Polymeric micro- and nanomaterials play a significant role in various current and emerging technologies. A liquid shear based method was developed to fabricate a wide range of polymeric materials, which include fibers, sheets, ribbons, rods and spheres in a scalable, cost-effective and simple way. During the process, droplet shearing, droplet deformation, droplet breaking up and polymer precipitation occur simultaneously. The size and morphology of the resultant structures are determined by the dominating process which is further controlled by the experimental parameters including polymer concentration, polymer molecular weight and antisolvent concentration.

Among all of these structures, nanofibers have attracted the latest research interest due to the unique properties. Current leading fiber production approaches in the market possess certain drawbacks. For example, the throughput of electrospinning is limited to around 2.5 kg/hr and the diameter of fiber produced by wet spinning cannot be below micrometer while melt spinning is only applicable to melt-processable polymers. The breakthrough of our liquid shear driven technique for fiber synthesis is that it produces fibers with diameter from 200 nm to several micrometers from a wide range of liquid-processable polymers with high commercial yield (up to 12 kg/hr). Thus in Chapter 2, the optimum parameters range for fiber formation is established and the effects of those parameters on fiber size are investigated.

In the original liquid shear method, medium with high viscosity is needed to exert strong shear stress on the droplet and to stretch the droplets to long strand. However, the viscous medium complicates the post sample washing procedure and introduces the potential slippery
danger in the working area. Thus a non-viscous medium shearing method is developed in Chapter 3 and it is the first time proposed that the synthesis of PLA or PS nanofibers can be completed in the aqueous ethanol medium.

Colloid science usually categorizes emulsion as oil in water (O/W) and water in oil (W/O) dispersions. Oil in oil emulsion can also be formulated from the immiscible organic liquid pairs. Using the phase separation in the PS-cyclohexane system, the emulsion are formed under continuous shearing while the continuous phase is solvent-rich and the disperse phase is polymer-rich. By shearing the emulsions, the fibers sizes are reduced around 10X due to the smaller initial polymer droplet size. The fiber sizes are further reduced to 100 nm which enhances the competitive advantages of liquid shear technique.

Controlled drug release combines the advantages of increased therapeutic efficacy, reduced toxicity and lower administration frequency. By dispersing model drugs in the spinning polymer solution, these drugs are successfully encapsulated inside the biodegradable matrix and the encapsulation efficiency is modulated by polymer concentration and fiber size while the release profile of the drug is determined by the degradation rate of the polymer matrix.
Shear Driven Synthesis of Polymeric Micro- and Nanomaterials

by
Tian Tian

A dissertation submitted to the Graduate Faculty of North Carolina State University in partial fulfillment of the requirements for the degree of Doctor of Philosophy

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DEDICATION

This dissertation is dedicated to my husband and my parents for their encouragement, support, sacrifices and unconditional love.

I also dedicate this dissertation to my son, Ricky, for opening another door of this wonderful world to me.
BIOGRAPHY

Tian Tian was born in Pingyu, a small town in Henan province of China. She graduated from Pingyu Elementary School, Pingyu Middle School and Zhumadian High School. She lived in Pingyu until 2005 to enter Jilin University (JLU), ranked as one of the top three Chinese universities in polymer science and engineering. Tian worked as a research assistant on nanoparticle assembly under the guidance of Xuemin Zhang in Professor Bai Yang’s group since 2006 summer. In 2009, Tian graduated from Jilin University with the bachelor major in polymer science and engineering. She got the permission to be admitted to China Academy of Science for her PhD study without exam. She chose North Carolina State University to pursue her graduate study by joining the department of Chemical and Biomolecular Engineering under the guidance of Dr. Orlin D. Velev.
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Chapter 1 Introduction
1.1 Development of Fiber Production

One-dimensional polymeric nanostructures, especially nanofibers, gained significant interest from industrial, academic and technological perspectives due to their numerous applications in many areas\(^1,2\). From the geometrical aspect, fibers are elongated, and threadlike structures with extreme long length. Hooke firstly examined the structure of silkworm fibres microscopically and suggested the possibility of artificial silk synthesis in 1664. In 1890, Chardonnet’s company made high profit by realizing the man-made artificial silk with product capacity approximately 1000 kg/day. In 1935, Dupont patented Nylon 66, the first artificial synthetic fiber materials obtained from the precursors in 1935. After around two centuries’ development, the biggest barrier for nanofiber researches and applications remains the lack of a scalable synthesis or production method in a safe, consistent, and cost-effective manner with high commercial yield\(^3\). In the following sections, several fiber production technologies in the market to date will be covered and the pros and cons of each method will be discussed.

1.1.1 Self-Assembly

Generally speaking, self-assembly refers to the formation of structures or patterns using small molecules as the building blocks through non-covalent forces such as hydrogen bonding, electrostatic reactions or hydrophobic forces\(^4\). It is a powerful bottom-up approach in nanostructure creation. Amphiphiles, one of the widely utilized building components for self-assembly structures, are molecules containing polar or hydrophilic groups as heads and non-polar or hydrophobic groups as tails connected by covalent bonds (Figure 1.1). Besides
nanofibers, a wide range of mesoscopic-scale structures, including vesicles and lamellas, are formed from various amphiphilic supermolecules including biomolecules (Figure 1.2). Being limited by the content of the thesis, only nanofiber type structures will be discussed here. In addition to classical amphiphiles shown in Figure 1.1, a wide range of synthetic amphiphiles including peptides, block copolymers, rod-like molecules and oligopeptides can assemble into nanofibers in aqueous or organic solvents under appropriate conditions (Figure 1.2).

Figure 1.1: Schematic chemical structures of traditional amphiphiles for fiber formation by self-assembly.1
In water, hydrogen bonding cannot be employed as the only direct driving force for self-assembly since the enthalpy increases because of the hydrogen bonding formation between molecules is compromised by the hydrogen bonding formation between water molecules and amphiphilic molecules. So other non-covalent interactions such as hydrophobic interaction and electrostatic interaction are required for self-assembly to happen in aqueous solutions. For example, after mixing alkylated chiral melamine (hydrophobic unit 1 in Figure 1.3) and derivatized azobenzene cyanuric acid (hydrophilic unit 2 in Figure 1.3) in aqueous solutions, helical fibers were formed with thickness around 14-28 nm and width around 30-50 nm (Figure 1.3) via self-assembly due to the synergy effect of hydrogen bonding and hydrophobic interactions. The hydrophilic cyanuric acid is located on the surface of the fibers while the hydrophobic part is in the interior. Besides hydrophobic interaction driven self-assembly, electrostatic molecular pairing approach can also be adopted to develop nanofibers (Figure 1.4). For example, the ion pairs of anionic guanosine 5’-monophosphate (GMP), cationic adenosine 5’-monophosphate (AMP) were mixed together to form helices and fibers with size from nano to micrometer in aqueous medium. For small
and neutral ionic molecules, such as zwitterionic amino acids, the above molecular paring approaches are not applicable. Pre-modification approaches are adopted to allow self-assembly between such molecules to happen. For example, by reacting with orthophthalaldehyde (OPA) and alkyl thiols, amino acids are converted into isoindole derivative. An anionic charge was added to the isoindole unit by mixing isoindole derivative with 2-Mercaptoethanesulfonic acid (MES) (Figure 1.5 A). The promoted moleculars association between charged isoindole derivative and cationic cyanic dye developed the fiber structures with width around 50 nm and length of micrometer (Figure 1.5 B).
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Figure 1.5: A). Schematic representation of amino acid premodification methods for making fiber precursors. B). TEM images of the mixture of isoindole-amino acids and dye. a) isoindole-Glu/1, b) isoindole-Ala/1, c) isoindole-Gly/1, and d) isoindole-Lys/18.
Nanofiber formation from diblock copolymer self-assembly also provides the possibility of nanofiber production. For example, one block copolymer consisting of a monodisperse oligo(p-phenylene-vinylen)(OPV) and a coil segment of polymer(ethylene oxide) (PEO), poly(propylene oxide) (PPO) or polyisoprene (PI) of varying length were synthesized(Figure 1.6). The molecules of this copolymer self-assembled into cylindrical micelles with cylindrical OPV core and PEO or PPO corona and these supramolecular structures were controlled by the solvent quality. At high poor solvent concentration, the cylinders aggregated into a hexagonal closed packing and fibers with 10 nm diameter and micrometers length were formed in the PEO-based systems.

**Figure 1.6:** Schematic representation of the self-assembly of copolymers in aqueous solution and fluorescence micrographs with short(left) and long (right) PPO blocks.
Nanofibers have been created from the self-assembly of organic/inorganic components by the use of metal coordination. The intervalence charge transfer absorption for [Pt(en)₂][PtCl₂(en)₂] was observed at 473 nm in chloroform with orange color, whereas it is observed at 513 nm in dichloromethane with red color. This observed solvatochromism significantly affected the morphology of the assemblies as shown in Figure 1.6. In orange chloroform dispersion, nanofibers with thickness of 20–200 nm and length of more than 20 μm were observed and rectangular nanocrystals (width 100 nm, length 200–300 nm) were observed in the red dichloromethane dispersion.

![Figure 1.7: TEM images of nanofiber formed from [Pt(en)₂][PtCl₂(en)₂] dispersions, a) in chloroform, b) in dichloromethane.](image)

In conclusion, self-assembly in aqueous medium or organic solvent provides an approach for formation of nanofibers. It allows construction of fibers with unique functions since the self-assembly units can be various molecular types. Despite the aforementioned advantages, self-assembly is only applicable for formation of fibers with diameters from 10 nm to 200 nm from specific molecules, such as amphiphils, ionic molecules and diblock polymers. The
yield is usually low and the procedure is tedious and expensive, which limits its wide application.

1.1.2 Phase Separation

In 1999, Ma and Zhang proposed one approach involving thermal induced liquid-liquid phase separation to produce poly-L-lactic acid nanofibrous structures\textsuperscript{11}. Four steps are needed for this procedure: polymer dissolution in THF, polymer gelation at low temperature, solvent extraction by water and freezing-drying (Figure 1.8). The diameter of the obtained fibers is in the 50-500 nm range with porosities up to 98.5%. The sizes and porosities can be tuned by the fabrication parameters including polymer concentration and gelation temperature. During this process, less equipment is needed with batch to bath consistency and 3D pore arrangement is guaranteed. However, the procedure is complex involving solvent exchange and freeze drying which are pretty expensive and the material selection is narrowed to PLA-THF at present.

\textbf{Figure 1.8}: a) Schematic representation of nanofiber creation from thermally induced phase separation. b) SEM image of nanofibers produced from this technique\textsuperscript{11}. 
1.1.3 Templating

Templating involves adopting a template or mold to fabricate a desired structure and is promising to control the hierarchical structures of nanomaterials. This technique involves synthesizing polymers chemically or electrochemically inside the pores of a template or drawing a polymer melt into the pores by capillary action. For example, to create nanofibers, aluminum membrane films are used as the template, which are fabricated by electrochemical oxidation of aluminum to coat the nanopores on the membrane surface. The length, diameter and interpore distance have been successfully controlled by varying the experimental parameters. As shown in Figure 1.9, the water pressure on one side of the template forces the polymer melt to flow through the pores to the other side of the template\textsuperscript{12}. The extruded melt solidifies upon contacting with the precipitation solutions. Fibers diameters can be tuned by using different templates and the length of the fibers can also be controlled by the melt time and temperature. However, to release the fibers, the template is sacrificed by dissolution or mechanical detachment. In other words, template technique is a destructive approach. Even though non-destructive approach has been proposed by producing reusable silica template (Figure 1.10)\textsuperscript{13}, the template fabrication procedure is complex and tedious while the length of the fiber remains limited by the template.
Figure 1.9: a) Schematic representation of nanofiber creation from destructive template approach. b) SEM image of nanofibers from PCL. c) b) SEM image of nanofibers from 50/50 PLGA.

Figure 1.10: (A) Schematic of the fabrication of polymer nanofibers using a nondestructive templating technique (grey: alumina template, green: resin, blue: polymer nanofibers, pink: silica replica template. (B) SEM images of 120nm (B&C) and 1 µm (D&E) polymer fibers fabricated by the above technique.
1.1.4 Mechanical Drawing

Polymeric nanofibers can be mechanical drawn directly from viscous polymer melt or solution $^{14,15,16,17}$. As exemplified in Figure 1.11, a tip of a rod made of iron or silica with radius of 125 μm is immersed into the molten PTT firstly. Then the rod tip is moved up and retracted from the molten polymer slowly with a speed of 0.1–1 m/s, leaving a PTT wire extended between the molten PTT and the tip. The extended PTT wire is quickly quenched in air and finally forms a PTT fiber with diameter as low as 60 nm and length up to 500 nm$^{14}$. Another example of drawing method is shown in Figure 1.12. First, a pipette filled with polymer solution is fixed perpendicularly above a given solvophilic substrate whose movement can be controlled by a motorized XYZ nanopositioner. Then the substrate is raised to contact the polymer droplet at the end of the pipette tip. After the droplet formation and adhesion, the pipette is moved down and stopped at certain height. Then the pipette is moved along following a predetermined trajectory to form the polymer fibers. After the drawing of the fiber, the substrate is raised again to form and adheres a new droplet on the substrate to form another suspended fiber$^{15}$. By repeating this procedure, fibers with controlled length can be produced. Unlike the approaches discussed previously, mechanical drawing can fabricate polymer fiber mixtures from different polymer species where each fiber contains only one specific type of polymer since one single fiber is formed at a time. The range of the fiber diameter is from tens of nanometers to several microns. One disadvantage of this method is also that one fiber forms at a time which limits its productivity. The other disadvantage is that heating specific substrate and complex control equipment are needed for the drawing procedure which makes its wide application impossible.
Figure 1.11: (A) Schematic demonstration of the drawing technique procedure. (B) Transmission electron microscope (TEM) image of a polymer nanofiber fabricated using the drawing technique\textsuperscript{14}.

Figure 1.12: (A) Schematic representation of suspended polymer fiber obtained by mechanical drawing. (B) Scanning electron microscope (SEM) images of (a) continuously drawn array of fibers on a silicon substrate, (b) a 37 nm nanofiber (c) a cross pattern of two fibers showing the fiber diameter control in the same drawing process, and (d) 2D fiber network\textsuperscript{15}.
1.1.5 Extraction

Nanofiber production through extraction is only limited to specific family of materials. For example, a two-step chemical-mechanical procedure is proposed to get fibers (diameters in 10 nm to 120 nm with length up to a few thousand nanometers) from agricultural residues such as wheat straw and soy hull (Figure 1.13)\textsuperscript{18}. The chemical treatment isolated cellulose from the wheat straw or soy hull while mechanical treatment separated the fibers from the cellulose. Chitin nanofibers (diameter in 3-4 nm with size in micrometer) have also been successfully extracted from squid pen β-chitin by simply mechanical treatment at pH=3 -4 under ultrasonication (Figure 1.14)\textsuperscript{19}.

![Chemical Treatment](image1) ![Mechanical Treatment](image2)

**Figure 1.13**: Images of natural wheat straw, wheat straw microfibers after chemical treatment and wheat straw nanofibers after mechanical treatment\textsuperscript{18}.

