Available online at www.worldscientificnews.com

World Scientific News

An International Scientific Journal

WSN 196 (2024) 83-113 EISSN 2392-2192

Nano Fiber Synthesis by Chemical Methods: A Review of Recent Progress and Applications

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ABSTRACT

Nano fibers, characterized by their one-dimensional structure and nanoscale diameters, exhibit exceptional properties, including high surface area, flexibility, and mechanical strength. This review article provides a comprehensive overview of recent advancements in chemical synthesis methods for nano fibers, including electrospinning, template-assisted synthesis, vapor-phase deposition, and self-assembly. The applications of nano fibers are diverse, encompassing biomedical engineering, energy storage, catalysis, sensors, and filtration. The tenability and versatility of nano fibers make them promising candidates for addressing current challenges in these fields. However, further research and development are necessary to optimize synthesis methods and explore new applications to fully realize the potential of nano fibers.

Keywords: Biomedical engineering, chemical synthesis, electrospinning, energy storage, filtration, nanotechnology, sensors, template-assisted synthesis,

(Received 18 July 2024; Accepted 15 August 2024; Date of Publication 29 August 2024)

INTRODUCTION

Nano fibers, with their unique one-dimensional structure and nanoscale diameters, have emerged as a fascinating class of materials, exhibiting an extraordinary combination of properties (Kuchibhatla et al. 2007; Barhoum et al. 2019). Their exceptionally high surface area, flexibility, and mechanical strength make them an attractive candidate for a wide range of applications (Kontturi et al. 2018; Benzigar et al. 2020). The ability to tailor their properties through various chemical synthesis methods has further expanded their potential, enabling the development of nanofibers with specific functionalities (Agarwal et al. 2009; Rivero et al. 2015).Recent advancements in chemical synthesis methods, including electrospinning, template-assisted synthesis, vapor-phase deposition, and self-assembly, have significantly improved the control over nanofiber morphology, composition, and properties (Keshavarz et al. 2022). These methods have enabled the production of nanofibers with precise diameters, lengths, and surface functionalities, opening up new avenues for their application in diverse fields (Lim. 2017).The applications of nanofibers are vast and varied, spanning from biomedical engineering, energy storage, and catalysis to sensors, filtration, and beyond (Ramakrishna et al 2010; Reddy et al. 2021). Their tenability and versatility make them an ideal candidate for addressing current challenges in these fields, where traditional materials have limitations (Prasad et al. 2017; Khan et al. 2020).

Tissue engineering has made substantial progress in recent years, driven by the development of nanofiber-based scaffolds (Hussain et al. 2014). Nanofibers offer distinct advantages in tissue engineering applications, including their high surface area-to-volume ratio, ability to mimic the natural extracellular matrix (ECM) structure, and potential for controlled release of therapeutic agents (Vasita and Katti 2006; Rim et al. 2013; Oprea et al. 2019). We will also examine several examples of nanofiber scaffolds used for the regeneration of various tissues, including skin, bone, cartilage, nerve, and heart (Prabhakaran et al. 2011). The fabrication, characterization, and application of nanofibrous systems as scaffolds for tissue engineering are currently active areas of research (Martins et al. 2007; Teixeira et al. 2019; Parham et al. 2020). Additionally, nanofiber-based systems are being explored for various biological and non-biological applications due to their potential (Ambekar and Kandasubramanian 2019; Ahmadian et al. 2023).The significance of nanofiber-based scaffolds in tissue engineering is substantial, and ongoing research in this field promises to yield new therapeutic options for patients with tissue damage or degeneration (Dahlin et al. 2011; Ogueri and Laurencin 2020). This review aims to provide a comprehensive understanding of the current state of nanofiber-based scaffolds in tissue engineering and their future prospects.

METHODS FOR NANOFIBER SYNTHESIS

Three primary techniques are employed for the synthesis of nanofibers including electrospinning, self-assembly, and phase separation (Greiner and Wendorff 2008; Wade and Burdick. 2014). Electrospinning is a widely used and popular technique for fabricating nanofibers (Islam et al. 2019). This process involves applying a high voltage to a polymer solution or melt, which is then ejected through a spinneret, creating a charged jet (Brown et al. 2016; Saleh-Hudin et al. 2018). The electrostatic forces cause the jet to elongate, reducing its diameter until the solvent evaporates, and solidifies into a continuous nanofiber (Reneker and Yarin 2008; Alghoraibi and Alomari. 2018). Electrospinning allows for the production of nanofibers with controlled diameters, morphology, and composition (Ahmadian et al. 2021; Valizadeh and Mussa Farkhani. 2014). Self-assembly is a technique that leverages the natural tendency of molecules to assemble into specific structures, such as nanofibers (Froimchuk et al. 2020; Ogueri and Laurencin. 2020). This method offers precise control over the size, morphology, and composition of the nanofibers, making it an attractive option for tissue engineering applications (Xie et al. 2010). Self-assembly enables the fabrication of complex and hierarchical structures, which are challenging to produce using other methods (Hedegaard and Mata. 2020). Phase separation is a technique that involves the separation of a polymer solution into distinct phases, resulting in the formation of nanofibers (Tipduangta et al. 2016; Almetwally et al. 2017). This method offers advantages in controlling the size, morphology, and composition of the nanofibers (Baji et al. 2010). However, phase separation has received relatively limited attention in the context of tissue engineering applications, and further research is needed to explore its potential (Ravichandran et al. 2012; Khorshidi et al. 2016). The use of radiofrequency-supported microwave plasmas for the synthesis of nanofibers (Biazar. 2017). The study of carbon and alumina nanofibers is restricted to their applications in tissue engineering (Vasita et al., 2006). These nanofibers have shown promise in various tissue engineering applications, including the fabrication of scaffolds for tissue regeneration, wound healing, and drug delivery (Sridhar et al., 2015; Nazarnezhad et al. 2020). The unique properties of nanofibers, such as their high surface area, porosity, and biocompatibility, make them attractive candidates for tissue engineering applications (Singla et al., 2019; Nazarnezhad et al. 2020).

