REVIEW ARTICLE

Electrospun Nanofibers for Biomedical Use: A Detailed Review of Process Parameters, Morphological Control, and Advanced Fabrication Methods

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Abstract

Electrospinning has emerged as a versatile and highly adaptable nanofiber fabrication technique capable of generating multifunctional scaffolds for biomedical applications, particularly in wound healing and regenerative medicine. This review provides a comprehensive analysis of the fundamental principles of electrospinning, the influence of solution, processing, and environmental parameters on nanofiber morphology, and the critical relationships between rheological behavior, chain entanglement, and fiber formation. Various classes of polymers, including synthetic, natural, and composite systems, are examined with respect to their spinnability, structural performance, biodegradation, and application-specific suitability. Advanced electrospinning methods such as coaxial, triaxial, emulsion, bubble, centrifugal, and microfluidic-assisted systems are critically evaluated for their ability to achieve controlled drug delivery, compartmentalized architectures, porous and hollow morphologies, and stimuli-responsive performance. In addition, the review highlights emerging nanofiber platforms such as conductive, biomimetic, hydrogel-integrated, and smart responsive systems that synergistically integrate bioactivity, mechanical adaptability, and diagnostic or therapeutic functionalities. Key biomedical applications, including antimicrobial dressings, angiogenic scaffolds, aligned fibers for tissue guidance, and multidrug delivery constructs, are discussed, supported by recent advances demonstrating enhanced healing outcomes, infection control, and microenvironment modulation. By synthesizing current progress in fabrication technologies, material innovations, and clinically oriented design strategies, this review underscores the expanding potential of electrospun nanofibers as next-generation wound care and regenerative platforms. Future perspectives emphasize scalable manufacturing, green electrospinning approaches, real-time sensing integrations, and multifunctional hierarchical scaffolds capable of addressing complex wound pathophysiology.

Key words: Biomedical scaffolds, coaxial electrospinning, drug delivery, electrospinning, nanofibers, smart materials, tissue regeneration, wound healing

INTRODUCTION

Electrospinning is a simple, low-cost method of forming nanofibers from a polymer solution due to the influence of a high electric field. Rayleigh discovered electrospinning in 1897, and the process has since been very much developed.[1] Key developments are the use of rotating electrodes by Cooley and the production of composite fibers by Formhals.[2,3] There are three primary components of the electrospinning process: a high-voltage power source, a syringe (spinneret), and a collector (electrode). When a polymer solution is exposed to a high electric field, charges accumulate on its surface, forming a Taylor cone that emits a charged jet.[4] The jet elongates and solidifies into fibers

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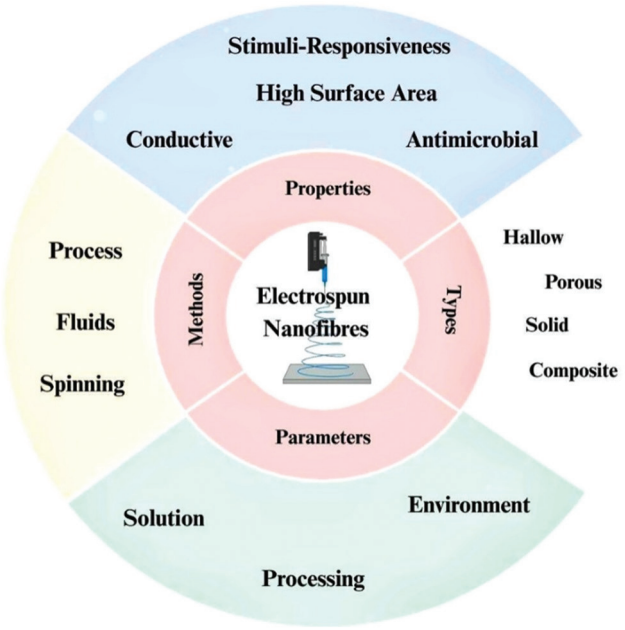
GRAPHICAL ABSTRACT



Legends: Visual summary highlighting the electrospinning process, material selection, fabrication strategies, and key biomedical uses such as wound healing and drug delivery.

as the solvent evaporates. The process can be vertically or horizontally mounted, and the quality of the nanofibers formed depends on various factors associated with the polymer solution, the method of processing, and the ambient environment.[5]

PARAMETERS INFLUENCING ELECTROSPINNING OF NANOFIBERS

The electrospinning process is controlled by various key parameters that have a direct impact on the morphology, diameter, and quality of the nanofibers. These parameters can be divided into three broad categories: Solution properties, process conditions, and environmental parameters [Figure 1].[6,7] These factors must be optimized to produce uniform, defect-free nanofibers designed for effective skin regeneration.

Solution parameters

The morphology and diameter of electrospun fibers are largely determined by the characteristics of the polymer solution. The critical factors are:

Concentration

Fong *et al*. performed one of the classic experimental studies that first linked low-concentration polymer solutions to bead formation and capillary breakup during electrospinning. They showed that at low polymer loadings, the jet is insufficiently viscoelastic to resist surface-tension-driven instabilities, producing droplets and beads-on-string morphologies; as concentration increases, the jet stabilizes, and continuous fibers appear. Fong's work is important because it explains bead formation as a balance between capillary forces and the viscoelastic nature of the solution, rather than just blaming low polymer concentration.[8]

Kong *et al*. (PMC) provided a practical rheological protocol linking macroscopic viscosity/viscoelastic measurements to electrospinnability for biopolymers. They demonstrated that measuring specific viscosity versus concentration and finding the change in scaling exponent allows identification of the entanglement transition (Ce). Their experiments on starch and pullulan show that the morphological transition, showing that the shape of fibers from droplets to beads to smooth fibers closely depends on how the solution concentration compares to Ce, and thus rheology can predict the minimum practical concentration for fiber formation.[9]