![A) Images of squid pen β-chitin nanofiber/water dispersion at 0.2% observed with cross polarizers. B) TEM micrograph of nanofiber prepared from squid pen β-chitin in water at pH=4\textsuperscript{19}.](image3)

**Figure 1.14**: A) Images of squid pen β-chitin nanofiber/water dispersion at 0.2\% observed with cross polarizers. B) TEM micrograph of nanofiber prepared from squid pen β-chitin in water at pH=4\textsuperscript{19}.
1.1.6 Polymerization

Polymerization has also been utilized to synthesize polymeric nanofibers from the monomers. Surface-induced polymerization (SIP) is a versatile technique for controlling surface properties of nanomaterials and widely used for the growth of nanofibers on substrates. For example, ECA, also branded as Super Glue, forms mechanically strong polymer with excellent adhesive properties under ambient conditions, which permits the polymer to be attached to a variety of surfaces. High aspect ratio PECA nanofibers (diameter with 100 nm to 400 nm) were formed on a silicon substrate at very high relative (>500) humidity with vapor since the polymerization of ECA rapidly proceeds in the presence of water (Figure 1.15). Plasma–induced polymerization is one kind of surface-induced polymerization that utilizes plasma to activate the surface for polymerization. It has also been applied to grow short nanofibers on substrates. However, surface-induced polymerization approaches for nanofiber synthesis is only limited to specific materials and the lengths of the fibers are also limited in micrometer range.

![Figure 1.15: SEM images of initial polymer fibers (15 min exposure to monomer and high humidity) growth on a ginger print at 30°C and relative humidity > 95%. a) low magnification view b) close-up view of the same (inset showing the top view of fiber). c) PECA nanofibers obtained by initiation with the synthetic mixture of linoleic acid and aqueous sodium chloride.](image-url)
Poly(vinyl alcohol) (PVA)-Poly(methyl methacrylate)(PMMA) nanofibers have been fabricated by radical-mediated dispersion polymerization with AIBN as the initiator for the polymerization and linearly aligned silver nanoparticles as template (Figure 1.16). Although silver – polymer nanofiber composites are promising for many application areas including biomaterials, medical devices and electronics, the removal of embedded silver nanoparticles from such nanofibers to get pure polymer fibers is still challenging.

![Figure 1.16](image-url)

**Figure 1.16**: (A) Schematic representation of silver nanoparticle embedded polymer nanofiber fabrication procedure. (B) SEM and TEM images of silver nanoparticle embedded polymer nanofibers.

Polyaniline (PANI) is one of the most widely used conducting polymers due to its high electrical conductivity, environmental stability and simple doping/dedoping chemistry. PANI nanofibers are expected to offer better properties compared to the bulk PANI pellets and have been synthesized by interfacial polymerization without structure-directing agents or template. During the synthesis process, the morphology is determined by the ways of the nucleation (Figure 1.17). In Figure 1.17, the fibers and dots represent polyaniline resulting from homogeneous and heterogeneous nucleation, respectively. At the initial stage,
polyaniline nanofibers form exclusively. Subsequently, if heterogeneous nucleation is favored, new molecules will grow on the preformed nanofibers, leading to the formation of thicker and agglomerated particles; if heterogeneous nucleation is suppressed and homogeneous nucleation is predominant, well-dispersed polyaniline nanofibers will be continuously synthesized. Typical SEM images of the products from the two different routes are presented next to the reaction vials. This method is simple and compatible to batch production; however, its application to other polymer molecules is limited.

**Figure 1.17:** Schematic illustrations and images showing how the nucleation mode of polyaniline is related to the shape and aggregation of the resulting particles during the synthetic process\textsuperscript{28}. 

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1.1.7 Spinning

Previously spinning was utilized to describe the conventional process of producing continuous polymeric fibers with spinneret extrusion and at present it is expanded to fiber synthesis without spinneret\textsuperscript{2}. Polymers with the capacity of fiber formation can be used in this process and the conversion of polymer to liquid state by dissolution, heating or pressurization is needed before spinning. It is generally categorized as melt spinning, solution spinning and emulsion spinning depending on the state of polymer liquid. These three general categories have been further classified into several approaches, which will be discussed in this section. Electrospinning is excluded from the part since it is compatible with polymer melt, polymer solution and emulsion and it will be introduced in a separate section of this chapter below.

1.1.7.1 Melt Spinning and Melt Blowing

Melt spinning is one of the most commonly used methods for non-woven production\textsuperscript{25}. During the conventional melt spinning process (Figure 1.18), the polymer is melted, pumped and forced to flow through the spinneret, which typically has several holes. Polymer fibers in melt form from holes are cooled at temperature below the melting temperature of the polymer. The solidified polymer fibers are collected on a collection wheel. The main advantage of melt spinning is the capability to easily spin multi-component systems. In addition, no solvent is needed during the process, which improves its environmental safety and enables a wide variety of biomedical applications. Also, the spinning speed achievable during the process provides high throughout. However, drawing instabilities would cause wide fiber diameter
distribution and the high viscosity of the melt requires strong mechanical forces to produce fibers with diameters below one micron.

To further reduce the fiber sizes, melt blowing (MB) has been proposed to further reduce the fiber diameters to 0.1 microns. Unlike melt spinning, during the melt blowing process, fibers are created by extruding the polymer melt through an orifice die and drawing down the extrudate with a jet of hot air (Figure 1.19). The air is supplied in the form of two streams that form a v-slot and the drag force. The air flow attenuates the melt extrudate into fibers and the fibers are collected by the specific collection device. The basic MB technology has been developed under US government sponsorship in the early 1950s and ExxonMobil has developed the most patents to produce microfiber nonwoven from MB equipment. Currently, various companies including 3M, Kimberly-Clark, Cummins and Johns Manviille have developed MB technologies out of ExxonMoil Chemical processes for commercial product formulation. For example, 3M successfully developed microfiber blends with better performance than ExxonMoil patents. However, the materials selection is limited since only polymer melts with low viscosity could be spun to avoid excessive polymer swelling at the spinneret exit. Also, currently MB used almost exclusively to produce microfibers rather than nanofibers although it has the capability of producing fibers as small as 100 nm. Another drawback is that the resultant fiber mats usually exhibit low strength due to the polymer with low molecule weight adopted to meet the viscosity needs. What is more, roping, shot and flying are the three main unavoidable defects during the melt spinning process. Roping is observed as a narrow, elongated, thick streak in the web is due to the uncontrolled turbulence in the air-stream and movement of fibers. Shot is observed when small spherical particles of
polymer are from high temperature or too low molecular weight. Fly is a defect where polymer contaminates the surrounding environment instead of going to the fiber mats from too violent blowing conditions.

Figure 1.18: Schematic illustrations of A) melt spinning and B) melt blowing.

1.1.7.2 Solution Spinning

Solution spinning describes the process of fiber formation from the polymer solution instead of polymer melt. It is particularly suitable for polymers which are thermally unstable or degrade under melting. Usually fibers from melted state exhibit inferior mechanical properties than those from solution state due to the higher amount of chain entanglements in the polymer melts. Depending on the mechanism of solvent removal, solution spinning is classified as wet spinning, dry-jet spinning (liquid crystal spinning), dry spinning and dry wet
spinning (gel spinning).

Wet spinning has the longest history among all the fiber spinning methods and has been first invented in the later 19\textsuperscript{th} century\textsuperscript{27}. Deoxyribonucleic acids (DNAs) from wet spinning have been studied in 1960s. In wet spinning, the polymer dissolved in the suitable solvent is forced to extrude from the spinneret with several holes and the spinneret is immersed in a coagulation bath containing a non-solvent of the polymer\textsuperscript{28}. After solvent removal from the fiber jet and fiber solidification, the polymer precipitation happens and the long stretched fiber structures are frozen. During this process, mass-transfer between polymer solvent and non-solvent occurs. The mass transfer rate during wet spinning is slower than both melt spinning, which uses heat transfer process to solidify the fibers and dry solution spinning, in which evaporation is used to solidify the fibers since solvent evaporation and diffusion into air is faster than solvent diffusion in a miscible liquid.

Wet spinning tends to produce fibers with pear or finger-shaped voids, which would impair the transparency and fibrillation of the fibers. To avoid the formation of voids during the wet spinning process, dry-jet wet spinning has been proposed. For dry-jet wet spinning, the spinning jet is in contact with the external gaseous environment very shortly before entering the coagulation bath. In order to complete this process, the coagulation medium is placed a few millimeters or a few centimeters below the spinneret\textsuperscript{29,30,31}. Dry spinning is different from both wet spinning and dry jet spinning because the fibers solidify under the steam of hot air or inert gas and the solvent removal is done by heating. Dry spinning is faster than wet spinning since the fiber solidification is formed by evaporation instead of precipitation\textsuperscript{32}. Due to safety and environmental concerns associated with solvent handling,
dry spinning is only adopted for polymers not suitable for melt spinning since the solvent is not recyclable. Dry jet spinning is also named as liquid crystal spinning since only lyotropic liquid crystal polymers and thermotropic liquid crystal polymers can form fibers with this process. Different from liquid crystals, polymer gels are saturated polymer solutions with high polymer concentration and high polymer molecular weight, which are fluid at the extrusion temperature and become gelled when cooled down to ambient temperature. The polymers for gel spinning have very long and flexible chains while polymers for liquid crystal spinning exhibit rigid rod-like molecular structures. Both technologies were widely used in industry for formation of fibers with high-tenacity and high-modulus. In summary, solution spinning is used in large-scale polymer fibers production from polymers which are not thermoplastic and can be dissolved in industrially safety-approved solvents. However, the fiber size obtained from solution spinning is still in micrometer range and wash and bleach of fibers are necessary before use.


1.1.7.3 Emulsion Spinning

Emulsion spinning is firstly patented by Dupont in 1956. Improvement was developed during the past decade to adopt emulsion spinning to produce composite fibers composed of one or more insoluble or non-melting compounds, such as inorganic nanoparticles, drugs and hydrophilic polymers\textsuperscript{34}. These compounds are finely grounded and mixed with various polymer solutions. Catalysts or emulsifiers are possible to be added to stabilize the mixture. The mixture is then extruded into a coagulation bath following the wet spinning procedure or through the hot air followed the dry spinning procedure. This approach is promising for production of fibers made of fluorocarbons with high melting point or blends with flame-retardant properties.

\textbf{Figure 1.19:} Schematic illustrations of melt spinning, dry blowing and wet spinning processes.
1.1.8 Electrospinning

Unlike the mechanical force driven approaches discussed before, electrospinning is an electrostatically driven method for polymeric nanofiber fabrication that can be adopted by both liquid polymer solution and polymer melt\textsuperscript{1, 35, 36, 37, 38}. Figure 1.20 exemplifies the schematic illustration of the basic experimental set up for electrospinning. A high voltage power supply (DC or AC), a spinneret (a metal needle or capillary tub) and a collector are the three components of this set up. The spinneret is usually connected to a syringe containing with polymer solution or polymer melt. The liquid will be fed through the spinneret to a high electric field at controllable and constant rate with the use of syringe pump and a pendant drop is formed at the end of the spinneret. Electric field in the kilovolt range is generated by the high voltage power. As the surface tension of the polymer droplet is overcome by electrostatic repulsion, a Taylor cone is formed and a thin liquid jet is ejected towards the collector from the droplet. This jet becomes a long and thin thread after the stretching and whipping process. As the jet is continuously elongated and the solvent is continuously evaporated, the diameter of the jet is reduced to as small as tens of nanometers and a fiber structure is formed. Various modifications have been proposed to the setup to further control the structures of the resultant fibers. Examples include using the rotating drum to collect electrospun fibers with uniform fiber orientation and using two coaxial capillaries to fabricate hollow nanofibers (Figure 1.21)\textsuperscript{39}.

The morphology and diameter of electrospun fibers are dependent on a number of processing parameters including strength of the applied field, the distance between the spinneret and collector, the feeding rate of the polymer solution, the type of polymer, the
conformation of polymer chain, viscosity, elasticity, electrical conductivity as well the polarity of the solvent\textsuperscript{40}. The effects of some of these parameters on fiber size and morphology are summarized and listed in Table 1. For example, minimal concentration is needed for fiber formation and below this minimal concentration, beaded fibers or only beads are formed. Above this critical concentration, the fiber diameter increases dramatically with the polymer concentration. Minimum solvent conductivity is needed for fiber formation; beads or beaded fibers are formed below this value; above this value, high conductivity of polymer solvent leads to the significant decrease of the fiber diameter.
Table 1.1: Effect of solution, process and other parameters on the electrospun fibers morphology

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Effect/Observation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Solution parameters</strong></td>
<td></td>
</tr>
<tr>
<td>Concentration</td>
<td>Increasing concentration results in bigger fibers</td>
</tr>
<tr>
<td></td>
<td>Very low concentration can form beads on fibers</td>
</tr>
<tr>
<td>Molecular weight</td>
<td>More bead formation at low molecular weight</td>
</tr>
<tr>
<td></td>
<td>Increasing molecular weight produces bigger and smoother fibers</td>
</tr>
<tr>
<td>Viscosity</td>
<td>Increasing fiber diameter with the increase of viscosity</td>
</tr>
<tr>
<td>Conductivity</td>
<td>Thinner fibers are formed with the increase of conductivity</td>
</tr>
<tr>
<td>Surface tension</td>
<td>Low surface tension generates smooth and uniform fibers at low electric field</td>
</tr>
<tr>
<td><strong>Process parameters</strong></td>
<td></td>
</tr>
<tr>
<td>Applied voltage</td>
<td>Generally, the fiber diameter is decreased with the increase in applied voltage</td>
</tr>
<tr>
<td>Feed rate</td>
<td>Very high feed rate produces beads on fibers while very low feed rate cannot continually produce fibers</td>
</tr>
<tr>
<td></td>
<td>Typical feed rate is below 1 ml/h</td>
</tr>
<tr>
<td>Collector</td>
<td>Different collector shapes are available depending on desired morphology</td>
</tr>
<tr>
<td></td>
<td>More uniform thickness of mat can be obtained using a rotating drum</td>
</tr>
<tr>
<td>Distance to the collector</td>
<td>Too far or too near distance would result in bead formation</td>
</tr>
<tr>
<td></td>
<td>Needs sufficient time to elongate and dry</td>
</tr>
<tr>
<td><strong>Other parameters</strong></td>
<td></td>
</tr>
<tr>
<td>Temperature</td>
<td>Increased temperature results in decreased fiber diameter</td>
</tr>
<tr>
<td>Humidity</td>
<td>High humidity can induce internal porosity of fiber</td>
</tr>
<tr>
<td>Post-spinning treatment</td>
<td>Sufficient drying should be done to evaporate the residual solvents</td>
</tr>
</tbody>
</table>
Although electrospinning can be used to create nanofibers from a number of different polymers with diameters ranging from less than 3 nm to greater than 1 μm, this process remains dependent on jet stability (which in turn depends on solvent viscosity, surface tension, and vapor pressure). Electrospinning also essentially produces one infinitely long fiber, which is collected as an unordered mesh and is difficult to manipulate into higher order architectures other than uniaxial alignment. The production capacity of electrospinning is low compared with wet spinning due to its low polymer fluid throughput. The technological advances to increase the nanofiber production volume include: (1) introduction of multi spinneret components for parallel multi-processing (2) free surface electrospinning. The multi spinnerets approach can be arranged in a uniaxial configuration or in a circular geometry (Figure 1.22). Besides increasing the throughput and thickness of resulting mats, it is also useful for large area deposition and fiber mixtures production from different materials. However, the voltage alternation induced from the close electrospinning is the main drawback of this approach. The other problem related to traditional electrospinning is the clogging at the spinneret nozzle from the fineness of the needle. The clogging can become more common at high solution concentration or solution mixture with particles. Free surface electrospinning without spinneret provide one approach to solve this problem. This process involves the formation of an electrospinning jet from the free surface of a liquid without any needle or nozzles. However, the variation on fiber size is wide and the fiber assembly configurability is limited.
Figure 1.20: A) Schematic illustration of a standard electrospinning setup. B) a SEM image of electrospun polyurethane nanofibers\textsuperscript{42}.