ELECTROSPINNING

Electrospinning is a versatile technique employed to fabricate nanofibers by harnessing the power of an electric field to manipulate a polymer solution or melt (Subbiah et al. 2005; Bhardwaj and Kundu 2010). The process commences with the ejection of the polymer solution from a fine nozzle, creating a charged jet that is subjected to an intense electric field (Reneker and Yarin 2008). This electric field exerts a stretching force on the jet, elongating and thinning it to an extraordinary degree, ultimately yielding ultrafine fibers (Lukáš et al. 2009). As the fibers travel through the electric field, they undergo a process known as "stretching and thinning," which reduces their diameter to the nanoscale (Rafiei et al. 2013). Upon reaching a collector, the fibers solidify, forming a nonwoven mat or scaffold (Sun et al. 2014). The collector's design and configuration play a crucial role in determining the final shape and orientation of the nanofibers (Wang et al. 2019).

The electrospinning process is a versatile method for producing nanofibers, offering several advantages that make it an attractive technique for various applications (Agarwal et al. 2009; Sahay et al. 2012). One of the primary benefits of electrospinning is its ability to produce fibers with high porosity and large surface area, making them well-suited for tissue engineering applications (Martins et al. 2008). These fibers can support cell growth and proliferation, making them ideal for use in tissue engineering scaffolds (Lannutti et al. 2007; Khorshid et al. 2016). Another significant advantage of electrospinning is its ability to control fiber diameter and composition (Boudriot et al. 2006). This allows researchers to tailor the fibers to specific applications, such as drug delivery or wound healing (Rieger et al. 2013). By adjusting the fiber diameter and composition, researchers can create fibers with specific properties that are optimized for their intended use (Karimah et al. 2021).

To further enhance the control over fiber properties, various modifications have been developed for the electrospinning setup (Sahay et al. 2011). These modifications include the use of multiple nozzles, the incorporation of magnetic fields, and the use of templates to guide fiber formation (Wychowaniec and Brougham. 2022). These modifications allow researchers to refine the electrospinning process and expand the potential applications of nanofibers in tissue engineering and drug delivery (Pillay et al. 2013). Polymeric nanofibers produced via electrospinning offer a range of beneficial properties, including a high surface area-to-volume ratio, high porosity, and high mechanical strength (Ibrahim and Klingner. 2020). These properties enable the fibers to mimic the natural extracellular matrix structure and promote cell adhesion and proliferation (Sell et al. 2007). Additionally, polymeric nanofibers provide a large surface area for drug loading, which can improve drug stability, solubility, and bioavailability (Wu et al. 2011).

The ability to control the composition of polymeric nanofibers allows researchers to tailor their properties for different applications (Wang et al. 2019). For example, the incorporation of nanofillers such as carbon nanotubes or graphene oxide can enhance the electrical conductivity and mechanical strength of the fibers, making them suitable for energy storage applications (Li et al. 2019). Overall, the electrospinning process is a powerful tool for producing nanofibers with specific properties, making it an attractive technique for a range of applications (Shi et al. 2015). Fibers ranging from 50nm to 1000nm or greater can be produced through electrospinning, offering versatility in creating nanofibers for various uses (Fadil et al. 2021).

The Taylor cone plays a crucial role in the electrospinning process, where the electric field at the tip causes the solution to be ejected as a jet (Haider et al. 2019). This jet is rapidly elongated by electrostatic forces and undergoes solvent evaporation, resulting in solidification and the formation of nanofibers (Saleh-Hudin et al. 2018). In contrast, electro-spraying involves the formation of small droplets due to the competition between electrostatic forces and surface tension, which then solidify into small particles or fibers (Leena et al. 2019). Both techniques can be easily scaled up for large-scale production using multiple capillary nozzles or electrospray nozzles, making them suitable for various applications (Deng et al. 2006). The ability to control process parameters such as polymer concentration, flow rate, and electrical potential allows for tailoring the size, shape, and morphology of the nanofibers, expanding their potential applications (Wang et al. 2019). As the jet is ejected from the Taylor cone, rapid solvent evaporation occurs, leading to the solidification of nanofibers with a high aspect ratio and diameter ranging from tens to hundreds of nanometers (Zhang et al. 2022). Electrospinning can be scaled up for large-scale production, and the use of various polymers and additives enables the creation of nanofibers with diverse properties and functionalities (Omer et al. 2021). Electrospun nanofibers can be further functionalized with biological or chemical molecules to enhance their performance for specific applications (Kriegel et al. 2008). On the other hand, electro-spraying produces nanoparticles by generating charged droplets from a polymeric solution, which are then collected as dried or partially dried particles (Sosnik. 2014). This technique is highly versatile and can produce particles with a range of diameters and compositions. Both electrospinning and electro-spraying are promising techniques for producing polymeric nanofibers and nanoparticles with a wide range of applications in areas such as biomedicine, environmental sensing and remediation, and energy storage and conversion (Asmatulu and Khan. 2018).

Electrospinning is a versatile technique that offers several advantages (**Figure 1**), including the ability to produce nanofiber meshes with high porosity and surface area (Ramesh Kumar et al. 2012).

Additionally, this technique can be applied to a wide variety of natural and synthetic polymers, making it a highly adaptable method (Sionkowska. 2011). This versatility allows researchers to experiment with different materials and create nanofibers with unique properties (Agarwal et al. 2009). However, electrospinning also has some limitations. One of the main drawbacks is the broad range of fiber thickness, which can result in inconsistent fiber diameters (Richard-Lacroix and Pellerin. 2015). Another limitation is the random orientation of nanofibers, which can affect the mechanical properties of the fiber meshes (Pauly et al. 2016). Furthermore, the mechanical properties of the fiber mesh themselves can be relatively low, which may limit their use in certain applications (Klosterhalfen et al., 2005). Despite these limitations, electrospinning remains a relatively robust and simple technique for producing nanofibers from a wide variety of polymers (Agarwal et al. 2009). Its versatility, high porosity, and surface area make it an attractive method for researchers and industries alike (Valtchev and Tosheva. 2013). With ongoing advancements and refinements, electrospinning is likely to continue playing a significant role in the development of nanofiber-based materials and applications (Anjum et al. 2022).