Liu *et al*. clearly showed how polymer concentration affects fiber formation in a poly(lactic-co-glycolic) acid (PLGA) hyaluronic acid system. They identified the critical entanglement concentration using viscosity measurements and analyzed it with standard error of the mean (SEM) images at different concentrations. Their results showed that smooth, uniform fibers formed only when the concentration was about 2–2.5 times higher than Ce. This study is notable since it presents precise numerical values and SEM data, making it an excellent illustration of how concentration optimization.[10]

Rajeev and Helms showed that in polycaprolactone (PCL) solutions, increasing the polymer entanglement ratio (c/Ce) changes fiber morphology from beaded structures below Ce to bead-on-string forms at 1–2×Ce and finally to smooth, mechanically stronger continuous fibers above 2×Ce, highlighting that entanglement controls not only fiber formation but also mechanical performance relevant for scaffold application.[11]

Xue *et al*. (Chem. Rev.) synthesize decades of single- and multisystem studies and frames the consensus (1) chain entanglement is the dominant factor controlling beading versus continuous fibers, (2) different polymers/solvents shift the numeric Ce widely, and (3) authors commonly report that bead-free electrospinning is achieved when solution concentration is roughly 2–3×Ce for many systems, while noting exceptions tied to solvent volatility, conductivity, molecular weight and applied field.[7]

Strong qualitative consensus has been found across the experimental (Fong, Liu, Rajeev) and review (Xue, Kong) literature: Low concentration results in beads, whereas sufficiently above Ce results in smooth fibers. There are significant variations in how studies quantify adequately

above Ce. Xue and Kong provide the consensus suggestion (2–3×Ce) and rheological methods to find Ce; Liu and other experimental teams provide system-specific numerical Ce values with SEM series, and Rajeev frames results through the dimensionless entanglement number (c/Ce) and correlates structure to dynamics.

Viscosity

An increased-viscosity solution produces fibers with higher diameters, and at low viscosity, bead formation occurs. Suitable viscosity is required to produce stable fibers [Figure 2].[12]

Processing conditions

Applied voltage

Recent systematic reviews and experimental studies show that increasing applied voltage most often reduces average fiber diameter by increasing electrostatic stretching of the jet, but the effect is neither strictly linear nor universal. Kalluri *et al*. summarized multiple systems and reported that higher voltages generally favor thinner fibers but can also increase jet instability and produce bimodal diameter distributions when the feeding rate or solution rheology is not adjusted simultaneously.[13] Abdulhussain *et al*. reviewed statistical analyses and found that applied voltage frequently had a stronger influence on diameter than flow rate, yet several polymers–solvent systems show little diameter change with voltage because the solution's viscoelasticity dominates jet behavior. The practical conclusion for optimization is to use voltage to fine-tune fiber diameter once solution entanglement and flow rate are within an acceptable window, avoid pushing voltage into regions that trigger secondary jets or satellite droplets, and always report the voltage–flow–distance operating map for reproducibility.[6]

Flow rate

Recent experimental series and optimization studies (Tariq *et al*., 2023; Kalluri *et al*., 2021) show that increasing flow rate tends to increase mean fiber diameter and raises the likelihood of incomplete solvent evaporation and bead formation. Tariq's statistical optimization work found clear trends: low flow rates produced thinner, more uniform fibers with fewer beads, whereas high flow rates produced thicker

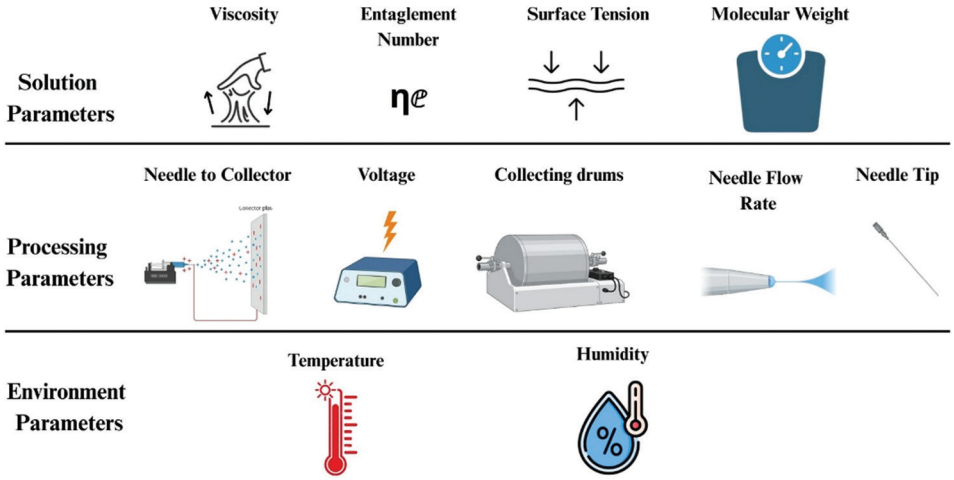


Figure 1: Three major types of parameters influencing the electrospinning of nanofibers. Legends: Illustrates the basic components and working principle of the electrospinning process, including Taylor cone formation and nanofiber deposition