Figure 1.21: Schematic illustrations of possible geometries of electrospinning collector\textsuperscript{39}.
Specific surface electrospinning set up has been designed to overcome these drawbacks. At present, Nanospider is the most successful free surface electrospinning approach. Nanospider, invented by Elmarco, a Czech company, has the capability of producing nanofibers of various polymers in large quality. Using polyvinyl alcohol (PVA) as an example, the smallest resultant fiber diameter is around 200 nm with 30% standard deviation with annual throughput up to 50 million m². This technique uses the rotating cylinder as the nanofiber generator and this rotated cylinder is immersed into the polymer solutions (Figure 1.23). At the high voltage, an enormous number of liquid jets is formed from the cylinder surface and upward oriented. Nanofibers were formed after solvent evaporation of the jets. However, its commercial yield is only 0.178 kg/h.
There are several other approaches to fabricate nanofibers, such as centrifuge spinning\(^{44,45}\), film splitting\(^3\) and island-sea spinning\(^{46}\), however, due to limited space in this thesis, only major ones are briefly discussed here and the disadvantages and advantages of each mentioned method are listed in Table 1.2. Depending on the various application needs, appropriate methods should be chosen. For example, for cell incorporation, melt based and organic solution based methods are not preferred since high temperature or toxic organic solvent is vitally harmful for cells. At present, the biggest challenge for nanofibers
commercialization remains the low productivity below market needs. Thus further improvement in the synthesis of nanofibers is needed to further integrate the potential of nanofibers in practical applications.
### Table 1.2: Advantages and disadvantages of fiber production methods

<table>
<thead>
<tr>
<th>Method</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Self-Assembly</td>
<td>3D pore arrangement</td>
<td>Lack of control on fiber orientation and arrangement</td>
</tr>
<tr>
<td></td>
<td>Easy cell incorporation</td>
<td>Limited fiber diameter (~2-30 nm) and length (~10 µm)</td>
</tr>
<tr>
<td></td>
<td>Injectable for in vivo assembly</td>
<td>Difficult to be scaled</td>
</tr>
<tr>
<td></td>
<td>Good for thin nanofibers</td>
<td>Limited material selection(amphiphiles)</td>
</tr>
<tr>
<td>Phase Separation</td>
<td>3D pore arrangement</td>
<td>Complex procedure</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lack of control fiber arrangement</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Difficult to be scaled</td>
</tr>
<tr>
<td>Templating</td>
<td>Wide material selection</td>
<td>Sacrificial substrates</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fiber dimension and arrangement limited</td>
</tr>
<tr>
<td></td>
<td>Control over fiber diameter/length</td>
<td>Limited to specific polymers</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Difficult to be scaled</td>
</tr>
<tr>
<td>Drawing</td>
<td>Wide material selection</td>
<td>Low productivity</td>
</tr>
<tr>
<td></td>
<td>Simple procedure</td>
<td>Not consistent fiber diameter</td>
</tr>
<tr>
<td>Extraction</td>
<td>Cheap natural materials as the starting material</td>
<td>Limited material selection</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Limited control of fiber diameter and length (a few microns)</td>
</tr>
<tr>
<td>Polymerization</td>
<td>Polymer synthesized directly to fibers</td>
<td>Limited material selection</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Limited control of fiber diameter and length (a few microns)</td>
</tr>
<tr>
<td>Electrospinning</td>
<td>Easy setup</td>
<td>2D pores or microstructure arrangement</td>
</tr>
<tr>
<td></td>
<td>Cost effective</td>
<td>Poor cell infiltration into the core of the scaffolds</td>
</tr>
<tr>
<td></td>
<td>Easy control over fiber diameter, microstructure</td>
<td>Usually toxic solvent used</td>
</tr>
<tr>
<td></td>
<td>and arrangement</td>
<td>Low throughput</td>
</tr>
<tr>
<td></td>
<td>Wide material selection</td>
<td>Complex procedure</td>
</tr>
<tr>
<td></td>
<td>Wide fiber size range (from several nanometer to</td>
<td></td>
</tr>
<tr>
<td></td>
<td>several microns)</td>
<td>Jet instability</td>
</tr>
<tr>
<td>Melt spinning</td>
<td>Easy to scale</td>
<td>Limited material selection (melt-processable polymer)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Limited fiber sizes (a few microns)</td>
</tr>
<tr>
<td>Wet spinning</td>
<td>Solvent recovery for reuse</td>
<td>Complex procedure</td>
</tr>
<tr>
<td></td>
<td>Oldest process</td>
<td>Weak fibers until dry</td>
</tr>
</tbody>
</table>
1.2 Nanofiber Features and Application

Nanofibers are attracting significant interest as a versatile one-dimensional mesostructure due to their unique features and properties. This section focuses on the introduction of these unique features and the novel applications of nanofibers for the past few decades.

1.2.1 Unique features of nanofibers

As discussed in the previous parts, dependent on production methods, the resultant fiber length varies from micron range to extremely long (~kilometers or to infinity) while the long fibers can be assembled into a three-dimensional porous mat. Additionally, fibers with small diameter would have high surface volume ratio and a high density of pores formed from the nanofibers entanglement. For example, for a nonwoven mat composed of Nylon-6 nanofibers from electrospinning, the Braunauer-Emmett-Telller(BET) surface area is from 9 to 51 m²·g⁻¹ and the porosity is from 25% to 80% while the pore size varies from 2.737 to 0.167 µm¹⁴⁷. Thus the pores in the fiber mats are relatively large and the pores can be fully interconnected to form a three-dimensional network. The surface area of nanofibers could be further increased by smaller pore formation on individual fiber surface by controlling the experimental parameters.

Fiber formation process usually involves the rapid stretching of polymer jets or polymer droplets, which leads to an extremely strong shear force on the polymer chains. The shearing force and rapid polymer solidification prevent the polymer chains from relaxing back to the equilibrium states which complicates the polymer chain orientation development and
crystalline. Besides controllable length, high surface volume ratio, high porosity and low density, the materials that form nanofibers can be organic, inorganic or hybrid, the orientation of fibers can be ordered or random, the internal morphologies can be core-sheath, hollow or even multichannelled. Thus the single fiber or mats formed from fibers have high flexibility on dimensionality, directionality, composition and morphology, which further promotes the potential application of nanofibers in various academic and industrial fields. We present here a short summary of the major application areas including energy conversion and storage, desalination membrane, composite enhancement and tissue engineering.

1.2.2 Nanofiber Application

1.2.2.1 Energy conversion and storage

Energy is vital in all aspects of modern society. Energy conversion and storage devices gained more interest in academic and industrial fields due to the increasing world population and energy needs. The next generation of efficient energy conversion and storage devices should meet the requirements of being rechargeable, reversible and highly durable. To satisfy all these needs, functional materials with improved performance, chemical and electrochemical stability as well as minimum environment effect are preferred. Nanofibers have attracted lots of attention in energy related device synthesis due to their unique properties including high surface area to volume ratio, low density, high pore volume and exceptional mechanical strength\textsuperscript{48,49,50}.

The fuel cell is a device able to covert the hydrogen electrochemical oxidation fuel or hydrogen-rich fuel into electrical energy at high efficiency. The biggest difference of fuel cell
from conventional electrochemical cell batteries is that a flow of chemical of hydrogen or only air is needed to generate the electricity\textsuperscript{51}. The chemical product from the fuel cell is only water which eliminates any possible pollution. Nanofibers have been developed to apply to all components of a fuel cell including electro-catalyst, electrolyte membrane and catalyst support material. Pt is the main component of the electrocatalyst and the spinning of Pt to an extremely fine fiber diameter (<10 nm) is initially difficult. Along with the popularity of electrospinning, catalytic electrospun (NWs) nanowires of Pt/Rh from electrospinning was first proposed and exhibited better performance than conventional catalyst of high dispersed PtRu NPs on carbon\textsuperscript{52}. The mixture system of Pt/Rh nanoparticle and nanowire system also showed improved catalyst capability. The polyamide-6 (PA 6) nanofibers coated with a Pt layer of ~ 85 nm thickness showed high current density and enhanced performance due to the large surface area, reduced diffusion resistance and excellent tolerance of CO poisoning\textsuperscript{53}.

Besides catalysts, the electrode supporting material is crucial for fuel cell development on the performance and durability. Carbon is the most widely used support material for fuel cell due to its large surface, high electronic conductivity and low cost. However, carbon corrosion is unavoidable during the long term fuel cell operation. Carbon nanofiber is a promising material for catalyst support. Carbon nanofibers from PAN nanofibers have been developed with improved conductivity over carbon particles due to easier electron transfer and better durability\textsuperscript{54}. What is more, by incorporating various amounts of heteropolyacid (HPAs) in the PAN precursor, the electrical conductivity of HPA-CNf exhibited have been improved with increasing HPA content\textsuperscript{55}. The HPA-CNf conductivity and thermal stability can be further improved by incorporating nickel nitrate\textsuperscript{56}. 
Nanofibers tend to form mats in an easy and spontaneous way. Such mats have been utilized in developing fuel cell membranes in the following two ways. One is to form a porous non-conductive or less conductive polymer fiber matrix acting as mechanical reinforcement and then have it filled with highly proton conducting components\textsuperscript{57,58}. Perflorosulfonic acid (PFSA) isomers such as Nafion are the most widely utilized polymer matrix\textsuperscript{59,60}. The other way is to form a conducting porous fiber mat first and then have it reinforced with a second polymer to provide mechanical stability. In either case, conductivity is significantly dependent on the volume fraction of the proton conductive component\textsuperscript{61,62}. However, several studies showed that mechanical and hydrolytic stability or reduced methanol permeability are largely improved when conductivity of the membrane is reduced due to the existence of non-conductive component\textsuperscript{63,64}. Thus balance among all the properties is needed for membrane development.

The production of lithium-ion batteries (LIB) is another energy related area with wide nanofiber utilization. Reversible insertion and extraction of lithium cations into/from a host matrix accompanying with the electron flow through an external circuit to generate electrical energy is needed inside the batteries\textsuperscript{65}. The main constituents of LIB are an anode, cathode and an electrolyte as electronic insulator while Li\textsuperscript{+} conductor is the main constituents of the LIB\textsuperscript{66}. A wide range of architectures and morphologies, such as hollow fibers, triaxial core-sheath, biaxial, nanonuggets, nanobelts, and nanowires, have been studied as the cathodes of lithium-ion batteries. LiCoO\textsubscript{2} is the most widely used commercial cathode material due to its high specific energy density and cycle life. LiCoO\textsubscript{2} fiber cathode with large surface areas and small pores has achieved high initial discharge capacity of 182 mA h
g\textsuperscript{-1} compared with 140 mA h g\textsuperscript{-1} from conventional powder and film electrodes\textsuperscript{67}. However, this kind of cathode suffers from the large loss of capacity during time since the Li\textsubscript{2}CO\textsubscript{3} and CoF\textsubscript{2} are formed due to the dissolution of cobalt and lithium cations during the charge-discharge process. Coating of the nanofibers is a promising strategy to address this problem. For example, coaxial fibers with LiCoO\textsubscript{2} fibers\textsuperscript{68} or LiNi\textsubscript{0.8}Co\textsubscript{9.1}O\textsubscript{2}\textsuperscript{69} as the core and MgO as the shell were synthesized and the MgO coating avoided impedance growth. These MgO coating protected the surface from passive film formation during cycling with improved reversibility. 90\% of the discharge capacity of LiCoO\textsubscript{2}/MgO was remained after 40 cycles while 52\% for the uncoated Li fiber electrode. The fiber coating strategy has already been applicable to other commonly used cathode materials such as LiFePO\textsubscript{4} and V\textsubscript{2}O\textsubscript{5} to improve the overall battery especially cycling stability.

Carbon is the most widely used anode material due to its high safety, low cost and great cell life. However, the low cell voltage, low specific charge and low rate capability still limit its application. Carbon nanofibers from thermal treatment of PAN nanofibers showed highest reversible capability and good rate capability due to the hierarchical structure which includes a mixture of disordered defects and dangling bonds\textsuperscript{70}. Doping nanofibers with Si or Sn nanoparticles is an approach allowing to both overcome the drawbacks of poor cycling performance due to large volume change and particle aggregates and utilize the high theoretical capacity\textsuperscript{71,72}. Improved reversible capacity and cycle stability were observed due to the favoring electronic and ionic transport through the surrounding media in Si@CNFs in nanofibrillar networks. Other inorganic particles including Co\textsubscript{3}O\textsubscript{4}\textsuperscript{73}, Fe\textsubscript{3}O\textsubscript{4}\textsuperscript{74} and MnO\textsubscript{x}\textsuperscript{75} have already been embedded inside carbon nanofibers anodes and improved performance
was demonstrated. Nanofiber matrix has also been proposed for LIB membrane due to the better interconnectivity for ionic conduction, good homogeneity, control over the morphology of the membrane and flexible inorganic particle incorporation\textsuperscript{76}.

The application of fibrous structures in other energy related fields including dye-sensitive solar cell and supercapacitor is not covered in this thesis due to the length limitation. In summary, nanofibers are promising to satisfy the challenges of energy related applications because of the unique properties.