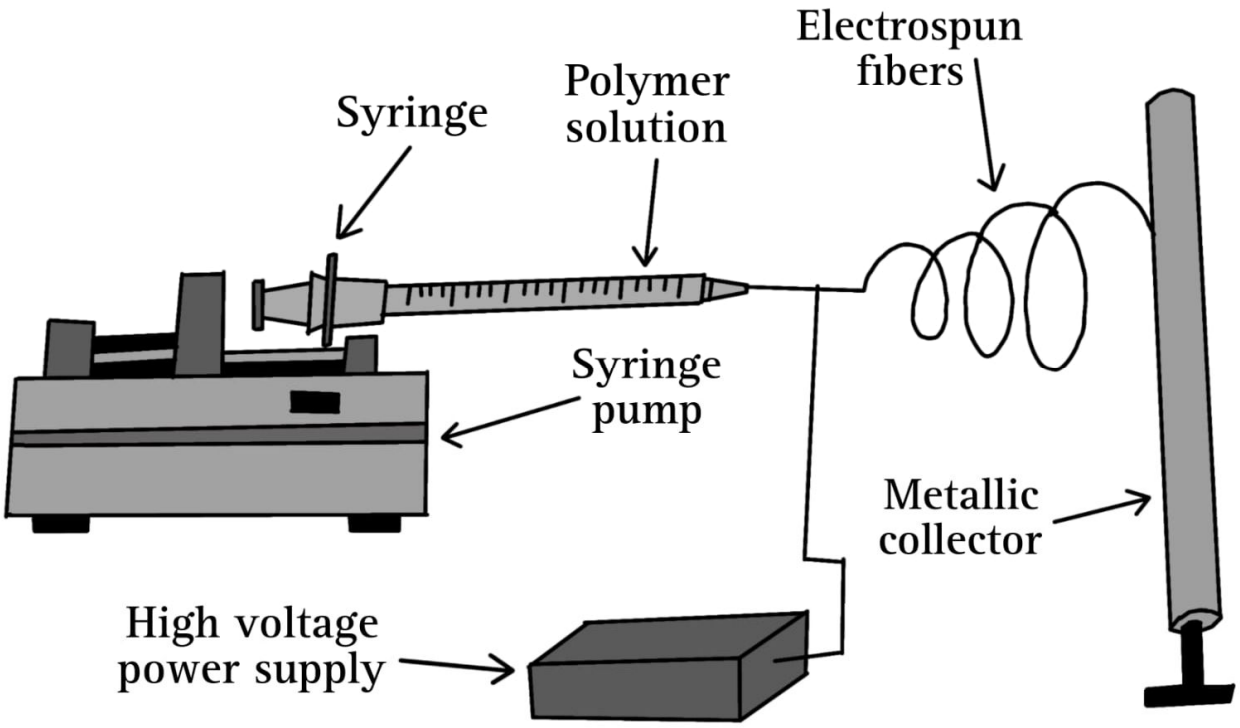

Figure 1: Schematic of the electrospinning process

TEMPLATE-ASSISTED SYNTHESIS

Template-assisted synthesis is a powerful method for fabricating nanofibers with precise control over their size, shape, and orientation (Pérez-Page et al. 2016). This technique utilizes a pre-existing template or mold, which can be a solid material, such as a porous membrane or a nanopatterned surface, or a liquid droplet (Mireles and Gaborski. 2017). A precursor material into or onto the template and transforming it into nanofibers through various processes, researchers can create nanofibers with uniform dimensions, ordered arrangements, and complex geometries (Greiner and Wendorff. 2008).The advantages of template-assisted synthesis are numerous. This method enables the creation of nanofibers with precise control over their properties, allowing for the incorporation of different materials within the nanofibers, such as core-shell structures or composite materials (Yarin et al. 2007). Additionally, template-assisted synthesis offers scalability and reproducibility, making it suitable for large-scale production (Poolakkandy and Menamparambath, 2020), The applications of template-assisted synthesized nanofibers are diverse and widespread (Pavlenko et al. 2022). In nanotechnology, they are used in areas such as electronics, photonics, and energy storage devices (Sygletou et al. 2017). In biomedical engineering, these nanofibers are employed for tissue engineering scaffolds, drug delivery systems, and biosensors (Cleeton et al. 2019). Furthermore, template-assisted synthesis finds applicability in filtration membranes, catalysis, and environmental remediation (Pavlenko et al. 2022).Overall, template-assisted synthesis is a versatile method for the fabrication of nanofibers with precisely controlled properties (template-assisted synthesis is a versatile method for the fabrication of nano fibers with precisely controlled properties (Pavlenko et al. 2022). Its wide range of applications makes it a valuable technique for various fields, offering opportunities for advancements in materials science and engineering. By leveraging this technique, researchers and industries can develop innovative solutions and products with enhanced performance and functionality.

PHASE SEPARATION

The phase separation method, introduced by Zhang and Ma, is a technique used to produce a 3D structure of collagen-like nanofibers through thermally induced liquid-liquid phase separation (Sabzi et al. 2020). This method consists of five main stages preparation of a homogeneous polymer solution, phase separation, gelation, extraction of the solvent, and freezing and freeze-drying under vacuum (Rezvankhah et al. 2020). The process begins with the preparation of a polymer solution by dissolving the polymer at room temperature (Miller-Chou and Koenig, 2003). The solution is then left to reach the gelation temperature, which is a critical step in the process (Almetwally et al. 2017).

The gelation process depends on the concentration of the polymer and the gelation temperature (Almetwally et al. 2017). When the polymer reaches the gelation temperature, platelet-like structures form due to the nucleation of crystals, making it essential to maintain the optimum temperature (Yu and Cölfen. 2004). After the gelation step is complete, the solvent is extracted from the gel using water, followed by freeze-drying. The freeze-drying stage requires minimal experimentation. The nanofiber matrix can be directly fabricated or adjusted by modifying the polymer concentration. The quality, morphology, and nanofibrous matrix are influenced by major factors such as polymer concentration, polymer type, and solvent type (Ciftci et al. 2017). However, a significant drawback of this technique is that only a limited range of polymers can be used to obtain nanofibers through phase separation, as not all polymers are compatible with this process due to the specific gelation capacity required (Ciftci et al. 2017). Despite this limitation, the phase separation method remains a valuable technique for producing collagen-like nanofibers with potential applications in various fields (Bürck et al. 2013).