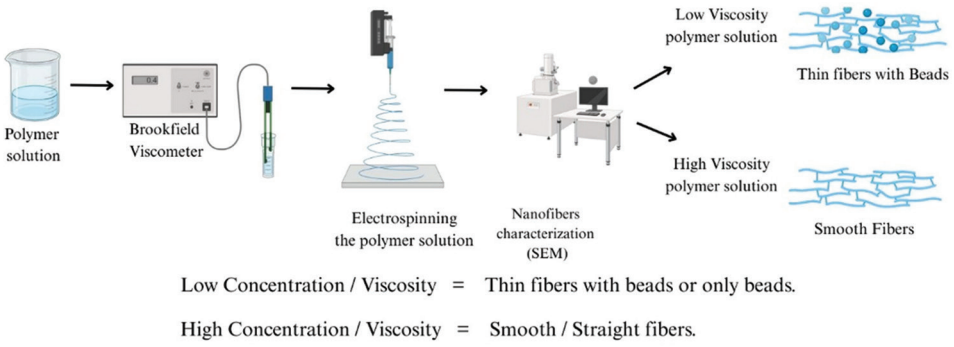


Figure 2: Impact of polymer viscosity on nanofiber morphology in electrospinning. Legends: Shows how solution, process, and environmental parameters influence fiber diameter, bead formation, and overall nanofiber quality

fibers and more beads unless counterbalanced by increases in voltage or tip-to-collector distance. Some exceptions occur when solvent volatility or ambient drying is fast (then higher flow can be tolerated), but the reviewer takeaway is robust: Set flow rate as the primary control for mass throughput and then tune voltage/distance to preserve fiber uniformity. Report volumetric flow (μL/min) and the Reynolds-like conditions for comparability.[14]

Collector type/alignment

Recent comparative reviews on alignment methods (Robinson *et al*., 2021) and subsequent experimental work (Switz *et al*., 2023; Ahmadi Bonakdar and Rodrigue, 2024) make two points clear: (1) Rotating drums and split-collector/electrodes reliably produce aligned fibers, and rotation speed controls alignment degree and can modestly affect fiber diameter through mechanical drawing; (2) Flat/static collectors produce random mats and are preferred when isotropic properties or high porosity are required. Robinson's review[15] contrasts limitations (e.g., substrate size, edge effects, and scaling) and recommends that method selection be driven by the application (tissue engineering vs. filtration). Practically, for aligned scaffolds, use a high-speed drum or dual-electrode setup and report drum speed (rpm), linear surface speed, and substrate geometry; for random mats, use a static flat collector but control humidity/temperature to avoid bead formation.[16]

Needle tip-to-collector distance (TCD)

Recent biomedical electrospinning reviews and experimental reports (Chinnappan *et al*., 2022) highlight TCD as a key parameter controlling solvent evaporation time and fiber solidification. Short distances can cause wet fibers, fused webs, or larger diameter (insufficient flight drying); long distances can produce bead-on-string morphologies if the jet thins excessively or ambient conditions promote instability. Chinnappan *et al*. summarized preferred ranges (roughly 10–20 cm depending on setup) and emphasized coupling with voltage (V); an operating map of V versus TCD is often necessary to identify a stable cone-jet regime.[13,17]

Needle (gauge) size

Recent literature (2021–2024) shows that smaller needles can reduce initial jet diameter and sometimes yield slightly thinner fibers, but needle size is a secondary effect compared with solution rheology, voltage, and flow rate. Smaller bore needles increase the chance of clogging, especially for viscous or particle-laden solutions, and can cause pressure build-up that disturbs steady flow. Reviews and practical setup papers therefore recommend choosing a needle gauge that balances desired throughput and clog risk (e.g., 21–27G commonly used), and focusing optimization on concentration/viscosity, then fine-tune needle size if necessary for subtle diameter control.[18]

Environmental variables

Temperature

Recent experimental and review studies consistently show that increasing temperature decreases solution viscosity and accelerates solvent evaporation, producing finer fiber diameters up to an optimal threshold, beyond which excessive heating destabilizes the Taylor cone or causes jet discontinuities. Heat-assisted electrospinning investigations report systematic diameter reduction and improved uniformity when modest heating is applied, but note a trade-off: Very high temperatures increase solvent volatility and can produce secondary jet instabilities or discontinuous fibers. Reviews and experimental compilations attribute these effects to two coupled mechanisms: (1) lower solution viscosity at elevated temperature facilitates jet stretching, and (2) increased solvent evaporation shortens the liquid jet lifetime, allowing earlier solidification, together driving diameter decrease until drying/instability limits are reached. For practical optimization, authors recommend measuring solution rheology across the intended temperature range and mapping diameter and jet stability (V–T and T–flow maps); typical useful temperature windows are system-dependent, but many solvent/polymer systems show beneficial effects in the mild heating range (25–50°C), with degradation of uniformity above system-specific thresholds.[17,19,20]

Humidity

Relative humidity (RH) critically affects fiber morphology, surface porosity, and continuity. Lauricella *et al*. and He *et al*. demonstrated that high RH increases the likelihood of water condensation on fiber surfaces, which induces micropore or crater formation when volatile solvents such as dimethylformamide (DMF) or acetone evaporate rapidly.[21] Zhang *et al*. experimentally varied RH (20–80%) during PVP and cellulose acetate electrospinning and found that pore density and size increased proportionally with humidity, attributed to phase separation between solvent vapor and ambient moisture.[22] In contrast, very low RH (<25%) caused premature solvent evaporation and needle clogging, as observed by Khalil *et al*. in polyacrylonitrile nanofibers, leading to uneven jet ejection and fiber breakage. Thus, humidity primarily governs the drying kinetics and surface texture of nanofibers: High humidity forms porous or cratered morphology; low humidity tends to brittle, discontinuous fibers.

PROPERTIES OF ELECTROSPUN NANOFIBERS

High surface area-to-volume ratio

Nanofibers have a high surface area that enhances cell adhesion, drug loading, and the exudate of wound interaction.[23] This enhances bioactive molecule delivery and adsorption of bacteria, which are critical in infected wounds.

Regulated porosity

The nanofiber mat possesses a nanostructure that is porous and organizes oxygen permeability, exudate absorption, and nutrient diffusion in a manner that replicates the native ECM.[24] Porosity is controlled by modifying conditions in electrospinning (e.g., humidity, solvent).[25]

Mechanical flexibility and strength

Nanofibers achieve a compromise between tensile strength (to resist mechanical stress) and flexibility (to be pliable to wounds). Mixing synthetic (PCL, polylactic acid [PLA]) and natural (collagen, chitosan) polymers improves these properties.[26]

Controlled degradation

Degradation rates can be regulated by the choice of polymer (e.g., fast-degrading gelatin vs. slow-degrading PCL) to match phases of wound healing. This avoids premature scaffold degradation.