1.2.2.2 Desalination membrane

Drinkable water supply shortage due to human consumption and irrigation is currently one of the major global problems. The alternative way to solve fresh water shortage is to treat seawater or wastewater into potable drinking water by desalination (Figure 1.24). In the past two years, research of the use of nanofiber on desalination membrane (MD) improvement has been significantly increased. Reverse osmosis (RO), nanofiltration (NF), ultrafiltration (UF) and microfiltration (MF) are four main membrane-based technologies and successful application of nanofibers membrane for these pressure-driven processes has been proposed\textsuperscript{77,78}. The PAN nanofibers with an active layer made of chitosan with porosity of 70\% exhibited higher flux rate than commercial NF membranes after 24 hours and the rejection rate of oily wastewater has been larger than 99.9\%\textsuperscript{79}. PAN nanofibers with a thin film of PVA layer deposition showed high rejection rate in an oil in water emulsion system at very low feed pressure\textsuperscript{80}. After drying the PVDF nanofibrous membrane with diameter around 500 nm for 24 h at room temperature and using the saline water at different NaCl
concentrations as the medium, the air gap membrane desalination (MD) test showed that the PVDF nanofibers rejection rate increased exponentially with increasing temperature difference and the salt concentration in membrane is below the concentration in drinking water. The PVDF membrane performance remains the same even after two months of continuous operation. DCMD performance of a polyvinilidenefluoride-co-hexafluoropropylene(PVDF-HFP) nanofibers membrane was also studied as these copolymers have higher hydrophobicity and free volume than PVDF. The salt rejection from this membrane is around 99.99% while the permeate flux is 4.28 kg/m². PVDF is the most popular polymer for MD synthesis due to its high mechanical and thermal integrity as well as good chemical resistance. One new class of proposed polymer for desalination of nanofiber MD is aromatic fluorinated polyoxadiazoles (F-POD), polyoxadiazole copolymer (Co-POD) and polytriazoles (F-PT) while the salt rejection ratio was more than 99.95% for all cases. Besides desalination of sea water, nanofibrous membranes have also been utilized for desalination of geothermal water (~from Sahah, Malaysia). During this process, high amount of energy to evaporate the feed water is not required which reduces the cost of water production. Research on separation of ethanol or other volatile organic compound (VOC) from water by using PVDF nanofibrous membrane has also been developed. For example, the chloroform concentration was found to decrease dramatically in the mixture of water and chloroform with the PVDF nanofiber membrane during the MD experiment. This good performance of rapid removal of VOC from water is due to the hydrophobicity, appropriate pore size and the high surface area provided by the nanofibrous membrane.
1.2.2.3 Composite enhancement

During the past several decades, composite materials have been used widely in every type of advanced structural applications including land, sea and air transport vehicles, space exploration, military defense, health and sporting items. Among all the various kinds of composites, fiber reinforced polymer (FRP) composite materials are the most widely used and versatile ones at present\textsuperscript{86, 87, 88}. FRP composite is a family of materials with a
thermoplastic or thermosetting polymer matrix in which the reinforcing fibers are embedded. The compositions of these two basic constitutes can be designed to tailor the property of the composite to satisfy the desired application requirement. Nanofibers are chosen as the composite component since they are continuous, extremely long structures with high aspect ratio and there are no fiber edges as stress concentration points. Also, the molecular orientation in fibers due to stretching increases the single fiber modulus and the fiber mats can be easily dispersed in the polymer matrix. Traditional FRP composite used the reinforcing fibers to reach specific mechanical performance. Fibers can be embedded in matrix at two extreme conditions: (1) composites containing short randomly oriented fibers and the resultant composites display isotropic mechanical property; (2) composites containing long unidirectional fibers and the resultant composites display orthotropic and strong reinforcing effect. Bulk composite structures and laminate composites are the two main types of composite structures. For the bulk composite structures, the fibers function as the reinforcement fill due to their good mechanical properties, large aspect ratio, high surface area to volume ratio, good fiber matrix adhesion (Figure 1.25). Figure 1.25 demonstrates the advantage of using nanofibers over microfibers for increasing the ultimate tensile strength and Young Modulus. Delamination along interlaminar planes is a severe problem for laminate composites and is the dominating failure mode in laminates subjected to impact and fatigue loading. Delamination is usually a result of the mismatch of anisotropic mechanical and thermal properties of the plies at free edges, joints and under out-of-plane loading. Various methods including stacking sequence, laminate stitching as well as braiding have been developed to solve this problem. Nanofibers are adopted to reinforce the small scale
area to hinder delamination since these small areas experience high stress concentration which directly results in structural failure (Figure 1.26). By incorporating high-strength, tough and continuous carbon nanofibers (CNFs) into the ultrathin resin-rich interlayers of laminated polymer, the materials with a high strength and fracture toughness were developed. What is more, by embedding core-shell healing-agent-loaded nanofibers, the FRP materials with unique interfacial damage self-healing property were fabricated\textsuperscript{89,90}.

Figure 1.25: Comparison of fiber composite ultimate tensile and Yong modulus performance\textsuperscript{87}. 

\begin{figure}
\centering
\includegraphics[width=\textwidth]{comparison.png}
\caption{Comparison of fiber composite ultimate tensile and Yong modulus performance.}
\end{figure}
1.2.2.4 Tissue Engineering

Tissue engineering is an interdisciplinary technology of bioscience and biotechnology involving the restoration or regeneration of injured tissue by using various combinations of biomaterials, cells and bioactive agents. Cells, growth factor and scaffold are the three major constituents of tissue engineering. The cells grown on a scaffold ex vivo from isolated cells originating from a patient were implanted at the injured site. The growth factor
determines the growth and differentiation of the cells. Scaffolds can be also directly delivered to the injured site of the patient to induce tissue formation in situ. Scaffold can serve as either a temporary and artificial extracellular matrix (ECM) to degrade over time or a reservoir to deliver the bioactive agents to promote the injured tissue regeneration. ECM is a crucial 1D structured component of tissue and it is the substrate where the cells of the particular tissue are embedded. Nanofibrous scaffolds have attracted significant interest in many areas of tissue engineering due to the structural similarity to native extracellular matrix, compatible with a wide family of materials, controllable fiber size and orientation. Nanofibers have already been used in skin, vasculature, nerve, bone, cartilage, bladder and tendon in vivo or in vitro regeneration.\textsuperscript{92,93,94} Nanofibrous scaffolds have two typical configurations: 2D mats and 3D cotton-like balls (Figure 1.27). 2D mats usually have a flat topography and tightly packed fibers, which would hinder the cell infiltration after implantation. 3D mats are more favorable unless the orientation or functionality of nanofibers is important due to the highly desirable proper pore size and interconnectivity.

For example, nanofibrous vascular graft made of PCL coated with an arginine-glycine-aspartic acid (RGD) named Nap-FFGRGD has been developed and the RGD and hydrophobic naphthalene groups can self-assemble on the hydrophobic surface to form a RGD containing layer. The endothelial cells on the RGD-PCL were confluent and formed structures resembled the native vessel while the EC on the PCL graft were randomly aligned and the endothelialization rates of RGB-PCL grafts were much higher than the PCL grafts.\textsuperscript{95} In the field of nerve tissue engineering, highly aligned nanofibers is necessary to prevent neurite deviation of the axonal outgrowth on fibers from the natural axis of growth
which may otherwise result in delaying axonal extension from one end to another in a scaffold. The neurite orientation and morphology dependent on the fiber orientation and substrate topography affects the neurite growth, survival and differentiation of gene expression. Since the main components of bone ECM are collagen (organic) and Hap (inorganic), nanofibers composite is widely utilized for bone tissue engineering, e.g., Hap/PLLA\textsuperscript{96}, beta-tricalcium phosphate (\(\beta\)-TCP)/poly(\(\varepsilon\)-caprolactone) (PCL)\textsuperscript{97}, Hap/PLLA/collagen\textsuperscript{98} and Hap/PLLA/poly-benzyl-L-glutamate(PLBG)/collagen\textsuperscript{99} and \(\beta\)-TCP/PCL/collagen\textsuperscript{100}. Tendons are fibrous connections between muscles to bones and ligament connects bone to bone. Co-electrospinning of PLLA/collagen and PCL/collagen fibers onto opposite sides of a mandrel can produce a dual scaffold. In this scaffolds, the regional variations in mechanical properties were observed and the strain trend is same as the native muscle-tendon junction\textsuperscript{101}.

**Figure 1.27:** Electrospun nanofibrous scaffolds. (A) 2D nanofibrous scaffolds and (B&C) 3D nanofibrous scaffolds\textsuperscript{94}. 


Despite the versatility on nanofiber morphology and compositions as well as promising application in a wide range of areas, the main issue remains to bring the promising research into industrial practice. Given the low production rate of present technologies, there is still a long way to improve nanofibers fabrication. Technique such as needleless electrospinning has been developed recently to tackle this widely recognized issue but is still in early stage. Moreover, process variables to control fiber morphology, functionality in applications of this new technique are yet to be studied. Thus, the technique of fiber production development which warrants further research and industrial application in many fields is still in urgent need.
1.3 Layout of This Dissertation

The main objective of my graduate research is the development of a novel liquid shear based method to produce a large class of nanomaterials including nanofibers, nanosheets, rods, spheres as well as nanoribbons. This approach is facile, scalable, inexpensive and compatible with a wide range of polymers, including PLA, PS, cellulose acetate, zein as well as chitosan. It is applicable for functional fiber synthesis by incorporating nanoparticles or small molecules inside the fiber matrix. The thesis is organized as follows.

Chapter 2 introduces the process and mechanism of the liquid shear driven method. By shearing of a polymer solution inside a viscous medium miscible with the solvent, polymer liquid droplets were stretched to generate strands with high surface/volume ratio under near zero interfacial tension. During this liquid shearing process, a range of processes including droplet emulsification, droplet stretching, solvent diffusion, polymer solidified skin formation and possible jet splitting happen simultaneously. The final product morphology of the final product is determined by dominating process. For example, dominating emulsification process produced spheres while dominating droplet stretching process generated long strand structures.

Among all the structures, nanofibers have aroused the most wide research interest due to the unique properties including high surface area to volume ratio, and controlled organization direction. Current fiber production development cannot satisfy neither the commercial nor the research needs. Chapter 3 focuses on the fiber synthesis process in batch and continuous liquid shear driving way and presents fiber size dependence on operational parameters,
polymer solution parameters as well as shearing medium compositions by adopting polystyrene (PS) and poly (lactic acid) (PLA) as the model polymers. It is suggested that fibers with diameters range from 200 nm to several microns can be produced from a wide range of polymers.

Chapter 4 proposed a novel method to produce ultrathin fiber formation from the heterogeneous oil in oil emulsion system instead of the homogeneous polymer solution. For the first time, phase-separated polymer solution containing one type of polymer and one type of solvent was adopted for fiber formation. The fiber size capacity for liquid shear technique is reduced from 200 nm to 100 nm, which significantly enhances its competitive strength with electrospinning.

Chapter 5 presents one application of fiber production from liquid shear process. Majority of the antibacterial drugs are embedded inside the biodegradable fiber matrix instead of on the fiber surface and the release of the drug can be controlled by the decomposing rate of fibers. Chapter 6 introduces other possible applications and future research directions for this project briefly, which includes process modeling by COMSOL multiphysics software and synthesis of inner/surface hierarchical fibers.
1.4 References


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Chapter 2 Liquid Shear Driven Synthesis of Polymer Micro- and Nanomaterials with Controllable Morphologies
2.1 Introduction

Polymeric micro- and nanomaterials with various morphologies play an important role in the diverse array of applications including drug delivery, functional material formulation as well as microfluidics. Particle shape is a crucial parameter to determine the particle functions. Several approaches, including self-assembly\(^1\), nonwetting template molding (Figure 2.1)\(^2\), photolithography (Figure 2.2)\(^3\) as well as the mechanical stretching of spherical particles (Figure 2.3)\(^4\), have been proposed to create polymeric materials with controlled shapes. Although some of these approaches have the advantages of easy to scale up, high yield and precise control on particle, the disadvantages, including high cost, particle size limitation, high operation temperature, low throughput and limited ability on particle synthesis in 3D, are difficult to avoid. What is more, the length of the obtained nanomaterials is all limited at micrometer range and fibers were never considered as a product of these approaches. Even for electrospinning, the available and controllable morphologies are only spheres, fibers and beads on a string (Figure 2.4)\(^5\). In summary, a simple, versatile, inexpensive approach with high throughput is still needed to further the application of polymeric materials in diverse areas.
Figure 2.1: A) Schematic demonstration of the experimental setup during the photolithography nanofabrication process. B) SEM images of microparticles formed using this approach. The scale bar in all of the figures is 10 µm².
Figure 2.2: A) Schematic illustration of the PRINT process in which the nonwetting nature of the fluorinated materials and surface allows the generation of the isolated particles. B) SEM images of shapes using PRINT: a) Trapezoidal particles; b) bar particles; c) conical particles; d) arrow particles. 

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Figure 2.3: A) Schematic illustration of making particles with different shapes. B) SEM images of shapes made from scheme A: a) spheres; b) rectangular disks; c) rods; d) worms; e) oblate ellipses; f) elliptical disks; b) UFOs; h) Circular disks. (Scale bars=2µm).
Nanofibers are essential materials for liquid and aerosol filtration, improved batteries, biotechnology, and tissue engineering\(^6\). Polymer nanofibers can be fabricated by mechanical drawing, force spinning, electrospinning, phase separation, template synthesis and self-assembly\(^7,8\). Mechanical drawing methods such as melt blowing and bicomponent spinning have high productivity, but they produce fibers from melt-processable polymers with relatively large diameter. Electrospinning is a versatile method that produces nanofibers with uniform diameters in a wide range, but of modest production rate even when scaled up by parallel operation of many nozzles, or by spinning from a drum\(^9\). Besides nanofibers, other one dimensional polymer nanomaterials have also been investigated from academic
areas and they could extend nanofibers applications to the ones requiring high surface area and strong adhesion. Materials in the form of nano- and microribbons are less investigated, but rod-like, sheet-like and other asymmetric particles are found to be useful as foams and emulsion superstabilizers, or as components of capsules, electro-optical media and viscosity modifiers. The formation of finely dispersed materials such as nanoparticles and nanofibers requires the creation of a large surface area (usually a highly energy-consuming process) and the ability to control and modify the characteristic sizes and shapes of the structures.

One of the major challenges of nanoscale engineering is the development of controllable, scalable, rapid and cost-effective processes for nanomaterials synthesis. In this chapter, we report a family of liquid-based processes that can be used to synthesize a broad variety of polymer nanostructures, including nano- and microfibers, ribbons and sheets, as well as rods and spheres. Such materials have numerous applications in current and emerging technologies.

2.2 Experimental Section

2.2.1 Materials

High molecular weight (MW) polystyrene (PS) (Mw ≈ 190,000 - 230,000, Mw/Mn ≈ 1.6), cellulose acetate (CA) (Mn ~ 30,000), and titanium (IV) isopropoxide (TIPP) were obtained from Sigma-Aldrich. Low MW PS (Mw = 5,780, Mw/Mn = 1.05) was obtained from Pressure Chemical (Pittsburgh, PA). Ingeo 6751D poly-(lactic acid) (Mw= 62,720, Mw/Mn= 2.880) was provided by NatureWorks Inc. Titan 470 carbon black was provided by
Cabot, Inc. Chloroform and denatured alcohol were obtained from Fisher Scientific, and oleic acid capped iron oxide nanocrystals (10 nm) were obtained from Ocean NanoTech (Fayetteville, AK). The PDMS precursor (Sylgard 184) was from Dow Corning.

2.2.2 Solution Characterization Method

The zero shear viscosity of the different solutions was measured with a stress controlled rheometer (AR2000, TA instrument) having a parallel plate geometry (Peltier plate in 40 mm diameter and upper cone geometries in 2° cone angles).

