A Review: Electrospinning of Biopolymer Nanofibers and their Applications

Article *in* Polymer Reviews · May 2008

DOI: 10.1080/15583720802022182

CITATIONS
397

READS
3,296

2 authors:

Jessica D Schiffman
University of Massachusetts Amherst
79 PUBLICATIONS **3,349** CITATIONS

SEE PROFILE

Caroline Schauer
Drexel University
85 PUBLICATIONS **3,562** CITATIONS

SEE PROFILE

Polymer Reviews, 48:317–352, 2008

ISSN 1558-3724 print/1558-3716 online
DOI: 10.1080/15583720802022182

A Review: Electrospinning of Biopolymer Nanofibers and their Applications

JESSICA D. SCHIFFMAN AND CAROLINE L. SCHAUER

Department of Materials Science and Engineering, Drexel University, Philadelphia, PA

Electrospinning is a fabrication technique, which can be used to create nanofibrous non-wovens from a variety of starting materials. The structure, chemical and mechanical stability, functionality, and other properties of the mats can be modified to match end applications. In this review, an introduction to biopolymers and the electrospinning process, as well as an overview of applications of nanofibrous biopolymer mats created by the electrospinning process will be discussed. Biopolymers will include polysaccharides (cellulose, chitin, chitosan, dextrose), proteins (collagen, gelatin, silk, etc.), DNA, as well as some biopolymer derivatives and composites.

Keywords biopolymers, electrospinning, nano-effects, nanofibers, non-wovens, polysaccharides

1 Introduction

1.1 Biopolymers

Innovative technologies focused around bio-based materials are currently of high urgency as they can decrease dependencies on fossil fuel.[1] Biopolymers are derived from naturally occurring matter such as: crustacean shells, mushrooms, or wood. While some applications look towards the use of biopolymers for their sustainability, eco-efficiency, industrial ecology, and renewable nature, the rationale for using biopolymers in this review is predominantly based on their inherent properties. Biopolymers are renewable resources,[2] but also intrinsically exhibit antibacterial activity, biodegradability, and biocompatibility.[3] Therefore, they are ideal for use in a wide variety of industries such as ophthalmology, medicine, agriculture, textiles, paper coatings, and automotive.[4–9] Non-woven electrospun fibrous mats composed of biopolymers could offer specific applications including air filtration, protective clothing, substitutes for agricultural pesticides, and nanocomposites.[10] More discussion about the applications of nanofibrous mats is found in Section 3.

It is important to note that working with biopolymers can be challenging. For example, chitin can be extracted from, crustacean shells,[4,11] insect cuticles,[12] or fungal biomass.[13–15] Based on the source, it will vary in molecular weight (MW), degree of deacetylation (DD), purity, distribution of charged groups[16,17] and crystallinity.[18,19] This

Received 5 December 2007; Accepted 16 January 2008.
Address correspondence to Caroline L. Schauer, Department of Materials Science and Engineering, Drexel University, Philadelphia, PA 19104. E-mail: cschauer@coe.drexel.edu

variation holds true for all biopolymers. As a result of material inconsistency, each bulk material requires unique processing conditions, which complicates controlled manufacturing.[20] Despite the aforementioned challenges, the intrinsic benefits cannot be overlooked; it is for this reason that macrofibers containing biopolymers such as chitosan,[21–27] alginate,[28–30] cellulose/chitin,[31] alginate/carboxymethyl (CM) chitosan,[32] collagen/poly(lactide-co-glycolide) (PLGA),[33] and alginate/soy[34] have previously been fabricated utilizing traditional fiber processing techniques. Research on macro-scale biopolymer and biopolymer composite fibers is ongoing. Constructing nano-scale biopolymer fibers are of additional interest, as will be discussed in Section 2.3 and throughout this review.

1.2 Nanofibers

While there are a few different methods to produce nanofibers including: phase separation,[35] island in the sea,[36] drawing,[37] template synthesis,[38–40] and self assembly,[41–45] an additional unique synthetic method, electrospinning, has received much attention lately. As can be seen in Fig. 1(a), there has been a significant upsurge in the annual number of scientific publications on electrospinning since 1994, the year that the term ''electrospinning'' was coined. Prior to this, it was known as "electro static spinning,"[46] and was patented 60 years earlier by Formhals.[47] Figure 1(b) displays the recent rise in the number of articles regarding biopolymer electrospun papers since 1997, when DNA[48] was first electrospun. The authors found that conducting a SciFinders scholar search including terms such as "electrospinning" and "biopolymer" was too limiting since a search of this nature misses many references. Therefore, Fig. 1(b) includes the articles reviewed in this work as the authors significantly tried to include all available articles concerning biopolymer-containing electrospun fibers. Since the statistics in Figs. 1(a) and 1(b) have different origins, the histograms are intended to demonstrate the trends in electrospinning research, rather than exact numbers.

One reason for the upsurge in nanofibers fabrication research in the 1990s, was due to new found interest in producing polymeric nanofibers under laboratory conditions.[49] Moreover, improved analytical tools now allowed for the produced fibers to be better

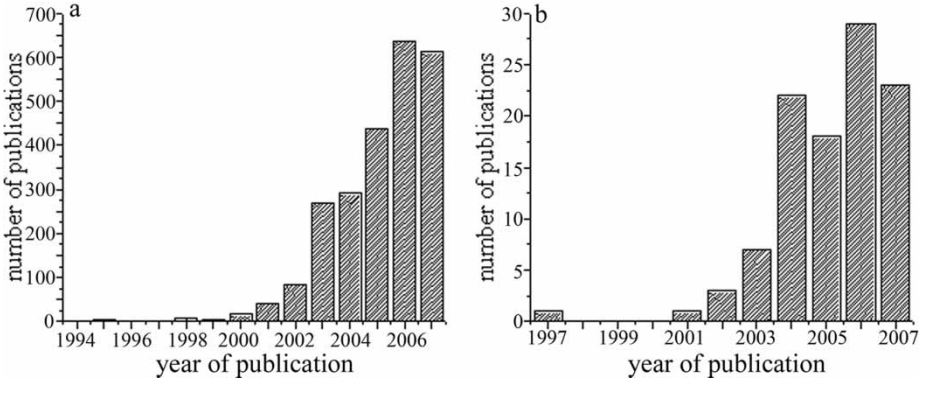

Figure 1. (a) Comparison of the annual number of scientific publications since 1994, when the term ''electrospinning'' was introduced. Data analysis completed using SciFinder Scholar search system with the term ''electrospinning'' on November 19, 2007. (b) All scientific journal publications on electrospun biopolymers found, accessed, and noted in this review.

observed and characterized. The electrospinning process became and remains attractive since it is a cost-effective method of producing nanofibers from a large variety of bulk starting materials in a moderately easy, repeatable, and simple fashion.[50,51] This review will focus on biopolymer and biopolymer-containing fibrous mats fabricated by the electrospinning process.

2 Electrospinning

2.1 Processing

As displayed in Fig. 2, the basic requirements of an electrospinning apparatus, include: (1) a capillary tube with a needle or pipette, (2) a high power voltage supply, and (3) a collector or target.[10] Electrical wires connect the high power supply to the capillary tube, which contains a polymeric solution, as well as to the target. The capillary tube and target are held at a relatively short distance from each other. Copper plates,[52,53] aluminum foil or plates,[54–57] rotating drums,[58–60] and human hands[61] have been utilized as targets to collect fibers during the electrospinning process.

The polymer solution is forced through the syringe pump to the needle, either by gravity or by an advancement pump. Initially, as a result of surface tension, pendant droplets of the solution are held in place. A conical protrusion,[62] known as a Taylor cone,[63] is formed when a critical voltage is applied to the system. For a few centimeters, an approximately straight jet emerges from the cone; however, this straight segment cannot hold for long. The jet therefore emerges into a diaphanous and conical shape, within which exists the complicated path taken by the jet.[64] Bending instabilities are experienced by the conically moving jet and its field is directed towards the collector, which has the opposite electrical charge. In the time it takes the jet to reach the collector, the solvent evaporates and dry polymer fibers are deposited.[5]

2.2 As-spun Nanofibers

Electrospinning produces seemingly endless ultra-fine fibers, which have been theoretically and experimentally proven to be continuous.[46,64] When the described electrospinning apparatus is utilized, fibers collect as a non-woven mat on the target. A recent review (2007) by Greiner and Wendorff[49] discussed the polymer, polymer

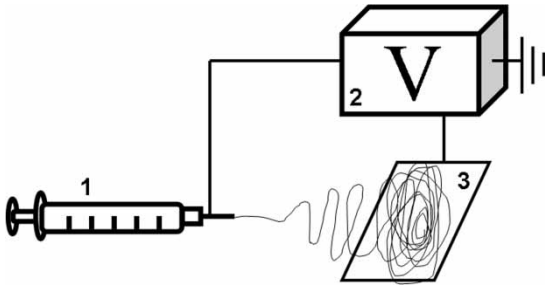

Figure 2. Schematic of a typical electrospinning apparatus, including: (1) syringe needle, (2) voltage supply, and (3) collector.

solution, and other properties that influence the ability to electrospin a solution as well as the morphology of the as-spun fibrous mats. These parameters are summarized in Table 1.

For many applications it is desirable to have aligned or a specific arrangement of accumulated nanofibers. By using patterned electrodes,[65] conductive substrates separated by a nonconductive gap,[66] disc collectors,[67] or other methods as outlined by Teo and Ramakrishna[68] (2006), varying degrees of fiber alignment can be achieved. While strides have been taken towards achieving aligned nanofibers,[66,69,70] it remains a challenge to align a substantial thickness of fibers. In some instances alignment would be beneficial. For example, cell elongation and proliferation have been demonstrated to occur along the direction of the nanofibers,[68] which, could improve tissue engineering applications. In terms of up-scaling and increasing the production rate of the electrospinning process, some challenges do exist, but can be overcome,[71] for example, using multiple jet electrospinning.[72–74]

2.3 Nano-effects

Specific surface area increases as dimensions decrease, and this is especially true when nano-scale dimensions are obtained; specifically, in this review, we are interested in the decrease of fiber diameters. Increasing the surface area means that a higher proportion of atoms are on the surface and thus, enhanced properties occur, which can be thought of as nano-effects.[75] Some of these nano-effects include: increased quantum efficiency, unusually high surface energy, raised surface reactivity, elevated thermal and electrical conductivity, high strength-to-weight ratios, and superparamagnetism.[76] Simply put, nano-effects are any behaviors that are observed on the nano-scale, which the bulk form of the same material do not display.[75]

3 Applications

The ability for natural polymers to match the demands of specialty markets creates a growing niche for them because the ability to tailor a product towards a particular consumer application is more important than the need for multimillion pound-per-year-sales.[20] Therefore, when the intrinsic properties of biopolymers are combined with the exciting nano-effects that nanofibrous mats have to offer, enhanced products can be manufactured.

Table 1
Parameters that effect the morphology of the electrospun fibers[49]

Polymer properties	Solution properties	Other properties
Molecular weight	Viscosity	Substrate properties
Molecular-weight distribution	Viscoelasticity	Solution feed rate
Glass-transition temperature	Concentration	Field strength
Solubility	Surface tension	Geometry of electrode(s)
	Electrical conductivity	Vapor pressure of the solvent
		Relative humidity

Biopolymer nanofibers could be used as particle filters in vivo, nanocomposite reinforcing fibers for nanotechnology, sutures,[77] filters for metal recovery,[78] as templates,[79–81] and in chemically and biologically protective clothing.[82] The porosity of electrospun fibers can be altered[83–85] and effects such as the number of anchoring points for cells, wetting-properties, and degradation rates can all be varied. Thus, medical textiles, chemical filtration, fuel cell membranes, catalysis, electrochemical cells, and nanoreinforcements would benefit from using a nanofibrous mat with increased porosity.[49,86]

Biopolymer nanofibrous mats have shown potential for applications within the medical field due to the aforementioned intrinsic properties of these renewable materials. For this reason, we will go into more depth regarding these applications. Medical and pharmaceutical fields could use nanofibers to fabricate wound dressings,[87,88] tissue engineering scaffolds for drug delivery,[89–93] or other medical devices. The success rate of artificially recreating the extracellular matrix and other tissue engineering applications, depends on the properties of the scaffolds, such as their biocompatibility, osteoconductivity, degradability, high surface-area-to-volume ratios, and mechanical properties.[89,93,94] Cellular and enzymatic behavior is influenced by the size of the substrate;[95,96] when the diameters of fibrous scaffolds are smaller than the diameter of a cell, it is theorized that cells can attach and organize around those fibers. This is desirable as it results in increased amounts of cell proliferation when compared to the behavior of cells when they are on larger diameter fibers. Additionally, by electrospinning fibrous mats, a three-dimension malleable[97] scaffold is fabricated. Thus, it could be molded around, spun directly onto, or into the pores of whatever size substrate that needs cell seeding.

Mechanical properties, degradation rate, as well as pore size, shape, and distribution of the tissue engineering scaffold must match the needs of the tissue of interest.[98] Nonwoven fibrous mats could conceivably resemble the extracellular matrix; however, it is also necessary that the effects that an artificial matrix have on cell growth, proliferation, and differentiation be thoroughly investigated. The geometrical and physicochemical properties of electrospun mats and their influence on cell attachment kinetics as well as the expression of binding and matrix proteins need to be better understood.[99] In many of the reports to follow, the particular application of interest noted in the articles will be highlighted.

4 Biopolymers Electrospun

4.1 Polysaccharides

Complications arise when working with polysaccharides because our theoretical understanding of charged biopolymers such as DNA, RNA, and polysaccharides[100] is rather limited compared to that of neutral polymers; consequently, so is our understanding of polyelectrolyte system properties.[100–102] Unlike neutral polymers, these materials experience both long-range electrostatic interactions and the presence of counter ions.[103,104] Of the biopolymers discussed below, chitosan is cationic in solution, while hyaluronic acid and alginic acid are anionic polyelectrolytes.

4.1.1A Cellulose. The most abundant natural, renewable, biodegradable polymer is cellulose. Cellulose is one of the longest studied polymers and is a polydispersed linear biopolymer of poly-β(1,4)-D-glucose units with asyndiotatic configuration. Despite

hardships with processing, cellulose has been found in textile, paper, plastic, food additives, and propellant applications.[105] Due to strong inter- and intra- molecular hydrogen bonds, cellulose does not dissolve in common solvents; it does dissolve in dimethylsulfoxide/paraformaldehyde[106] or sulfur dioxide.[107] However, these solvents were not suitable for electrospinning.[108] Due to the problems associated with dissolving cellulose, it is common to use cellulose derivatives, which do dissolve in common solvents. In some cases, the disadvantage of cellulose derivatives, is the reduced stability and degradation of the cellulose structure.[109]

In the first patent dealing with electrospinning, Formhals[47] spun two derivatives of cellulose, cellulose acetate and propionyl cellulose. The solution used was comprised of equal parts, 44 g of chemically pure acetone and alcohol, and 1 g of softening agent (Solactol and Palatinol). However, it was not until many years later that cellulose, cellulose-derivatives, or cellulose-containing fibers were spun again. In the remainder of this section, as well as in Table 2, many of the documented cases of those systems are described.

Commercial cellulose fibers have previously been fabricated[110] using the dry-jet wet spinning process with N-methylmorpholine oxide (NMMO)/water (H_2O) (known as the Lyocell process).[111] Kang et al.,[112] used NMMO to electrospin cellulose, and then, utilizing nitrogen dioxide and perfluorocarbon, oxidized the mats to prevent the adhesion of human tissues. Also utilizing NMMO as a solvent, cellulose was electrospun by Kulpinski[108] in 2005. Fibers were electrospun from 2% mercerized cellulose at 90–95°C and raw cellulose at 95–100°C. Most had diameters between 200–400 nm; however, some fibers were up to 700 nm in diameter. In the same year, Frey et al.[113] additionally electrospun celluloses; however, they utilized lithium chloride (LiCl) and N, N-dimethylacetamide (DMAc) as the solvent system. Lithium was used to overcome the electrostatic interactions between cellulose and DMAc. This study determined that dry and stable cellulose fibers could be spun from 3% cellulose solutions by using a water coagulation bath (for removal of LiCl) and heated collectors (for solvent removal). Frey et al. suggest that cellulose nanofibers have promise for filtration applications.