Cellular interactions and bioactivity

Surface modification (i.e., heparin, RGD peptides) is employed to promote cell growth and ECM deposition.[27,28] Angiogenesis, for example, is induced by bioactive glass nanofibers.[29]

Antimicrobial properties

Silver nanoparticles (AgNPs), chitosan, or antibiotics inhibit biofilm formation. Polyvinyl alcohol (PVA)-ciprofloxacin fibers electrospun decrease colonization by 99% in *Pseudomonas aeruginosa*.[30]

Stimuli-responsiveness

Smart nanofibers are pH-sensitive, temperature-sensitive, or enzyme-sensitive for on-demand release of drugs. pH-sensitive fibers release antibiotics only in infected (acidic) wounds.[31]

Electrical conductivity

Conductive polymers (e.g., polypyrrole) or carbon nanofibers produce electroactive wound dressings that enhance healing through electrical stimulation.[32]

Dynamic mechanical properties

Higher-order nanofibers also demonstrate strain-stiffening behavior similar to native tissue, with mechanically regulated fibroblast activation. Shape-memory polyurethane nanofibers are able to contract upon exposure to body temperature and apply the optimal tension to wound edges.[33,34] Such "smart" mechanical properties minimize scarring in full-thickness wounds.

Multidrug temporal release profiles

Next-generation nanofibers achieve complex release kinetics through core-shell designs for sequential antibiotic/growth factor delivery,[35] Surface-eroding polymers for time-programmed release, and enzyme-responsive bonds for infection-triggered drug release.[36]

TAILORING NANOFIBERS THROUGH POLYMER SELECTION

The choice of polymer significantly influences fiber morphology, mechanical properties, and functionality. Polymers used in electrospinning can be broadly classified into synthetic, natural, and composite-based systems.

Synthetic polymers

The most commonly used are those in electrospinning due to their excellent spinnability, mechanical strength, and tunable degradation profiles. Examples include PCL, PLA, PVA, and polyethylene oxide (PEO).[37] These polymers typically produce uniform, bead-free fibers with good structural integrity. Their high molecular weight and consistent viscosity allow for stable jet formation, essential for smooth electrospinning.[12] However, synthetic polymers are often bioinert and require surface modification or blending to improve biocompatibility or bioactivity. A detailed comparison of different synthetic polymers used in nanofiber production is provided in Table 1.

Natural polymers

Such as chitosan, gelatin, collagen, alginate, and cellulose derivatives offer intrinsic biological properties such as biodegradability, cell affinity, and antimicrobial activity.[38] These are especially attractive for wound healing, tissue regeneration, and drug delivery.[39] However, they pose challenges in electrospinning due to poor solubility, rigid molecular structure, or polyelectrolyte nature, which can lead to bead formation, jet instability, or even failure to form fibers. As a result, natural polymers often require blending with synthetic carriers like PEO or PVA to enhance viscosity and fiber-forming capability.[40] Table 2 provides a comparative overview of natural polymers in nanofiber fabrication, including their solvents, key applications, advantages, and challenges.

Table 1: Comparison of synthetic polymers in electrospinning

Polymer	Solvent	Key applications	Advantages	Limitations
PCL	DCM, Chloroform	Tissue engineering, wound healing (↑ 3D scaffolds)	Biodegradable, flexible	Hydrophobic, slow degradation
PLA	HFIP, Chloroform	Drug delivery, sutures (↑ aligned fibers)	High strength, FDA-approved	Brittle, slow degradation
PAN	DMF	Carbon nanofiber precursors (↑ supercapacitors)	High thermal stability	Toxic solvent (DMF)
PVDF	DMF, Acetone	Piezoelectric sensors (↑ wearables)	High β-phase content	Requires poling
PVA	Water	Wound dressings (↑ Ag NP loading)	Water-soluble, biocompatible	Poor mechanical strength

PCL: Polycaprolactone, PLA: Polylactic acid, PAN: polyacrylonitrile, PVDF: Polyvinylidene fluoride, PVA: Polyvinyl alcohol, DCM: Dichloromethane, DMF: Dimethylformamide, HFIP: Hexafluoro isopropanol, Ag NP: Silver nanoparticles, ↑: Enhanced or increased performance, FDA: Food and Drug Administration

Table 2: Natural polymers in electrospinning

Polymer	Solvent	Key applications	Advantages	Challenges
Chitosan	Acetic acid	Antimicrobial dressings (↑ ZnO nanocomposites)	Antibacterial, biodegradable	Poor electrospinnability
Collagen	HFIP, Acetic acid	Skin/cartilage regeneration (↑ crosslinking)	ECM-mimicking	Batch variability
Silk fibroin	Formic acid, Water	Neural scaffolds (↑ aligned fibers)	High strength, biocompatible	Slow degradation
Alginate	Water (with PEO)	Wound healing (↑ Ca^{2+} crosslinking)	Hemostatic properties	Low mechanical strength

HFIP: Hexafluoroisopropanol, PEO: Polyethylene oxide, ECM: Extracellular matrix, ZnO: Zinc oxide, ↑: Enhanced or increased performance, Ca^{2+}: Calcium ions

Composite or hybrid systems

They are formed by co-spinning synthetic and natural polymers. These systems allow customization of mechanical properties, biodegradation rates, and drug release behavior, depending on the proportion and interaction of each component.[41] For example, a PCL/gelatin composite may yield fibers with enhanced cell attachment from gelatin and long-term mechanical support from PCL. Core–shell and coaxial electrospinning techniques are also used in composites to load multiple drugs or protect sensitive bioactives.[42,43] These systems offer greater functional flexibility, such as dual-drug delivery or stimuli-responsive behavior, often making them ideal for advanced biomedical and pharmaceutical applications [Table 3].