2.2.3 Apparatus and Procedure

A benchtop Couette flow apparatus with a 2.3 mm gap (Figure 2.5) was constructed with a rotating cylindrical shaft (radius \( r_i = 5.0 \) mm) and a disposable, stationary polypropylene tube (ID = 14.6 mm, Evergreen Scientific). Shaft rotation was digitally controlled (150 - 6000 rpm) by a Cole-Parmer Servodyne Mixer, Model # 50003. The solidified polymer products were formed by liquid-liquid shear-dispersion in a viscous antisolvent medium, similarly to the process previously used to fabricate anisotropic polymer rods. Typically 0.05 ml of polymer solution, injected into 7-8 ml of antisolvent, was sheared at 2000 to 6000 rpm for 2 min. The shearing medium was mixture of glycerol and polymer antisolvent. The rpm range in our device yielded \( \tau \) ranging from \( \approx 34 \) to 204 Pa.

Our initial experiments at higher shear rates showed significant increase in polydispersity from instabilities at the top free liquid-air interface. This instability was suppressed by introducing a top baffle made of cured PDMS with uniform thickness to prevent drawing of air into the liquid medium during shear. The maximal shear rate in such a
device could be limited by an onset of turbulence in Taylor-Couette flow as predicted by the critical Taylor number. In addition to eliminating the free top surface with baffles, the flow can be additionally stabilized by modulating the speed of the rotor, introducing liquid flow in the axial direction, periodic movement of the central cylinder in the axial direction, or by increasing the medium viscosity.

Figure 2.5: Modified batch liquid shear device with a PDMS baffle to prevent turbulence by eliminating the top free liquid surface.

A continuous liquid shear fabrication device, which has a number of advantages to the batch unit described above and was used for making of the smallest size fibers reported in this paper. The key principles of the process are the same, but instead of a Couette shear flow,
the continuously operating device is using Poiseuille flow through simple cylindrical pipe. The polymer solution is injected through a small side inlet into the larger pipe where the viscous antisolvent is pumped at high flow rates (Figure 2.6). The high pressure continuous shear flow device uses a triplex positive displacement pump (CAT Pumps, Model#2SF30ES) to push the viscous antisolvent medium through 4 foot long 4.57 mm ID stainless steel tube. The polymer solution is injected using a syringe pump (New Era Pump Systems, Model# NE-1000). The process is somewhat sensitive to the location of injection of the polymer solution in the flowing antisolvent, but overall is extremely robust and controllable. The nanofibers samples produced by the instrument are typically of less than 200 nm in diameter and tight size distribution (Figure 2.7). The device produces a continuous stream of nanofibers dispersed in liquid medium (up to 10 kg/h at a rate of medium circulation of 1.8 m$^3$/h while the throughput of Nanospider from Elmarco is only 0.171 kg/h$^{14}$). These liquid-borne nanofibers are easily amenable to wet-laying, and thus can be easily integrated in a number of common filter and nonwoven manufacturing lines$^{15}$. This continuous fiber product device was named Xanoshear patented by Xanofi and no more details will be discussed in this thesis.
Figure 2.6: A) A prototype device for continuous fabrication of fibers by liquid shear. The injected polymer solution is subjected to shear in an antisolvent medium flowing in a pipe, rather than a Couette flow device. The polymer is broken up into droplets, which are sheared simultaneously in the liquid to form the fibers. B) Sample of PS nanofibers produced by our XanoShear™ device.

Figure 2.7: SEM images and size distribution histogram of cellulose acetate nanofibers produced by XanoShear™ continuous flow shear device.

Despite the advantages of Xanoshear™ including continuous product synthesis, compatible with syringe pump, flexible for mat formation composing of more than one polymer, all the presented experiment results are based on batch process since it needs
minimum equipment investment and materials.

2.2.4 Characterization

Optical microscopy (Olympus BX-61 microscope with a DP-70 digital CCD camera) was adopted to characterize the sample structures in micrometer range. The JEOL 2000FX Scanning Transmission Electron Microscope (SEM) was used to study the sample morphology and size below micrometer. Each sample was coated with gold using a sputtering machine for 60 s prior to observations under the SEM. The average diameter and standard deviation of each sample were determined by at least 50 measurements from the SEM or optical microscopy images. Measurements were conducted by an image-processing program named ImageJ (NIH).

2.3 Mechanism Study

2.3.1 Taylor-Couette Flow

The classical Taylor-Couette flow is the motion of a viscous incompressible fluid in the region between two rigid coaxial cylinders, which rotate at constant angular velocities\(^{16}\). For the equipment we adopted, the outer cylinder is held fixed while the angular velocity of the inner cylinder is controlled digitally. It is demonstrated that the flow in the gap between two cylinders is dependent on Reynolds number (Re)\(^{17,18,19,20}\). At low Re, the flow is laminar, steady and purely azimuthal and is referred as circular Couette flow (CCF). As the Reynolds number of the inner cylinder is increased to a certain value (Re\(_0\)), the laminar flow becomes unstable resulting in axially periodic Taylor vortex flow which is axisymmetric. The resulting
velocity of the Taylor vortex has an azimuthal component on top of the existing CCF velocity component as well as axial and radial components, which leads to the rational motion in the (r,z)-plane (Figure 2.8 A). Increasing the Reynolds number further above the other critical value (Re_{cr2}), chaotic and turbulent Taylor vortex flow (Wavy vortex flow) containing a wide range of bifurcations is generated.

**Figure 2.8:** Schematic illustration of A). Taylor vortex flow when circular Couette flow becomes unstable. The axisymmetric vortices are stacked on top of each other in the axial direction. B). Wavy vortex flow when Taylor vortices become unstable to non-axisymmetric perturbations and rotate with some wavespeed around the axis of rotation^{21}.

The geometry of the Taylor-Couette equipment is defined by the height to gap aspect ratio, \( \Gamma=L/d \) where \( L \) is the axial dimension of the domain and \( d \) is the gap width, the radius
ratio, $\eta = R_1/R_2$, where $R_1$ and $R_2$ are the inner and outer cylinders radius collectively and the ration rate ratio $\omega_2/\omega_1$, where $\omega_1$ and $\omega_2$ are the inner and outer cylinders rotation rates. Reynolds number is defined as the ratio of inertial force to viscous force:

$$Re = \frac{R_1\omega_1(R_2 - R_1)}{\nu} = \frac{U_0d}{\nu}$$  \hspace{1cm} (2.1)

where $U_0$ is the inner cylinder rotation velocity and $\nu$ is the kinematic viscosity of the fluid.

The flow is filled in the cylindrical domain between two rotating cylinders:

$$\Omega = \Sigma \times R, \Sigma = \{(x, y) \in R^2; R_1^2 < x^2 + y^2 < R_2^2 \}$$  \hspace{1cm} (2.2)

And the velocity $V$ of the fluid and the pressure $p$ satisfy the Navier-Stokes equations:

$$\begin{cases}
\frac{\partial V}{\partial t} + (V \cdot \nabla)V + \frac{1}{\rho} \nabla p = \nu \Delta V + f \\
\nabla \cdot V = 0
\end{cases}$$  \hspace{1cm} (2.3)

Where $\rho$ is the medium density, $p$ is the pressure, $V$ is the fluid velocity vector and $f$ is the density of external force per unit mass. $\nabla$ is the gradient operator, $(V \cdot \nabla)$ is the divergence and $\Delta$ is the Laplace operator. $f$ equals zero for standard situation since gravity can be incorporated in the pressure term $p$. so Navier-Stokes equations for an incompressible Newtonian liquid on $\Omega$ become:

$$\begin{cases}
\frac{\partial V}{\partial t} + Re(V \cdot \nabla)V + \nabla p = \Delta V \\
\nabla \cdot V = 0
\end{cases}$$  \hspace{1cm} (2.4)

Two geometric idealizations are made to simplify the calculation: $\eta \to 1$ and $\Gamma \to \infty$. Under limit of $\eta \to 1$, curvature effects become negligible. Under limit of $\Gamma \to \infty$ and the assumption
of axial z direction periodicity, azimuthal velocity is only dependent on r. The boundary conditions are:

\[ v_r=v_z=0, v_\theta=1, \text{ at } r=\eta/(1-\eta) \] and \[ v_\theta=\omega/\eta \text{ at } r=1/(1-\eta) \] (2.5)

The problem has a steady-state solution, the Couette flow, expressed by the following equations in cylindrical coordinates \((r, \theta, z)\):

\[
\begin{cases}
V^{(0)} = (0, v_\theta^{(0)}(r), 0) \\
p^{(0)} = \text{Re} \int \frac{[v_\theta^{(0)}(r)]^2}{r} dr \\
v_\theta^{(0)}(r) = Ar + \frac{B}{r}, A = \frac{\omega_2 - \omega_1 \eta^2}{1-\eta^2}, B = \frac{R_2^2 (\omega_1 - \omega_2)}{1-\eta^2}
\end{cases}
\] (2.6)

The external cylinder is fixed: \(\omega_2=0\). Thus \(A = \frac{-\omega_1 \eta^2}{1-\eta^2}, \quad B = \frac{\omega_1 R_2^2}{1-\eta^2}\)

This solution is independent of \(z\) and \(\theta\) and the streamlines are circles centered the rotation axis as shown in Figure 2.8. This model is idealized based on the assumptions of non-slippery boundary condition, infinite cylindrical length or the aspect ratio is close to zero. Under these conditions, the end effects can be ignored. However, the actual case is more complicated involving vortices. As a consequence of the vortices, high speed fluid near the inner cylinder is carried outward in the outflow region while low speed fluid near the outer cylinder is carried inward in the inflow regions between vortices. Thus the angular momentum of the fluid in the annulus is redistributed.

The criterion of the flow type of inviscid liquid inside the cylinder gap can be expressed as the following equation:
\[
\frac{d}{dr}(r^2 \nu^2) > 0 \quad \text{for} \quad R_1 \leq r \leq R_2
\] (2.7)

Substituting the equation 2.6 in equation 2.7 leads to the criterion that

\[
\frac{\omega_2}{\omega_1} > \eta^2
\] (2.8)

However, for the fixed external cylinder, the criterion cannot be met since \(\omega_2=0\). Thus, the flow is Taylor vortex while the velocity in axial and radical directions cannot be neglected. For the viscous liquid, the criterion for circular Couette flow is the Reynolds number below \(\text{Re}_0\), which is only dependent on radius ratio (Figure 2.9). For the batch experimental setup we adopted, all the related parameters are listed in Table 2.1 and the \(\text{Re}_0\) is appropriately 80. The Re values is in the range of 60 ~ 180 for 50% v/v Ethanol 50% Glycerol from at external shearing increases from 2000 rpm to 6000 rpm.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>(R_1/m)</td>
<td>0.005</td>
</tr>
<tr>
<td>(R_2/m)</td>
<td>0.0073</td>
</tr>
<tr>
<td>(\eta)</td>
<td>0.684932</td>
</tr>
<tr>
<td>(\omega_1/rpm)</td>
<td>0</td>
</tr>
<tr>
<td>(\omega_2/rpm)</td>
<td>2000</td>
</tr>
<tr>
<td>(\omega)</td>
<td>0</td>
</tr>
</tbody>
</table>

Table 2.1: Parameters of batch process
2.3.2 Droplet Shearing/Emulsification

Formation of liquid droplets suspended in another immiscible liquid subjected to shear flow is the strategy of emulsion preparation. It is proposed by fluid dynamics and computer modeling researchers that droplets begin to deform if the droplets are dispersed in another immiscible liquid under shear flow and the droplets have the potential to break up into fragments if the local shear rate is sufficiently large (Figure 2.10)\textsuperscript{22}. The viscosity ratio of the droplet to medium liquid is defined as $\lambda = \frac{\mu_d}{\mu_m}$. The time scale for droplet stretching is $\tau_r$.
and that for droplet shape relaxation is $\tau_0$. The capillary number is the ratio of these time scales:

$$Ca = \mu_m \gamma a / \sigma$$ (2.10)

where $a$ is the droplet diameter, $\sigma$ is the interfacial tension and $\gamma$ is the shear rate.

When the droplet is very viscous ($\lambda >> 1$), the rate of droplet elongation is relatively small to the droplet relaxation. Thus the high viscous droplets cannot break. The critical viscosity ratio $\lambda^*$ for droplet break up is roughly 3. The value is not fixed since it is dependent on several parameters, such as rheology property of medium and flow geometry. However, no calculation procedure has been established for this parameter. For $\lambda < \lambda^*$, the criterion is critical capillary number ($Ca_c$), above which the droplet eventually breaks. For capillary number below the critical value, a steady drop shape exists when the droplet is sheared. When the droplet is sheared in the regime at $Ca \sim Ca_c$, it breaks up through the “end-pinching” mechanism separated by smaller droplets (Figure 2.10 after T=50). Accurate critical capillary number calculation is complex due to the divergence of time required to reach steady state and the available modeling and experimental data to date are plotted in Figure 2.11.
Figure 2.10: 3D volume-of-fluid simulation of drop breakup in simple shear A) for Ca=0.45, Re=0.125, \( \lambda = 1 \), equal densities B) for Ca=0.555, \( \lambda = 0.77 \), equal densities\(^{22}\).
Figure 2.11: Critical capillary numbers dependence on viscosity ratio from numerical simulation and experimental data\textsuperscript{22}. 
Figure 2.12: Plotting of droplet breakup mechanism as a function of $\lambda$ and Ca based on the experimental results\textsuperscript{24}.

The aforementioned droplet shearing researches are based on two immiscible Newtonian liquids while the polymer solution is usually shearing thinning liquid exhibiting more complicated properties subject to external shearing\textsuperscript{25,26}. Polymer solution is a viscoelastic fluid. Majority of viscoelastic materials are high viscous and exhibiting non-Newtonian (shear thinning) property. Unlike pure Newtonian droplet deformation, the deformation of non-Newtonian droplet in a Newtonian medium is more complex. Extra parameters are defined to characterize the shearing process:

$$\lambda = \frac{\Psi_{10}}{2\eta_p}$$  \hspace{1cm} (2.11)
\[ Ec = \frac{\lambda_s \gamma}{\eta_m a} \]  \hspace{1cm} (2.12)

Where \( \Psi_{10} \) is the coefficient of the first normal stress difference due to the droplet viscoelasticity; \( \eta_p \) is the polymeric contribution to viscosity. \( Ec \) is the elastocapillary number (\( Ec \)) which is the ratio of the droplet viscoelasticity and external shear stress. \( \lambda_s \) is the timescale of stress evolution.

Two deformation modes exist for the polymeric viscoelastic drop under shearing: a) Droplet deforms at flow direction. Similar to Newtonian liquid, droplet elongates in the flow direction from spheres to ellipsoidal shape and to a long thread shape. This deforming mode happens at low \( Ec \) where the viscoelastic force is weak enough to be neglected. b) Droplet deformation in the vortices direction. Droplet elongates in the flow direction from spheres to ellipsoidal shape initially. Then contraction of droplet in the flow direction and elongation in the vortices direction happen simultaneously. This deforming mode is common for high \( Ec \) number due to the dominant restoring effect from the viscoelastic property\textsuperscript{27,28}. No matter at which direction the droplet deforms, the deforming mechanism remains the same and is dependent on \( \lambda \) and Ca.
In summary, for polymer droplet, $\text{Ec}$ is the crucial parameter to determine the droplet deformation direction while $\text{Ca}$ and $\lambda$ determine whether the droplet breaks.