NATURAL POLYMERIC MATERIALS FOR NANOFIBERS

Natural polymers, such as collagen, hyaluronic acid, gelatin, chitosan, elastin, and silk, are being used as biomaterials due to their similarity and sometimes identity to micro-molecular substances present in the human body (Taneja et al. 2021). Collagen, the most popular biomaterial, is compatible with various cell types, including myoblasts and chondrocytes (Taneja et al. 2021). The mechanical strength of collagen nanofibers is enhanced due to intermolecular interactions with polyethylene oxide (Chen et al. 2008). Chitosan, another natural biomaterial, is used to produce nanofibers that maintain structural integrity in water, enhancing the attachment of human osteoblasts and chondrocytes (Tao et al. 2020). These nanofibers preserve the characteristic morphology of the cells (Venugopal et al. 2008). Hyaluronic acid, however, requires advanced techniques like electroblowing, combined with electro-spinning and air flow, to produce high-quality nanofibers (Dias et al. 2020). Gelatin, a natural biomaterial, can be combined with synthetic materials to produce composite nanofibers with improved chemical strength and wettability (Kim et al. 2009). This combination enhances the mechanical properties of natural biomaterials for tissue engineering applications (Heidari et al. 2016). Silk fibroin is another promising natural material used to produce nanofiber scaffolds (Kundu et al. 2013). These natural polymers offer great potential for tissue engineering and regenerative medicine due to their biocompatibility, biodegradability, and ability to support cell growth and differentiation (Asadi et al. 2020). The development of advanced techniques and composite materials has improved the quality and functionality of natural polymer nanofibers, making them suitable for various biomedical applications.

SELF-ASSEMBLY

Self-assembly is a fundamental principle that occurs at multiple length scales, from atomic to macroscopic levels, and is observed in nature, from crystal formation to biological systems like proteins and DNA (Grzybowski et al. 2009). In the context of nanofibers, self-assembly refers to the spontaneous arrangement of nanofibers into hierarchical structures through non-covalent interactions, such as electrostatic interactions, hydrogen bonding, van der Waals forces, or π-π stacking (Gao et al. 2023). These interactions enable the formation of various self-assembled structures, including networks, gels, membranes, or scaffolds, depending on the properties of the nanofibers and environmental conditions (Venugopal et al. 2008). The self-assembly of nanofibers offers several advantages, including structure control and functional properties (Greiner and Wendorff. 2008). By manipulating environmental parameters like temperature, pH, or concentration, researchers can guide the self-assembly process to obtain specific structures with desired properties. Self-assembled nanofiber networks, for example, can exhibit high surface area, porosity, and mechanical strength, making them suitable for applications like filtration membranes or tissue engineering scaffolds (Greiner and Wendorff. 2008). Additionally, incorporating functional molecules or nanoparticles into the self-assembled structures can enable extra functionalities, such as drug delivery capabilities or sensing abilities (Ekiz et al. 2016). Overall, self-assembly is a powerful technique for creating complex and functional structures from nanofibers, with significant potential for various applications in materials science, biotechnology, and nanotechnology.

APPLICATION OF NANOFIBARS IN TISSUE ENGINEERING

In the field of tissue engineering, various methods have been explored for fabricating scaffolds, but in recent years, nanofibrous systems have emerged as a promising option. These systems offer several advantages, including high surface area and porosity, which can enhance cell adhesion and proliferation. Moreover, the 3D architecture of nanofibrous systems closely resembles the natural extracellular matrix (ECM), providing an ideal micro and nano environment for cells to grow and perform their regular functions (Sell et al. 2007).The unique properties of nanofibrous systems make them an attractive choice for tissue engineering applications. Their high surface area and porosity allow for efficient nutrient and waste exchange, while their 3D structure provides mechanical support and guidance for cell growth (Loh and Choong 2013). As a result, nanofibrous systems have been extensively pursued as scaffolds for tissue engineering, with the potential to support the regeneration of various tissues and organs.

By mimicking the natural ECM, these systems can create a conducive environment for cells to thrive, making them a promising tool for advancing tissue engineering and regenerative medicine.

NANOFIBERS FOR MUSCULOSKELETAL TISSUE ENGINEERING

Bone tissue is composed of an organic bone matrix, primarily consisting of collagen fibers and inorganic compounds like hydroxyapatite crystals (Farbod et al. 2014). Traditional treatment approaches for bone injuries or deformities, such as tumors or infectious bone loss due to trauma, involve autografts, allografts, or xenografts (Damien and Parsons, 1991). However, these methods are associated with several problems, including inflammation, scarring, infection, immunological graft rejection, hematomas, and high-cost procedures (Wu et al. 2017). Bone tissue engineering (BTE) aims to produce a scaffold that can be implanted in the defect area and remodeled by the patient's own cells (Alonzo et al. 2021). The design of the scaffold is inspired by the structure and function of healthy bone tissue (Li et al. 2013). A wide range of biomaterials can be used to mimic the function, structure, and composition of bone ECM for bone tissue regeneration (Ferreira et al. 2012). However, if the scaffolds are not biodegradable, surgery is necessary to remove them, which can cause irritation to the patient and bring infection (Dorati et al. 2017). This method is also costly to perform. In contrast, biodegradable scaffolds can be designed to degrade over time, eliminating the need for removal surgery (Dorati et al. 2017). The use of 3D scaffolds has been successful in promoting cell differentiation, as evidenced by the change in cell shape from round to spindle-like form (Ji et al. 2015). This indicates that the scaffold is providing a conducive environment for cells to grow and differentiate, paving the way for effective bone tissue regeneration (Figure 2).