Table 3: Impact of polymer blends and additives

Polymer blend	Additive	Effect on fiber properties	Application
PCL/ Gelatin	–	↑ Cell adhesion, mechanical strength	Skin regeneration
PLA/ PEG	CNTs	↑ Conductivity, flexibility	Wearable sensors
PVDF/ ZnO	ZnO NPs	↑ Piezoelectric and antibacterial activity	Air filters

PCL: Polycaprolactone, PLA: Polylactic acid, PVDF: Polyvinylidene fluoride, PEG: Polyethylene glycol, CNTs: Carbon nanotubes, ZnO NPs: Zinc oxide nanoparticles, ↑: Enhanced or increased performance

TYPES OF ELECTROSPUN NANOFIBERS FOR WOUND HEALING APPLICATIONS

The types of electrospun nanofibers for wound healing applications were classified into various types [Figure 3].

Porous nanofibers

Porous nanofibers have internal or surface pores, which increase surface area, breathability, and exudate uptake, all required for wet wound healing.[44,45] The pores are created by phase separation (e.g., water vapor-induced phase separation) or solvent systems (e.g., tetrahydrofuran/DMF mixtures). Polystyrene porous fibers, for instance, have tunable porosity for controlled drug release. Recent research emphasizes their application in oxygen-permeable diabetic wound dressings.[46,47]

Solid nanofibers

Tough nanofibers, with a dense, non-porous structure, provide mechanical strength and controlled drug release.[48] Polymers such as PCL and PLA are favored since they

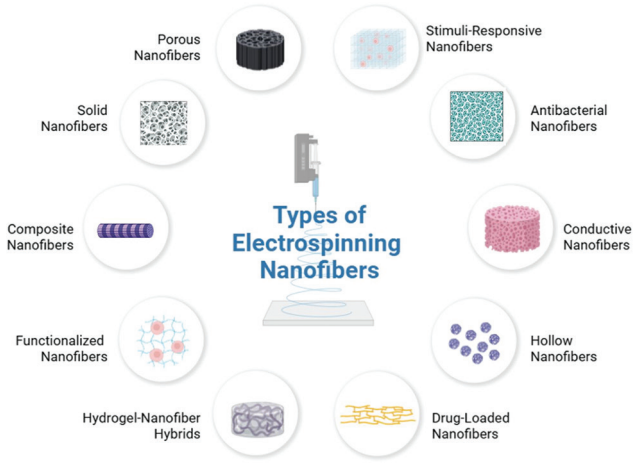


Figure 3: Types of electrospinning nanofibers

degrade naturally and are biocompatible. These fibers are best suited for the treatment of chronic wounds, where it is essential to maintain the structure intact.

Composite nanofibers

Composite nanofibers couple synthetic and natural polymers to exploit mechanical and bioactive functionalities. PCL-gelatin composite, for example, promotes fibroblast growth.[49] AgNPs hybrids incorporate antimicrobial functionalities.[50]

Functionalized nanofibers

Surface-modified nanofibers incorporate bioactive molecules (e.g., growth factors, peptides) by covalent attachment or adsorption. Heparin-functionalized PCL fibers promote burn wound angiogenesis.[51] Antibody-conjugated fibers provide targeted therapy.[52]

Hollow nanofibers

Hollow nanofibers can be synthesized by coaxial electrospinning or core elimination.[53] The fibers can be drug-loaded or growth factor-loaded. PLGA vascular endothelial growth factor (VEGF)-loaded hollow fibers promote the growth of blood vessels in the case of deep wounds.[54] They can be applied for slow release because they possess high drug-loading capability.[55]

Core-shell nanofibers

Core-shell nanofibers, fabricated through coaxial electrospinning, facilitate dual-drug delivery and delivery of sensitive bioactive molecules. Therapeutic drugs (e.g., antibiotics or growth factors) are typically encapsulated in the core, and controlled release kinetics are provided by the shell. It has been recently demonstrated that VEGF-loaded core-shell fibers are efficient in promoting diabetic wound angiogenesis.[56] Premature drug degradation is prevented by a compartmentalized structure without sacrificing fiber integrity.

Aligned nanofibers

Aligned nanofibers also provide topographical signals to direct migration and collagen deposition, required in orderly tissue repair.[57] Rotating drum collectors or electrostatic field manipulation lead to aligned architectures.[58] Aligned PCL/collagen nanofibers exhibited 40% improved re-epithelialization with respect to random fibers in burns. The aligned architecture is especially advantageous in the nerve regeneration of the deep wound.[59]

Stimuli-responsive nanofibers

These "smart" fibers react to alterations in the wound microenvironment (pH, temperature, enzymes). pH-sensitive metronidazole-loaded fibers release drugs selectively in infected (acidic) wounds.[60] Temperature-responsive poly(n-isopropylacrylamide) (PNIPAM)-containing fibers shrink at body temperature, applying gentle pressure for healing.[61]

Antibacterial nanofibers

The incorporation of antimicrobial agents such as AgNPs, chitosan, or antibiotics creates infection-free dressings. AgNP-decorated zein nanofibers show 99.9% inhibition of MRSA and cytocompatibility.[62-64] New approaches involve photosensitizer-encapsulated fibers for photodynamic antimicrobial therapy.[65]

Conductive nanofibers

Conductive polymers (polypyrrole, PEDOT: PSS) or carbon nanomaterials form electroactive dressings that facilitate wound healing by electrical stimulation.[66] PEDOT: PSS/gelatin fibers improved diabetic wound healing by 35% by electrical cueing of fibroblast migration.[67] These types of fibers also facilitate real-time monitoring of wounds when coupled with sensors.