As noted in the paragraph above, two solvent systems have been used to electrospin cellulose and each has various advantages and disadvantages. LiCl/DMAc dissolves celluloses from different origins, at various concentrations, and notably does so without side reactions; however, solution preparation can be challenging. NMMO/H_2O solutions require elevated temperatures and have a limited range appropriate for spinning; however, this solvent system is simpler than the first.[109,114–118] Kim et al.[119] reiterated that both solvent systems produced cellulose fibers; however, the as-spun fibers differed structurally. Fibers from LiCl/DMAc were found to be amorphous while those from NMMO/H_2O had varying amounts of crystallinity. Additionally, using nitric acid (HNO_3)/phosphoric acid (H_3PO_4) and sodium nitrite ($NaNO_2$), Kim et al. oxidized the as-spun fibers and explored the degradation characteristics under a physiological environment. Oxidized cellulose is of interest because it degrades under physiological conditions and is bioresorbable; it has been used as a resorbable homeostatic dressing, in cosmetic preparations, fibrin formation catalysis-agents, and adhesion barriers.[120–122]

4.1.1B Cellulose Acetate. A derivative of cellulose, cellulose acetate, has common applications in the fabrication of semi-permeable membranes for dialysis, ultrafiltration, and reverse osmosis.[123] Cellulose acetate has been electrospun as outlined in Table 2. In 1998, Jaeger et al.[124] electrospun cellulose acetate/acetone solutions resulting in fibers with "beads on the string" morphology. Possibly this was a result of the gelation

Table 2
Table displays all known electrospinning of cellulose and cellulose-derivative solutions. Contains information regarding polymer, solvent(s), and reference (Ref)

Polymer(s)	Solvent(s)	Ref
Cellulose	NMMO	112
α-cellulose (mercerized cellulose pulp)	1/1 NMMO/H_2O	108
α-cellulose (spruce cellulose pulp)		
Cellulose (S) cellulose (S 470 cotton linter paper)	8 wt% LiCl/DMAc	113
Cellulose (surgical cotton batting)		
Fibrous cellulose	8% LiCl/DMAc	113, 119
Cellulose (surgical cotton batting)	1/1 NMMO/H_2O	
Cellulose acetate	1/1 Acetone/alcohol + softening agent	47
Cellulose acetate	Acetone	124
Propionyl cellulose		
Cellulose acetate	2/1 Acetone/DMAc 3/1 Acetic acid/DMAc 3/1 Acetic acid/acetone	125
Cellulose acetate	1/9-3/17, 4/1 Acetone/H_2O	126–127, 132
Cellulose acetate	3/1/1 Acetone/DMF/ trifluoroethylene	133
Cellulose acetate	2:1 Acetone/DMAc	135,138
Cellulose acetate	17/3 Acetone/H_2O	134
Cellulose acetate/PVA	2:1 Acetone/DMAc	73
Ethyl–cyanoethyl cellulose	THF	139
Ethyl cellulose	100/0-1/4 THF/DMAc	141
CM cellulose[a]	MeOH/H_2O	267
CM cellulose sodium salt/PEO	H_2O	153
Hydroxypropyl cellulose	Anhydrous ethanol or anhydrous 2-propanol	143
Hydroxypropyl methylcellulose	1/1 H_2O/Ethanol	153
Methylcellulose	1/1 H_2O/Ethanol	
Enzymatically treated cellulose	8% LiCl/DMAc	
Cellulose acetate/hydroxyapatite	Acetone or 1/1 acetone/AA	165

[a]Electrosprayed.

of the polymer, low viscosity solutions, or due to the low boiling point of acetone. Based on the inconsistent fiber morphology previously reported, Liu and Hsieh (2002)[125] investigated using acetone, acetic acid (AA), and dimethylacetamide as the solvent since cellulose acetate only dissolves in liquids with a Hildebrand solubility parameter between 9.5 and 12.5 $(cal/cm^3)^{1/2}$. Utilizing the solvent system acetone/dimethylacetamide yielded the most consistent fibers with diameters ranging from 100 nm to 1 μm. Various collectors, wetting properties, and adsorption behavior of the non-wovens were also evaluated.

Son et al.[126] tried a new solvent system, acetone/H_2O, and found increased success of electrospinning cellulose acetate under basic pH conditions. The as-spun fibers were then deacetylated into cellulose fibers with an activation energy of 10.3 kcal/mol; they retained their non-woven morphology. The same year, Son et al.[127] oxidized their previously deacetylated cellulose acetate mats[126] utilizing a mixture of HNO_3/H_3PO_4-$NaNO_2$ as previously demonstrated by Banker and Kumar.[128] The oxidized cellulose nanofibers displayed a lower crystallinity than cellulose fibers and the carboxyl content increased as the amount of $NaNO_2$ increased.

Electrospun polyacrylonitrile containing silver nanoparticles were prepared[129] and are of interest due to the antimicrobial properties that the silver nanoparticles might provide to the fibers.[130,131] In their third report on the subject, Son et al.[132] added and proceeded to electrospin 0.01–0.5 wt% silver nitrate ($AgNO_3$) to 10 wt% cellulose acetate in 4/1 acetone/H_2O solution; the as-spun fibers were then photoreduced. The cellulose acetate fibers with 0.0, 0.05, 0.3, and 0.5 wt% $AgNO_3$ had average diameters of 1910, 680, 640, and 610 nm, respectively. When the cellulose acetate non-wovens with 0.05 wt% $AgNO_3$ were tested against S. aureus, E. coli, K. pneumoniae, and P. aeruginosa, all bacteria were reduced 99.9% post-incubation.

Ma, et al.[133] also electrospun cellulose acetate in 2005. Structural and mechanical improvements were determined to have occurred with 1 h heat treatment, while alkaline treatment served to regenerate cellulose. The mats, which consisted of fibers ranging from 200 nm to 1 μm, could be used to specifically capture bovine serum albumin or bilirium after Cibacron Blue F3GA was covalently bonded to the mats.

Frey et al.[134] electrospun cellulose acetate citing important factors, which differed from the previous method.[125] They utilized a mixed solvent system of acetone/H_2O and the polymeric solution was cooled to 5°C. The as-spun fibers were deacetylated into cellulose fibers whose absorbency of dyes and liquids and degree of hydrophilicity were compared to both electrospun and conventional fabrics.

Supaphol et al.[135] in 2007, electrospun 16 w/v% cellulose acetate containing 0.5 wt% vitamin A (retinoic acid) or 5.0 wt% vitamin E (α-tocopherol) for cosmetic applications. Vitamin A has been proven to reduce wrinkles, normalize keratinization, lighten brown spots, and smooth skin, while vitamin E is an antioxidant that provides photoprotection.[136,137] The as-spun fibers had average fiber diameters between 247 and 265 nm. Over the testing period, a gradual and monotonous increase in the release of vitamins was mainly observed. Supaphol et al.[138] also electrospun 16 w/v% cellulose acetate and functionalized the mats for topical drug delivery. They incorporated 20 wt% (based on the weight of the cellulose acetate powder) four non-steroidal anti-inflammatory drugs: naproxen, indomethacin, ibuprofen, and sulindac. The drugs were well-incorporated into the 263–297 nm fibers. Drug-loaded fibers showed enhanced swelling over the pure-cellulose acetate fibers and it was determined that the fibers loaded with naproxen released the most drug. In both of these studies,[135,138] the fibers were compared to films containing the vitamins or drugs respectively.

4.1.1C Other Cellulose Derivatives. In 2004, Zhao et al.[139] first prepared ethyl–cyanoethyl cellulose from ethyl-cellulose and acrylonitrile as previously described.[140] The ethyl–cyanoethyl cellulose was then dissolved in tetrahydrofuran (THF) and successfully electrospun into porous fibers. As the applied voltage was increased, the as-spun fibers were more crystalline; however, at higher voltages, the crystallinity again decreased.

Ethyl cellulose has good thermostability as well as electric properties. In 2005, Wu et al.[141] electrospun the cellulose ether in a solvent system of THF/DMAc and tested

the effects of various solvent ratios. It was determined that the solvent composition influenced the fiber size distribution and diameter. Higher concentration ranges of polymer were spun upon the addition of DMAc.

Another derivative of cellulose is hydroxypropyl cellulose, which is used in the production of nanocrystalline ceramic oxide powders as steric stabilizers.[142] In 2005, Shukla et al.[143] demonstrated that hydroxypropyl cellulose could be electrospun utilizing two different solvents at a variety of applied voltages and two different tip-to-collector distances (10 and 15 cm). Interestingly, as-spun fibrous mats were appropriate for use as templates for producing tin oxide nano and macro porous fiber networks on microelectromechanical system (MEMS) devices.

Poly(ethylene oxide) (PEO), is a biocompatible polymer[144] that has been used as a wound dressing[145] and as injectable cartiledge.[146] PEO has been electrospun solo[62,147–150] and can be added to facilitate electrospinning.[151,152] In 2007, PEO was used as a carrier polymer by Fretnot et al.[153] to spin a number of cellulose derivatives: hydroxypropyl methylcellulose (HPMC), methylcellulose, 3% enzymatically treated cellulose (supplier: Tampere University of Technology (TUT), Finland), and CM cellulose sodium salt. They were able to later extract the PEO from the fibers. The cellulose derivatives were investigated to identify the role that MW, degree of substitution, and substitution pattern have on microstructure, which was observed using a scanning electron microscope (SEM). It was determined that MW and degree of substitution did not significantly affect the electrospinning of HPMC and CM cellulose fibers. Upon PEO extraction from all of the cellulose derivatives, SEM displayed that the fibers differed as a result of various substitution patterns.

4.1.1D Cellulose Composites. In addition to PEO, another polymer, poly(vinyl alcohol) (PVA), is also commonly used to facilitate electrospinning or provide different chemical and mechanical properties of the as-spun composite. It has been electrospun solo numerous times without difficulty,[154–156] and has good fiber-forming capabilities.[157–160] PVA is a biocompatible, non-toxic, and chemically resistant polymer, which has been utilized in biomedical applications such as contact lenses,[161,162] implants,[163] and artificial organs.[164] In 2004, Ding et al.[73] fabricated non-wovens composed of cellulose acetate/PVA by multi-jet electrospinning, potentially for filters and biomedical applications. These mats were found to have a uniform dispersion purely by blending the polymers, i.e., there were no chemical interactions. Changing the cellulose acetate/PVA ratio altered the mechanical properties of the fibers. Cellulose acetate/hydroxyapatite (HA) fibers, as well as cellulose acetate/polyvinylpyrolidone (PVP) fibers were electrospun by Bishop et al.[165] Studies demonstrated that the cellulose acetate was better than PVP for dispersing the HA. Various amounts of the solvents, acetone and AA, yielded different HA dispersions and the cellulose acetate/HA mats have potential use as advanced biocompatible prosthetics.

4.1.2 Chitin. After cellulose, chitin is the most abundant organic material produced by biosynthesis. However, use of chitin in many applications has been limited due to its insolubility in most organic solvents. The neutrally charged biopolymer is soluble in 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP), hexafluoroacetone, chloroalcohols in conjunction with aqueous (aq) solutions of mineral acids, and DMAc containing 5% LiCl.[4]

Table 3 displays the only known instances of electrospun chitin, which all utilized HFIP as the solvent. The process parameters for the electrospinning of chitin and chitin-containing solutions, including: MW, degree of deceleration (DD), solvent used,

Table 3

Table displays all known electrospinning of chitin and chitin-containing solutions. Contains information regarding molecular weight (MW), degree of deacetylation (DD), solvent, special processing requirements, electrospinning conditions (including: applied voltage, separation distance, advancement speed of solution), and reference (Ref)

Polymer(s)	MW	DD	Solvent	Processing	Conditions	Ref
Chitin	910 k	8%	HFIP	Chitin irradiated mixed 3 days	15 kV, 7 cm	166
Chitin	920 k	8%	HFIP	Chitin irradiated mixed 20 days	17 kV, 7 cm	167
Practical grade chitin		9%	HFIP	Mixed 3–4 days	24 kV, 6 cm, 1.2 mL/h	168
Chitin/PGA	91 k	8%	HFIP	Chitin irradiated	17 kV, 7 cm, 4 mL/h	169
Chitin/SF	91 k	8%	HFIP	Chitin irradiated silk dissolved in $CaCl_2/EtOH/H_2O$	17 kV, 7vm, 4 mL/h	170

PGA – poly(glycolic acid); SF – silk fibroin.

special polymer processing, electrospinning parameters (including: applied voltage (kV), separation distance between needle and collector (cm), and advancement speed of solution (mL/h), and reference (Ref) are given in Table 3. In some instances, the information might not have been provided in the original article.

Park et al.[166] utilized irradiation to facilitate the dissolution of chitin since the as-is solubility of chitin is only approximately 65% in HFIP. However, upon doing so, there was a decrease in the MW of the polymer. The chitin fibers were analyzed utilizing an SEM custom code image analysis program and they had a maximum and minimum fiber diameter of 460 and 50 nm respectively with an average diameter of 163 nm. Deacetylation of the fiber mats transformed them into chitosan fibers, as confirmed by Fourier transform infrared spectroscopy (FTIR) and x-ray diffraction (XRD). Park et al.[167] then compared the degradation behavior of their 163 nm diameter electrospun chitin fibers to 8.77 μm diameter commercial chitin macrofibers both in vitro and in vivo. Since the electrospun fibers have an increased surface area-to-volume ratio, they promoted cell attachment and the spreading of normal human fibroblasts and keratinocytes better than the commercial fibers. Therefore, Park et al. suggested that tissue scaffolding or wound dressings could be fabricated from the mats.

Schiffman et al.,[168] electrospun practical grade chitin (Sigma-Aldrich) using HFIP as the solvent. Figure 3(a) contains a histogram that displays the as-spun practical grade chitin fiber diameter distribution. Using a Zeiss Supra 50/VP field emission scanning electron microscope (FESEM) to average fifty random fiber diameters, the maximum and minimum fiber diameter observed were 41 nm and 391 nm respectively. The average fiber diameter was 152 ± 70 nm, which is within standard deviation with the findings of Park et al.[166] Figure 3(b) contains an SEM micrograph displaying cylindrical fibers of practical grade chitin, 1 μm marker displayed. Analysis regarding how the crystallinity of bulk chitin changes during the electrospinning process and the mechanical properties of the fibers were evaluated. According to the authors, this information is needed for electrospun non-wovens to be used in technical medical and environmental applications.

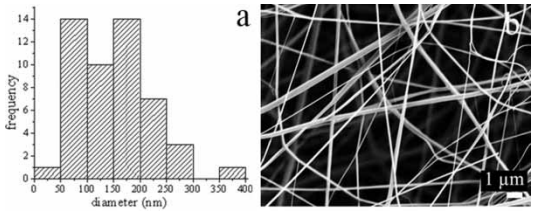

Figure 3. (a) Histogram displaying the as-spun practical grade chitin fiber diameter distribution. (b) SEM micrograph of as-spun practical grade chitin nanofibers, 1 μm marker displayed. (Unpublished images, experiment performed by Jessica D. Schiffman)

With respect to the chitin-component fibrous mats, Park et al. have two cited works (see Table 3) in which they mimicked the extracellular matrix. Since poly(glycolic acid) (PGA) is both biocompatible and biodegradable, chitin/PGA fibers[169] were fabricated. The blended fibers degraded faster than pure PGA fibers; in vitro degradation studies were conducted in phosphate buffered saline, pH 7.2. Chitin/silk fibroin (SF)[170] fibers were also electrospun. It was thus determined by cell studies that fibrous mats composed of 25% PGA or SF and 75% chitin experienced the most attachment and proliferation of normal human epidermal fibroblasts (NHEF).[169,170] Based upon this behavior, the chitin/PGA fibers, which had a bovine serum albumin coating might be a good candidate for tissue engineering scaffolds. The highest spreading of NHEF and normal human epidermal keratinocytes (NHEK) were observed on the chitin/SF non-wovens; these scaffolds might be suitable for wound healing and skin regeneration purposes.

Derived from the shells of Penaeus merguiensis shrimps, α-chitin whiskers were utilized in a nanocomposite fibrous mat of electrospun PVA by Junkasem et al. (2006).[171] When the chitin whisker to PVA ratio was approximately 5.1%, a maximum tensile strength value of 5.7 ± 0.6 MPa was obtained; however, increasing the chitin content after this point decreased the strength of the fibrous mats. PVA/H_2O had previously been electrospun[155] and nanocomposites containing α-chitin whiskers within a chitin/PVA film had been previously fabricated.[172,173]

4.1.3A Chitosan. The *N*-deacetylated derivative of chitin is chitosan, though a sharp nomenclature difference between the two biopolymers based on the degree of *N*-deacetylation has never been precisely defined. Typically, commercial chitosan is approximately 85% deacetylated, which leads to a $-NH_2$ functionality on the C-2 of the D-glucosamine repeat unit.[3,4] As a result of this process, chitosan is soluble in aq acidic solvents that chitin is not soluble in, such as AA, formic acid (FA), malic acid (MA), and others.

