

# Biomaterials, Cells, And Stimulation For Spinal Cord Repair

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## Introduction

Neural tissue engineering represents a promising frontier for addressing the debilitating effects of spinal cord injury (SCI) by developing sophisticated scaffolds designed to emulate the native extracellular matrix, facilitate the delivery of therapeutic agents, and actively guide axonal regeneration. This field is continuously evolving, with recent breakthroughs focusing on innovative biomaterial development, including advanced hydrogels and electrospun fibers, which are being integrated with cell-based therapies. These therapies often involve stem cells and neural progenitor cells, aiming to promote significant functional recovery in injured spinal cords [1].

The application of stem cell therapy stands out as a leading strategy in neural tissue engineering for SCI, with particular emphasis on mesenchymal stem cells (MSCs) and induced pluripotent stem cells (iPSCs). These versatile cells possess the remarkable ability to differentiate into various neural lineages, secrete essential neurotrophic factors that support neuronal health, and effectively modulate the often-detrimental inflammatory response characteristic of SCI. The synergistic combination of stem cells with biocompatible scaffolds further amplifies their therapeutic potential by providing a nurturing microenvironment conducive to cell survival and seamless integration with the host neural circuitry [2].

Hydrogels have emerged as widely adopted materials for use as scaffolds in neural tissue engineering. Their inherent properties, such as high water content, excellent biocompatibility, and their capacity to closely mimic the native extracellular matrix, make them ideal candidates for regenerating nervous tissue. Contemporary hydrogel designs are increasingly incorporating bioactive cues, including peptides and growth factors, to actively stimulate cell adhesion, enhance proliferation, and guide differentiation. Furthermore, the development of injectable hydrogels offers a less invasive method for delivering therapeutic interventions to the injured spinal cord site [3].

The integration of electrical stimulation with established neural tissue engineering strategies holds significant potential to substantially enhance axonal regeneration and improve functional recovery following SCI. Electroactive scaffolds are being engineered to deliver electrical cues that precisely replicate physiological signals, thereby fostering neuronal growth and promoting differentiation. This combined approach seeks to overcome the inhibitory factors that are prevalent in the environment of the injured spinal cord and to effectively guide the formation of new, functional neural connections [4].

Three-dimensional (3D) bioprinting technology is ushering in a revolutionary era for neural tissue engineering, offering unprecedented control over the precise fabrication of complex, cell-laden scaffolds. This technology allows for meticulous

control over scaffold architecture and the spatial distribution of therapeutic agents, enabling the creation of constructs that more accurately replicate the intricate microarchitecture of the spinal cord. Consequently, this leads to more effective neural regeneration and restoration of lost function. A key advantage of this method is its capability for the precise layering of different cell types and biomaterials [5].

The extracellular matrix (ECM) plays an indispensable role in orchestrating cellular behavior and driving tissue regeneration processes. Engineered biomaterials derived from the ECM, such as decellularized spinal cord tissue, represent a promising avenue for the development of biomimetic scaffolds. These advanced scaffolds are designed to support neural regeneration by delivering native biochemical and physical cues. Such materials are capable of guiding cell adhesion, migration, and differentiation, which are critical steps in facilitating the integration of transplanted cells and promoting the formation of new neural connections [6].

Exosomes, which are minute extracellular vesicles secreted by cells, are rapidly gaining recognition as potent therapeutic agents within the field of neural tissue engineering for SCI. These vesicles are packed with a diverse cargo of proteins, lipids, and nucleic acids that possess the ability to modulate cellular functions, stimulate neurogenesis, and mitigate inflammatory responses. Exosomes derived from stem cells, in particular, are highly attractive due to their inherent capacity to deliver beneficial factors directly to the injured site, thereby promoting regeneration and facilitating functional recovery [7].