### 2.3.3 Phase Separation

In liquid shear process, the diffusion between the polymer solvent and shearing medium causes the polymer to precipitate from the solution, which is called coagulation. Coagulation is crucial since it determines the morphology and throughput of this technique without involving chemical reaction. The kinetics of the fiber coagulant is controlled by the solvent diffusion. While the droplet deforms, solvent diffuses in two ways: one is from the polymer droplet to surface and the other is from the droplet surface to the medium. The former process leads to the solidified layer on the droplet surface while the latter results in the solidification of inner core of the polymer droplets. Solvent diffusion is a crucial step for various processes, such as coating drying and polymer processing. Diffusion coefficient ($D$)
is the parameter to characterize the diffusion rate and can be calculated by Stokes-Einstein equation:

\[ D = \frac{k_B T}{6\pi \eta r} \]  

(2.13)

Where \( k_B \) is Boltzmann’s constant, \( T \) is the absolute temperature, \( \eta \) is viscosity and \( r \) is the radius of the molecule. There are several limitations for Stokes-Einstein equation, such as only valid at low Reynolds number, sphere molecules assumption. Many deviations from the relationship have been observed. For solvent diffusion in the polymer solution, the case is much more complicated and the Stoke-Einstein equation is not reliable. However, it is a simple form to describe the relationship between diffusion coefficient and medium viscosity and is enough for my research at present. For precise quantification of the shear driven process, which is out of the range of this thesis, it is not applicable.

Under these mechanisms, the shearing of a polymer solution inside a viscous medium generates liquid droplets and the liquid droplets deform to strands with high surface/volume ratio. The solvent diffusion, due to the miscibility between antisolvent in the medium and the solvent, leads to the polymer precipitation. Thus the combination of shear-driven fluid extension with antisolvent-induced polymer precipitation is used for the synthesis of a broad range of nano- and microstructures in this part. These structures include nanofibers, nanoribbons, nanosheets and anisotropic particles (Figure 2.13), whose morphologies are critically dependent on the dominating process. To simplify the results and discussion part, the following parameters are defined:

\( \tau_c \): time scale for droplet reaches the steady state upon given shear rate.
\( \tau_d \): time scale for polymer solvent diffuses inside the droplet (~inner core solidification)

\( \tau_s \): time scale for solvent diffuses from surface to the medium (~solidified skin formation)

\( D_b \): diffusion coefficient for solvent diffusion in the polymer bulk

\( D_s \): diffusion coefficient for solvent diffusion from the droplet surface to the shearing medium
2.4 Results and Discussion

The class of synthesis processes reported here is based on direct injection of polymer solutions in the bulk of a viscous medium under shear. The medium is chosen to be miscible with the polymer solvent, while also inducing antisolvent precipitation of the dissolved polymer. The typical media contains glycerin and 20%-90% of antisolvent, such as water or ethanol, inducing polymer precipitation in the injected sheared solution.
For the shearing devices having a common concentric cylinder (Taylor–Couette) geometry and assuring controlled uniform shear rate, a typical procedure for synthesizing the materials on a laboratory scale includes injecting 0.05 ml of polymer solution into 6.5 ml of viscous medium sheared between rotating concentric cylinders of diameters 10 and 14.6 mm.

Our key finding is that under shear, the ultralow interfacial tension between the droplets and the medium enables the formation of high surface area liquid structures, which can serve as templates for the formation of diverse classes of polymer materials, at least one characteristic dimension of which may be on the nanoscale. As the sheared solution droplets become highly stretched, the solvent diffuses out of the polymer-containing liquid phase, while the antisolvent in the medium infuses it (Fig 2.13). As the composition of the solvent medium changes, the polymer precipitates into solid mass. The interplay of these effects (which occur rapidly and mostly simultaneously) results in the formation of a surprisingly rich variety of structures. We distinguished five general types of material morphology outcomes, and illustrated them in Figure 2.13 with polystyrene structures synthesized under different conditions.

2.4.1 Polymeric Sphere Formation

The first, largely trivial, case is realized when the antisolvent concentration in the medium is so low that the polymer precipitation would take too long to allow the stretched and string-like structure to be frozen (τ<sub>e</sub> ≪ τ<sub>d</sub>, τ<sub>e</sub> ≪ τ<sub>s</sub>). Thus, capillary fragmentation of droplets under shears happens and spheres are obtained. The resultant sphere sizes showed increasing trend with higher antisolvent solvent until the antisolvent concentration reaches
the value for fiber formation (Figure 2.14). Two spheres or multispheres connected structures attributed to the incomplete capillary fragmentation process were also observed from the SEM (Figure 2.15). Two processes contribute to the wide distribution of sphere size: a) End-pinching droplet breaking up produces the smaller satellite droplets between larger ones. b) The shear rate on droplets has gradient.

![SEM images of PLA spheres from 5%v/v Ethanol and 95% Glycerol.](image)

**Figure 2.15:** SEM images of PLA spheres from 5%v/v Ethanol and 95% Glycerol.
Low polymer concentration is another strategy for sphere formation, however, the formed spheres tend to aggregate, for example, sphere aggregates connected by short fibers or embedded in fiber matrix (Figure 2.16). Low polymer concentration not only increases the trend of droplet fragmentation but also reduces the possibility of droplet deforming at vortices direction. The combination of droplet fragmentation and fast diffusion process due to reduced polymer droplet viscosity leads to sphere formation. Droplets containing higher polymer concentration would resist capillary fragmentation and get sheared into anisometric structures. The resulting liquid fingers or strands begin solidifying into long continuous polymer structures (Figure 2.13 Path B).
2.3.2 Polymeric Rods Formation

The droplet experiences a tensile stress due to the velocity gradient of the surrounding liquid. The stretched droplet breaks and produces short threads if the external drag forces exceed its tensile strength. Rods structures are formed if the short thread solidifies. Two approaches of polymeric rods formation from liquid shear driven method based on the stretching-breaking mechanism will be introduced.

Our group has reported earlier that by shearing the SU-8 polymer solution (Mn~7000±1000) in the mixture of glycerol and ethanol medium, the suspension of polymer microrods with flat ends and uniform sizes can be fabricated. Aqueous foams can be stabilized solely with this kind of rods structures. The method is rapid, scalable, and robust. This rod formation technique can be expanded to other type of polymers, for example, PS. The stretched fibrous precipitates subject to secondary fragmentation (Figure 2.13 Path C) yields polymer microrods, similar to SU-8 rods reported earlier. The fragmentation of the
protofibers can be avoided by using polymers with higher molecular weights. For example, solutions of two batches of polystyrene of MW = 5.78 k and 230 k, sheared under nearly identical conditions, yielded short rods for the low MW polymer, and long fibers for the high molecular weight one (Figure 2.13 path E).

The morphology variation of structures sheared from polymer solution with different molecular weight can be explained by the different level of chain overlap in the polymer solution. Chain overlap refers to entanglement of the polymer molecules which can be described by entanglement number. The solution entanglement number \((n_e)_{soln}\) is defined as the ratio of the polymer molecular weight to its solution entanglement molecular weight:

\[
(n_e)_{soln} = \frac{M_w}{(M_e)_{soln}} = \frac{(\phi_f M_w)}{M_e}
\]  

(2.14)

Where \(M_w\) is the weight average molecular weight, \((M_e)_{melt}\) is the entanglement molecular weight in melt, \((M_e)_{soln}\) is the entanglement molecular weight in solution and \(\phi_f\) is the polymer volume fraction.

The number of entanglements per chain is then calculated by \((n_e)_{soln}-1\) as per entanglement involves two chains. For example, if \((n_e)_{soln} = 2\), each polymer molecular chain entangles with one polymer chain. Chain entanglements in the polymer solution limit the drop subdivision and oppositely the limited chain entanglement favors the generation of smaller droplets which forms uniform beads after solvent removal. During the electrospinning process, the following progression of observed fiber morphology due to increase of polymer entanglement can be observed: 1) beads only, 2) beads with incipient
fibers, 3) beaded fibers, 4) fibers only and 5) globular fibers/macrobeads. Researchers have also demonstrated that stable and complete fibers can be formed if the number of entanglements per chain is larger than or equal to 2.5 (Error! Reference source not found.) while incipient and incomplete fibers can be obtained at one entanglement per chain (Error! Reference source not found.) based on the study of a large range of polymer/solvent system.

The entanglement molecular weight of polystyrene is around 18,000. If Mw = 5800, Error! Reference source not found. from the above equation and no entanglements are formed in the polymer solution, which means that the droplet would subdivide into smaller droplets and be elongated into short rods under the shear (Figure 2.17, 2.18). If Mw = 230,000, Error! Reference source not found. >> 2.5 and the degree of entanglement in the polymer solution is high enough to prevent the droplets from further breaking up and to stabilize the synthesized fibers (Figure 2.17).
Figure 2.18: Schematic illustration of the mechanism of rod and fiber formation using solvent attrition under nanoshearing. a) Polymer solution droplet is deformed by shear. b) Droplet breaks up until shear forces are balanced by interfacial tension forces. c) Droplets elongate and stiffen as the polymer solvent diffuses out and antisolvent diffuses into the proto-fibers. d) Hypothesis of the role of polymer molecular weight in the rod/fiber formation process. e) Optical micrographs of (left) short polymer rods formed from 5.8k MW polystyrene solution and (right) long fibers from 230k MW polystyrene solution after shearing at 2000 rpm for 3 min in 75 % glycerol : 25 % ethanol. Scale bars = 100 µm.

Figure 2.19: SEM images of PS rods with Mw= a) 5.78K and b) 9.7K.

The resultant rod size is dependent on several parameters. A paper involving the SU-8 microrods formation published in 2006 by our group has presented majority of these parameters except molecular weight. Thus only the molecular weight effect on rod diameter is demonstrated (Figure 2.19). Rods diameter increases from 2 µm to 6 µm due to stronger
molecular entanglement and higher viscosity ratio. Equation 2.9 provides the other possible explanation that increased interfacial tension (\( \gamma \)) leads to larger droplet diameter (a).

![Graph showing rod diameter dependence on PS molecular weight.](image)

**Figure 2.20:** Rod diameter dependence on PS molecular weight.

The other strategy for polymeric rod formation is post-treating the resultant fibers to break these long continuous structures into short rods. For example, at low shear rate (120 rpm, 150 rpm, 500 rpm), PS fibers with diameter above 20 microns are fabricated. Upon vacuum (50 millitorrs) for 90s, the long, stretched fiber will break up and formed short rods (Figure 2.19). It was also observed that fiber breaking happens less when diameter decreases, which fits the theory that the tensile strength of single fiber decreases with increasing fiber diameter. Thus large fibers are easier to be broken.
In summary, by liquid shear driven method, polymeric rods with molecular weight both above and below entanglement molecular weight can be fabricated by breaking up the stretched structures mechanically. For polymer with low molecular weight, the break up happens in the Taylor Couette flow during the droplet shearing while mechanical force is exerted on resultant fibers for polymer with high Mw.

2.4.2 Polymeric Ribbon/Sheet/Thin Sheet Formation

Inside the polymer droplet, removal of solvent from the coagulating filament and the solidification of polymer happen simultaneously. The polymer on the surface precipitates to form a solidified skin layer firstly due to large diffusion rate and short diffusion length. One side of the layer is unsolidified and soft polymer with certain amount of solvent and the other side of the layer is Newtonian liquid medium. Both the rigid skin layer and the inner core start move inwards with time due to further volume drop due to solvent removal\textsuperscript{31,32,33,34}. The relative moving rate of the outer skin and inner core determinates the morphology of the fiber cross-section. If the coagulant rate of the core is low (\(\tau_s < \tau_d\)), a large volume change happens after skin formation and the moving rate of the solidified layer is lower than that of inner part,
which results in cross-section collapse. If the coagulant rate of the core is low ($\tau_c > \tau_d$), the moving rate of the solidified boundary is faster than that of inner part and the inner core merges into the skin. One extreme case is $\tau_s << \tau_d$, at which the rigid skin peels from the surface before moving inward due to the weak adhesion force between the soft core and solidified skin. The unbalanced surface solidification and core precipitation is the direct reason for cross section morphology deformation. If $\tau_s \sim \tau_d$, the morphology deformation is limited.

It is discussed in sphere formation part that the polymer concentration has to exceed a critical value before high-aspect ratio precipitated structures were formed and had a strong effect on the morphology above this critical threshold. The existence of a critical concentration can be correlated to the molecular entanglement of the polymer chains in the semi-liquid proto-fibers, a well-documented effect in wet-spinning and electrospinning. The molecular chain entanglement can be characterized by the functional dependence of the viscosity on the polymer concentration. In Figure 2.20 we present a log-log plot of the zero shear viscosities of poly-lactic acid (PLA) solutions and correlate them to the type of structures formed while shearing these solutions in glycerol/ethanol mixture. The plot shows a clear change in power-law line slopes between the semi-dilute unentangled, and the entangled regimes just below 2% w/w PLA (although due to solution non-ideality and polymer polydispersity the slope of the entangled PS solution line is lower than Rouse model prediction for neutral polymers in good solvents. In excellent correlation, the formation of fibers and fibrous materials was first observed at concentrations around this entanglement point. While more complex effects, related to the viscoelasticity of the proto-fibers and the
fragility of the solvent-swollen polymer, may be potentially involved, the polymer entanglement during the shearing process proved essential parameter for the formation of fibers and other continuous structures.

Figure 2.21: Effect of polymer concentration on the viscosity of solution of PLA (MW = 62.7k) in CHCl₃. The entanglement concentration is determined by the change in the slope of the log-log plot of the zero shear viscosity vs. concentration of the polymer solution. The SEM images in the insets demonstrate the result of shearing these PLA solutions at 2000 rpm in glycerin containing 50% v/v ethanol. Discontinuous aggregates from spheres are observed when the sheared solutions are below the entanglement concentration (path A in Fig. 1). Fibers are formed above the entanglement level.