The capability to electrospin a polymer is dependent upon finding the optimal solvent system, among optimizing many other parameters. Chitosan intrinsically has a larger solvent choice for electrospinning than chitin since it is soluble in more solvents. Despite this, after protonation, chitosan changes into a polyelectrolyte in acidic solutions; thus becoming the only pseudonatural cationic polymer.[3] There are only a few reports on ionic polymers or polyelectrolytes that have successfully been electrospun.[174] Min et al.[166] theorized that due to the high electrical force applied during electrospinning, repulsive forces between ionic groups within the polymer backbone arise and often produce particles since the formation of continuous fibers is restricted. Work towards developing an empirical equation for fiber diameter, which includes the effects that polyelectrolytes have on electrospinning have been conducted by Mckee et al.[175,176]

Chitosan has successfully been electrospun using trifluoroacetic acid (TFA) and AA. Table 4 contains information on chitosan, chitosan-containing, or chitosan derivatives that have been electrospun. The table includes the polymer, MW and DD of the polymer, solvent system used, electrospinning conditions (such as applied voltage (kV), separation distance (cm), and advancement speed of the pump), and reference number (ref).

Homogenous bead-free fibers from chitosan10 (Wako Pure Chemical Industries, Ltd., Japan) were electrospun by Ohkawa et al. (2004)[177] using a solution of 70/30 TFA/dichloromethane (MC). Utilizing 8 wt% chitosan10 solutions yielded fibers with a minimum and maximum fiber diameter of 210 and 650 nm respectively and an average diameter of 330 nm. Electrospinning utilizing 0.2 M AA, 0.1 M hydrochloric acid (HCl), neat FA, dichloroacetic acid, and mixtures with methanol, ethanol, and 1,4-dioxane, MC as well as with aprotic solvents N,N-dimethylformamide and dimethylsulfoxide were also attempted but failed. It has been proposed that solutions primarily containing TFA facilitate the electrospinning of chitosan because

1. the amino groups of the chitosan can form salts[178] thus destroying the rigid interactions between the chitosan molecules and because
2. the electrified polymer jet can be solidified as a result of the high volatility of the solvent.

In an effort to decrease the average fiber diameter, in 2006, Ohkawa[179] focused on idealizing the viscosity of their solutions.[46,180] It was determined that there was a linear increase of fiber diameter as the concentration of chitosan in solution decreased, thus fiber diameter and polymer concentration had an inverse relationship.

In 2007, Schiffman and Schauer[52] electrospun, utilizing TFA as the solvent, four bulk chitosans as supplied from Sigma-Aldrich without further purification. They were low, medium, and high MW as well as practical grade chitosan and resulted in fibrous mats containing an average fiber diameter of 74 ± 28 nm, 77 ± 29 nm, 108 ± 42 nm, and 58 ± 20 nm, respectively. Foreign contaminants are often contained within the practical grade of chitosan, thus, the spinnablity of this poorly characterized system, which was not purified in any manner, is of great interest. Practical grade chitosan fibers displayed comparable properties to the better purified chitosans. Hence, this implies that discarded waste products of the seafood and other industries could be easily be recycled into useable materials. Figure 4(a) is an SEM micrograph of as-spun practical grade chitosan nanofibers. These fibers appeared similar in morphology to the low, medium, and high MW chitosan fibers spun. A 500 nm marker is displayed. Figure 4(b) is a histogram displaying the as-spun practical grade chitosan fiber diameter distribution.

However, prior to their use in applications, the chemical stability of the chitosan fibers needs to be improved. A two-step process was implemented to crosslink the fibers; first, the chitosan solutions were spun into fibers, and second, a vapor-phase glutaraldehyde (GA) was exposed to the as-spun fiber mats overnight while in a vaporization chamber. Figure 4(c) displays an SEM micrograph of these two-step crosslinked practical grade chitosan nanofibers with a 4 μm marker displayed. It is evident that upon crosslinking the continuous and cylindrical fiber morphology is retained. This is true for the low, medium, and high MW fibers as well. Figure 4(d) displays a histogram of the diameters of the two-step crosslinked practical grade chitosan fibers. The average diameters for the two-step crosslinked low MW, medium MW, high MW, and practical grade were 387 ± 183 nm, 172 ± 75 nm, 137 ± 59 nm, and 261 ± 160 nm, respectively. SEM micrographs supported uniaxial tensile testing proving that crosslinking caused all the

Table 4
Table displays all known electrospinning of chitosan and chitosan-containing solutions. Contains information regarding molecular weight (MW), degree of deacetylation (DD), solvent, electrospinning conditions (including: applied voltage, separation distance, advancement speed), and reference (Ref)

Polymer(s)	MW	DD	Solvent	Conditions	Ref
Chitosan 10	$^{+}$3210 k	78%	TFA/MC	15 kV, 15 cm	177
Chitosan 10	$^{+}$210 k	78%	TFA	15 kV, 15 cm,	179
Chitosan 100	$^{+}$1310 k	77%		No pump pressure	
Chitosan 500	$^{+}$1580 k				
Chitosan 1000	$^{+}$1800 k				
Low MW chitosan	70 k	74%	TFA	26 kV, 6.4 cm, 1.2 mL/h	52
Medium MW chitosan	190–310 k	83%			
High MW chitosan	500–700 k	72%			
Practical grade chitosan	190–375 k	75%			
Chitosan	190–310 k	83%	TFA/GA	26 kV, 6.4 cm, 1.2 mL/h	53
Chitosan	210 k	91%	TFA/MC	25 kV, 15 cm, 2 mL/h	182
Chitosan		95%	TFA/MC	25 kV, 20 cm	181
Chitosan	106 k	54%	aq AA	3–5 kV, 20 μL/min	183
Chitosan	190–310 k	75–85%	aq AA	20 kV, 10 cm, 0.3 mL/h	184
Chitosan 10/PVA	$^{+}$210 k	78%		15 kV, 15 cm	177
Chitosan 100/PVA	$^{+}$1300 k	77%			
Low MW chitosan/PVA		75–85%	aq AA	22 kV, 15 cm, 0.6 mL/h	191
Chitosan/PVA	1600 k	82.5%	aq AA	18 kV, 25 cm	157
Chitosan/PVA	165 k	90%	aq AA	10, 15 cm, 10–20 kV, 0.06–0.24 mL/h	185
Chitosan/PVA		78%	aq AA	15 cm, 15 kV	158
Chitosan/PVA	120 k	82.5%	aq AcrA	15–30 kV, 13 cm	160
Chitosan/PVA	120 k	82.5%	aq AcrA	22 kV, 12 cm	159
Chitosan/PEO			aq AA	15 kV, 20 cm, 0.1 mL/h	174
High chitosan/PEO			aq AA	10–28.5 kV, 10 cm	193
Chitosan/PEO	190 k	85%	aq AA	20–25 kV, 17–20 cm	194
Pharmaceutical grade		90%	aq AA	20 kV, 15 cm	195

(*continued*)

Table 4
Continued

Polymer(s)	MW	DD	Solvent	Conditions	Ref
Chitosan/PEO					
Chitosan/PET		85%	TFA/HFIP	12–20 kV, 10–15 cm, 0.3–0.7 mL/h	200
Chitosan/collagen	1000 k		TFA/HFIP	20 kV, 130 cm, 0.8 mL/h	243
Chitosan/collagen			TFA/HFIP		260
Chitosan/silk fibroin	220 k	86%	FA	16 kV, 8 cm, 1.0 mL/h	255
Hexanoyl chitosan	576 k	88%	Chloroform	8–18 kV, 12 cm	211
CE chitosan/PVA	390 k		H_2O	*1.6 kV/cm, 7.5 cm	212, 213
Q chitosan/PVA	400 k	80%	H_2O	*1.5–3.5 kV/cm	214
CM chitosan/PEO			H_2O	20 kV, 20 cm, 0.1 mL/h	195

[+]Indicates viscosity average MW.
*Indicates applied field strength (AFS).

chitosan fiber mats to decrease in elasticity, Young's modulus, and ultimate tensile strength.

Schiffman and Schauer[53] also fabricated a crosslinked chitosan fibrous mat utilizing a one-step process. Here, the solution to be electrospun was combined with 1 mL of GA liquid prior to the electrospinning; the resultant non-wovens were insoluble in acidic, basic, and aq solutions for at least 72 h. An average diameter of 77 ± 29 nm was observed for medium MW chitosan fibers, which was less than the 172 ± 75 nm evaluated for the two-step crosslinked fibers fabricated from the same chitosan.[52] It was therefore concluded that one-step electrospinning could produce finer crosslinked chitosan fibers faster and with theoretically improved mechanical properties than the two-step method.

An alternative method of crosslinking or neutralizing chitosan nanofibers was reported by Sangsanoh and Supaphol[181] after they noted that electrospun non-woven mats, prepared by Ohkawa et al.'s method[177] dissolved when exposed to sterilized 70% ethanol solutions or phosphate buffer saline. To remedy this, they submerged the fibrous mats in 5 M aq sodium carbonate (Na_2CO_3) solutions for 3 h to neutralize the remnant TFA. Schwann cells were able to attach to the mats after this neutralization. Matsuda et al.[182] reported that chitosan non-wovens also became neutralized and insoluble in water after immersing them in 28% aq ammonium solution.

In addition to utilizing TFA as a solvent, strong aq AA can sometimes be used to electrospin chitosan. Geng et al.,[183] attempted to electrospun three kinds of demineralized and deproteinized chitosan powders. However, uniform fibers were only generated from a 7% solution of the chitosan that had a MW of 106,000 and a DD of 54% in 90% AA. Other chitosans, which had a MW and DD of 30,000, 56% and 398,000, 65% respectively, did not form fibers. Surface tension and charge density were theorized to be the key factors in

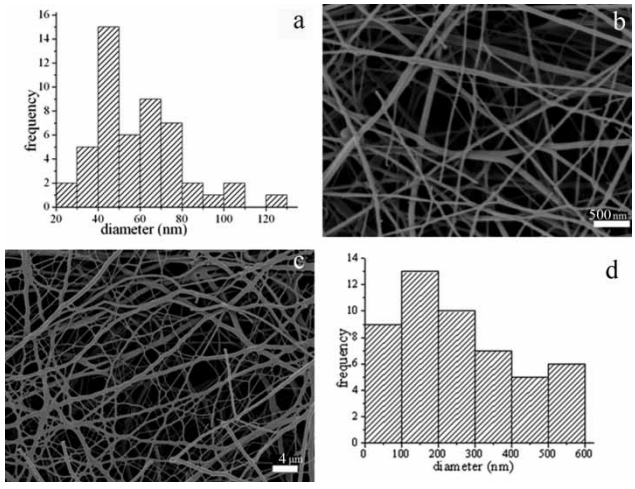

Figure 4. (a) SEM micrograph of as-spun practical grade chitosan nanofibers, 500 nm marker displayed. (b) Histogram displaying the as-spun practical grade chitosan fiber diameter distribution. (c) SEM micrograph of two-step crosslinked practical grade chitosan nanofibers, 4 μm marker displayed. (d) Histogram displaying the two-step crosslinked practical grade chitosan fiber diameter distribution. (Unpublished images, experiment performed by Jessica D. Schiffman)

determining the spinnability of the system. In a feasibility study conducted by De Vrieze et al.[184] it was determined that chitosan could be electrospun in strong AA solutions but not in FA, lactic acid or HCl. In the future, chitosan fibrous mats might aide in wound or other medical applications, or the removal of metals from solutions for environmental applications.

Notably, electrospinning of chitosan in AA solutions was unsuccessful for Sangsanoh and Supaphol,[181] Li and Hsieh,[157] as well as previous attempts in 2004[54] and current attempts by the author of this section in 2007. Possibly, this is because inappropriate MWs of chitosan were tested.[181,183]

4.1.3B Chitosan/PVA. Ohkawa et al.[177] electrospun chitosan10/PVA and chitosan100/PVA at the same time that they spun pure chitosan10. With a 30/70 chitosan10/PVA ratio, fibers with an average diameter of 120 nm were fabricated; thicker fibers were observed when higher ratios were employed. As a comparison, PVA/deionized H_2O electrospun without additional polymers had an average diameter of 470 nm. By adding PVA to chitosan, Li and Hsieh (2006)[157] increased entanglements and decreased the repelling interactions of the polycationic chitosan molecules. Also, 25/75 chitosan/PVA nanofibers ranging from 20–100 nm were electrospun in 2% aq AA solutions. Zhang et al. (2007)[185] also spun 40/60 chitosan/PVA fibers in 2% AA solutions. Transmission electron microscopy (TEM) and energy dispersive spectroscopy (EDS) identified that the as-spun fibers and beads both contained chitosan. They believe that chitosan/PVA nonwovens might be suitable for wound dressings based on their high water up-take capabilities. In 2006, Zhou et al. electrospun fibers from chitosan/PVA in aq acrylic acid (AcrA) solutions[160] and later thermally crosslinked the fibrous mats using triethylene glycol dimethcrylate (TEGDMA) for 2 h at 80°C in 2007.[159] Zhou et al. spun up to 90/10 chitosan/PVA

solutions in as high as a 90% AcrA; neat AcrA did not allow for spinning. It was noted that some chitosan remained undissolved.[160]

Due to the polyelectrolytic nature of chitosan, it has a high viscosity in dilute aq solutions. Therefore, it can be desirable to use chitosan as a thickener, especially since it is compatible with other biocompatible polymers such as PVA[186,187] and PEO.[188] Sometimes beads are observed when electrospinning. To counter this, additives such as salts[150] or surfactants[189] can be used. Similarly, cationic and anionic polyelectrolytes[190] could increase the conductivity of a solution and thus decrease fiber diameter. In 2006, Lin et al.[191] electrospun a combination of 1% chitosan with 5-8% PVA. The addition of chitosan was observed to reduce fiber diameter and yielded thinner, uniform, bead free fibers as noted by Lin et al. and Jia et al.[158,191] In 2007, Jia et al.,[158] and others,[149,192] additionally noted that electrospinning restricts the formation of a crystalline microstructure due to (1) the rapid solidification of the stretched molecular chains and (2) high elongation rates.

4.1.3C Chitosan/PEO. Duan et al.[174] noted that with a mass ratio of chitosan/PEO of 1/2 or 1/1, conductivity, surface tension, and solution viscosity enhanced electrospinning. FTIR, x-ray photoelectron spectroscopy (XPS), and differential scanning calorimetry (DSC) determined that the smaller fibers were primarily composed of chitosan while larger fibers were mainly composed of PEO. Around the same time, Spasova et al.[193] published the successful electrospinning of chitosan/PEO when the mass ratios were equal to or less than one. With increased amounts of chitosan, the fiber diameter increased, just as Duan[174] observed. Spasova et al.[193] also tested the effect of incorporating the broad-spectrum antimicrobial and antimycotic agent, potassium 5-nitro-8-quinolinolate (K5N8Q) against Gram negative and positive bacteria E. coli and S. aureus and the fungus C. albicans. Sterile zones were observed for the electrospun mats with K5N8Q, however no zones were observed for control samples.

Instead of adding chitosan as a thickener, Bhattrai et al. (2005)[194] added PEO to reduce the viscosity of chitosan solutions, therefore a higher polymer concentration would be spinnable. Chitosan/PEO mats (9/1) retained structural integrity in H_2O and promoted good adhesion of chondrocyte and osteoblast cells, and might be appropriate for bone tissue engineering. Bhattrai et al. noted that the solubility of PEO in water is desirable when fast degradation times are needed, such as for controlled drug release. Alternatively, when mechanical stability is necessary, like for tissue repair and remodeling, where cell attachment, differentiation, and growth are needed, a scaffold primarily composed of chitosan is more suitable. Vondran[195] has also electrospun mats of chitosan/PEO and evaluated the mechanical properties of as-spun and GA-vapor cross-linked[52] mats. Uniaxial tensile tests, nanoindentation, solubility studies, SEM studies, and FTIR analysis were conducted.

4.1.3D Chitosan/PET. Poly(ethylene terephthalate) (PET) is common in the textile and plastic industry due to its antibacterial properties,[196,197] mechanical properties, and fair biocompatibility. It has been used in cardiovascular implants such as artificial blood vessels and artificial heart sewing rings.[198] PET has also been electrospun solo.[199] In 2007, Jung et al.[200] fabricated chitosan/PET mats for medical applications. Using TFA/HFIP as the solvent, chitosan/PET, and chitin/PET were electrospun and antibacterial activity experiments were conducted. The mats that contained chitosan inhibited the growth much more effectively than both the pure PET and the chitin/PET non-wovens.

4.1.3E Chitosan Tri-component Systems. In 2004, Jiang et al.[201] spun ibuprofen-loaded PLGA/poly(ethylene glycol) (PEG)-*g*-chitosan mats appropriate for atrial fibrillation based on their ultrafine fibers, high porosity, and capability to conform to movements.[202] Fast degradation rates of the mats helped to prevent accumulation of byproducts on the delivery site. The ibuprofen was incorporated using two different methods

1. electrostatically conjugated during the electrospinning process; and
2. covalently conjugated to the PEG-*g*-chitosan prior to spinning.

Crosslinking was not necessary since the tri-component system was soluble in organic solvents, while being insoluble in neutral pH H_2O.[203] Within the system, the hydrophilicity, membrane shrinkage, and rate of drug release could be controlled.