Biomimetic nanofibers

These fibers mirror native ECM composition, often collagen, elastin, or decellularized matrix elements.[68] New studies with amniotic membrane-derived nanofibers showed enhanced epithelialization without scarring.[69] Certain designs replicate the hierarchical structure of native skin layers.

Drug-loaded nanofibers

In addition to conventional drug encapsulation, sophisticated loading techniques have been developed. Among these,

Janus fibers fabricated through side-by-side electrospinning permit the spatial separation of therapeutic agents, enabling independent and tunable release profiles for dual-drug delivery systems, such as antibiotics and growth factors.[71,72] nanoparticle-embedded fibers: PLGA nanoparticles in PVA fibers for sustained release, layer-by-layer fibers: Alternating drug/polymer layers for sequential release.

Hydrogel-nanofiber hybrids

Hybridization of electrospun fibers with hydrogels provides wet, porous, yet mechanically strong dressings. New structures are fiber-reinforced hydrogels (Silk fibroin fibers in alginate hydrogel) and fiber-hydrogel bilayer structures (PCL nanofiber mat + chitosan hydrogel). These hybrids have the optimal moisture balance without allowing fiber mat collapse.[72,73]

This broader categorization encompasses new nanofiber morphologies with dedicated wound healing benefits. Each class responds to particular clinical requirements, ranging from protection against infection (antibacterial fibers) to chronic wound cure (conductive/biomimetic fibers). New advances focus on multifunctionality through mixing materials and responsive smartness.

METHODS OF ELECTROSPINNING FOR NANOFIBER PRODUCTION

Electrospinning has become a multiaspect fabrication technique with a variety of processing techniques, each with its own merits in generating nanofibers with specific properties. The following section provides a comprehensive overview of the different electrospinning processes, classified according to their working principles, fluid systems, and spinning mechanisms [Figure 4 and Table 8].

Types of electrospinning processes

Coaxial electrospinning

Coaxial electrospinning employs a twin-capillary spinneret to produce core-shell nanofibers for drug encapsulation, growth factor encapsulation, or sensitive bioactive molecules. The core-shell structure offers protection for the sensitive

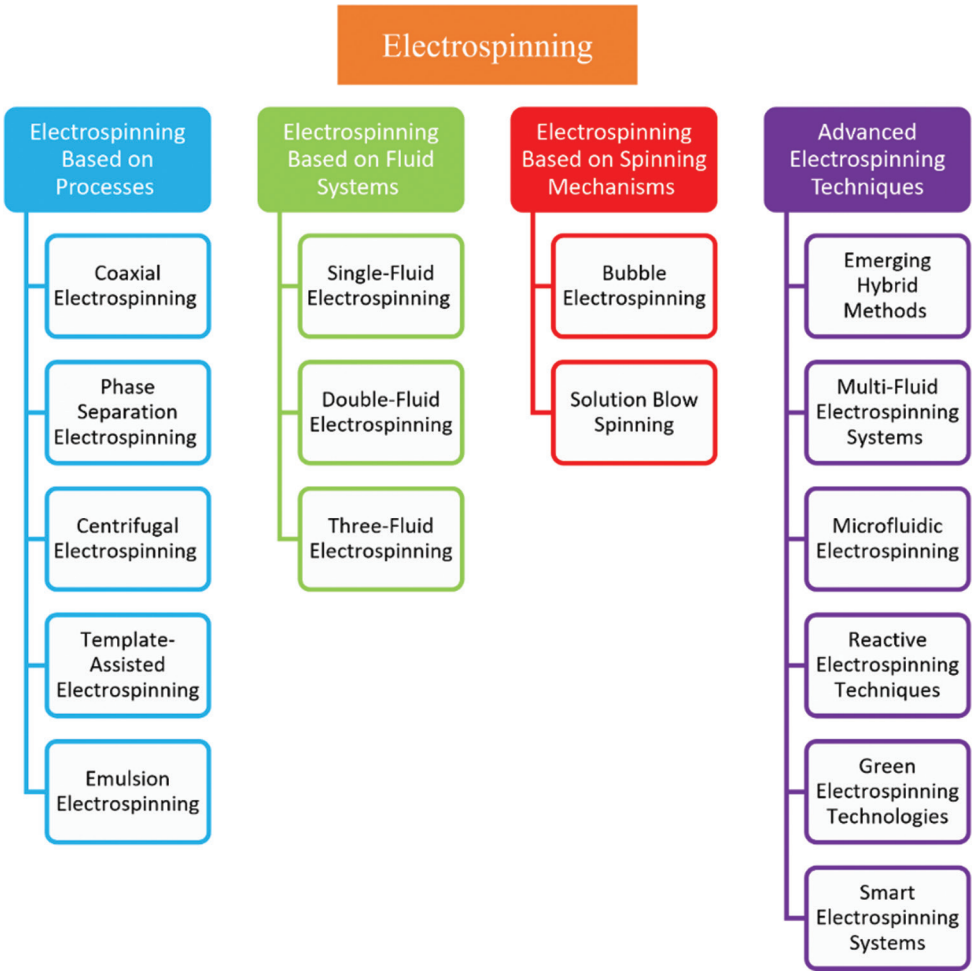


Figure 4: Methods of electrospinning for nanofiber production

Table 4: Comparison between bubble electrospinning and solution blow spinning

Feature	Bubble electrospinning	Solution blow spinning
Mechanism	Uses gas bubbles in a polymer solution	Uses high-pressure gas to eject polymer solution
Production speed	Moderate (faster than needle electrospinning)	Very high (up to 10×electrospinning)
Fiber uniformity	Less uniform due to bubble instability	More controllable, but slightly thicker fibers
Applications	Filtration, tissue engineering	Industrial-scale nanofibers, filtration, flexible electronics
Key challenge	Controlling bubble size and fiber consistency	Achieving sub-100 nm fibers

nm: Nanometers; ↑: Enhanced or increased performance

cargoes with a controlled release mechanism.[74] Triaxial electrospinning has also been emerging as a method to generate multilayered fibers for sequential drug delivery.[75,76]