The shearing of polymers solutions above the entanglement threshold yielded a variety of nanofibers, ribbons, sheets and thin sheets (Fig 2.13, Paths D-G). The specific morphology is dependent on the pattern of polymer precipitation into the sheared liquid finger, controlled
by solvent efflux into and antisolvent influx from the medium. The rate of antisolvent infusion is strongly dependent on its concentration in the medium, and critically affects both the morphology and characteristic dimensions of the resulting structures. The typical effect of the antisolvent concentration on the formation of nanofibers and ribbons from polylactic acid is illustrated in Figure 2.13B. Ethanol concentrations up to ca. 20% v/v produced spherical particles with increasing diameter (as the antisolvent concentration is insufficient to solidify the polymer before the liquid fingers break up into droplets). Above this critical concentration the sheared material solidified into uniform long fibers with sub-micron diameter (Path E in Fig. 2.13). Further increasing the EtOH concentration led to increase of the fiber cross-section and deformation from circular to oval cross-section, forming ribbons (Path 1F in Fig. 2.13). The deformation is likely a consequence of the rapid formation of a thick solidified skin before all of the solvent has left the protofiber core. Rapid skin formation at low polymer concentrations just above the entanglement threshold could also lead to synthesis of very thin sheet-like structures (Path D in Fig.2.13). While these sheets appear somewhat similar to the ribbons formed at high antisolvent concentrations, they are uniformly thin and likely formed by polymer skins that had peeled off the interfaces.
Figure 2.22: Effect of polymer concentration on cross section. Samples are from shearing PLA-chloroform solutions in a medium of 50% glycerol: 50% ethanol (v/v) at 2000 rpm.

Figure 2.23: Effect of antisolvent concentration on cross section. Fibers are from shearing 10% w/w PLA-chloroform solution in different medium (v/v) at 2000 rpm.
By adding antisolvent to PLA solution to further reduce the time length required for skin formation, skin peeling happens since the adhesive force between solidified skin and liquid core is so weak to protect the skin from external shearing (Figure 2.10). To distinguish from the sheet formed by double layer skin collapsing, the sheet here from skin peeling is named as thin sheet since it is from single layer skin. The skin peeling process explains the coexistence of fibers and thin sheet in SEM images since the fibers is from the solidified core formed after skin peeling. These thin sheets are especially promising for applications requiring large interfacial area, like composite reinforcement and foam stabilization.

Figure 2.24: SEM images of thin sheets formation from skin peeling (red dot area).
In summary, by control the time scale required for surface solvent diffusion (skin formation) and internal solvent diffusion (core solidification), polymeric long string-like structures including sheets, ribbon, fibers as well as thin sheet can be fabricated.

2.4.3 Fiber Formation

Uniform nanofibers are one valuable type of material, which can be readily formed at specific conditions, such as moderate polymer and antisolvent concentrations. The resultant fiber diameter is in the range of 200nm to several microns and it could be controlled by the operational and polymer parameters. Detailed information about fiber formation will be discussed in next chapter.

In summary, we demonstrate a simple, scalable and versatile technique for creating a few classes of polymer nanomaterials in the bulk of liquid by the combined action of shear extension in a viscous medium and phase separation. The appropriate combination the process parameters selection yields fibers, ribbons, sheets or thin sheets from diverse classes of polymers, including many that can only be processed from solution. This method is promising to expand the area of nanomanufacturing as it takes place in the bulk of liquid and is readily scalable. Such efficient fabrication of nanofibers and nanoribbons at unprecedented rates and volumes could make them as widespread as the common wet- or dry-spun fibers, and could enable their use as bulk components of a wide range of products, from filters to bioscaffolds.
2.5 References


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Chapter 3 Scalable Synthesis of Polymeric Nanofibers by Fluid Shear Driven Method
3.1 Introduction

Fibers with diameter below 1 micron are generally considered as nanofibers and are expected to bring revolutionary advances to many science and technology fields due to the unique properties. For example, nanofibers with a diameter of 100 nm have a ratio of geometrical surface area to mass of approximately 100 m$^2$/g$^2$. This high specific surface area and the fine pore size of nanofiber nonwoven fabrics not only create selectively permeable membranes but also greatly improve the mechanical efficiency of both liquid and aerosol filtration with only a modest increase in the pressure drop. Biocompatible and biodegradable nanofibers are considered essential for the future development of scaffolds in tissue engineering. Inorganic nanofibers with high surface area, yet much easier handling than powders, have wide applications in catalysis and photovoltaics. Fiber-based reinforcement has been considered as one effective way for composite material strength enhancement since the nanofibers would improve the interaction between fibers and materials due to its high surface to volume ratio.

To enable wider application of nanofibers in filters, tissue engineering scaffolds, protein purification, smart textiles, catalysts and photovoltaics, polymeric fiber synthesis has become a topic of great interest for the past few years. The existing methods for the fabrication of nanofibers include mechanical drawing, electrospinning, phase separation, template synthesis and self-assembly. At present only the first two have shown potential for commercial scale nanofibers production. The drawing methods (melt blowing and bicomponent spinning) have very high productivity, but are limited only to melt-processable polymers and currently to
fiber diameters \( d > \sim 0.5 \text{ mm} \). Electrospinning is the most popular commercial method that can fabricate nanofibers from polymer solutions. Electrospinning produces fibers with uniform diameters in a wide range \( (d = 20 \sim 2000 \text{ nm}) \), but its production rate is limited up to a few \( g/\text{min} \) for the largest commercial units due to the “one nozzle, one fiber” paradigm. The production capacity may be expanded by using multi nozzles in parallel. However, it requires large technology investment and additional complexity from the interactions between nozzles was introduced. Alternatively, the highest capacity electrospinning technology (Elmarco’s Nanospider) initiates the fibers formation from a polymer solution-coated rotating drum. However, the rate still cannot satisfy the industrial needs at present. Production methods capable of several orders of magnitude higher throughput than electrospinning or nanospider type devices could largely expand the practical applications of nanofiber materials.

The scalable method we introduce here adopts shear forces and antisolvent-induced phase separation. The fibers are synthesized by introducing polymer solution in the bulk of a viscous medium under shear. The medium is chosen so that it is miscible with the polymer solvent, but also precipitates the polymer. The breakthrough in the ability to draw very thin fibers comes from the ultra-low interfacial tension between the droplets and the medium, which allows high degree of stretching and generation of materials with high surface area. As the solution droplets are highly stretched in parallel by shear, the solvent diffuses out of the droplets leaving polymer fibers in the diameter range of 100 nm – several \( \mu \text{m} \) behind. As a result, the fibers are formed in the bulk liquid without using nozzles or spinnerets by the combined action of shear and phase separation.
In order to gain further understanding of fiber formation process, during which emulsification, viscous shear and breakup of the droplets, solvent attrition in the medium, solidification and possible further solidified polymer breakup happens simultaneously, the effects of the following parameters on fiber sizes and distribution will were demonstrated:

a) Process parameters related to operational condition such as the intensity of applied shearing, the feeding rate for the polymer solution, total feeding amount, distance between stirring impeller and injection location.

b) Parameters related to polymer solutions such as the type of polymer, the conformation of polymer chains, viscosity and concentration of the polymer solutions, molecular weight, molecular-weight distribution, architecture (branched, linear etc.) and elasticity of the polymer.

c) Variables related to disperse medium composition like antisolvent concentration in the medium, viscous solvent concentration in the medium.

Besides these parameters, the humidity and temperature of the surrounding medium may also play an important role in determining the morphology and diameter of fibers, which will not be covered here.

3.2 Experimental Section

3.2.1 Materials

High molecular weight (MW) polystyrene (PS) \((M_w \approx 190,000 - 230,000, M_w/M_n \approx 1.6)\), cellulose acetate (CA) \((M_n \sim 30,000)\) were obtained from Sigma-Aldrich. Ingeo 6751D
poly-(lactic acid) (Mw= 62,720, Mw/Mn= 2.880) was provided by NatureWorks Inc. Chloroform, denatured alcohol and glycerol were obtained from Fisher Scientific. The PDMS precursor (Sylgard 184) was from Dow Corning.

3.2.2 Preparation of Solutions

Polymer solution with certain concentration by weight was prepared by dissolving the polymer solid (PS or PLA) in the solvent (chloroform) under 1200 rpm shearing for 3 hrs. Disperse medium with certain antisolvent concentration by volume was prepared by mixing polymer antisolvent (ethanol or water) and viscous solvent (glycerol or glycerin).

3.2.3 Fiber Synthesis Method

A benchtop Couette flow apparatus with a 2.3 mm gap was constructed with a rotating cylindrical shaft (radius $r_i = 5.0$ mm) and a disposable, stationary polypropylene tube (ID = 14.6 mm, Evergreen Scientific). Shaft rotation was digitally controlled (150 - 6000 rpm) by a Cole-Parmer Servodyne Mixer, Model # 50003. The fibers were formed by liquid-liquid shear-dispersion in a viscous antisolvent medium, similarly to the process previously described in chapter 2. Typically 0.05 ml of polymer solution, injected into 6.5 ml of antisolvent, was sheared at 2000 to 6000 rpm for 2 minutes.

The initial experiment at higher shear rates showed significant increase in polydispersity from instabilities of the top free liquid-air interface, which were suppressed by introducing a top baffle made of cured PDMS with precise thickness to prevent drawing of air into the liquid medium during shear. This decrease could be potentially limited by an onset of turbulence in Taylor-Couette flow as predicted by the critical Taylor number. In addition to
eliminating the free top surface with baffles, the flow can be additionally stabilized by modulating the speed of the rotor, introducing liquid flow in the axial direction, periodic movement of the central cylinder in the axial direction, or by increasing the medium viscosity.

**Figure 3.1:** Schematic illustration of Modified batch liquid shear device with a PDMS baffle to prevent turbulence by eliminating the top free liquid surface.

### 3.2.4 Fiber Characterization Method

Optical microscopy (Olympus BX-61 microscope with a DP-70 digital CCD camera) was adopted to characterize the polymer solution and fiber structures. The JEOL 2000FX Scanning Transmission Electron Microscope (SEM) operated at 5 kV was used to study the
fiber morphology and sizes. The samples were sputter coated (Technics Inc, Hummer II) with Au-Pd at a thickness of 100 Å to produce the conductive surface.

3.2.5 Fiber Diameter Measurement Method

The fiber diameter analysis method has been developed and used earlier for characterizing of fiber diameter distribution of meltblown fibers and electrospun fibers at the Nonwovens Cooperative Research Center, Nonwovens Institute (NCRC) at NC State University. To ensure unbiased results of distribution measurements we adapted a procedure from industry standard methods ASTM D 629 and AATCC Test Method 20A “Fiber counting in microscopical analysis”:

1. 4-5 SEM images were taken randomly from each samples. Magnification used ranged, usually 4000-5000X, optimized to provide enough resolution for small fibers while still can capture large fibers in the field of view.

2. From each image, fiber diameters were measured, starting at the center of the image’s left edge and moving in the horizontal direction to the center of the right edge, while measuring and recording diameter of all fibers in between. In a similar manner, fiber diameters were measured by moving vertically from the top edge center point to the bottom edge center point of the image.

3. This procedure was repeated for all the images taken and the fiber diameter measurement results from all the images (4-5 per sample) were combined and analyzed. Total 50-100 fibers were analyzed and reported for each of the samples.

Measurements were conducted by an image-processing program named ImageJ (NIH).
3.3 Results and Discussion

3.3.1 Process Parameters

The process parameters we investigated here include shear stress, feed rate, feed amount and location of polymer injection. Their roles and mechanisms of operation are discussed below.

3.3.1.1 Shear Stress

The first parameter related to the diameters of the fibers we investigated is the shear stress. Thinner fibers with narrower distribution were produced from PS-chloroform solution by increasing the shear rate from 2000 rpm to 6000 rpm (Figure 3.2). The initial process taking place during fiber formation is the elongation and extension of the polymer solution droplets in a sheared Newtonian fluid medium. The Couette flow between the concentric rotating cylinders (Fig. 3.1) produces uniform shear stress throughout the whole device volume. The shear stress, which would deform the droplets, is opposed by the interfacial tension, which acts to minimize the droplet surface area. The balance of those two tensions can be expressed by the dimensionless capillary number $Ca$:

$$Ca = \frac{\tau a}{\gamma} \quad (3.1)$$

$$\tau \approx \frac{\mu \omega r_i}{\Delta r} \quad (3.2)$$

Here $\tau$ is the shear stress, $a$ is the droplet radius, $\gamma$ is the interfacial tension, $\mu$ is the fluid
viscosity, \( r_i \) and \( \omega_i \) are the radius and angular velocity of the inner cylinder, and \( \Delta r = r_o - r_i \) is the intercylinder spacing. For \( Ca > 1 \) the shear stress dominates and the droplets stretch into long cylinders. At a critical value, \( Ca_{cr} \), these cylinders could break up into smaller drops which continue to deform according to their new radius and capillary number. \( Ca_{cr} \) depends on the ratio of viscosities of the polymer droplets and the media, and varies in the range 0.3-20 in our experiments. The use of viscous medium in the experiments was critical for obtaining thin fibers at a typical shear stress \( \tau \approx 70 \) Pa. The interfacial tension between the two miscible liquid phases is not well defined and it is reasonable to assume \( \gamma \approx 0.01 - 0.1 \) mN/m. For a given critical capillary number \( Ca_{cr} \), higher \( \tau \) would result in a decrease of the diameter of shear-deformed solution droplets \( d = 2a \) (Eqn. 1) which were proved by the experimental results (Figure 3.2).
Although larger shear stress leads to the synthesis of smaller fibers, minimal shear stress is required for uniform and complete fiber formation. For 10% w/w PS-chloroform solution (Figure 3.3), either merged fiber structures due to incomplete polymer solidification when the fiber structures contact between each other (120 rpm) or spindle shaped structures (150 rpm) from incomplete droplet stretching were observed. At 500 rpm, the product was mostly uniform and complete fibers structures due to the balanced time between droplet stretching and polymer precipitation. However, defect structures can still be observed. In either case (120 rpm, 150 rpm, 500 rpm), polymeric rods from the breaking up of stretched solidified polymer structures existed. Detailed information on rod formation from high molecular weight and low molecular weight PS were already discussed with detailed information in Chapter 2.
The phenomenon that shear stress can reduce the fiber size is based on the process during which solvent diffusion is dominating ($\tau_c >> \tau_d, \tau_s$). In other words, before the droplet reaches the steady state diameter, the stretched structures are already precipitated from the polymer solution. Thus higher shear stress would leads to stronger stretch during the same time scale required for phase separation.

### 3.3.1.2 Volume Feeding Rate

To vary the feeding rate, the same amount of PLA- chloroform solutions were injected in
the medium under external shearing uniformly at different time lengths. Larger fibers with wider distribution were produced when the rate increased from 0.03 ml/s to 0.000208 ml/s (Figure 3.4) regardless of whether the polymer concentration is 5% w/w or 10% w/w. The injection rate is calculated by dividing the injected amount with time used. Fast inject rate produces larger droplets at the end of the syringe needle. So the conclusion that larger droplets result in larger fibers agrees with the conclusion that droplets with smaller size would produce thinner fibers based on the fiber synthesis researches from polymeric oil in oil emulsion (more detail will be presented in chapter 4). As discussed in shear stress part, the dominating diffusion process determined the time length for polymer precipitation. Under same time length and shear stress, larger droplet results in fibers with larger diameters.