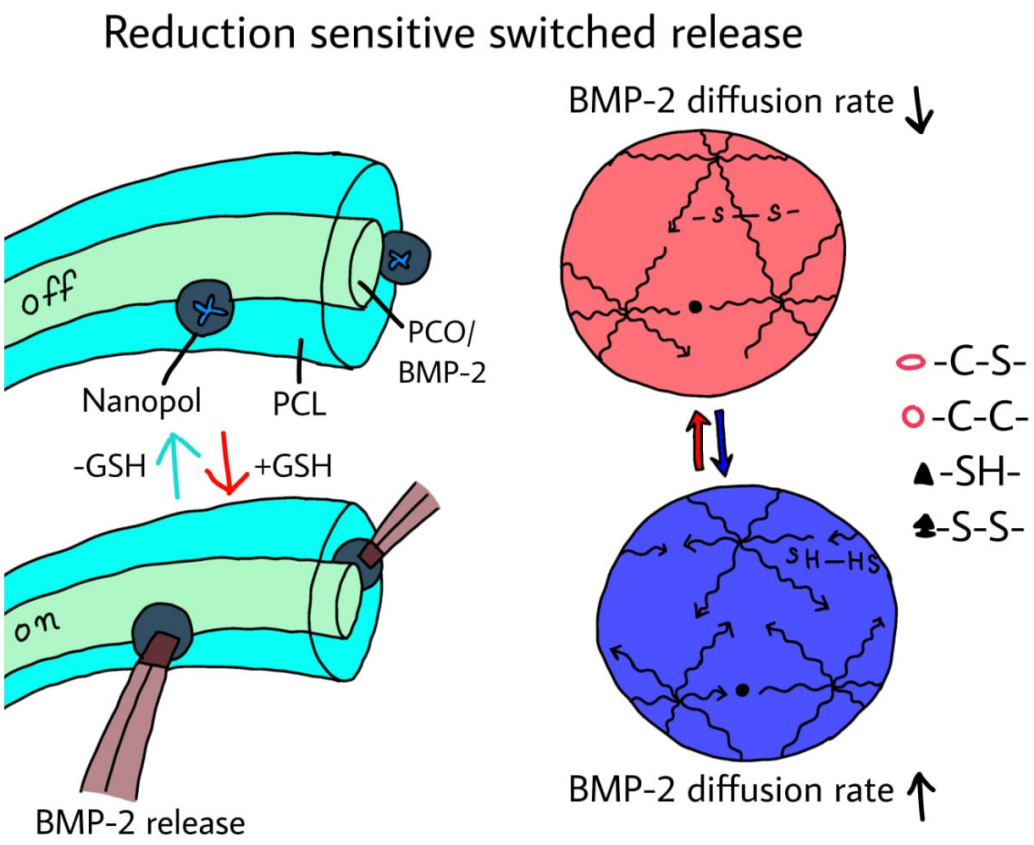

Figure 2: Reduction-Sensitive Switched Release

NANOFIBERS FOR CARTILAGE TISSUE ENGINEERING

Polymeric nanofibers have shown great promise in cartilage tissue engineering due to their ability to mimic the natural extracellular matrix (ECM) of articular cartilage and provide an optimal microenvironment for chondrocyte growth and proliferation (Eftekhari et al. 2020). One of the key challenges in engineering cartilage tissue is to produce scaffolds that mimic the unique mechanical properties of cartilage, such as stiffness and elasticity, which are critical for proper chondrocyte differentiation and function (Wasyłeczko et al. 2020). Electrospinning techniques can be used to produce highly organized and aligned nanofiber scaffolds with mechanical properties similar to native cartilage (Wasyłeczko et al. 2020).

Nanofiber scaffolds can also be functionalized with different biochemical cues, such as growth factors, cytokines, and extracellular matrix proteins, to promote cellular adhesion, proliferation, and differentiation, as well as to mimic the natural environment of cartilage tissue (Setayeshmehr et al. 2019).

Additionally, nanofiber scaffolds can be used to deliver drugs and gene therapy agents to promote tissue growth and regeneration, taking advantage of their high surface area to volume ratio for efficient release kinetics (Ji et al. 2011). Studies have demonstrated the potential of polymeric nanofiber scaffolds for cartilage tissue engineering. For example, adult bone marrow-derived MSCs were seeded onto PCL nanofibers and induced to differentiate into chondrocytes, showing comparable results to cell aggregates or pellets (Li et al. 2005). Furthermore, self-assembling peptide hydrogels have been shown to support chondrocyte proliferation, ECM production, and phenotype maintenance, making them a suitable candidate for cartilage tissue engineering (Kisiday et al. 2002). Overall, polymeric nanofiber scaffolds provide a promising approach for cartilage tissue engineering due to their unique mechanical properties, ability to mimic the natural environment of cartilage, and flexibility to incorporate different biochemical cues and therapeutic agents.

NANOFIBERS FOR LIGAMENT TISSUE ENGINEERING

Polymeric nanofibers have demonstrated great potential for ligament tissue engineering due to their ability to mimic the extracellular matrix (ECM) of native tissues, providing an optimal microenvironment for cellular growth and proliferation (Sell et al. 2007). The alignment and orientation of nanofibers can be controlled through various electrospinning techniques, allowing for the fabrication of highly organized scaffolds that mimic the anisotropic structure of ligament tissue (Xing et al. 2022). This is crucial, as the mechanical properties of ligament tissue are highly dependent on the degree of alignment and orientation of the collagen fibers that make up the tissue (Kew et al. 2011). Nanofiber scaffolds can be functionalized with biochemical cues such as growth factors, cytokines, and extracellular matrix proteins to promote cellular adhesion, proliferation, and differentiation (Figure 3) (Cheng et al. 2014).