Phase separation electrospinning

This method uses solvent-solvent interactions to generate porous or hollow nanofibers. By varying polymer-solvent combinations (e.g., PCL in THF/water), high surface area fibers with variable porosity are generated, which are applicable to wound exudate.[77,78]

Centrifugal electrospinning

Combining centrifugal force with electric fields, this method enhances production rates (~50 g/h) while maintaining fiber alignment. It is particularly useful for scaling up aligned nanofiber production for nerve regeneration.[79]

Template-assisted electrospinning

A sacrificial template (e.g., microfiber meshes) is used to direct fiber deposition, and intricate 3D structures such as helical or branched nanofibers are facilitated. The technique is applied to vascular graft scaffolds.[80]

Emulsion electrospinning

Oil-in-water or water-in-oil emulsions are electrospun to create multicompartment fibers for the dual delivery of drugs.[81] Hydrophobic drugs in the oil phase and hydrophilic drugs in the aqueous phase, for instance, may be co-delivered.[82]

Electrospinning based on fluid systems

Single-fluid electrospinning

It involves a homogeneous polymer solution or melt at high voltage to produce nanofibers by jet stretching and solvent evaporation. This basic process can allow for accurate control of fiber diameters (usually 50–1000 nm) via solution viscosity, conductivity, and processing conditions.[83] Recent developments include green electrospinning with water solvents and melt electrospinning of thermosensitive solvents without solvents.[84]

Double-fluid electrospinning

It involves coaxial (concentric) and side-by-side arrangements, enabling intricate fiber morphologies. The coaxial process generates core-shell fibers that provide encapsulation efficiencies greater than 90% for fragile biomolecules, while side-by-side spinning generates Janus fibers with bimodal surface properties.[77,85] Difficulties are ensuring stable compound Taylor cones and avoiding phase separation during spinning.

Table 5: System configurations

Type	Layers	Feature size	Applications
Triaxial	3	50 nm–2 μm	Chronotherapeutic delivery
Quad axial	4	100 nm–5 μm	Multistimuli responsive systems

nm: Nanometers; μm: Micrometers

Table 6: Sustainability metrics comparison

Parameter	Conventional (%)	Green improvement (%)
Energy use	100	Reduced by 40
Solvent waste	100	Reduced by 95
Carbon footprint	100	Reduced by 60

Table 7: Summary of advanced techniques

Technique	Key advantage	Example application
Hybrid Methods	Multiprocess integration	3D-printed nanofiber scaffolds
Multifluid	Layered drug delivery	Sequential growth factor release
Microfluidic	Precise compositional control	Janus vascular grafts
Reactive	*In situ* crosslinking	UV-cured waterproof fibers
Green	Eco-friendly production	Solvent-free PCL membranes
Smart	Stimuli-responsive functionality	pH-triggered drug release

PCL: Polycaprolactone, UV: Ultraviolet, pH: Potential of Hydrogen (acidity/basicity)

Three-fluid electrospinning

Is the cutting-edge, with triaxial spinnerets spinning fibers with: An innermost drug-loaded core, A middle-level

Table 8: Summary of various biofabrication methods, their resulting outcome products, incorporated polymers and drugs, and the intended biomedical applications

Method	Outcome product	Polymer (s) used	Drug (s) Incorporated	Application	References
Co-axial electrospinning	Core-shell nanofibers promoting diabetic wound healing	PVA, Cellulose acetate	Rhubarb anthraquinones, honey, borneol	Multifunctional wound dressings addressing diabetic ulcers	[97]
Phase separation electrospinning	Nanofibrous scaffolds with tunable mechanical properties	PLA, PEG	Not specified	Tissue engineering matrices for wound healing	[2]
Template-assisted electrospinning	Micropatterned fibrous scaffold with enhanced cell proliferation and wound healing	PCL	None specified	Wound healing scaffold promoting fibroblast alignment and accelerated healing	[98]
Emulsion electrospinning	Nanofibers with controlled drug release	Various polymers	Antibiotics, antiseptics, anti-inflammatory drugs, biomolecules	Wound healing applications	[99]
Single-fluid electrospinning	Nanofibrous membranes with embedded bioactive agents	PCL, chitosan	Antibiotics, growth factors	Wound healing applications	[98]
Double-fluid electrospinning	Core-shell nanofibers with controlled drug release	PCL (shell), chitosan (core)	Antibiotics, growth factors	Wound healing applications	[98]
Three-fluid electrospinning	Triaxial nanofibers with multilayered drug release	EC, PVP	Ibuprofen	Controlled drug delivery for wound healing	[75]
Bubble electrospinning	Nanofibrous membranes with potential for wound dressing	Various polymers (e.g., PVA, PCL)	Not specified	Potential applications in wound healing	[100]
Solution blow electrospinning	Nanofibrous scaffolds promoting fibroblast growth	Chitosan	Not specified	Dermal wound healing	[101]
Emerging hybrid electrospinning	Cell-encapsulated nanofibers promoting tissue regeneration	Polymers such as PCL or PVA	Living cells (e.g., fibroblasts)	Scaffold for tissue engineering and wound healing	[102]
Multifluid electrospinning systems	Janus fibers with dual functionality	PVA, PCL	Ag NP, dexamethasone	Antibacterial and anti-inflammatory wound dressing	[103]
Microfluidic electrospinning	Nanofiber membranes with antibacterial properties	PVA, Chitosan	Ag NP	Antibacterial wound dressings	[104]
Reactive electrospinning techniques	pH-responsive nanofibers with infection detection capability	PMMA-co-MAA, PAA	Bromothymol blue dye	Wound dressings with visual infection monitoring	[105]
Green electrospinning technologies	Eco-friendly antibacterial nanofibrous film	PVA, Green-synthesized Ag NP	Ag NP	Antibacterial wound dressing	[106]
Smart electrospinning	Intelligent nanofibrous membranes with sensors and drug delivery	Various biodegradable polymers	Antimicrobial agents, growth factors	Real-time monitoring and on-demand treatment of wounds	[67]

