead to increased tissue stiffness and electrical resistance after an infarction.

By improving the mechanical softness and electrical conductivity of damaged cardiac tissue, electro-conductive biomaterials support better electromechanical coupling and synchronized heartbeats, resulting in enhanced heart function [42, 43].

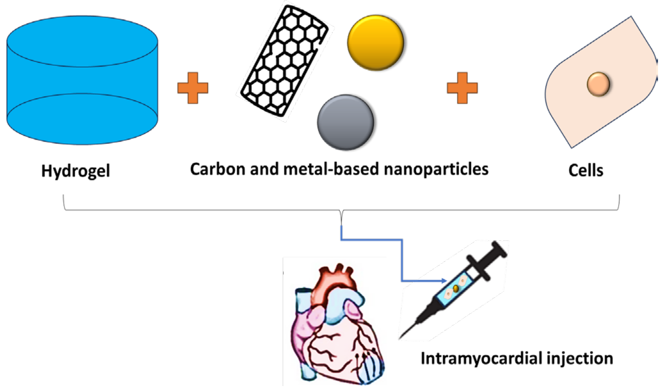

Fig. 2. Injectable conductive hydrogels for cardiac tissue engineering, facilitating electrical coupling and delivery of therapeutic agents.

3.3. Bone and Musculoskeletal Regeneration

Electro-conductive biomaterials have become very promising for bone and musculoskeletal regeneration because they mimic the natural electrophysiological environment of bone tissue. Since bone is an electroactive and electro-responsive tissue, regenerative efforts are significantly improved by implanting materials that conduct electrons, which facilitates electron transfer at the cell-material interface [44, 45]. This transfer enhances cell-substrate interactions, supports intercellular communication, and promotes osteogenesis of adult stem cells and osteoprogenitors even without external electrical stimulation [44].

Yu et al.'s [46] recent research highlighted progress in nano-conductive hydrogels made from materials like calcium phosphate, PEDOT:PSS, magnesium titanate, and methacrylated alginate. These hydrogels demonstrated strong electro-activity, biocompatibility, and osteoinductivity, promoting calcium influx locally and activating signaling pathways such as TGF-β/Smad2, which are essential for bone formation. In vivo experiments showed that when combined with electrical stimulation, these hydrogels could fully repair bone defects within weeks, underscoring their potential for clinical use in electro-inspired bone regeneration. Additionally, electroactive biomaterials support osteogenesis while also promoting chondrogenesis, angiogenesis, antibacterial activity, and drug delivery, serving as multifunctional platforms for musculoskeletal tissue engineering [47, 48]. By integrating electrical, biochemical, and mechanical cues, these biomaterials offer a biomimetic approach to effectively restore bone and cartilage functions [49].

3.4. Wound Healing

Conductive biomaterials play multiple roles in wound healing. They act as bioactive dressings that not only serve as physical barrthe wound healing processiers but also promote cell attachment, growth, and movement [50, 51]. For instance, PPy-based conductive films integrated into polymer matrices have been shown to support the viability and growth of human skin fibroblasts by Yu et al. [52], especially when combined with electrical stimulation. This method influences the expression of cytokines like IL-6 and IL-8, as well as growth factors such as FGF-1 and FGF-2, which are essential for forming granulation tissue and collagen production. Consequently, this approach enhances the healing process beyond what traditional dressings can achieve.

Wang et al [53]. suggested that conductive biomaterials can be designed to incorporate functions like electronically controlled drug release, antibacterial effects through agents like silver nanowires, and photo-thermal properties. These features improve the healing environment. Such multifunctional electro-conductive biomaterials are flexible and can be used for various wounds, including chronic and diabetic ulcers, which are typically difficult to treat.

4. Challenges and Future Perspective

Electro-conductive biomaterials offer significant potential for tissue engineering and regenerative medicine by delivering electrical stimuli directly to cells, thereby boosting functions such as growth, migration, adhesion, proliferation, and differentiation. These materials, like conducting polymers including polyaniline, PEDOT, and poly-pyrrole, combine the mechanical strengths of polymers with the electrical properties of metals, enabling adjustable conductivity and biocompatibility tailored to various tissues [7, 54]. However, challenges remain in their practical application, especially regarding their stability and biodegradability within the body. Conducting polymers tend to degrade slowly, which can cause inflammation and require surgical removal, prompting research into biodegradable alternatives. Additionally, successful integration of these materials into complex tissue environments demands precise control over surface properties and conductivity to support cell behavior and tissue regeneration. The development of electro-conductive hydrogels also faces hurdles such as mismatched mechanical properties with native tissues, environmental durability, susceptibility to damage, interface compatibility, and bacterial contamination all issues that must be addressed to unlock their full potential in bioelectronics and tissue engineering [54, 55].

Looking ahead, the development of electro-conductive biomaterials depends on overcoming current challenges by adopting innovative fabrication techniques like 3D bio-printing [56]. This technology allows for the creation of precisely structured, cell-loaded constructs with adjustable electrical properties that better resemble native tissues. Research in material design focuses on balancing conductivity with mechanical flexibility, while also improving biodegradability and biocompatibility to avoid immune reactions [6, 57]. Combining electrical stimulation with conductive scaffolds has produced synergistic effects, especially in cardiac and neural tissue engineering, emphasizing the importance of integrating these methods. Additionally, bringing these materials into clinical practice will require solving issues such as long-term stability, monomer toxicity, and proper integration with host tissues. Ongoing interdisciplinary efforts are crucial for developing "smart" electro-conductive biomaterials that can adapt to physiological needs, support tissue growth, and effectively communicate with bio-electronic devices, creating new opportunities for treating various diseases and injuries [56, 57].

5. Conclusion

Electro-conductive biomaterials have become an essential innovation in tissue engineering, bridging bioelectronics and regenerative medicine by mimicking the electrical properties of natural extracellular matrices. These materials support vital cellular activities such as growth, migration, proliferation, and differentiation across various tissues like cardiovascular, neural, bone, and muscle. Using conductive scaffolds with electrical stimulation offers combined benefits, enhancing functional recovery in nerve repair and the maturation of cardiac tissue.

Although there have been promising results, challenges remain in understanding long-term biocompatibility, cell-material interactions, and scalable manufacturing processes. Future research should focus on developing intelligent scaffold designs that incorporate structural, mechanical, and dynamic electrical signals, along with thorough clinical translation efforts. The ongoing development of electroconductive biomaterials has the potential to significantly enhance the restoration of complex tissue functions.

Author Contributions

Mojdeh Rezaei-khamseh: Conceptualization, Writing – original draft, Writing – review & editing. ***Soroush Etebarian:*** Writing – original draft, Writing – review & editing. All authors read and approved the final version of manuscript.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data Availability

No data is available.

Ethical issues

The authors confirm full adherence to all ethical guidelines, including the prevention of plagiarism, data fabrication, and double publication.

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