Nanomaterials are offering unique and substantial advantages in the realm of neural tissue engineering for SCI, largely due to their exceptionally high surface area-to-volume ratio and their readily tunable properties. Nanofibers, nanoparticles, and nanostructured surfaces can be meticulously engineered to closely mimic the nanoscale architecture of the neural ECM, thereby enhancing cell adhesion and facilitating the targeted delivery of therapeutic agents. Their diminutive size also enables improved penetration into the complex architecture of the injured spinal cord tissue [8].

Biomimetic scaffolds that accurately replicate the intricate biochemical and physical cues present in the native spinal cord environment are fundamentally crucial for achieving successful outcomes in neural tissue engineering. Current strategies involve the incorporation of specific signaling molecules, the precise mimicking of topographical features found in natural tissues, and the careful tuning of mechanical properties. The collective goal of these efforts is to promote neuronal survival, stimulate robust axonal outgrowth, and ensure functional integration of regenerated neural tissue, ultimately aiming to restore lost motor and sensory functions by bridging the lesion site and encouraging remyelination [9].

Tissue engineering approaches that adeptly combine multiple therapeutic modalities, encompassing biomaterials, cellular components, and bioactive molecules,

are demonstrating progressively greater success in tackling the complex and multifaceted challenges presented by SCI. These sophisticated multi-component strategies are meticulously designed to cultivate a highly conducive environment for regeneration. They achieve this by simultaneously promoting the survival of transplanted cells, actively reducing the formation of inhibitory glial scars, and effectively guiding the regrowth of axons. The precise engineering and integration of these composite constructs are paramount to achieving meaningful and sustained functional recovery [10].

## Description

Neural tissue engineering is significantly advancing the repair of spinal cord injuries (SCI) by creating intricate scaffolds that meticulously replicate the native extracellular matrix, deliver vital therapeutic agents, and actively guide the regeneration of axons. The cutting edge of this research is characterized by innovations in biomaterials, such as advanced hydrogels and electrospun fibers, which are increasingly being combined with sophisticated cell-based therapies. These therapies frequently involve the use of stem cells and neural progenitor cells, with the overarching objective of promoting substantial functional recovery in individuals affected by SCI [1].

A prominent and highly promising strategy within neural tissue engineering for SCI is the utilization of stem cell therapy. This approach predominantly employs mesenchymal stem cells (MSCs) and induced pluripotent stem cells (iPSCs), both of which exhibit remarkable plasticity. These cells are capable of differentiating into diverse neural lineages, secreting crucial neurotrophic factors that support neuronal viability and function, and importantly, modulating the inflammatory cascade that often exacerbates SCI. The synergistic effect of combining stem cells with biocompatible scaffolds further augments their therapeutic efficacy by providing an optimized microenvironment that supports cell survival and fosters integration with the existing neural circuitry [2].

Hydrogels have become a cornerstone in the development of scaffolds for neural tissue engineering, largely owing to their intrinsic properties. Their high water retention capacity, excellent biocompatibility, and inherent ability to closely mimic the native extracellular matrix make them exceptionally well-suited for applications in neural regeneration. Modern hydrogel designs are being engineered with sophisticated bioactive cues, such as specific peptides and growth factors, which are crucial for promoting cell adhesion, enhancing cell proliferation, and guiding cellular differentiation. Moreover, the advent of injectable hydrogels presents a less invasive delivery mechanism for therapeutic interventions targeting the site of spinal cord injury [3].

The synergistic combination of electrical stimulation with established neural tissue engineering methodologies is showing considerable promise in significantly accelerating axonal regeneration and improving functional recovery subsequent to SCI. Electroactive scaffolds are being designed to deliver precise electrical cues that mimic endogenous physiological signals, thereby actively stimulating neuronal growth and promoting cellular differentiation. This integrated approach aims to surmount the various inhibitory factors present within the microenvironment of the injured spinal cord and to effectively direct the formation of new, functional neural connections [4].