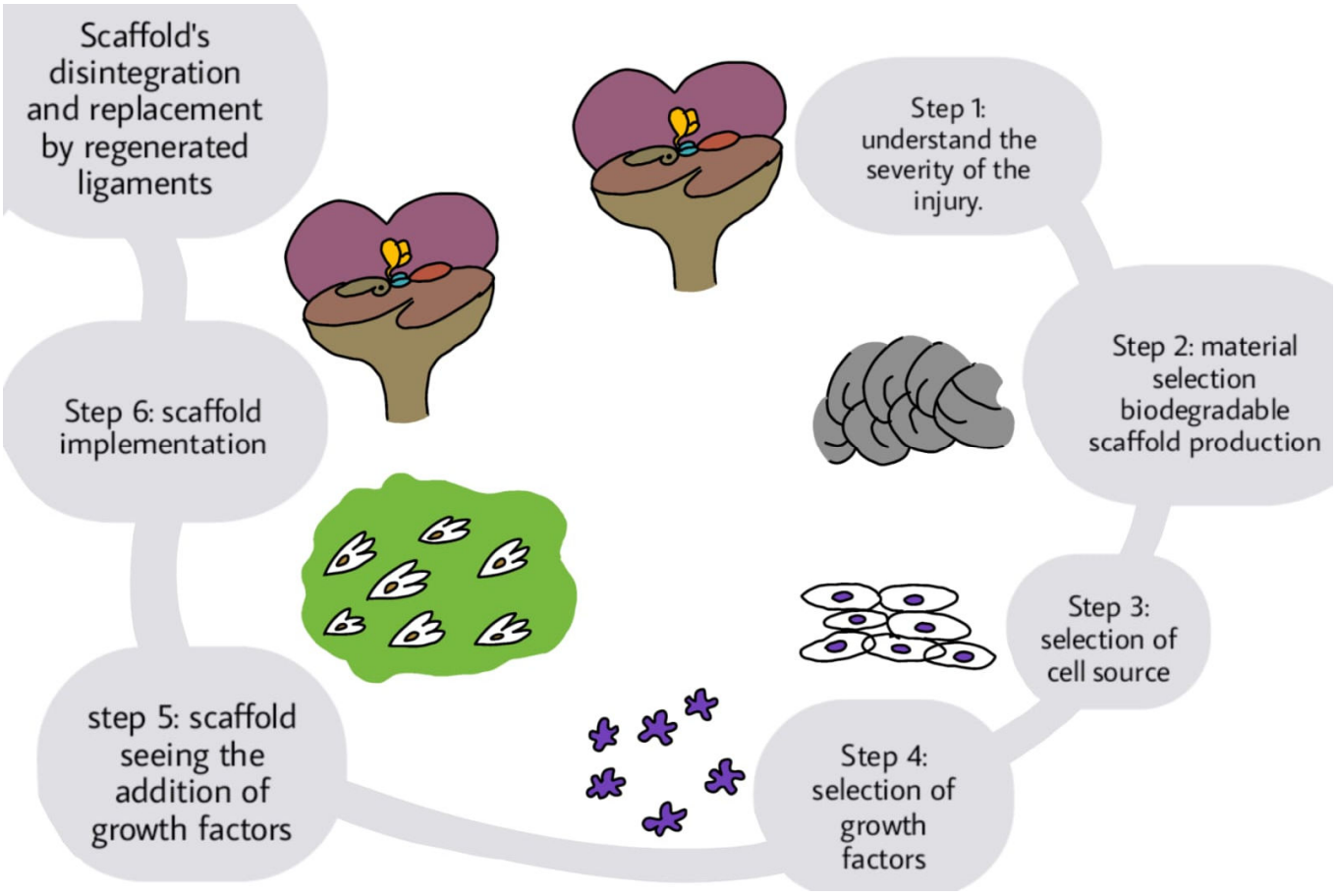

Figure 3: Seaffold's degradation, and replacement by regenerated ligament

The incorporation of these cues enhances the biocompatibility and bioactivity of the scaffolds, improving their ability to promote tissue regeneration (Chen et al. 2018). Additionally, nanofiber scaffolds have shown superior mechanical properties compared to conventional scaffold materials, such as hydrogels and sponges, due to their high surface area to volume ratio, high porosity, and ability to control fiber diameter and mechanical properties. Studies have demonstrated the potential of polymeric nanofiber scaffolds for ligament tissue engineering. For example, human ligament fibroblasts (HLFs) were seeded onto aligned nanofibers, showing enhanced synthesis of ECM proteins, such as collagen, compared to randomly oriented nanofibers (Lee et al. 2005). Furthermore, the direction of mechanical stimuli was shown to influence the ECM produced by HLFs, with aligned nanofibrous scaffolds demonstrating promise for use in ligament tissue engineering (Martins et al. 2008). Overall, polymeric nanofiber scaffolds represent a promising approach for ligament tissue engineering due to their ability to mimic the structure and function of native tissues, provide an optimal microenvironment for cellular growth, and offer superior mechanical properties (Han et al. 2021).

NANOFIBERS FOR SKELETAL MUSCLE TISSUE ENGINEERING

Skeletal muscles have a limited capacity for regeneration, and significant damage can lead to permanent loss of muscle tissue and function, resulting in impaired movement and reduced quality of life (Tieland et al. 2018). While small muscle injuries can be repaired naturally, larger injuries or diseases that result in substantial muscle loss are challenging to treat and regenerate (Figure 4). Tissue engineering approaches, combining biomaterials and cells, have emerged as a promising strategy to address muscle injuries and diseases (Liu et al. 2018).

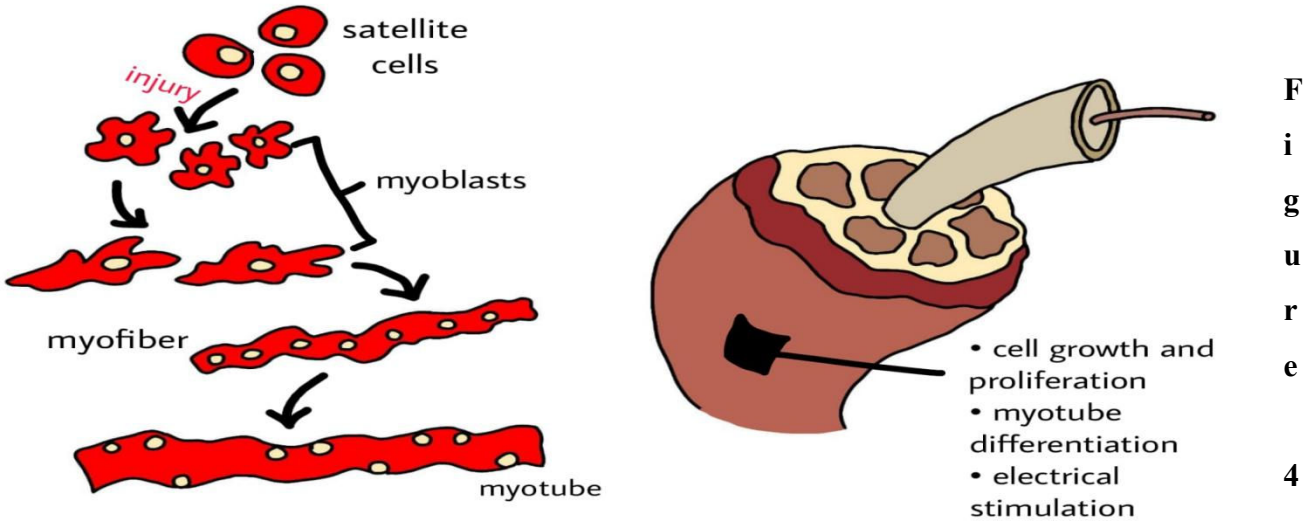

Figure 4: Seaffolds for skeletal muscle regeneration

NANOFIBERS FOR SKIN TISSUE ENGINEERING

Skin wounds typically heal by forming epithelialized scar tissue, rather than regenerating full skin (Monavarian et al. 2019). However, polymeric nanofibers have shown promise in skin tissue engineering due to their ability to mimic the structure and function of the natural extracellular matrix (ECM) of the skin (Sell et al. 2007). Nanofiber scaffolds can provide a suitable environment for skin cell growth and proliferation, promoting wound healing and regeneration. These scaffolds can be produced with similar morphology and biochemical properties as the native ECM, supporting the growth, adhesion, and proliferation of various skin cells, including keratinocytes, fibroblasts, and melanocytes (Cichorek et al. 2013). The aligned nanofibers can also mimic the orientation of collagen fibers in the skin, which is crucial for the mechanical strength and elasticity of the tissue (Law et al. 2017).