Utilizing two syringes, Duan et al.[204] (2006) simultaneously electrospun PLGA for mechanical properties and chitosan/PVA for bioactivity onto a rotating drum. The as-spun fibers were crosslinked with 25% GA-vapor for 4 h at 37°C, and then the remainder of the exposed aldehyde groups were blocked by 0.1M glycine solution.[33] These systems have a potential in skin tissue engineering since they promoted fibroblast attachment and proliferation. Their fiber morphology, shrinkage, absorption in phosphate buffered solution, and mechanical properties were investigated. In 2007, Duan et al.[205] conducted a 10 wk in vitro degradation investigation in phosphate buffered solution, to determine the mechanical properties and functionality of the mats as a scaffold for human embryo skin fibroblasts (hESFs). More cells were on the composite mats than the pure PLGA scaffolds. Cellular penetration into the pores on the mats were observed after several days of culture.[206,207]

4.1.3F Chitosan Derivatives. A derivative of chitosan, hexanoyl chitosan is antithrombogenic and resistant to hydrolysis by lysosome,[208] therefore could be useful for medical applications.[209] Hexanoyl chitosan[210] was electrospun by Neamnark et al.[211] As-spun fibers had a ribbon-like morphology with diameters ranging from 0.64 to 3.93 μm. Rashkov et al. electrospun and crosslinked N-carboxyethyl (CE) chitosan/PVA[212,213] as well as quaternized (Q) chitosan/PVA[214] fiber mats. Both CE and Q chitosan fibrous mats show potential for tissue engineering applications.

CM chitosan is a functional derivative of the glucoasmine subunit of chitosan and has high moisture retention, gel-forming capability, antibacterial function, and lack of cytotoxicity.[215,216] CM chitosan is soluble in water[217,218] when prepared with reaction temperatures between 0 and 10°C. In 2007, Vondran[195] electrospun 3 wt% 1/1 CM chitosan/PEO in H_2O. Some beading was observed; the average fiber diameter was 118.19 ± 40.48 nm. SEM, FTIR, DSC, and solvatochromatic fluorescent dye studies were conducted.

4.1.4 Alginate and Hyaluronic Acid. It has been theorized that alginic acid (alginate) cannot be electrospun due to the repulsive forces that exists because of the polyelectrolyte character of alginate[219–221] and that solution viscosity is not the limiting factor.[219] To date, researchers have been unsuccessful in electrospinning the anionic biopolyelectrolyte, alginate. However, electrospinning of alginate fibers was successful when a carrier polymer was utilized. In 2006, after blending with PEO, Lu et al.[219] and Bhattarai et al.[222] as well as Safi et al.[220] in 2007 electrospun fibers containing alginate. The repulsive forces among the polyanionic molecules were reduced due to the blending

of solutions, as evident by conductivity changes and FTIR.[219] Also, the viscosity was reduced, and there was an increase in intermolecular interactions of the co-polymer through hydrogen bonding.[220] Bhattarai et al. utilized XRD to observe an increase in crystallinity that was most likely a result of the alginate chains realigning during the electrospinning process. The peaks noted were only those of the PEO.[222] Safi et al.[220] also demonstrated that blending with PVA had the same effects as PEO.

With some difficulties, nanofibers from an additional anionic biopolyelectrolyte, hyaluronic acid have been fabricated. Hsiao et al.[223,224] modified the electrospinning process to include an air blowing feature. They called their system an electro-blowing apparatus. It was theorized[223] that electrospinning of this biopolymer is challenging because aq hyaluronic acid solutions exhibit unusually high surface tension and viscosity. Hsiao et al.[225] were also able to use a traditional electrospinning apparatus to fabricate hyaluronic acid fibers in DMF/H_2O. A ratio of 1 or 1.5 generated an average fiber diameter of 200 nm or 250 nm, respectively.

4.1.5 Dextran. A bacterial polysaccharide, dextran consists of α -l,6 linked D-glucopyranose residues with some α-1, 2-, α-1, 3-, or α-1, 4-linked side chains; it has been explored for the delivery of drugs, proteins, and imaging agents.[226,227] Using a solvent solution of dimethyl sulfoxide (DMSO)/H_2O or DMSO/dimethylformamide (DMF) Hsiao et al.[228] electrospun methacrylated dextran[229] into mats with bovine serum albumin or lysozyme.

4.2 Proteins

Nature itself displays protein fibers as the quintessential part of motility, stabilization, elasticity, scaffolding, protection of cells, tissues, and organisms.[230] Despite being a major category of biopolymers, on which close to a century of research has been conducted, it is still challenging to process proteins into fibers. Proteins have complex macromolecular and three-dimensional structures in conjunction with strong inter- and intra- molecular forces. Despite this, efforts have been renewed due to advances in protein engineering. There is an increased understanding of how they function in biology, which has influenced researchers to transform these biopolymers into products for medical and other technical applications.[230,231]

4.2.1 Collagen and Gelatin. Collagen is the main structural component of the extracellular matrix of many native tissues.[232] In 2001, PEO was added to facilitate collagen electrospinning.[152] Initially, in 2004, Bowlin et al.,[232,233] electrospun type I collagen from calfskin and type III collagen isolated from human placenta with HFIP as the solvent. Various concentrations, input voltages, air gap separations, delivery rates, and mandrel motion were evaluated for their impacts on the collection of non-woven fibers. Pure elastin (bovine ligamentum nuchae), as well as blends of type I and III collagen with and without elastin were also electrospun since elastin alternates with collagen in many native tissues.[234] Aortic smooth muscle cells and dermal fibroblasts were seeded, as part of the three-layered vascular construct that Bowlin et al. fabricated. Type II collagen from lyophilized, chicken sternal cartilage was electrospun utilizing the same solvent, HFIP that spun types I and III. The mats were crosslinked using 3% vapor-GA.[235] Cell growth was demonstrated to occur, encouraging the use of the mats for the bioengineering of cartilage.[236] In 2007, Bowlin et al.[237] determined that crosslinking

with 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDC) dissolved in pure ethanol resulted in superior chemical and mechanical properties than those crosslinked with GA. Rho et al.[238] and Shih et al.[239] also electrospun type I collagen, utilizing vapor-GA and EDC to crosslink their as-spun mats respectively. Rho et al. experimented with cytocompatibility, cell behavior, cell interactions, and open wound healing on rats.[238] The morphology, growth, adhesion, motility, and osteogenic differentiation of human bone marrow-derived mesenchymal stem cells was studied on the fibrous mats spun by Shih et al.[239]

Additionally collagen-composite fibrous mats have been fabricated with PEO,[152,240] polycaprolactone (PCL),[207,241] chondroitin sulfate,[242] and chitosan.[243] Kidoaki et al.[244] fabricated tri-layered electrospun mats composed of type I collagen (from bovine skin), ST-gelatin as previously fabricated,[245,246] and segmented polyurethane by both multilayering and mixed electrospinning. This was conducted as a prototype scaffold for creating artificial grafts or other tissue engineering applications.

Gelatin has a quite similar composition and biological properties as collagen, from which it is derived. It is highly polar and therefore has a polyelectrolytic character. Additionally, while it readily dissolves in H_2O, gelatin could not be electrospun utilizing aq solutions.[206,247,248] In 2004, Ramakrishna et al.[206,247] electrospun 7.5% mass concentration gelatin in 2,2,2-trifluoroethanol to produce bead free fibers. The mechanical properties at various mass concentrations were tested. In one article[206] gelatin/PCL fibers were also electrospun and cell experimentation conducted, which could lead to tissue engineering applications. In 2005, gelatin was again electrospun but by utilizing a ratio of 49/1 FA/H_2O as the solvent. However, some degradation of the gelatin was observed.[248] FTIR and circular dichroism (CD) indicated that electrospun fibers had a random coil and helical conformation as confirmed by XRD and DSC. Li et al.[249] determined that 8% gelatin, 10% collagen, 20% tropoelastin, and 20% elastin in HFIP spun into bead-free fibers. Crosslinking for 1 h at room temperature was conducted utilizing 10% by volume 1,6-isocyanatohexane (HMDI) in isopropanol for mats on which cell studies were conducted; SEM, atomic force microscopy (AFM), and microtensile testing was additionally carried out.

4.2.2 Silk. Silks are spun into fibers by lepidoptera larvae including: silkworms, spiders, scorpions, mites and flies. Depending upon the source from which they are derived, they can vary in composition, structure, and properties. For example, the silk of various evolutionarily advanced spiders is comprised of different amino acid compositions and also have various mechanical properties as required for their particular function. These functions include lifeline support, web construction, lines for prey capture, etc. Bombyx mori (B. mori) are the most thoroughly studied silk producers whose silk has been used as a suture in biomedical applications for centuries[250] since it is biocompatible, biodegradable, has low inflammatory responses, and good oxygen and water vapor permeability.[251–253] Interest in using silk is due to its enhanced environmental stability, significant crystallinity, impressive combination of strength and toughness, high elasticity, and resistance to failure in compression (even when compared to Kevlar). However, they are insoluble in common solvents including: H_2O, dilute acids, and alkali.[250] Silk was first electrospun and patented by Zarkoob et al.[77,254] in 2000. PEO was added to facilitate the electrospinning of silk[151] in 2002 and silk/chitin[170] was electrospun in 2006. Park et al. electrospun chitosan/SF[255] before the solo electrospinning of chitosan was demonstrated (Table 4). Chitosan/SF (30/70) fibers were created using FA as a solvent and the effects of a

methanol treatment on the secondary structure of SF versus chitosan/SF fibers was investigated.

In addition, research regarding the electrospinning of silk and silk-containing nanofibers is outlined in Tables 5 and 6. Table 5 contains information regarding the source of the silk electrospun, the solvent used, interesting facts concerning the research conducted, and the reference (Ref). Table 6 contains other articles where the mechanical properties of electrospun silk were evaluated, since as noted, silk is historically known to have impressive strength. The table includes the solvent, post-electrospinning treatment, Young's modulus (MPa), elongation (%), tensile modulus (MPa), and reference (Ref).

4.2.3 Other Proteins. In addition to their work on collagen, Bowlin et al.[256] electrospun human and bovine fibrinogen fraction I from plasma in 9/1 HFIP/MEM (10X minimal essential medium) Earle's without L-glutamine and sodium bicarbonate at a concentration

Table 5
Contains information regarding electrospun silk, solvent used, research conducted, and reference (Ref)

Polymer(s)	Solvent	Research conducted	Ref
B. mori N. clavipes spiders	HFIP	8–1000 nm fiber diameters. stable under nitrogen: N. clavipes: 280.8ºC, B. mori: 245.8ºC	77, 268
Raw silk fibers	98% FA	50% aq methanol for crystallization: cell studies	88, 269
Fibroin silk fibers	98–100% FA	Effect of spinning parameters on fiber morphology & diameter	270, 271
B. mori/PEO/green fluorescent protein	H_2O	Potentially create fibers w/uniform non-linear optical properties	272
B. mori/PEO/BMP2 B. mori/PEO/ nHAP B. mori/ PEO/BMP2/nHAP	H_2O	hMSC growth & differentiation toward osteogenic outcomes highest Ca deposition & upregulation of BMP-2	92
B. mori/PEO	H_2O	Two-fluid e-spinning produced core/ shell fibers	273
B. mori in 9.3M LiBr	H_2O	Use of a concentrated aq solution to produce silk fibers	274
B. mori silk yarn	HFIP	Effects of vapor: H_2O, methanol, ethanol, & propanol	275
B. mori 1/1 B. mori/ wool keratose	98% FA	Post-spin methanol treatment displayed high performance for removing & recovering heavy metals ion from water	78
Thai silkworm Chinese/Japanese silkworm	85% FA	Mouse osteoblast-like cells appeared to adhere & proliferate possible bone scaffold	276

Abbreviations used on Table: BMP2 is bone morphogenetic protein 2, nHAP are nanoparticles of hydroxyapatite, and human bone marrow-derived mesenchymal stem cells is abbreviated hMSCs.

Table 6
Contains mechanical properties of electrospun silk solutions including solvent, post-electrospinning treatment, Young's modulus (MPa), elongation (%), tensile modulus (MPa), and reference (Ref)

Polymer(s)	Solvent	Treatment	Young's mod (MPa)	Elongation (%)	Tensile modulus (MPa)	Ref
B. mori	Hexa-fluoroacetone	None	15	40		277
S. c. ricini			20	40		
4/1 B. mori/PEO	H_2O	9/1 Methanol/H_2O	13.6 ± 1.4	4.0 ± 2.0	624.9 ± 0.9	278
B. mori/PEO	H_2O	None	*0.75 ± 0.06			279
		9/1 methanol/H_2O	*1.28 ± 0.08			
		H_2O extracted	*8 ± 2.98			
B. mori	98-100% FA	None	515	3.2	7.25	280
Silk yarn	HFIP	None	1.3 ± 0.2	7.6 ± 1.7	17.7 ± 6.8	281
		H_2O-vapor	2.6 ± 0.4	8.5 ± 2.0	30.4 ± 4.4	
		Methanol	4.6 ± 0.5	4.4 ± 0.7	104.3 ± 13.7	
Silk fibers	HFIP	9/1 methanol/H_2O	498.61 ± 15.84	5.54 ± 0.25	17.63 ± 1.73	282
Silk/1% type I collagen			$387\ 69 \pm 10.34$	6.26 ± 0.63	17.85 ± 1.54	
Silk/1% PLAGA			203.32 ± 9.67	9.86 ± 0.22	15.13 ± 1.4	

*Data acquired by AFM.

of 0.083 g/mL. SEM revealed an average fiber diameter of 80 ± 30 nm. Xie and Hsieh[231] electrospun casein, a milk protein with PEO or PVA and crosslinked the fibers with 4,4'-methylenebis(phenyl diisocyanate) (MDI) in THF. Lipase enzyme was successfully incorporated into PEO and PVA mats and demonstrated an increased catalytic activity towards hydrolyzing olive oil than cast films.

A wool protein, isolated as S-sulfo-kerateins was combined with PEO[257] and electrospun. A major protein of corn, zein[258] and zein/hyaluronic acid/PVA[259] were both dissolved into 7/3 ethanol/H_2O solution, electrospun, and the resultant fibrous mats crosslinked with hexamethylene diisocyanate (HDI). The goal is to use these materials for medical and packaging applications. Various polymer and solvent concentrations were evaluated by SEM and by tensile testing.

4.2.4 Polysaccharide/Protein Composites. In an effort to create a biomimetic of the extracellular matrix, Chen et al.[243] (2007) electrospun chitosan/collagen composite fibrous mats. At the time of this research both collagen and chitosan had been electrospun.[52,177,232,235,238] A 90/10 HFIP/TFA solvent mixture produced the best fibers. As the ratio of chitosan to collagen increased, fiber diameter decreased.

Also in 2007, Mo et al.[260] electrospun chitosan/collagen in HFIP/TFA as well as poly(L-lactid-co-ε-caprolactone) (P(LLA-CL)). Smooth muscle cells attached to the collagen nanofibers remained attached after 30 days of culture. As the chitosan/collagen ratio was varied, mechanical properties were measured using a Hounsfield H5K-S Testing system. Based upon the variation of stress-strain properties observed, theoretically a 50/50 ratio of chitosan/collagen ratio could be considered useful as a blood vessel scaffold whereas an 80/20 mat might be suitable for applications requiring flexibility such as skin tissue scaffolding.

4.3 Deoxyribonucleic Acid (DNA)

The only known nucleic acid to be electrospun is DNA, which is known to contain the genetic specificity of biological development of all living organisms.[261] The first known successful electrospinning of DNA was in 1997 by Fang and Reneker.[48] DNA fibers had previously been fabricated using conventional fiber techniques, such as wet-spinning.[262,263] Reneker electrospun 0.3-1.5% fibrous calf thymus Na-DNA (MW: 10^9 g/mol) in a mixture of 7/3 H_2O/ethanol. As thin as 30 nm fibers were observed, beads were also present. This was followed by Takahashi et al.[264] whom electrospun onto a mica surface large DNA molecules from a 7/3 H_2O/ethanol solutions and examined them using AFM. They discovered that the fibers had an average height of 1.8 nm and a length of 1 μm or longer. Hsiao et al.[93] in 2003 investigated a block co-polymer of PLA-*b*-PEG-*b*-PLA, in which plasmidic DNA was incorporated and then released structurally intact from the non-woven mat over a twenty day experiment. Craighead et al.[265] (2006) fabricated electrospun mats with stretched and oriented fluorescently labeled DNA molecules within PEO fibers. Recently, in 2007 Wallace et al.[266] electrospun DNA/PEO fibers ranging from 50 to 250 nm in diameter from an aq solution to study the conductivity, surface tension, and viscosity of the solutions.