PVA: Polyvinyl alcohol, PLA: Polylactic acid, PEG: Polyethylene glycol, PCL: Polycaprolactone, EC: Ethyl cellulose, PVP: Polyvinylpyrrolidone, PMMA-co-MAA: Poly (methyl methacrylate-co-methacrylic acid), PAA: Poly (acrylic acid). Numbers in parentheses correspond to reference citations

diffusion-controlling layer, and a protective outer layer. This system enables temporal control of multiple drug releases (e.g., initial release of an antibiotic with subsequent delivery of a growth factor). Recent developments include microfluidic-assisted three-fluid systems that enable <5% variation in diameter and electro-responsive middle layers that enable control of release profiles.[86]

Electrospinning based on spinning mechanisms

Bubble electrospinning

Bubble electrospinning is a novel technique in which gas bubbles are incorporated into a polymer solution. The bubbles burst when an electric field is applied, and numerous nanofibers are generated simultaneously. This technique significantly enhances the manufacturing efficiency over the conventional needle-based technique of electrospinning. The bursting bubbles give a fast fiber-generating process, which is well-suited for mass production of nanofibers for use in products such as air filters and wound dressings. It is still challenging to control how homogeneous the fibers are, however, because bubble formation and bursting can be a random process.[87]

Solution blow spinning (SBS)

SBS is a high-pressure alternative to electrospinning, with a polymer solution being pushed out of a nozzle by high-pressure gas rather than an electric field. SBS facilitates fast fiber production (up to 10 times as fast as electrospinning) with nanoscale diameters (100–1000 nm). SBS is well-suited for bulk production of nanofibers for filtration, biomedical scaffolds, and flexible electronics. Its disadvantage is that it is more difficult to produce ultra-fine fibers (<100 nm) than with electrospinning.[88] The comparison between bubble electrospinning and SBS is discussed in Table 4.

Advanced electrospinning techniques

Emerging hybrid methods

Electrospinning + 3D printing, a hybrid technique using 3D-printed templates or conductive collectors to create spatially organized nanofibrous structures, enabling pore sizes >100 μm while preserving the nanoscale fiber texture.[89]

Multifluid electrospinning systems

Multifluid electrospinning (greater than coaxial) utilizes triaxial or quadaxial spinnerets for the production of compartmentalized drug-release layered nanofibers or multimaterial cores.[90] Triaxial fibers, for example, are used to deliver VEGF (inner core), platelet-derived growth factor (middle layer), and an outer protective shell for sequential wound healing. Quad-axial systems further enable thermo-responsive hydrogels as intermediate layers for smart drug delivery, as described in Table 5.[91]

Microfluidic electrospinning

Microfluidic electrospinning combines microfluidic chips and electrospinning to obtain regulated fiber morphology and composition. Microfluidic electrospinning can produce Janus fibers with spatially distinct proteins (e.g., elastin and collagen for vascular grafts) and gradient fibers for mechanical stiffness transition gradually. Microchannel laminar flow avoids premature mixing of polymers.

Reactive electrospinning techniques

Reactive electrospinning utilizes *in situ* crosslinking or polymerization in the course of fiber fabrication. For instance, ultraviolet-curable acrylates are electrospun and immediately cured to form solvent-resistant fibers, and enzymatic crosslinking (e.g., transglutaminase in gelatin fibers) increases scaffold stability. This process is especially suitable for insoluble polymers and *in situ* hydrogel formation.

Green electrospinning technologies

Green electrospinning uses harmless solvents such as water and ionic liquids, and biodegradable materials such as PLA and chitosan. Water-based electrospinning of pullulan/PVA blends minimizes toxicity,[92] and melt electrospinning of PCL without solvent stops VOC emissions.[93] These ways of working are in line with the goals of a circular economy. The sustainability metrics comparison is described in Table 6.

Smart electrospinning systems

Smart electrospinning yields fibers that change if they sense pH, temperature, or light. They are, for instance: pH-sensitive fibers with Eudragit® for treatment of burn wounds,[94] Thermo-responsive PNIPAM fibers for releasing items,[95] conductive MXene-loaded fibers for flexible strain sensors.[96]

The summary of advanced techniques is described in Table 7.

CONCLUSION

Electrospun nanofibers represent a rapidly advancing class of biomaterials uniquely capable of combining nanoscale architecture, tunable porosity, mechanical adaptability, and controlled therapeutic delivery. Insights into the interplay between polymer chemistry, solution rheology, and process parameters have enabled precise morphological control and enhanced functional performance across diverse biomedical applications. Innovations such as coaxial, triaxial, emulsion, and microfluidic electrospinning have further expanded the design space, enabling multidrug release, encapsulation of fragile biomacromolecules, and the creation of complex hierarchical structures. Emerging smart fibers responsive to pH, temperature, and enzymes demonstrate significant promise in addressing the dynamic nature of chronic and infected wounds. Moreover, biomimetic and conductive nanofiber systems increasingly support angiogenesis,

cellular alignment, and regenerative signaling. While challenges related to large-scale production, solvent safety, and standardization persist, ongoing developments in green electrospinning, hybrid fabrication, and integrated sensing platforms are paving the way for clinically translatable, multifunctional wound care solutions. Overall, electrospinning continues to evolve as a powerful fabrication technology capable of producing next-generation therapeutic scaffolds, with substantial potential to transform wound management and broader biomedical engineering applications.

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