Nanofiber scaffolds can be functionalized with bioactive molecules, such as growth factors, cytokines, and extracellular matrix components, to promote cell adhesion, proliferation, and differentiation (Cichorek et al. 2013). These molecules can facilitate wound healing and accelerate skin tissue regeneration by promoting angiogenesis, collagen synthesis, and re-epithelialization (Rousselle et al. 2019). Furthermore, nanofiber scaffolds can serve as a carrier for drug delivery, enabling targeted and controlled release of therapeutics for various skin disorders, such as skin cancer, dermatitis, and psoriasis (Goyal et al. 2016). This makes them a versatile tool for skin tissue engineering and regenerative medicine, offering a promising solution for improving wound healing outcomes and skin regeneration (Goyal et al. 2016).

NANOFIBERS FOR BLOOD VESSEL TISSUE ENGINEERING

Polymeric nanofibers have been explored for their potential use in blood vessel tissue engineering due to their ability to provide a suitable environment for endothelial cell growth and proliferation, as well as mimic the structure and function of the natural extracellular matrix (ECM) of blood vessels (Jia et al. 2019). Nanofiber scaffolds can be produced with similar morphology and mechanical properties as the native ECM of blood vessels, such as collagen and elastin fibers, supporting the growth, adhesion, and proliferation of endothelial and smooth muscle cells (Xie et al. 2020).

Aligned nanofibers can mimic the alignment of fibers in the vascular ECM, crucial for mechanical strength and elasticity (Xu et al. 2015). Researchers have developed methods to produce aligned nanofibers, such as using a rotating collector disc, to fabricate tubular scaffolds for engineering blood vessels (Hu et al. 2012). These aligned nanofibers have been shown to mimic the dimensions of natural ECM, provide mechanical properties comparable to human coronary arteries, and form a well-defined architecture for smooth muscle cell adhesion and proliferation (Jia et al. 2019). The nanoscale-textured surface roughness of nanofibers has been found to significantly impact cell response, with cells attaching and organizing well around fibers with diameters smaller than them (Anselme et al. 2010). To enhance cell adhesion and proliferation, researchers have modified the surface of nanofibers by grafting gelatin onto PET nanofibers (Ma et al. 2005). This modification has been shown to promote endothelial cell spreading and proliferation while preserving their phenotype, making gelatin-modified PET nanofibers potential candidates for vascular graft engineering (Ma et al. 2005).

NANOFIBERS FOR NEURAL TISSUE ENGINEERING

In the nervous system, degeneration of neurons or glial cells, or unfavorable changes in the extracellular matrix of neural tissue, can lead to a wide range of clinical disorders (Soleman et al. 2013). Unfortunately, neural tissue repair is a significant challenge, as almost all neural injuries result in irreversible loss of function (Dietz and Curt. 2006). However, polymeric nanofibers have shown promise in neural tissue engineering due to their ability to mimic the structure and function of the natural extracellular matrix (ECM) of the nervous system, providing a suitable environment for neural cell growth and proliferation (Jia et al. 2019). Neural tissue engineering aims to repair neural tissue by combining biological tools, such as cells and ECM equivalents, with synthetic tools like biomaterials for scaffold design and drug delivery systems (Subramanian et al. 2009).

Nanofiber scaffolds can be designed to mimic the morphology and biochemical properties of the native ECM of the nervous system, supporting the growth, adhesion, and proliferation of neural cells, including neurons and glial cells (Tian et al. 2015). The aligned nanofibers can also replicate the orientation of fibers in the nervous system, crucial for the directional growth of axons and growth cones (Sirkkunan et al. 2021). Furthermore, nanofiber scaffolds can be functionalized with bioactive molecules, such as growth factors, cytokines, and neural cell adhesion molecules, to promote cell adhesion, proliferation, differentiation, and neurite outgrowth (Jia et al. 2019). These molecules can facilitate the formation of neural networks and enhance the functional integration of new neural tissue into the host tissue, offering a promising approach for neural tissue repair and regeneration (Goyal et al. 2016).

NANOFIBERS FOR CONTROLLED DRUG DELIVERY

Nanofibers have emerged as a promising tool for controlled drug delivery, thanks to their unique properties, including high surface area-to-volume ratio, large pore size, and interconnected porous structure (Goyal et al. 2016). These features enable enhanced drug loading, sustained release, and targeted delivery, making nanofibers an attractive option for various medical applications (Goyal et al. 2016). Nanofibers can be fabricated from a range of materials, such as polymers, ceramics, and metals, and can be engineered to possess specific properties, including biocompatibility, biodegradability, mechanical strength, and surface charge, depending on the intended use (Agarwal et al. 2009). Drug molecules can be incorporated into the nanofiber matrices through various methods, including electrospinning, phase separation, and layer-by-layer assembly, ensuring uniform and high drug loading while preventing burst release (Jeckson et al. 2021).

Furthermore, nanofiber scaffolds can be functionalized with bioactive molecules, such as growth factors, cytokines, and antibodies, to enhance drug targeting and efficacy, as well as facilitate tissue regeneration and repair (Du et al. 2020). Additionally, nanofiber scaffolds can respond to various stimuli, including temperature, pH, and light, triggering drug release at specific time points or locations in the body (Contreras-Cáceres et al. 2019). This can minimize side effects and maximize therapeutic potential. Overall, nanofibers hold great promise for controlled drug delivery, offering improved drug loading, sustained release, targeting, and efficacy. They also enable personalized medicine and disease management, making them a valuable tool in the development of advanced healthcare solutions.