5 Conclusion

Unquestionably, in the area of electrospinning, more progress has been made in the last decade than ever before, and the advances continue to occur. It has only been within

the 21st century that researchers have discovered how to successfully electrospin pure solutions of chitosan, cellulose, hyaluronic acid, etc. However, special processing such as degumming, irradiation, harsh solvents, elevated temperatures, etc, are often needed to spin biopolymers such as silk, chitin, and cellulose. However, once the biopolymers are spinning, they will precede with the same degree of ease. Alternatively, while hyaluronic acid and alginic acid easily dissolve in water, these aqueous solutions fail to electrospin. For this reason, blending with water soluble, biocompatible, synthetic polymer such as PLA or PVA is a good option as they can reduce repulsive forces within the charged biopolymer solutions and allow fiber spinning. Nonetheless, researchers are continuing to have a better understanding of what comprises an appropriate solution so that more biopolymers can be electrospun.

From this new knowledge, research has moved forward in many preliminary attempts towards functionalizing the biopolymer fibrous mats, for example, towards creating a biomimic of the extracellular matrix. However, specifically for this and other biomedical applications, the scaffolds must match the requirements of the tissues ranging from appropriate mechanical properties, degradation rate, optimized drug release profiles, as well as pore size, shape, and distribution. Once fabricated, all pure-biopolymer and composite fibrous mats will have unique topological, mechanical, and chemical properties. Additionally, the capability of a cell to adhere and proliferate on these mats will vary. It is important to remember that anytime something is implanted, a foreign body response is expected.

The as-spun fibrous mats have easily been modified. For example, chitosan has been crosslinked or neutralized to gain the chemical stability of chitin mats. Vitamins have successfully been loaded into cellulose acetate fibers and plasmidic DNA can be incorporated and then released from PLA-*b*-PEG-*b*-PLA non-wovens. However, more analysis and head-to-head comparison concerning the functionality and biodegradability of these fibrous mats is necessary. For example, chitosan and alginic acid are known chelators. However, it is unclear at the present time which is a more effective heavy metal chelator: a fibrous mat composed purely of chitosan or a composite of alginic acid/PEO. In terms of effectiveness, many factors must be taken into consideration, including: detection limits, metal selectivity, chemical and mechanical stability, and cost effectiveness. Also, an understanding of how to integrate these fibers as a component of a hierarchical assembly of well assembled nanostructures and devices that can function as a filter or as advanced coatings, nanofillers, or nanocomposites is needed.

For large-scale manufacturing of new products containing these biopolymer nanofibers to occur, a few significant challenges also need to be addressed. Methodology to fabricate reproducible, uniform nanofibers, which have particular morphologies, mechanical and chemical properties, that are oriented for the demands of particular tasks remains a work in progress. While the advancements in fabricating biopolymer non-wovens are appreciated, much work still remains.

Acknowledgment

JDS would like to thank the National Science Foundation-Integrative Graduate Education and Research Traineeship (NSF IGERT) (DGE-0221664) and Graduate Assistance in Areas of National Need-Drexel Research and Education in Advanced Materials (GAANN-DREAM) (P200A060117) which is funded by the Department of Education's Office of Postsecondary Education for funding.

References

1. Mohanty, A. K.; Misra, M.; Drzal, L. T. "Sustainable bio-composites from renewable resources: Opportunities and challenges in the green materials world", *J. Polym. Environ.* **2002**, *10*, 19–26.
2. Kaplan, D. L. *Biopolymers from Renewable Resources*; Springer: New York, 1998.
3. Rinaudo, M. "Chitin and chitosan: Properties and applications", *Prog. Polym. Sci.* **2006**, *31*, 603–632.
4. Kumar, M. N. V. R. "A review of chitin and chitosan applications", *React. Funct. Polym.* **2000**, *46*, 1–27.
5. Subbiah, T.; Bhat, G. S.; Tock, R. W.; Parameswaran, S.; Ramkumar, S. S. "Electrospinning of nanofibers", *J. Appl. Polym. Sci.* **2005**, *96*, 557–569.
6. Berger, J.; Reist, M.; Mayer, J. M.; Felt, O.; Peppas, N. A.; Gurny, R. "Structure and interactions in covalently and ionically crosslinked chitosan hydrogels for biomedical applications", *Eur. J. Pharm. Biopharm.* **2004**, *57*, 19–34.
7. Chirkov, S. N. "The antiviral activity of chitosan (review)", *Appl. Biochem. Micro +* . **2002**, *38*, 1–8.
8. Dodane, V.; Vilivalam, V. D. "Pharmaceutical applications of chitosan", *Pharm. Sci. Technol. To.* **1998**, *1*, 246–253.
9. Vartiainen, J.; Motion, R.; Kulomen, H.; Ratto, M.; Skytta, E.; Ahvenainen, R. "Chitosan-coated paper: Effects of nisin and different acides on the antimicrobial activity", *J. Appl. Polym. Sci.* **2004**, *94*, 986–993.
10. Huang, Z. M.; Zhang, Y. Z.; Kotaki, M.; Ramakrishna, S. "A review on polymer nanofibers by electrospinning and their applications in nanocomposites", *Compos. Sci. Technol.* **2003**, *63*, 2223–2253.
11. Tolaimate, A.; Desbrieres, J.; Rhazi, M.; Alagui, A.; Vincendon, M.; Vottero, P. "On the influence of deacetylation process on the physicochemical characteristics of chitosan from squid chitin", *Polymer* **2000**, *41*, 2463–2469.
12. Zhang, M.; Haga, A.; Sekiguchi, H.; Hirano, S. "Structure of insect chitin isolated from beetle larva cuticle and silkworm (bombyx mori) pupa exuvia", *Int. J. Biol. Macromol.* **2000**, *27*, 99–105.
13. Wu, T.; Zivanovic, S.; Draughon, F. A.; Sams, C. E. "Chitin and chitosan-value-added products from mushroom waste", *J. Agric. Food Chem.* **2004**, *52*, 7905–7910.
14. Pochanavanich, P.; Suntornsuk, W. "Fungal chitosan production and its characterization", *Lett. Appl. Microbiol.* **2002**, *35*, 17–21.
15. Suntornsuk, W.; Pochanavanich, P.; Suntornsuk, L. "Fungal chitosan production on food processing by-products", *Process Biochem.* **2002**, *37*, 727–729.
16. Nwe, N.; Stevens, W. F. "Effect of urea on fungal chitosan production in solid substrate fermentation", *Process Biochem.* **2004**, *39*, 1639–1642.
17. Teng, W. L.; Khor, E.; Tan, T. K.; Lim, L. Y.; Tan, S. C. "Concurrent production of chitin from shrimp shells and fungi", *Carbohydr. Res.* **2001**, *332*, 305–316.
18. Jaworska, M.; Sakurai, K.; Gaudon, P.; Guibal, E. "Influence of chitosan characteristics on polymer properties. I: Crystallographic properties", *Polym. Int.* **2003**, *52*, 198–205.
19. Ogawa, K.; Yui, T.; Okuyama, K. "Three D structures of chitosan", *Int. J. Biol. Macromol.* **2004**, *34*, 1–8.
20. Daly, W. H. *Polymers from Biobased Materials*; H. L. Chun Noyles, Data Corporation: Park Ridge, 1991, pp. 81–89.
21. Modrzejewska, Z.; Eckstein, W. "Chitosan hollow fiber membranes", *Biopolymers* **2004**, *73*, 61–68.
22. Knaul, J. Z.; Creber, K. A. M. "Coagulation rate studies of spinnable chitosan solutions", *J. Appl. Polym. Sci.* **1997**, *66*, 117–127.
23. Qin, Y.; Zhu, C.; Chen, J.; Zhong, J. "Preparation and characterization of silver containing chitosan fibers", *J. Appl. Polym. Sci.* **2007**, *104*, 3622–3627.

24. El-Tahlawy, K.; Hudson, S. M. "Chitosan: Aspects of fiber spinnability", *J. Appl. Polym. Sci.* **2006**, *100*, 1162–1168.
25. Tuzlakoglu, K.; Alves, C. M.; Mano, J. F.; Reis, R. L. "Production and characterization of chitosan fibers and 3-D fiber mesh scaffolds for tissue engineering applications", *Macromol. Biosci.* **2004**, *4*, 811–819.
26. Lee, S.-H.; Park, S.-Y.; Choi, J.-H. "Fiber formation and physical properties of chitosan fiber crosslinked by epichlorohydrin in a wet spinning system: The effect of the concentration of the crosslinking agent epichlorohydrin", *J. Appl. Polym. Sci.* **2004**, *92*, 2054–2062.
27. Knaul, J.; Hooper, M.; Chanyi, C.; Creber, K. A. M. "Improvements in the drying process for wet-spun chitosan fibers", *J. Appl. Polym. Sci.* **1998**, *69*, 1435–1444.
28. Kim, Y. J.; Yoon, K. J.; Ko, S. W. "Preparation and properties of alginate superabsorbent filament fibers crosslinked with glutaraldehyde", *J. Appl. Polym. Sci.* **2000**, *78*, 1797–1804.
29. Yimin, Q. "Alginate fibres: An overview of the production processes and applications in wound management", *Polym. Int.* **2007**, *9999*, n/a.
30. Tong, D. P. "Process for the production of alginate fibre material and products made" **1985**.
31. Marsano, E.; Conio, G.; Martino, R.; Turturro, A.; Bianchi, E. "Fibers based on cellulose-chitin blends", *J. Appl. Polym. Sci.* **2002**, *83*, 1825–1831.
32. Fan, L.; Du, Y.; Zhang, B.; Yang, J.; Zhou, J.; Kennedy, J. F. "Preparation and properties of alginate/carboxymethyl chitosan blend fibers", *Carbohydr. Polym.* **2006**, *65*, 447–452.
33. Chen, G.; Sato, T.; Ushida, T.; Hirochika, R.; Shirasaki, Y.; Ochiai, N.; Tateishi, T. "The use of a novel plga fiber/collagen composite web as a scaffold for engineering of articular cartilage tissue with adjustable thickness", *J Biomed. Mater. Res. A* **2003**, *67A*, 1170–1180.
34. Wang, Q.; Du, Y.; Hu, X.; Yang, J.; Fan, L.; Feng, T. "Preparation of aginate/soy protein isolate blend fibers through a novel coagulation bath", *J. Appl. Polym. Sci.* **2005**, *101*, 4251–4431.
35. Ma, P. X.; Zhang, R. "Synthetic nano-scale fibrous extracellular matrix", *J. Biomed. Mater. Res.* **1999**, *46*, 60–72.
36. Nakata, K.; Fujii, K.; Ohkoshi, Y.; Gotoh, Y.; Nagura, M.; Numata, M.; Kamiyama, M. "Poly(-ethylene terephthalate) nanofibers made by sea-island-type conjugated melt spinning and laser-heated flow drawing", *Macromol. Rapid Commun.* **2007**, *28*, 792–795.
37. Ondarçuhu, T.; Joachim, C. "Drawing a single nanofibre over hundreds of microns", *Europhys. Lett.* **1998**, *42*, 215–220.
38. Duvail, J. L.; Retho, P.; Garreau, S.; Louarn, G.; Godon, C.; Demoustier-Champagne, S. "Transport and vibrational properties of poly(3,4-ethylenedioxythiophene) nanofibers", *Synth. Met.* **2002**, *131*, 123–128.
39. Wu, C.-G.; Bein, T. "Conducting polyaniline filaments in a mesoporous channel host", *Science* **1994**, *264*, 1757–1759.
40. Feng, L.; Li, S.; Li, H.; Zhai, J.; Song, Y.; Jiang, L.; Zhu, D. "Super-hydrophobic surface of aligned polyacrylonitrile nanofibers", *Angew. Chem. Int. Ed.* **2002**, *41*, 1221–1223.
41. Liu, D.; Zhang, H.; Grim, P. C. M.; De Feyter, S.; Wiesler, U. M.; Berresheim, A. J.; Mullen, K.; De Schryver, F. C. "Self-assembly of polyphenylene dendrimers into micrometer long nanofibers: An atomic force microscopy study", *Langmuir* **2002**, *18*, 2385–2391.
42. Liu, G.; Qiao, L.; Guo, A. "Diblock copolymer nanofibers", *Macromolecules* **1996**, *29*, 5508–5510.
43. Yan, X.; Liu, G.; Liu, F.; Tang, B. Z.; Peng, H.; Pakhomov, A. B.; Wong, C. Y. "Superparamagnetic triblock copolymer/Fe_2O_3 hybrid nanofibers", *Angew. Chem. Int. Ed.* **2001**, *40*, 3593–3596.
44. Hartgerink, J. D.; Beniash, E.; Stupp, S. I. "Self-assembly and mineralization of peptide-amphiphile nanofibers", *Science* **2001**, *294*, 1684–1688.
45. Masuda, M.; Hanada, T.; Okada, Y.; Yase, K.; Shimizu, T. "Polymerization in nanometer-sized fibers: Molecular packing order and polymerizability", *Macromolecules* **2000**, *33*, 9233–9238.

46. Baumgarten, P. K. "Electrostatic spinning of acrylic microfibers", *J. Colloid Interface Sci.* **1971**, *36*, 71–79.
47. Formhals, A. "Process and apparatus for preparing artificial threads", **1934**.
48. Fang, X.; Reneker, D. H. "DNA fibers by electrospinning", *J. Macromol. Sci., Phys.* **1997**, *36*, 169–173.
49. Greiner, A.; Wendorff, JoachimH. "Electrospinning: A fascinating method for the preparation of ultrathin fibers", *Angew. Chem. Int. Ed.* **2007**, *46*, 5670–5703.
50. Jayaraman, K.; Kotaki, M.; Zhang, Y.; Mo, X.; Ramakrishnab, S. "Recent advances in polymer nanofibers", *J. Nanosci. Nanotechnol.* **2004**, *4*, 52–65.
51. Ramakrishna, S.; Fujihara, K.; Teo, W.-E.; Lim, T.-C.; Ma, Z. *An Introduction to Electrospinning and Nanofibers*; World Scientific Printing Co. Pte. Ltd: Singapore, 2005.
52. Schiffman, J. D.; Schauer, C. L. "Cross-linking chitosan nanofibers", *Biomacromolecules* **2007**, *8*, 594–601.
53. Schiffman, J. D.; Schauer, C. L. "One-step electrospinning of cross-linked chitosan fibers", *Biomacromolecules* **2007**, *8*, 2665–2667.
54. Schiffman, J. D. *Masters of Engineering*; Cornell University, 2004.
55. Li, L.; Bellan, L. M.; Craighead, H. G.; Frey, M. W. "Formation and properties of nylon-6 and nylon-6/montmorillonite composite nanofibers", *Polymer* **2006**, *47*, 6208–6217.
56. Ji, Y.; Li, B.; Ge, S.; Sokolov, J. C.; Rafailovich, M. H. "Structure and nanomechanical characterization of electrospun PS/clay nanocomposite fibers", *Langmuir* **2006**, *22*, 1321–1328.
57. Gopal, R.; Kaur, S.; Feng, C. Y.; Chan, C.; Ramakrishna, S.; Tabe, S.; Matsuura, T. "Electrospun nanofibrous polysulfone membranes as pre-filters: Particulate removal", *J. Membr. Sci.* **2007**, *289*, 210–219.
58. Wannatong, L.; Sirivat, A.; Supaphol, P. "Effects of solvents on electrospun polymeric fibers: Preliminary study on polystyrene", *Polym. Int.* **2004**, *53*, 1851–1859.
59. Kim, K. W.; Lee, K. H.; Khil, M. S.; Ho, Y. S.; Kim, H. Y. "The effect of molecular weight and the linear velocity of drum surface on the properties of electrospun poly(ethylene terephthalate) nonwovens", *Fibers and Polymers* **2004**, *5*, 122–127.
60. Chew, S. Y.; Wen, J.; Yim, E. K. F.; Leong, K. W. "Sustained release of proteins from electrospun biodegradable fibers", *Biomacromolecules* **2005**, *6*, 2017–2024.
61. Kenawy, E. R.; Layman, J. M.; Watkins, J. R.; Bowlin, G. L.; Matthews, J. A.; Simpson, D. G.; Wnek, G. E. "Electrospinning of poly(ethylene-co-vinyl alcohol) fibers", *Biomaterials* **2003**, *24*, 907–913.
62. Shin, Y. M.; Hohman, M. M.; Brenner, M. P.; Rutledge, G. C. "Experimental characterization of electrospinning: The electrically forced jet and instabilities", *Polymer* **2001**, *42*, 09955–09967.
63. Taylor, G. "Disintegration of water drops in an electric field", *Proc. R. Soc. London, Ser. A* **1964**, *280*, 383–397.
64. Reneker, D. H.; Yarin, A. L.; Fong, H.; Koombhongse, S. "Bending instability of electrically charged liquid jets of polymer solutions in electrospinning", *J. Appl. Phys.* **2000**, *87*, 4531–4547.
65. Li, D.; McCann, J. T.; Xia, Y. "Electrospinning: A simple and versatile technique for producing ceramic nanofibers and nanotubes", *J. Am. Ceram. Soc.* **2006**, *89*, 1861–1869.
66. Li, D.; Wang, Y.; Xia, Y. "Electrospinning of polymeric and ceramic nanofibers as uniaxially aligned arrays", *Nano Lett.* **2003**, *3*, 1167–1171.
67. Theron, A.; Zussman, E.; Yarin, A. L. "Electrostatic field-assisted alignment of electrospun nanofibres", *Nanotechnology* **2001**, 384.
68. Teo, W. E.; Ramakrishna, S. "A review on electrospinning design and nanofibre assemblies", *Nanotechnology* **2006**, *17*, R89–R106.
69. Li, D.; Wang, Y.; Xia, Y. "Electrospinning nanofibers as uniaxially aligned arrays and layer-by-layer stacked films", *Adv. Mater.* **2004**, *16*, 361–366.
70. Li, D.; Ouyang, G.; McCann, J. T.; Xia, Y. "Collecting electrospun nanofibers with patterned electrodes", *Nano Lett.* **2005**, *5*, 913–916.