Thirty-dimensional (3D) bioprinting technology is fundamentally transforming the landscape of neural tissue engineering. It facilitates the precise fabrication of complex, cell-laden scaffolds, offering exquisite control over their architecture and the spatial arrangement of therapeutic agents. This advanced capability allows for the creation of engineered constructs that more accurately recapitulate the intricate microarchitecture of the spinal cord, ultimately promoting more effective neural re-

generation and functional restoration. A key advantage of this technology lies in its ability to precisely layer different cell types and biomaterials in a controlled manner [5].

The extracellular matrix (ECM) is a critical regulator of cell behavior and plays a pivotal role in orchestrating tissue regeneration processes. Engineered biomaterials derived from the ECM, including decellularized spinal cord tissue, offer a highly promising avenue for generating biomimetic scaffolds. These scaffolds are designed to actively support neural regeneration by providing native biochemical and physical cues. Such materials are adept at guiding essential cellular processes like adhesion, migration, and differentiation, thereby facilitating the integration of transplanted cells and promoting the formation of new neural connections within the injured site [6].

Exosomes, which are small extracellular vesicles secreted by cells, are emerging as potent therapeutic agents for spinal cord injury (SCI) within the field of neural tissue engineering. These vesicles contain a rich cargo of proteins, lipids, and nucleic acids that can effectively modulate cell function, stimulate neurogenesis, and reduce inflammation. Exosomes derived from stem cells are particularly sought after due to their inherent ability to deliver beneficial factors directly to the injured spinal cord environment, thereby promoting regeneration and enhancing functional recovery [7].

Nanomaterials are conferring unique and significant advantages to neural tissue engineering strategies aimed at treating SCI. Their exceptionally high surface area-to-volume ratio and tunable physical and chemical properties make them ideal for mimicking the nanoscale intricacies of the neural extracellular matrix. Nanofibers, nanoparticles, and other nanostructured surfaces can be precisely engineered to enhance cell adhesion, facilitate the targeted delivery of therapeutic agents, and improve penetration into the complex and often dense injured tissue environment [8].

Biomimetic scaffolds that effectively replicate the complex biochemical and physical milieu of the native spinal cord environment are indispensable for achieving successful outcomes in neural tissue engineering for SCI. Current research strategies focus on incorporating specific signaling molecules, precisely mimicking topographical features, and meticulously tuning the mechanical properties of scaffolds. The overarching objectives are to promote neuronal survival, stimulate axonal outgrowth, and ensure functional integration of regenerated neural tissue, with the ultimate aim of restoring lost function by bridging the lesion site and promoting remyelination [9].

Tissue engineering approaches that judiciously integrate multiple therapeutic modalities, including biomaterials, cellular components, and bioactive molecules, are showing increasing efficacy in addressing the multifaceted challenges associated with SCI. These advanced multi-component strategies are designed to create an optimal regenerative environment by simultaneously promoting cell survival, mitigating the formation of inhibitory glial scars, and actively guiding axonal regrowth. The precise engineering and orchestrated assembly of these composite constructs are crucial for achieving significant and lasting functional recovery [10].

## Conclusion

Neural tissue engineering offers significant promise for spinal cord injury (SCI) repair through advanced biomaterials like hydrogels and electrospun fibers, combined with cell therapies such as stem cells and neural progenitor cells. Key strategies include leveraging stem cells (MSCs, iPSCs) for their differentiation and neurotrophic factor secretion capabilities, and utilizing hydrogels that mimic the extracellular matrix and can be delivered minimally invasively. Electrical stimulation

and electroactive scaffolds aim to enhance axonal regeneration. 3D bioprinting allows precise construction of complex neural tissues. Extracellular matrix-derived biomaterials and nanomaterials are employed to replicate native cues and improve cell integration. Exosomes, particularly from stem cells, deliver regenerative factors. Biomimetic scaffolds replicating native cues are essential for survival and outgrowth. Multimodal approaches combining biomaterials, cells, and bioactive molecules are proving increasingly successful in addressing SCI complexity and promoting functional recovery.

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## Conflict of Interest

None.

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