NANOFIBERS FOR DNA, PROTEIN, AND ENZYME DELIVERY

The selection of a suitable gene delivery vehicle is crucial for meeting the needs of a specific therapeutic application, given the availability of multiple gene delivery systems (Pack et al. 2005). Currently, viral- and plasmid-based delivery vehicles are used to produce therapeutic proteins, eliciting a desired biological response (Cid and Bolívar. 2021). Gene delivery systems have been explored for various tissue engineering applications, with cationic liposomes and condensing agents like poly(ethyleneimine) and poly(l-lysine) being the most commonly used carrier-based systems (Wang et al. 2013). Recently, biomaterial-based gene delivery systems have gained attention, with materials like poly (ethylene glycol) (PEG), PLGA, and PLA-PEG copolymers being investigated for gene and protein delivery (Tsekoura et al. 2017). DNA delivery using nanofibers holds great promise for gene therapy, as they can protect DNA from degradation, facilitate cellular uptake, and enable efficient gene expression (Riley and Vermerris. 2017). Additionally, nanofibers can be functionalized with targeting ligands for cell-specific delivery (Yoo et al. 2009). Scaffolds for gene delivery must provide structural stability, site-specific delivery, and protection of genes from the biological system until release (Elfinger et al. 2008). The released DNA must retain its structural integrity until taken up by the desired cells (Stojanov and Berlec. 2020). Moreover, nanofibers can facilitate controlled protein and enzyme delivery, providing a sustained and localized therapeutic effect. They can also immobilize enzymes, enhancing their stability and reusability. The use of nanofibers for DNA, protein, and enzyme delivery can overcome limitations of conventional approaches, such as rapid degradation, low stability, and poor bioavailability (Sebe et al. 2015). Nanofiber-based delivery systems can enhance therapeutic efficacy, minimize toxic effects, and enable personalized medicine and disease management.

APPLICATION OF CARBON NANOFIBERS IN TISSUE ENGINEERING

Carbon nanofibers have shown great promise for orthopedic and dental tissue engineering applications due to their exceptional mechanical properties, which surpass those of bone tissue (Vasita and Katti. 2006). With a strength three times that of bone tissue, carbon nanofibers have the potential to provide a strong and durable scaffold for tissue growth (Peng et al. 2020). Additionally, their nanoscale fiber dimensions are similar to those of natural bone fibers, such as hydroxyapatite and collagen, making them an attractive option for mimicking the natural bone environment (Pina et al. 2015). Furthermore, carbon nanofibers have also been found to exhibit excellent conductivity, making them potential candidates for neural tissue engineering applications (Peng et al. 2020). Unlike conventional metal alloy implants, carbon nanofiber-based implants have shown excellent cyto-compatibility properties and do not release metal ions, which can lead to complications (Saliev. 2019). This makes them a promising alternative for orthopedic implants (Saliev. 2019).

Research has been conducted to explore the use of carbon nanofibers for bone tissue engineering. Studies have compared osteoblast adhesion on carbon nanofibers to that of conventional carbon fibers, showing greater adhesion on carbon nanofibers (Saliey. 2019). To understand the properties responsible for this enhanced adhesion, researchers have also studied osteoblast adhesion on PLGA-coated carbon nanofibers, which also showed improved adhesion compared to conventional carbon fibers (Peng et al. 2020). These findings suggest that carbon nanofibers have the potential to provide a suitable scaffold for bone tissue engineering (Peng et al. 2020).

APPLICATION OF ALUMINA NANOFIBERS IN TISSUE ENGINEERING

Osteointegration, the process by which bone tissue integrates with an implant, is a crucial requirement for successful bone and dental implantation (Insua et al. 2017). Research has shown that reducing the surface feature size of an implant can enhance osteointegration, leading to a stronger bond between the implant and surrounding bone tissue. Alumina, titania, hydroxyapatite (HA), and their composites are among the most extensively studied materials for orthopedic and dental applications (Park and Webster. 2005). Notably, alumina nanofibers have been identified as a promising material due to their physical geometry, which is similar to that of HA (Park and Webster. 2005). This similarity led researchers to hypothesize that alumina nanofibers may enhance osteointegration, making them a potential candidate for orthopedic and dental tissue engineering applications (Bhat et al. 2021). The studies discussed above highlight the potential of both carbon and alumina nanofibers as promising materials for orthopedic and dental tissue engineering applications.

Their unique properties and ability to enhance osteointegration make them attractive options for developing more effective and durable implants (Park and Webster. 2005).

CONCLUSIONS

Nanofibers have emerged as a promising material for various biomedical applications, including tissue engineering, wound healing, drug delivery, and implantable devices (Contreras-Cáceres et al. 2019). Their unique properties, such as high surface area, porosity, and ability to mimic natural tissue structures, make them an attractive option for developing innovative solutions for various medical challenges. Research has shown that nanofibers can be used to create scaffolds for tissue engineering, promote wound healing, and deliver drugs in a controlled and targeted manner. Additionally, nanofibers have been explored for their potential use in implantable devices, such as orthopedic and dental implants, due to their ability to enhance osteointegration and biocompatibility (Park and Webster. 2005).Mimicking the complex architecture and functionality of native extracellular matrix (ECM) is crucial for successful tissue engineering (Fernandes et al. 2009). ECM provides essential support, organization, and signals to cells in tissues and organs. To replicate this, synthetic ECM scaffolds can be prepared using various approaches, including electrospinning, self-assembly, and 3D printing. Among these methods, electrospinning of nanofibers has gained significant attention due to its ability to produce highly aligned and interconnected fiber networks with a morphology similar to native ECM.

Electrospinning is a simple and cost-effective technique that uses an electric field to draw fibers from a polymer solution and deposit them onto a surface. This method can produce nanofibers with a range of diameters and controlled mechanical properties. Furthermore, electrospun nanofibers can be functionalized with various molecules, such as growth factors, enzymes, and antibodies, to enhance cell adhesion, proliferation, and differentiation (Jia et al. 2019). The nanoscale structure of electrospun scaffolds provides a high surface area-to-volume ratio, supporting cellular processes and enabling efficient exchange of nutrients and waste products (Rnjak-Kovacina and Weiss. 2011). Additionally, electrospinning can produce not only single nano- or microfibers but also composite materials integrating nanofibers with other materials, such as ceramics, metals, and hydrogels (Fadil et al. 2021). The 3D printing of electrospun fibers can also create complex architectures with controlled mechanical and biological properties (Wang et al. 2021). Nanofibers, regardless of their synthesis method, offer scaffolds with high surface area and enhanced porosity. These properties significantly impact cell adhesion, proliferation, and differentiation, making nanofibrous matrices an attractive option for various tissue engineering applications (Jia et al. 2019).

Currently, nanofiber-based scaffolds are being explored for musculoskeletal tissue engineering, skin tissue engineering, neural tissue engineering, vascular tissue engineering, and controlled delivery of drugs, proteins, and DNA (Vasita and Katti. 2006). The results of these studies demonstrate the excellent potential of nanofiber-based scaffolds for tissue engineering applications.

Overall, the versatility and potential of nanofibers make them a promising tool for advancing biomedical research and developing innovative solutions for improving human health. Further research and development are needed to fully realize the potential of nanofibers in biomedical applications.

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