71. Pham, Q. P.; Sharma, U.; Mikos, A. G. "Electrospinning of polymeric nanofibers for tissue engineering applications: A review", *Tissue Eng.* **2006**, *12*, 1197–1211.
72. Theron, S. A.; Yarin, A. L.; Zussman, E.; Kroll, E. "Multiple jets in electrospinning: Experiment and modeling", *Polymer* **2005**, *46*, 2889–2899.
73. Ding, B.; Kimura, E.; Sato, T.; Fujita, S.; Shiratori, S. "Fabrication of blend biodegradable nanofibrous nonwoven mats via multi-jet electrospinning", *Polymer* **2004**, *45*, 1895–1902.
74. Chiu, J.; Luu, Y. K.; Hsiao, B. S.; Chu, B.; Hadjiargyrou, M. "Electrospun nanofibrous scaffolds for biomedical applications", *J. Biomed. Nanotechnol.* **2005**, *1*, 115–132.
75. He, J.-H.; Wan, Y.-Q.; Xu, L. "Nano-effects, quantum-like properties in electrospun nanofibers", *Chaos, Solitons & Fractals* **2007**, *33*, 26–37.
76. Bean, C. P.; Livingston, J. D. "Superparamagnetism", *J. Appl. Phys.* **1959**, *30*, 120S–129S.
77. Zarkoob, S.; Reneker, R. H.; Eby, R. K.; Hudson, S. D.; Erley, D.; Adams, W. W. U.S. Patent 6,110,590, 2000.
78. Ki, C. S.; Gang, E. H.; Um, I. C.; Park, Y. H. "Nanofibrous membrane of wool keratose/silk fibroin blend for heavy metal ion adsorption", *J. Membr. Sci.* **2007**, *302*, 20–26.
79. Bognitzki, M.; Hou, H.; Ishaque, M.; Frese, T.; Hellwig, M.; Schwarte, C.; Schaper, A.; Wendorff, J. H.; Greiner, A. "Polymer, metal, and hybrid nano- and mesotubes by coating degradable polymer template fibers (TUFT process)", *Adv. Mater.* **2000**, *12*, 637–640.
80. Caruso, R. A.; Schattka, J. H.; Greiner, A. "Titanium dioxide tubes from sol-gel coating of electrospun polymer fibers", *Adv. Mater.* **2001**, *13*, 1577–1579.
81. Muller, K.; Quinn, J. F.; Johnston, A. P. R.; Becker, M.; Greiner, A.; Caruso, F. "Polyelectrolyte functionalization of electrospun fibers", *Chem. Mater.* **2006**, *18*, 2397–2403.
82. Gibson, P.; Schreuder-Gibson, H.; Rivin, D. "Transport properties of porous membranes based on electrospun nanofibers", *Colloids Surf., A* **2001**, *187–188*, 469–481.
83. McCann, J. T.; Marquez, M.; Xia, Y. "Highly porous fibers by electrospinning into a cryogenic liquid", *J. Am. Chem. Soc.* **2005**, *128*, 1436–1437.
84. Casper, C. L.; Stephens, J. S.; Tassi, N. G.; Chase, D. B.; Rabolt, J. F. "Controlling surface morphology of electrospun polystyrene fibers: Effect of humidity and molecular weight in the electrospinning process", *Macromolecules* **2004**, *37*, 573–578.
85. Bognitzki, M.; Czado, W.; Frese, T.; Schaper, A.; Hellwig, M.; Steinhart, M.; Greiner, A.; Wendorff, J. H. "Nanostructured fibers via electrospinning", *Adv. Mater.* **2001**, *13*, 70–72.
86. Dayal, P.; Kyu, T. "Porous fiber formation in polymer-solvent system undergoing solvent evaporation", *J. Appl. Phys.* **2006**, *100,* 043512 043511–043516.
87. Khil, M. S.; Cha, D. I.; Kim, H. Y.; Kim, I. S.; Bhattarai, N. "Electrospun nanofibrous polyurethane membrane as wound dressing", *J Biomed Mater Res B Appl Biomater* **2003**, *67B*, 675–679.
88. Kim, S. H.; Nam, Y. S.; Lee, T. S.; Park, W. H. "Silk fibroin nanofiber. Electrospinning, properties, and structure", *The Society of Polymer Science, Japan* **2003**, *35*, 185–190.
89. Li, W. J.; Laurencin, C. T.; Caterson, E. J.; Tuan, R. S.; Ko, F. K. "Electrospun nanofibrous structure: A novel scaffold for tissue engineering", *J. Biomed. Mater. Res.* **2002**, *60*, 613–621.
90. Zeng, J.; Xu, X.; Chen, X.; Liang, Q.; Bian, X.; Yang, L.; Jing, X. "Biodegradable electrospun fibers for drug delivery", *J. Controlled Release* **2003**, *92*, 227–231.
91. Verreck, G.; Chun, I.; Rosenblatt, J.; Peeters, J.; Dijck, A. V.; Mensch, J.; Noppe, M.; Brewster, M. E. "Incorporation of drugs in an amorphous state into electrospun nanofibers composed of a water-insoluble, nonbiodegradable polymer", *J. Controlled Release* **2003**, *92*, 349–360.
92. Li, C.; Vepari, C.; Jin, H.-J.; Kim, H. J.; Kaplan, D. L. "Electrospun silk-BMP-2 scaffolds for bone tissue engineering", *Biomaterials* **2006**, *27*, 3115–3124.
93. Luu, Y. K.; Kim, K.; Hsiao, B. S.; Chu, B.; Hadjiargyrou, M. "Development of a nanostructured DNA delivery scaffold via electrospinning of PLGA and PLA-PEG block copolymers", *J. Controlled Release* **2003**, *89*, 341–353.

94. Murphy, W. L.; Peters, M. C.; Kohn, D. H.; Mooney, D. J. "Sustained release of vascular endothelial growth factor from mineralized poly(lactide-co-glycolide) scaffolds for tissue engineering", *Biomaterials* **2000**, *21*, 2521–2527.
95. Rosenberg, M. D. "Cell guidance by alterations in monomolecular films", *Science* **1963**, *139*, 411–412.
96. Jia, H.; Zhu, G.; Vugrinovich, B.; Kataphinan, W.; Reneker, D. H.; Wang, P. "Enzyme-carrying polymeric nanofibers prepared via electrospinning for use as unique biocatalysts", *Biotechnol. Prog.* **2002**, *18*, 1027–1032.
97. Burger, C.; Hsiao, B. S.; Chu, B. "Nanofibrous materials and their applications", *Annu. Rev. Mater. Res.* **2006**, *36*, 333–368.
98. Yang, S.; Leong, K. F.; Du, Z.; Chua, C. K. "The design of scaffolds for use in tissue engineering. Part I. Traditional factors", *Tissue Eng.* **2001**, *7*, 679–689.
99. Boudriot, U.; Dersch, R.; Greiner, A.; Wendorff, J. H. "Electrospinning approaches toward scaffold engineering—a brief overview", *Artif. Organs* **2006**, *30*, 785–792.
100. Stevens, M. J.; Plimpton, S. J. "The effect of added salt on polyelectrolyte structure", *The European Physics Journal B* **1998**, *2*, 341–245.
101. de Gennes, P. G. *Scaling Concepts in Polymer Physics*; Cornell University Press: Ithaca, 1979.
102. Micka, U.; Kremer, K. "Persistence length of the Debye-Huckel model of weakly charged flexible polyelectrolyte chains", *Physical Review E* **1996**, *54*, 2653.
103. Mann, B. A.; Everaers, R.; Holm, C.; Kremer, K. "Scaling in polyelectrolyte networks", *Europhys. Lett.* **2004**, *67*, 786–792.
104. Holm, C.; Joanny, J. F.; Kremer, K.; Netz, R. R.; Reineker, P.; Seidel, C.; Vilgis, T. A.; Winkler, R. G. *Polyelectrolytes with Defined Molecular Architecture II*; Springer: Berlin, 2004; pp. 67–111.
105. Hon, D. N. S. "Cellulose: A random walk along its historical path", *Cellulose* **1994**, *1*, 1–25.
106. Johnson, D. C.; Nicholson, M. D.; Haigh, F. C. U.S. Patent 3,447,939, 1969.
107. Hata, K. U.S. Patent 3,424,702, 1969.
108. Kulpinski, P. "Cellulose nanofibers prepared by the N-methylmorpholine-N-oxide method", *J. Appl. Polym. Sci.* **2005**, *98*, 1855–1859.
109. Roder, T.; Morgenstern, B.; Schelosky, N.; Glatter, O. "Solutions of cellulose in N,N-dimethylacetamide/lithium chloride studied by light scattering methods", *Polymer* **2001**, *42*, 6765–6773.
110. Turbak, A. F.; El-Kafrawy, A.; Snyder, F. W.; Auerbach, A. B. U.S. Patent 4,302,252, 1981.
111. Klemm, D.; Heublein, B.; Fink, H.-P.; Bohn, A. "Cellulose: Fascinating biopolymer and sustainable raw material", *Angew. Chem. Int. Ed.* **2005**, *44*, 3358–3393.
112. Kang, V. S.; Kim, H. Y.; Ryu, Y. J.; Lee, D. R. "Manufacturing the cellulose web by using electro-spinning and in-vitro behaviour of oxidized cellulose web", *Journal of the Korean Fiber Society* **2002**, *39*, 14–20.
113. Kim, C. W.; Frey, M. W.; Marquez, M.; Joo, Y. L. "Preparation of submicron-scale, electrospun cellulose fibers via direct dissolution", *J. Polym. Sci., Part B: Polym. Phys.* **2005**, *43*, 1673–1683.
114. Matsumoto, T.; Tatsumi, D.; Tamai, N.; Takaki, T. "Solution properties of celluloses from different biological origins in LiCl · DMAc", *Cellulose* **2002**, *8*, 243–320.
115. El-Kafrawy, A. "Investigation of the cellulose/LiCl/dimethylacetamide and cellulose/LiCl/N-methyl-2-pyrrolidinone solutions by 13C NMR spectroscopy", *J. Appl. Polym. Sci.* **1982**, *27*, 2435–2443.
116. Kim, D. B.; Lee, W. S.; Jo, S. M.; Lee, Y. M.; Kim, B. C. "Physical properties of lyocell fibers spun from different solution-dope phases", *J. Appl. Polym. Sci.* **2002**, *83*, 981–989.
117. Biganska, O.; Navard, P. "Phase diagram of a cellulose solvent: N-methylmorpholine-n-oxide-water mixtures", *Polymer* **2003**, *44*, 1035–1039.
118. Morgenstern, B.; Kammer, H.-W. "Solvation in cellulose LiCl-DMAc solutions", *Trends Polym. Sci.* **1996**, *4*, 87–92.

119. Kim, C.-W.; Kim, D.-S.; Kang, S.-Y.; Marquez, M.; Joo, Y. L. "Structural studies of electrospun cellulose nanofibers", *Polymer* **2006**, *47*, 5097–5107.
120. Banker, G. S.; Kumar, V. U.S. Patent 5,405,953, 1995.
121. Wiseman, D. M.; Saferstein, L.; Wolf, S. U.S. Patent 6,500,777, 2002.
122. Galgut, P. N. "Oxidized cellulose mesh: I. Biodegradable membrane in periodontal surgery", *Biomaterials* **1990**, *11*, 561–564.
123. Edgar, K. J.; Buchanan, C. M.; Debenham, J. S.; Rundquist, P. A.; Seiler, B. D.; Shelton, M. C.; Tindall, D. "Advances in cellulose ester performance and application", *Prog. Polym. Sci.* **2001**, *26*, 1605–1688.
124. Jaeger, R.; Bergshoef, M. M.; Batlle, C. M. i.; Schoenherr, H.; Vansco, G. J. "Electrospinning of ultra thin polymer fibers", *Macromol. Symp.* **1998**, *127*, 141–150.
125. Liu, H.; Hsieh, Y. L. "Ultrafine fibrous cellulose membranes from electrospinning of cellulose acetate", *J. Polym. Sci., Part B: Polym. Phys.* **2002**, *40*, 2119–2129.
126. Son, W. K.; Youk, J. H.; Lee, T. S.; Park, W. H. "Electrospinning of ultrafine cellulose acetate fibers: Studies of a new solvent system and deacetylation of ultrafine cellulose acetate fibers", *J. Polym. Sci., Part B: Polym. Phys.* **2004**, *42*, 5–11.
127. Son, W. K.; Youk, J. H.; Park, W. H. "Preparation of ultrafine oxidized cellulose mats via electrospinning", *Biomacromolecules* **2004**, *5*.
128. Banker, G. S.; Kumar, V. U.S. Patent 5,780,618, 1998.
129. Yang, Q. B.; Li, D. M.; Hong, Y. L.; Li, Z. Y.; Wang, C.; Qiu, S. L.; Wei, Y. "Preperation and characterization of a PAN nanofibre containing Ag nanoparticles via electrospinning", *Synth. Met.* **2003**, *137*, 973–974.
130. Sondi, I.; Salopek-Sondi, B. "Silver nanoparticles as antimicrobial agent: A case study on e. Coli as a model for gram-negative bacteria", *J. Colloid Interface Sci.* **2004**, *275*, 177–182.
131. Balogh, L.; Swanson, D. R.; Tomalia, D. A.; Hagnauer, G. L.; McManus, A. T. "Dendrimer-silver complexes and nanocomposites as antimicrobial agents", *Nano Lett.* **2001**, *1*, 18–21.
132. Son, W. K.; Youk, J. H.; Lee, T. S.; Park, W. H. "Preparation of antimicrobial ultrafine cellulose acetate fibers with silver nanoparticles", *Macromol. Rapid Commun.* **2004**, *25*, 1632–1637.
133. Ma, Z.; Kotaki, M.; Ramakrishna, S. "Electrospun cellulose nanofiber as affinity membrane", *J. Membr. Sci.* **2005**, *265*, 115–123.
134. Xiang, C.; Frey, M. W.; Taylor, A. G.; Rebovich, M. E. "Selective chemical absorbance in electrospun nonwovens", *J. Appl. Polym. Sci.* **2007**, *106*, 2363–2370.
135. Taepaiboon, P.; Rungsardthong, U.; Supaphol, P. "Vitamin-loaded electrospun cellulose acetate nanofiber mats as transdermal and dermal therapeutic agents of vitamin A acid and vitamin E", *Eur. J. Pharm. Biopharm.* **2007**, *67*, 387–397.
136. Cho, S.; Lowe, L.; Hamilton, T. A.; Fisher, G. J.; Voorhees, J. J.; Kang, S. "Long-term treatment of photoaged human skin with topical retinoic acid improves epidermal cell atypia and thickens the collagen band in papillary dermis", *J. Am. Acad. Dermatol.* **2005**, *53*, 769–774.
137. Shapiro, S. S.; Saliou, C. "Role of vitamins in skin care", *Nutrition* **2001**, *17*, 839–844.
138. Tungprapa, S.; Jangchud, I.; Supaphol, P. "Release characteristics of four model drugs from drug-loaded electrospun cellulose acetate fiber mats", *Polymer* **2007**, *48*, 5030–5041.
139. Zhao, S.; Wu, X.; Wang, L.; Huang, Y. "Electrospinning of ethyl-cyanoethyl cellulose/tetrahydrofuran solutions", *J. Appl. Polym. Sci.* **2004**, *91*, 242–246.
140. Huang, Y.; Chen, M. C.; Li, L. S. "Study on lyotropic liquid crystal of ethyl-cyanoethyl cellulose", *Acta Chim Sinica* **1988**, *46*, 367–371.
141. Wu, X.; Wang, L.; Yu, H.; Huang, Y. "Effect of solvent on morphology of electrospinning ethyl cellulose fibers", *J. Appl. Polym. Sci.* **2005**, *97*, 1292–1297.
142. Li, X.; Liu, H.; Wang, J.; Cui, H.; Zhang, X.; Han, F. "Preparation of YAG:Nd nano-sized powder by co-precipitation method", *Materials Science and Engineering: A* **2004**, *379*, 347–350.

