Chapter 6

Electroactive Biomaterials for Cell Behavior Regulation and Tissue Regeneration

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ABSTRACT

Endogenous electric fields widely occur in bone, skin, cardiac, and nerve tissues, significantly influencing organ development, wound healing, and tissue regeneration. Generated primarily by transmembrane potentials resulting from ion concentration gradients (e.g. Na+, K+, Ca2+), these fields inspire electroactive biomaterials designed with built-in electric fields. Unlike external electrical stimulation, such biomaterials precisely regulate cellular behavior through direct electron/charge interactions and protein-mediated signal transduction. By tailoring physical and chemical properties, these biomimetic materials replicate natural bioelectric cues. This review summarizes endogenous electrical signals, details fabrication methods and regulatory mechanisms of electroactive biomaterials, highlights applications in bone, nerve, and skin regeneration, and discusses clinical challenges and future perspectives.

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1. INTRODUCTION

Tissue regeneration plays a crucial role in the repair and restoration of damaged or lost tissue functions in the body. It involves a complex interplay of cellular activities, including cell migration, differentiation, proliferation, and extracellular matrix formation, which together contribute to the reconstruction of functional tissue.(Xia et al., 2018) However, current therapeutic strategies for enhancing tissue regeneration often fall short in promoting efficient, natural, and precise healing, particularly in cases of chronic wounds or severe tissue damage. In recent years, the application of electroactive biomaterials has emerged as a promising solution to improve tissue regeneration by leveraging endogenous electrical signals that govern cellular behavior and tissue repair.(Liu et al., 2021; Ning et al., 2018)

Endogenous electric fields are an intrinsic part of biological systems, present across various tissues such as bone, skin, nerve, and cardiac tissues.(Thrivikraman et al., 2018) These electric fields are primarily generated by the transmembrane potential, resulting from the difference in ion concentrations, such as sodium (Na^{+}), potassium (K^{+}), and calcium (Ca^{2+}), across the cell membrane.(Nowicka-Bauer & Szymczak-Cendlak, 2021) These fields not only contribute to cellular homeostasis but also regulate key physiological processes, such as wound healing, nerve regeneration, and bone remodeling. For example, during tissue injury, electric fields can guide the migration of cells to the wound site, promote cellular differentiation, and stimulate tissue repair by influencing the behavior of various cell types, including fibroblasts, stem cells, and endothelial cells.(Preetam et al., 2024) These endogenous electrical signals have been recognized for their ability to control cellular activities at a precise spatial and temporal level, thereby playing a pivotal role in tissue regeneration.(Das et al., 2024)

To mimic the beneficial effects of these natural electric cues and enhance tissue repair, electroactive biomaterials have been developed. These materials are designed to generate or respond to electric fields and provide electrical stimuli that directly influence cellular behavior.(Liu et al., 2021) Unlike traditional external electrical stimulation methods, which rely on bulky devices and invasive electrodes, electroactive biomaterials offer several advantages. They can be fabricated with built-in electric fields that operate at the material interface, enabling a more localized, direct, and sustained modulation of cellular functions. Furthermore, electroactive biomaterials are designed to interact with cells at the molecular level through charge-based interactions, triggering signal transduction pathways that regulate cellular processes such as migration, proliferation, and differentiation.(Chen et al., 2024a) The fabrication of electroactive biomaterials requires a careful design process to ensure that their physical, chemical, and electrical properties closely resemble those found in natural tissues.(Chen et al., 2024a; Esmaeili et al., 2022) These materials can be engineered to possess specific characteristics such as conductivity, piezoelectricity, and electrochemical activity, which are essential for eliciting the desired cellular responses.(Casella et al., 2021) By tailoring the composition and structure of electroactive biomaterials, researchers can fine-tune their ability to create electric fields that influence cellular behavior, providing a versatile tool for enhancing tissue regeneration across a wide range of applications.(Deng et al., 2022)

This chapter aims to provide a comprehensive overview of the role of electroactive biomaterials in regulating cell behavior and promoting tissue regeneration. First, we explore the physiological endogenous electric fields that exist in living organisms and tissues, highlighting their importance in regulating cellular processes. Next, we discuss the various fabrication methods used to develop electroactive biomaterials, focusing on how the design of these materials can generate or respond to electric fields. We then delve into the mechanisms by which electroactive biomaterials modulate cellular behavior, discussing how electric cues interact with cell surface receptors, ion channels, and functional proteins to influence cell

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