143. Shukla, S.; Brinley, E.; Cho, H. J.; Seal, S. "Electrospinning of hydroxypropyl cellulose fibers and their application in synthesis of nano and submicron tin oxide fibers", *Polymer* **2005**, *46*, 12130–12145.
144. Griffith, L. G. "Polymeric biomaterials", *Acta Materialia* **2000**, *48*, 263–277.
145. Yoshii, F.; Zhanshan, Y.; Isobe, K.; Shinozaki, K.; Makuuchi, K. "Electron beam crosslinked PEO and PEO/PVA hydrogels for wound dressing", *Radiat. Phys. Chem.* **1999**, *55*, 133–138.
146. Sims, C. D.; Butler, P. E.; Casanova, R.; Lee, B.; Randolph, M.; Lee, A. W. P.; Vacanti, C. A.; Yaremchuk, M. J. "Injectable cartilage using polyethylene oxide polymer substrates", *Plast. Reconstr. Surg.* **1996**, *98*, 843–850.
147. Doshi, J.; Reneker, D. H. "Electrospinning process and applications of electrospun fibers", *Journal of Electrostatics* **1995**, *35*, 151–160.
148. Deitzel, J. M.; Kleinmeyer, J. D.; Hirvonen, J. K.; Beck Tan, N. C. "Controlled deposition of electrospun poly(ethylene oxide) fibers", *Polymer* **2001**, *42*, 8163–8170.
149. Deitzel, J. M.; Kleinmeyer, J.; Harris, D.; Beck Tan, N. C. "The effect of processing variables on the morphology of electrospun nanofibers and textiles", *Polymer* **2001**, *42*, 261–272.
150. Fong, H.; Chun, I.; Reneker, D. H. "Beaded nanofibers formed during electrospinning", *Polymer* **1999**, *40*, 4585–4592.
151. Jin, H. J.; Fridrikh, S. V.; Rutledge, G. C.; Kaplan, D. L. "Electrospinning bombyx mori silk with poly(ethylene oxide)", *Biomacromolecules* **2002**, *3*, 1233–1239.
152. Huang, L.; Nagapudi, K. P.; Apkarian, R.; Chaikof, E. L. "Engineered collagen-PEO nanofibers and fabrics", *J. Biomater. Sci., Polym. Ed.* **2001**, *12*, 979–993.
153. Frenot, A.; Henriksson, M. W.; Walkenström, P. "Electrospinning of cellulose-based nanofibers", *J. Appl. Polym. Sci.* **2007**, *103*, 1473–1482.
154. Koski, A.; Yim, K.; Shivkumar, S. "Effect of molecular weight on fibrous PVA produced by electrospinning", *Mater. Lett.* **2004**, *58*, 493–497.
155. Ding, B.; Kim, H.-Y.; Lee, S.-C.; Shao, C.-L.; Lee, D.-R.; Park, S.-J.; Kwag, G.-B.; Choi, K.-J. "Preparation and characterization of a nanoscale poly(vinyl alcohol) fiber aggregate produced by an electrospinning method", *J. Polym. Sci., Part B: Polym. Phys.* **2002**, *40*, 1261–1268.
156. Zhang, C.; Yuan, X.; Wu, L.; Han, Y.; Sheng, J. "Study on morphology of electrospun poly(vinyl alcohol) mats", *Eur. Polym. J.* **2005**, *41*, 423–432.
157. Li, L.; Hsieh, Y.-L. "Chitosan bicomponent nanofibers and nanoporous fibers", *Carbohydr. Res.* **2006**, *341*, 374–381.
158. Jia, Y. T.; Gong, J.; Gu, X. H.; Kim, H. Y.; Dong, J.; Shen, X. Y. "Fabrication and characterization of poly (vinyl alcohol)/chitosan blend nanofibers produced by electrospinning method", *Carbohydr. Polym.* **2007**, *67*, 403–409.
159. Zhou, Y. S.; Yang, D. Z.; Nie, J. "Preparation and characterization of crosslinked chitosan-based nanofibers", *Chin. Chem. Lett.* **2007**, *18*, 118–120.
160. Zhou, Y.; Yang, D.; Nie, J. "Electrospinning of chitosan/poly(vinyl alchol)/acrylic acid acrylic solutions", *J. Appl. Polym. Sci.* **2006**, *102*, 5692–5697.
161. Liu, L.; Jones, L.; Sheardown, H. "Wetting agent release from contact lenses", *Invest. Ophthalmol. Vis. Sci.* **2005**, *46*, 908.
162. Sickler, S. G.; Carter, J. W.; Winterton, L. C.; Lally, J. M.; Gabriel, M. M. "PVA containing hydrogel lens affects bacterial adherence", *Invest. Ophthalmol. Vis. Sci.* **2005**, *46*, 924.
163. Allen, M. J.; Schoonmaker, J. E.; Bauer, T. W.; Williams, P. F.; Higham, P. A.; Yuan, H. A. "Preclinical evaluation of a poly (vinyl alcohol) hydrogel implant as a replacement for the nucleus pulposus", *Spine* **2004**, *29*, 515–523.
164. Chen, D.-H.; Leu, J.-C.; Huang, T.-C. "Transport and hydrolysis of urea in a reactor-separator combining an anion-exchange membrane and immobilized urease", *J. Chem. Technol. Biotechnol.* **1994**, *61*, 351–357.
165. Bishop, A.; Balázsi, C.; Yang, J. H. C.; Gouma, P.-I. "Biopolymer-hydroxyapatite composite coatings prepared by electrospinning", *Polymers for Advanced Technologies* **2006**, *17*, 902–906.

166. Min, B. M.; Lee, S. W.; Lim, J. N.; You, Y.; Lee, T. S.; Kang, P. H.; Park, W. H. "Chitin and chitosan nanofibers: Electrospinning of chitin and deacetylation of chitin nanofibers", *Polymer* **2004**, *45*, 7137–7142.
167. Noh, H. K.; Lee, S. W.; Kim, J. M.; Oh, J. E.; Kim, K. H.; Chung, C. P.; Choi, S. C.; Park, W. H.; Min, B. M. "Electrospinning of chitin nanofibers: Degradation behavior and cellular response to normal human keratinocytes and fibroblasts", *Biomaterials* **2006**, *27*, 3934–3944.
168. Schiffman, J. D.; Stolga, L. A.; Schauer, C. L. "Crystallization of chitin and chitosan: Transformations due to the electrospinning process", *J. Polym. Sci.*, Part B: Polym. Phy. Submitted.
169. Park, K. E.; Kang, H. K.; Lee, S. J.; Min, B.-M.; Park, W. H. "Biomimetic nanofibrous scaffolds: Preparation and characterization of PGA/chitin blend nanofibers", *Biomacromolecules* **2006**, *7*, 635–643.
170. Park, K. E.; Jung, S. Y.; Lee, S. J.; Min, B.-M.; Park, W. H. "Biomimetic nanofibrous scaffolds: Preparation and characterization of chitin/silk fibroin blend nanofibers", *Int. J. Biol. Macromol.* **2006**, *38*, 165–173.
171. Junkasem, J.; Rujiravanit, R.; Supaphol, P. "Fabrication of α-chitin whisker-reinforced poly(vinyl alcohol) nanocomposite nanofibres by electrospinning", *Nanotechnology* **2006**, *17*, 4519–4528.
172. Sriupayo, J.; Supaphol, P.; Blackwell, J.; Rujiravanit, R. "Preparation and characterization of [alpha]-chitin whisker-reinforced chitosan nanocomposite films with or without heat treatment", *Carbohydr. Polym.* **2005**, *62*, 130–136.
173. Sriupayo, J.; Supaphol, P.; Blackwell, J.; Rujiravanit, R. "Preparation and characterization of alpha-chitin whisker-reinforced poly(vinyl alcohol) nanocomposite films with or without heat treatment", *Polymer* **2005**, *46*, 5637–5644.
174. Duan, B.; Dong, C.; Yuan, X.; Yao, K. "Electrospinning of chitosan solutions in acetic acid with poly(ethylene oxide)", *J. Biomater. Sci., Polym. Ed.* **2004**, *15*, 797–811.
175. McKee, M. G.; Elkins, C. L.; Long, T. E. "Influence of self-complementary hydrogen bonding on solution rheology/electrospinning relationships", *Polymer* **2004**, *45*, 8705–8715.
176. McKee, M. G.; Hunley, M. T.; Layman, J. M.; Long, T. E. "Solution rheological behavior and electrospinning of cationic polyelectrolytes", *Macromolecules* **2006**, *39*, 575–583.
177. Ohkawa, K.; Cha, D.; Kim, H.; Nishida, A.; Yamamoto, H. "Electrospinning of chitosan", *Macromol. Rapid Commun.* **2004**, *25*, 1600–1605.
178. Hasegawa, M.; Isogai, A.; Onabe, F.; Usuda, M.; Atalla, R. H. "Characterization of cellulose-chitosan blend films", *J. Appl. Polym. Sci.* **1992**, *45*, 1873–1879.
179. Ohkawa, K.; Minato, Ken-Ichi; Kumagai, G.; Hayashi, S.; Yamamoto, H. "Chitosan nanofiber", *Biomacromolecules* **2006**, *7*, 3291–3294.
180. Fridrikh, S. V.; Yu, J. H.; Brenner, M. P.; Rutledge, G. C. "Controlling the fiber diameter during electrospinning", *Phys. Rev. Lett.* **2003**, *90*, 144502-144501-144504.
181. Sangsanoh, P.; Supaphol, P. "Stability improvement of electrospun chitosan nanofibrous membranes in neutral or weak basic aqueous solutions", *Biomacromolecules* **2006**, *7*, 2710–2714.
182. Matsuda, A.; Kagata, G.; Kino, R.; Tanaka, J. "Preparation of chitosan nanofiber tube by electrospinning", *J. Nanosci. Nanotechnol.* **2007**, *7*, 852–855.
183. Geng, X.; Kwon, O.-H.; Jang, J. "Electrospinning of chitosan dissolved in concentrated acetic acid solution", *Biomaterials* **2005**, *26*, 5427–5432.
184. Vrieze, S. D.; Westbroek, P.; Camp, T. V.; Langenhove, L. V. "Electrospinning of chitosan nanofibrous structures: Feasibility study", *J. Mater. Sci.* **2007**, *42*, 8029–8034.
185. Zhang, Y.; Huang, X.; Duan, B.; Wu, L.; Li, S.; Yuan, X. "Preparation of electrospun chitosan/poly(vinyl alcohol) membranes", *Colloid Polym. Sci.* **2007**, *285*, 855–863.
186. Zheng, H.; Du, Y.; Yu, J.; Huang, R.; Zhang, L. "Preparation and characterization of chitosan/poly(vinyl alcohol) blend fibers", *J. Appl. Polym. Sci.* **2001**, *80*, 2558–2565.
187. Miya, M.; Iwamoto, R.; Mima, S. "FT-IR study of intermolecular interactions in polymer blends", *J. Polym. Sci., Part B: Polym. Phys.* **1984**, *22*, 1149–1151.

188. Yilmaz, E.; Erdenizci, N.; Yilmaz, O. "Miscibility of chitosan and poly(ethylene oxide) in dilute solution", *J. Polym. Anal. Ch.* **2003**, *8*, 327–338.
189. Lin, T.; Wang, H.; Wang, H.; Wang, X. "The charge effect of cationic surfactants on the elimination of fibre beads in the electrospinning of polystyrene", *Nanotechnology* **2004**, *15*, 1375–1381.
190. Son, W. K.; Youk, J. H.; Lee, T. S.; Park, W. H. "The effects of solution properties and polyelectrolyte on electrospinning of ultrafine poly(ethylene oxide) fibers", *Polymer* **2004**, *45*, 2959–2966.
191. Lin, T.; Fang, J.; Wang, H.; Cheng, T.; Wang, X. "Using chitosan as a thickener for electrospinning dilute PVA solutions to improve fibre uniformity", *Nanotechnology* **2006**, *17*, 3718–3723.
192. Zong, X.; Kim, K.; Fang, D.; Ran, S.; Hsiao, B. S.; Chu, B. "Structure and process relationship of electrospun bioabsorbable nanofiber membranes", *Polymer* **2002**, *43*, 4403–4412.
193. Spasova, M.; Manolova, N.; Paneva, D.; Rashkov, I. "Preperation of chitosan-containing nanofibers by electrospinning of chitosan/poly(ethylene oxide) blend solutions", *e-Polymers* **2004**, *56*, 1–12.
194. Bhattarai, N.; Edmondson, D.; Veiseh, O.; Matsen, F. A.; Zhang, M. "Electrospun chitosan-based nanofibers and their cellular compatibility", *Biomaterials* **2005**, *26*, 6176–6184.
195. Vondran, J. L. *Masters of Science*; Drexel University; 2007.
196. Yang, M. R.; Chen, K. S.; Tsai, J. C.; Tseng, C. C.; Lin, S. F. "The antibacterial activities of hydrophilic-modified nonwoven pet", *Materials Science and Engineering: C* **2002**, *20*, 167–173.
197. Huh, M. W.; Kang, I. K.; Lee, D. H.; Kim, W. S.; Lee, D. H.; Park, L. S.; Min, K. E.; Seo, K. H. "Surface characterization and antibacterial activity of chitosan-grafted poly(ethylene terephthalate) prepared by plasma glow discharge", *J. Appl. Polym. Sci.* **2001**, *81*, 2769–2778.
198. Karck, M.; Forgione, L.; Haverich, A. "The efficacy of controlled antibiotic release for prevention of polyethyleneterephthalate- (dacron-) related infection in cardiovascular surgery", *Clin. Mater.* **1993**, *13*, 149–154.
199. Ma, Z.; Kotaki, M.; Yong, T.; He, W.; Ramakrishna, S. "Surface engineering of electrospun polyethylene terephthalate (PET) nanofibers towards development of a new material for blood vessel engineering", *Biomaterials* **2005**, *26*, 2527–2536.
200. Jung, H.-H.; Huh, M.-W.; Meng, W.; Yuan, J.; Hyun, S. H.; Bae, J.-S.; Hudson, S. M.; Kangt, I.-K. "Preparation and antibacterial activity of PET/chitosan nanofibers", *J. Appl. Polym. Sci.* **2007**, *105*, 2816–2823.
201. Jiang, H.; Fang, D.; Hsiao, B.; Chu, B.; Chen, W. "Preparation and characterization of ibuprofen-loaded poly(lactide-co-glycolide)/poly(ethylene glycol)-g-chitosan electrospun membranes", *J. Biomater. Sci., Polym. Ed.* **2004**, *15*, 797–811.
202. Reneker, D. H.; Chun, I. "Nanometre diameter fibres of polymer, produced by electrospinning", *Nanotechnology* **1996**, *7*, 216–223.
203. Ouchi, T.; Nishizawa, H.; Ohya, Y. "Aggregation phenomenon of PEG-grafted chitosan in aqueous solution", *Polymer* **1998**, *39*, 5171–5175.
204. Duan, B.; Yuan, X.; Zhu, Y.; Zhang, Y.; Li, X.; Zhang, Y.; Yao, K. "A nanofibrous composite membrane of PLGA-chitosan/PVA prepared by electrospinning", *Eur. Polym. J.* **2006**, *42*, 2013–2022.
205. Duan, B.; Wu, L.; Li, X.; Yuan, X.; Li, X.; Zhang, Y.; Yao, K. "Degradation of electrospun plga-chitosan/pva membranes and their cytocompatibility in vitro", *J. Biomater. Sci., Polym. Ed.* **2007**, *18*, 95–115.
206. Zhang, Y.; Ouyang, H.; Lim, C. T.; Ramakrishna, S.; Huang, Z.-M. "Electrospinning of gelatin fibers and gelatin/PCL composite fibrous scaffolds", *J. Biomed. Mater. Res.* **2005**, *72B*, 156–165.
207. Zhang, Y. Z.; Venugopal, J.; Huang, Z.-M.; Lim, C. T.; Ramakrishna, S. "Characterization of the surface biocompatibility of the electrospun PCL-collagen nanofibers using fibroblasts", *Biomacromolecules* **2005**, *6*, 2583–2589.

208. Lee, K. Y.; Ha, W. S.; Park, W. H. "Blood compatibility and biodegradability of partially N-acylated chitosan derivatives", *Biomaterials* **1995**, *16*, 1211–1216.
209. Hirano, S.; Noishiki, Y. "The blood compatibility of chitosan and N-acylchitosans", *J. Biomed. Mater. Res.* **1985**, *19*, 413–417.
210. Zong, Z.; Kimura, Y.; Takahashi, M.; Yamane, H. "Characterization of chemical and solid state structures of acylated chitosans", *Polymer* **2000**, *41*, 899–906.
211. Neamnark, A.; Rujiravanit, R.; Supaphol, P. "Electrospinning of hexanoyl chitosan", *Carbohydr. Polym.* **2006**, *66*, 298–305.
212. Mincheva, R.; Manolova, N.; Paneva, D.; Rashkov, I. "Preparation of polyelectrolyte-containing nanofibers by electrospinning in the presence of a non-ionogenic water-soluble polymer", *J. Bioact. Compat. Pol.* **2005**, *20*, 419–435.
213. Mincheva, R.; Manolova, N.; Rashkov, I. "Bicomponent aligned nanofibers of N-carboxyethylchitosan and poly(vinyl alcohol)", *Eur. Polym. J.* **2007**, *43*, 2809–2818.
214. Ignatova, M.; Starbova, K.; Markova, N.; Manolova, N.; Rashkov, I. "Electrospun nano-fibre mats with antibacterial properties from quaternised chitosan and poly(vinyl alcohol)", *Carbohydr. Res.* **2006**, *341*, 2098–2107.
215. Chen, R. N.; Wang, G. M.; Chen, C. H.; Ho, H. O.; Sheu, M. T. "Development of N,O-(carboxy methyl)chitosan/collagen matrixes as a wound dressing", *Biomacromolecules* **2006**, *7*, 216.
216. Chen, X. G.; Wang, Z.; Liu, W. S.; Park, H. J. "The effect of carboxymethyl-chitosan on proliferation and collagen secretion of normal and keloid skin fibroblasts", *Biomaterials* **2002**, *23*, 4609–4614.
217. Chen, X. G.; Park, H. J. "Chemical characteristics of O-carboxymethyl chitosans related to the preparation conditions", *Carbohydr. Polym.* **2003**, *53*, 355–359.
218. Muzzarelli, R. A. A.; Ilari, P.; Petrarulo, M. "Solubility and structure of N-carboxymethylchitosan", *Int. J. Biol. Macmmol.* **1994**, *16*, 177–180.
219. Lu, J. W.; Zhu, Y. L.; Guo, Z. X.; Hu, P.; Yu, J. "Electrospinning of sodium alginate with poly(ethylene oxide)", *Polymer* **2006**, *47*, 8026–8031.
220. Safi, S.; Morshed, M.; Hosseini, S. A.; Ghiaci, R. M. "Study of electrospinning of sodium alginate, blended solutions of sodium alginate/poly(vinyl alcohol) and sodium alginate/poly (ethylene oxide)", *J. Appl. Polym. Sci.* **2007**, *104*, 3245–3255.
221. Whistler, R. L.; Bemiller, J. N. *Indsutrial Gums Polysaccharides and their Derivatives*; Academic Press: San Diego, 1993.
222. Bhattarai, N.; Li, Z.; Edmondson, D.; Zhang, M. "Alginate-based nanofibrous scaffolds: Structural, mechanical, and biological properties", *Adv. Mater.* **2006**, *18*, 1463–1467.
223. Um, I. C.; Fang, D.; Hsiao, B. S.; Okamoto, A.; Chu, B. "Electro-spinning and electro-blowing of hyaluronic acid", *Biomacromolecules* **2004**, *5*, 1428–1436.
224. Wang, X.; Um, I. C.; Fang, D.; Okamoto, A.; Hsiao, B. S.; Chu, B. "Formation of water-resistant hyaluronic acid nanofibers by blowing-assisted electro-spinning and non-toxic post treatments", *Polymer* **2005**, *46*, 4853–4867.
225. Li, J.; He, A.; Han, C. C.; Fang, D.; Hsiao, B. S.; Chu, B. "Electrospinning of hyaluronic acid (HA) and HA/gelatin blends", *Macromol. Rapid Commun.* **2006**, *27*, 114–120.
226. Mehvar, R. "Dextrans for targeted and sustained delivery of therapeutic and imaging agents", *J. Controlled Release* **2000**, *69*, 1–25.
227. Hennink, W. E.; Nostrum, C. F. v. "Novel crosslinking methods to design hydrogels", *Advanced Drug Delivery Reviews* **2002**, *54*, 13–36.
228. Jiang, H.; Fang, D.; Hsiao, B. S.; Chu, B.; Chen, W. "Optimization and characterization of dextran membranes prepared by electrospinning", *Biomacromolecules* **2004**, *5*, 326–333.
229. Dijk-Wolthuis, W. N. E. v.; Talsma, F. H.; Steenbergen, M. J. v.; Bosch, J. J. K.-v. d.; Henninkt, W. E. "Synthesis, characterization, and polymerization of glycidyl methacrylate derivatized dextran", *Macromolecules* **1995**, *28*, 6317–6322.
230. Scheibel, T. "Protein fibers as performance proteins: New technologies and applications", *Curr. Opin. Biotechnol.* **2005**, *16*, 427–433.

231. Xie, J.; Hsieh, Y.-L. "Ultra-high surface fibrous membranes from electrospinning of natural proteins: Casein and lipase enzyme", *J. Mater. Sci.* **2003**, *38*, 2125–2133.
232. Matthews, J. A.; Wnek, G. E.; Simpson, D. G.; Bowlin, G. L. "Electrospinning of collagen nanofibers", *Biomacromolecules* **2002**, *3*, 232–238.
233. Bowlin, G. L.; Wnek, G.; Simpson, D. G.; Terracio, L. U.S. Patent 6,592,623, 2003.
234. Boland, E. D.; Matthews, J. A.; Pawlowski, K. J.; Simpson, D. G.; Wnek, G. E.; Bowlin, G. L. "Electrospinning collagen and elastin: Preliminary vascular tissue engineering", *Front. Biosci.* **2004**, *9*, 1422–1432.
235. Matthews, J. A.; Boland, E. D.; Wnek, G. E.; Simpson, D. G.; Bowlin, G. L. "Electrospinning of collagen type II: A feasibility study", *J. Bioact. Compat. Pol.* **2003**, *18*, 125–134.
236. Shields, K. J.; Beckman, M. J.; Bowlin, G. L.; Wayne, J. S. "Mechanical properties and cellular proliferation of electrospun collagen type II", *Tissue Eng.* **2004**, *10*, 1510–1517.
237. Barnes, C. P.; Pemble, C. W.; Brand, D. D.; Simpson, D. G.; Bowlin, G. L. "Cross-linking electrospun type ii collagen tissue engineering scaffolds with carbodiimide in ethanol", *Tissue Eng.* **2007**, *13*, 1593–1605.
238. Rho, K. S.; Jeong, L.; Lee, G.; Seo, B.-M.; Park, Y. J.; Hong, S.-D.; Roh, S.; Cho, J. J.; Park, W. H.; Min, B.-M. "Electrospinning of collagen nanofibers: Effects on the behavior of normal human keratinocytes and early-stage wound healing", *Biomaterials* **2006**, *27*, 1452–1461.
239. Shih, Y. R. V.; Chen, C. N.; Tsai, S. W.; Wang, Y. J.; Lee, O. K. "Growth of mesenchymal stem cells on electrospun type I collagen nanofibers", *Stem Cells* **2006**, *24*, 2391–2397.
240. Buttafoco, L.; Kolkman, N. G.; Engbers-Buijtenhuijs, P.; Poot, A. A.; Dijkstra, P. J.; Vermes, I.; Feijen, J. "Electrospinning of collagen and elastin for tissue engineering applications", *Biomaterials* **2006**, *27*, 724–734.
241. Venugopal, J. R.; Zhang, Y.; Ramakrishna, S. "In vitro culture of human dermal fibroblasts on electrospun polycaprolactone collagen nanofibrous membrane", *Artif. Organs* **2006**, *30*, 440–446.
242. Zhong, S. P.; Teo, W. E.; Zhu, X.; Beuerman, R.; Ramakrishna, S.; Yung, L. Y. L. "Formation of collagen-glycosaminoglycan blended nanofibrous scaffolds and their biological properties", *Biomacromolecules* **2005**, *6*, 2998–3004.
243. Chen, Z.; Mo, X.; Qing, F. "Electrospinning of collagen-chitosan complex", *Mater. Lett.* **2007**, *61*, 3490–3494.
244. Kidoaki, S.; Kwon, I. K.; Matsuda, T. "Mesoscopic spatial designs of nano- and microfiber meshes for tissue-engineering matrix and scaffold based on newly devised multilayering and mixing electrospinning techniques", *Biomaterials* **2005**, *26*, 37–46.
245. Nakayama, Y.; Matsuda, T. "Photocurable surgical tissue adhesive glues composed of photoreactive gelatin and poly(ethylene glycol) diacrylate", *J. Biomed. Mater. Res.* **1999**, *48*, 511–521.
246. Okino, H.; Nakayama, Y.; Tanaka, M.; Matsuda, T. ""*In situ* hydrogelation of photocurable gelatin and drug release"" **2002**, *59*, 233–245.
247. Huang, Z. M.; Zhang, Y. Z.; Ramakrishna, S.; Lim, C. T. "Electrospinning and mechanical characterization of gelatin nanofibers", *Polymer* **2004**, *45*, 5361–5368.
248. Ki, C. S.; Baek, D. H.; Gang, K. D.; Lee, K. H.; Um, I. C.; Park, Y. H. "Characterization of gelatin nanofiber prepared from gelatin-formic acid solution", *Polymer* **2005**, *46*, 5094–5102.
249. Li, M.; Mondrinos, M. J.; Gandhi, M. R.; Ko, F. K.; Weiss, A. S.; Lelkes, P. I. "Electrospun protein fibers as matrices for tissue engineering", *Biomaterials* **2005**, *26*, 5999–6008.
250. Altman, G. H.; Diaz, F.; Jakuba, C.; Calabro, T.; Horan, R. L.; Chen, J.; Lu, H.; Richmond, J.; Kaplan, D. L. "Silk-based biomaterials", *Biomaterials* **2003**, *24*, 401–416.
251. Sakabe, H.; Ito, H.; Miyamoto, T.; Noishiki, Y.; Ha, W. S. "In vivo blood compatibility of regenerated silk fibroin", *Sen'i Gakkaishi* **1989**, *451*, 487–490.
252. Santin, M.; Motta, A.; Freddi, G.; Cannas, M. "In vitro evaluation of the inflammatory potential of the silk fibroin", *J. Biomed. Mater. Res.* **1999**, *46*, 382–389.

253. Park, W. H.; Ha, W. S.; Ito, H.; Miyamoto, T.; Inagaki, H.; Noishiki, Y. "Relationships between antithrombogenicity and surface free energy of regenerated silk fibrion films", *Fibers and Polymers* **2001**, *2*, 58–63.
254. Zarkoob, S. PhD Dissertation, 1998.
255. Park, W. H.; Jeong, L.; Yoo, D. I.; Hudson, S. "Effect of chitosan on morphology and conformation of electrospun silk fibroin nanofibers", *Polymer* **2004**, *45*, 7151–7157.
256. Wnek, G. E.; Carr, M. E.; Simpson, D. G.; Bowlin, G. L. "Electrospinning of nanofiber fibrinogen structures", *Nano Lett.* **2003**, *3*, 213–216.
257. Thomas, H.; Heine, E.; Wollseifen, R.; Cimpeanu, C.; Moller, M. "Nanofibers from natural and inorganic polymers via electrospinning", *International Nonwovens Journal* **2005**, *14*, 12–18.
258. Yao, C.; Li, X.; Song, T. "Electrospinning and crosslinking of zein nanofiber mats", *J. Appl. Polym. Sci.* **2007**, *103*, 380–385.
259. Yao, C.; Li, X.; Song, T. "Fabrication of zein/hyaluronic acid fibrous membranes by electrospinning", *J. Biomater. Sci., Polym. Ed.* **2007**, *18*, 731–742.
260. Mo, X.; Chen, Z.; Weber, H. J. "Electrospun nanofibers of collagen-chitosan and P(LLA-CL) for tissue engineering", *Frontiers of Material Science in China* **2007**, *1*, 20–23.
261. Watson, J. D.; Crick, F. H. C. "Genetical implications of the structure of deoxyribonucleic acid", *Nature* **1953**, *161*, 964–967.
262. Rupprecht, A. "Mechanochemical study of wet-spun lithium-DNA fibers", *Biopolymers* **1970**, *9*, 825–842.
263. Hakim, M. B.; Lindsay, S. M.; Powell, J. "The speed of sound in DNA", *Biopolymers* **1984**, *23*, 1185–1192.
264. Takahashi, T.; Taniguchi, M.; Kawai, T. "Fabrication of DNA nanofibers on a planar surface by electrospinning", *Jpn. J. Appl. Phys., Part 1* **2005**, *44*, L860–L862.
265. Bellan, L. M.; Cross, J. D.; Strychalski, E. A.; Moran-Mirabal, J.; Craighead, H. G. "Individually resolved DNA molecules stretched and embedded in electrospun polymer nanofibers", *Nano Lett.* **2006**, *6*, 2526–2530.
266. Liu, Y.; Chen, J.; Misoska, V.; Wallace, G. G. "Preparation of novel ultrafine fibers based on DNA and poly(ethylene oxide) by electrospinning from aqueous solutions", *React. Funct. Polym.* **2007**, *67*, 461–467.
267. Kessick, R.; Fenn, J.; Tepper, G. "The use of AC potentials in electrospraying and electrospinning processes", *Polymer* **2004**, *45*, 2981–2984.
268. Zarkoob, S.; Eby, R. K.; Reneker, D. H.; Hudson, S. D.; Ertley, D.; Adams, W. W. "Structure and morphology of electrospun silk nanofibers", *Polymer* **2004**, *45*, 3973–3977.
269. Min, B. M.; Lee, G.; Kim, S. H.; Nam, Y. S.; Lee, T. S.; Park, W. H. "Electrospinning of silk fibroin nanofibers and its effect on the adhesion and spreading of normal human keratinocytes and fibroblasts in vitro", *Biomaterials* **2004**, *25*, 1289–1297.
270. Sukigara, S.; Gandhi, M.; Ayutsede, J.; Micklus, M.; Ko, F. "Regeneration of bombyx mori silk by electrospinning–Part 1: Processing parameters and geometric properties", *Polymer* **2003**, *44*, 5721–5727.
271. Sukigara, S.; Gandhi, M.; Ayutsede, J.; Micklus, M.; Ko, F. "Regeneration of bombyx mori silk by electrospinning. Part 2. Process optimization and empirical modeling using response surface methodology", *Polymer* **2004**, *45*, 3701–3708.
272. Putthanarat, S.; Eby, R. K.; Kataphinan, W.; Jones, S.; Naik, R.; Reneker, D. H.; Farmer, B. L. "Electrospun bombyx mori gland silk", *Polymer* **2006**, *47*, 5630–5632.
273. Wang, M.; Yu, J. H.; Kaplan, D. L.; Rutledge, G. C. "Production of submicron diameter silk fibers under benign processing conditions by two-fluid electrospinning", *Macromolecules* **2006**, *39*, 1102–1107.
274. Wang, H.; Shao, H.; Hu, X. "Structure of silk fibroin fibers made by an electrospinning process from a silk fibroin aqueous solution", *J. Appl. Polym. Sci.* **2006**, *101*, 961–968.
275. Jeong, L.; Lee, K. Y.; Liu, J. W.; Park, W. H. "Time-resolved structural investigation of regenerated silk fibroin nanofibers treated with solvent vapor", *Int. J. Biol. Macromol.* **2006**, *38*, 140–144.

276. Meechaisue, C.; Wutticharoenmongkol, P.; RujiraWaraput Huangjing, T.; Ketbumrung, N.; Pavasant, P.; Supaphol, P. "Preparation of electrospun silk fibroin fiber mats as bone scaffolds: A preliminary study", *Biomedical Materials* **2007**, *2*, 181–188.
277. Ohgo, K.; Zhao, C.; Kobayashi, M.; Asakura, T. "Preparation of non-woven nanofibers of bombyx mori silk, samia cynthia ricini silk and recombinant hybrid silk with electrospinning method", *Polymer* **2003**, *44*, 841–846.
278. Jin, H. J.; Chen, J.; Karageorgiou, V.; Altman, G. H.; Kaplan, D. L. "Human bone marrow stromal cell responses on electrospun silk fibroin mats", *Biomaterials* **2004**, *25*, 1039–1047.
279. Wang, M.; Jin, H. J.; Kaplan, D. L.; Rutledge, G. C. "Mechanical properties of electrospun silk fibers", *Macromolecules* **2004**, *37*, 6856–6864.
280. Ayutsede, J.; Gandhi, M.; Sukigara, S.; Micklus, M.; Chen, H.-E.; Ko, F. "Regeneration of bombyx mori silk by electrospinning. Part 3: Characterization of electrospun nonwoven mat", *Polymer* **2005**, *46*, 1625–1634.
281. Min, B. M.; Jeong, L.; Lee, K. Y.; Park, W. H. "Regenerated silk fibroin nanofibers: Water vapor-induced structural changes and their effects on the behavior of normal human cells", *Macromol. Biosci.* **2006**, *6*, 285–292.
282. Gandhi, M.; Yang, H.; Shor, L.; Ko, F. "Regeneration of bombyx mori silk by electrospinning: A comparative study of the biocompatibility of natural and synthetic polymers for tissue engineering applications", *Journal of Biobased Materials and Bioenergy* **2007**, *1*, 274–281.