Continuous device mentioned in chapter 2 is promising to better characterize the relationship between volume rate and fiber size since it is more compatible with injection rate control equipment like syringe pump.
Various amounts of PLA-chloroform solutions were introduced to the medium under external shearing at same volume injection rate. The conclusion that polymeric fiber sizes are independent of polymer solution amount can be drawn from Figure 3.4. After injection of polymer solution, the polymer precipitates while the polymer solvent dissolves with shear medium, which changes not only the interfacial tension between polymer solution and shear medium but also the viscosity of medium. However, the volume of added solvent is negligible (0.45 ml) compared to original disperse medium volume (7-9 ml), so the interfacial tension and medium viscosity did not change much and the fiber size remains in the same range according to eqn 3.1 and 3.2.
3.3.1.4 Needle Size

During the liquid shear process, polymer solution is forced through a syringe to form a droplet at the tip of the syringe needle. We used syringe needles having various sizes (Table 3.1) to add the same amount of polymer solutions with same concentration to the disperse medium during same time length. It is shown that the change in needle diameter did not lead to morphology or size variation of resultant fibers (Figure 3.5). It is because that the droplets were forced to leave the needle tip before reaching the final size attributed to the external shear stress and the injection rate plays a more important role on droplet sizes than needle diameter.

**Figure 3.4:** Effect of injection volume of PLA solution on size average fiber diameter and distribution.
Table 3.1: Syringe needle size

<table>
<thead>
<tr>
<th>Needle Gauge (G)</th>
<th>Needle Diameter (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>16</td>
<td>1.194</td>
</tr>
<tr>
<td>18</td>
<td>0.838</td>
</tr>
<tr>
<td>22</td>
<td>0.413</td>
</tr>
<tr>
<td>25</td>
<td>0.26</td>
</tr>
<tr>
<td>27</td>
<td>0.21</td>
</tr>
<tr>
<td>30</td>
<td>0.159</td>
</tr>
</tbody>
</table>

Figure 3.5: Effect of syringe needle size on average fiber diameter and distribution.
3.3.1.5 Injection Location

Three different input locations were chosen between the outer side of impeller and inner side of the plastic tube for polymer solution injection. In Figure 3.6, the x axis is the distance between the injection location and the inner impeller and the y axis represents the diameters of the obtained samples. It is observed that the fibers size seems to be in the same range and not affected by the injection location. After rewriting equation 3.2, the shear stress is uniform in the gap and independent of the injection location which explains the results.

The other way to explain this results is that the Re number is 62, close to the critical Reynolds number shown in Figure 2.9. Thus instead of circular flow, which only has azimuthal velocity component, the velocity in axial and radial directions are not negligible. Thus the shear rate on any single polymer droplet is not a constant value and the initial injection location makes no difference which explains the independence of fiber sizes on injection location.
3.3.2 Polymer Solution Parameters

As discussed in chapter 2, uniform nanofibers are one valuable type of nanomaterials, which readily formed at proper polymer solution parameters. Here, the effect of these parameters on fiber sizes is investigated.

3.3.2.1 Polymer Molecular Weight

It was proposed in chapter 2 that the polymeric molecular weight (MW) is the determining parameter between fiber-forming and the rod-forming. High MW can result in a high level of entanglement of the polymer solution, which is necessary to form necessary
entanglement to protect the fibers from breaking up for producing the fibers while a low entanglement level, by contrast, would result in polymer rods formation. At fiber forming range, the molecular weight plays no role in fiber sizes at low antisolvent concentration (~20% v/v and ~25% v/v) and polymer at higher molecular weight would result in larger fibers with wider distribution if the antisolvent concentration is high. During the fiber formation process, emulsification, viscous shear, solvent attrition, polymer solidification and precipitation happens simultaneously and the resulted morphology is determined by the competing effect of all these process (Figure 3.7).

At low antisolvent concentration, the solvent diffusion is slow compared to droplet stretching ($\tau_d$, $\tau_s$,$\tau_c$) and the droplets have enough time to be stretched to its steady state diameter which is only dependent on shear stress and interfacial tension. At high antisolvent concentration, the solvent diffusion rate is increased ($\tau_d$, $\tau_s$,$\tau_c$) and the stretch time for each droplet is fixed. For droplet with high molecular entanglement, the droplet is stretched less under the same time length due to the increased viscosity.
3.3.2.2 Polymer Concentration

The other parameter found to be critical for fiber formation was the polymer solution concentration. It was discussed in Chapter 2 that an initial polymer concentration at or above the entanglement level is required to form nanofibers, similarly to electrospinning. Above this initial concentration, the fiber sizes increase with polymer concentration due to the larger entanglement between polymer chains at higher polymer concentration at 50% v/v ethanol medium while the fiber sizes are independent of the polymer concentration at 25% v/v ethanol medium due to the dominating shear process. The explanation is similar to the...
molecular weight part, if the antisolvent concentration is low, the diffusion process is dominating and the fibers are stretched to the steady state diameter determined by shear stress and interfacial tension. However, the interfacial tension between different polymer droplets with different polymer concentration does not change much. Thus the size remains in the same range. At high antisolvent concentration, $\tau_d, \tau_s < \tau_e$ and polymer droplets with high concentration are stretched less during same time length due to the high droplet viscosity.
Figure 3.8: Effect of polymer concentration on size average fiber diameter and distribution: A) 25% v/v ethanol 75% v/v glycerol; B) 50% v/v ethanol 50% v/v glycerol.
3.3.3 Shearing Medium Parameters

Shearing medium is the crucial component of the fiber formation process and it determines shear stress, the solvent diffusion rate and polymer precipitation rate. It is of importance to investigate the effect of the shearing medium parameters on fiber sizes.

3.3.3.1 Antisolvent Concentration

The process of fiber formation and the resulting fiber diameters are also strongly affected by the concentration of antisolvent (usually ethanol) in the shearing medium. A minimal antisolvent concentration is required, so upon mixing with the solvent from the introduced polymer solution, the resulting medium is still capable of precipitating the polymer (20% v/v for PS and 25% v/v for PLA). Increasing the antisolvent concentration further, in a medium where the rest of the medium content is glycerol, simultaneously decreases the viscosity \( \eta \) and increases the diffusion coefficient \( D \) of the medium \( (D = kT/4\eta \pi a) \). Both of these effects are likely to increase the fiber diameters, either due to lower shear stress deformation of the polymer droplets, or to earlier solidification of the stretching droplets, respectively. Indeed, media with 20% v/v ethanol produced the smallest average diameter fibers, \( d_{10.90\%} = 250-850 \) nm, though some of them were fused to each other, indicating that 20% ethanol is close to the minimum required for an effective antisolvent medium. 25 % v/v ethanol produced the smallest fibers which were separated from each other, \( d_{10.90\%} = 520-1560 \) nm. For 25% < [ethanol] < 63 % v/v, the average fiber diameter and polydispersity increased rapidly (Figure 3.9a). The increasing trend of fiber sizes with polymer concentration was also observed in PLA (Figure 3.9b).
Figure 3.9: Effect of antisolvent concentration on fiber diameter and distribution: A) PS; B) PLA.
3.3.3.2 Disperse Medium Composition

The medium is a mixture of polymer antisolvent, miscible with the polymer solvent, to precipitate the polymer and the viscous solvent to produce strong shear stress (usually glycerol or glycerin). However, glycerol is not only highly viscous which would bring potential slipping danger in working area but also miscible with water and ethanol (the two most common and inexpensive polymer antisolvent) which complicates the recycling process for mass fiber production. To solve these problems, water or polymer solvent is added to the medium to replace glycerol.

The x axis of Figure 3.10 is the volume concentration of polymer solvent in the shearing medium while glycerol concentration is kept at 50% v/v and y axis is the size average fiber diameters and distribution. It is shown that the fiber size initially reduces with polymer solvent concentration in the medium but no fibers were produced if the polymer solvent concentration is higher than 10%. Polymer solvent in disperse medium not only reduces the interfacial tension between polymer solution and the medium, which results in thin fibers but also increases the solvent diffusion time which leads to the irregular polymeric structures formation (optical images in Figure 3.10). If the solvent concentration in the medium is low, the reduced interfacial tension effect dominates, which results in the smaller fiber synthesis. However, if the antisolvent concentration in the medium is high, the slow solvent diffusion dominates and the polymer precipitation is not able to happen, which leads to irregular structures on the microscope glass slides after solvent evaporation.
Under the theory of capillary droplet stretching, viscous medium is necessary to yield the high shear stress to stretch the droplets to strands. In the following part, the necessity of viscous medium is questioned. Fibers with diameters from 100 nm to several microns are produced from the aqueous ethanol medium, which has never been done by any other researchers before.

It is shown in Figure 3.11 that if the ethanol concentration is 31.7% v/v, adding water reduces the fiber size (Figure 3.11a) while water plays no role in fiber sizes if the ethanol concentration is 50% v/v (Figure 3.11b). If the glycerol concentration is constant (50% v/v), smaller fibers are synthesized with higher water concentration. More specifically, for
PS-chloroform and PLA-chloroform solution, glycerol is not needed to produce fibers if the ethanol concentration is higher than 35% v/v (Table 2.2 and 2.3) and the resultant fiber sizes are either smaller than or similar to those from glycerol/ethanol medium.
Figure 3.11: Effect of water concentration in disperse medium on size average fiber diameter and distribution: A) 31.7% v/v ethanol; B) 50% v/v ethanol; C) 50% v/v glycerol.
A) 

![Graph A](image)

B) 

![Graph B](image)
Table 3.2: Minimum glycerol concentration for PLA fiber formation at various ethanol concentrations

<table>
<thead>
<tr>
<th>$C_{\text{ethanol}}$ (% v/v)</th>
<th>25</th>
<th>30</th>
<th>35</th>
<th>40</th>
<th>45</th>
<th>55</th>
<th>60</th>
<th>65</th>
<th>70</th>
</tr>
</thead>
<tbody>
<tr>
<td>$C_{\text{glycerol}}$ (% v/v)</td>
<td>50</td>
<td>50</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Figure 3.12: Effect of ethanol concentration in water-ethanol mixture and glycerol-ethanol mixture on size average fiber sizes.
Table 3.3: Minimum glycerol concentration for PS fiber formation at various ethanol concentrations

<table>
<thead>
<tr>
<th>$C_{\text{ ethanol}}$(% v/v)</th>
<th>30</th>
<th>35</th>
<th>40</th>
<th>45</th>
<th>55</th>
<th>60</th>
<th>65</th>
<th>70</th>
</tr>
</thead>
<tbody>
<tr>
<td>$C_{\text{ glycerol}}$(% v/v)</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Figure 3.13: SEM images and size average diameters of PS fibers from shearing 10%PS w/w in mixture of ethanol and DI water.

40 v/v% Ethanol 60 v/v% DI water
$712 \pm 397$ nm

45 v/v% Ethanol 55 v/v% DI water
$791 \pm 471$ nm

50 v/v% Ethanol 50 v/v% DI water
$1162 \pm 631$ nm

60 v/v% Ethanol 40 v/v% DI water
$2055 \pm 1722$ nm
Figure 3.14: Viscosity measurement of a) 50% Ethanol and 50% Glycerol shear medium at different water concentration; b) Glycerol/Ethanol and Water/Ethanol at different ethanol concentration.

The viscosity is reduced significantly by replacing glycerol with water, which further
reduces $\tau_d$, $\tau_s$ and increases $\tau_e$. Thus the stretched strands with larger diameters precipitate to produce bigger fibers which are inconsistent with the experimental results. Capillary breakup theory is not applicable in medium with low viscosity and new model is needed to investigate this fiber formation process.

The theory proposed for the fiber formation in non-viscous medium is that the deformation of polymeric droplets is in the vortex direction. Unlike the deformation mode of Newtonian droplet under external shearing, which can only be at flow direction, two deformation modes exist for the polymeric viscoelastic drop under shearing: a) Droplet deforms at flow direction. Similar to Newtonian liquid, droplets elongate in the flow direction from spheres to ellipsoidal shape and to a long thread shape. This deforming mode happens at low Ec where the viscoelastic force is weak enough to be neglected. b) Droplet deformation in the vortices direction. Droplet elongates in the flow direction from spheres to ellipsoidal shape initially. Then contraction of droplet in the flow direction and elongation in the vortices direction happen simultaneously. This deforming mode is common for high Ec number due to the dominant restoring effect from the viscoelastic property. Ec is the abbreviation of elastocapillary number which is ratio of the droplet viscoelasticity and external shear stress (Equation 3.1):

$$Ec = \frac{\lambda_s \gamma}{\eta_m a}$$ (3.1)

Where $\Psi_{10}$ is the coefficient of the first normal stress difference due to the droplet viscoelasticity; $\gamma$ is the interfacial tension. Ec is the elastocapillary number (Ec) which is the ratio of the droplet viscoelasticity and external shear stress. $\lambda_s$ is the time scale of stress
The flow type in the Taylor–Couette device is controlled by Reynolds number. Above the $Re_0$ (~80 for the device we used), laminar flow becomes unstable and axisymmetric vortices in the gap are initiated (Figure 2.8). Increasing the Reynolds further results in chaotic, turbulent and nonaxisymmetric Taylor vortex flow. Reynolds number is the ratio of inertial force to viscous force:

$$Re = \frac{R_1 \omega I (R_2 - R_1)}{\nu} = \frac{U_0 d \rho}{\mu_m} \quad (3.2)$$

Where $U_0$ is the inner cylinder rotation velocity, $\rho$ is the density of the fluid and $\mu_m$ is the medium viscosity.

Reduced $\mu_m$ not only results in increased $Re$ but also increased $Ec$ while the latter produces vortices flow and the latter leads to droplet stretching in the vortices direction which is vertical to the flow direction. Thus stretched droplet diameter is determined by the shear stress in the vortices direction which is much stronger than those in flow direction. Even though $\tau_d, \tau_s$ is reduced, the reduced $\tau_c$ dominates and produces fibers with similar sizes to or smaller sizes than those from glycerol/ethanol mixture.

Fiber design requires a very fundamental understanding of the correlation between the intrinsic structure of a fiber and its properties and the relationship between fiber properties and its functions. The understanding of how particular fiber - characteristic intrinsic structures can be achieved via the selection of appropriate fiber processing techniques and via the choice of suitable processing parameters is also necessary. The liquid shear driven approach provides a novel way to construct technical elements from fibers. In summary, we
demonstrate that fluid shear-driven method is a facile and versatile technique for creating nanofibers from several micron to 200 nm from a large number of polymers (Figure 3.14), including those that can only be processed from solution. Similar to electrospinning, the new method creates nanofibers from solution at room temperature, which is highly desired in the processing of functional polymers, such as biodegradable polymers for biomedical application. The mild processing conditions could also benefit numerous other applications, such as generation of biocomposite fibers containing active enzymes or whole live cells. For certain polymers, the appropriate combination of solvent – antisolvent system would make the nanofibers possible.

The physical effect making possible to extend the droplets into nanofibers and to create high interfacial area is the low resistance of the extremely low interfacial tension between the mutually miscible solvent and the medium to shear extension in viscous medium. The bulk shear process of fiber formation needs no extrusion nozzles, which is straightforward to scale-up to large volume nanofiber manufacturing. It was shown that the shear can also be accomplished in continuous flow device (Figure 2.2), having the potential to produce nanofibers at very high output rates (6-12 kg h\(^{-1}\) while the yield of Elmarco is only around 0.171 kg h\(^{-1}\)). Thus, the technique has the potential to significantly decrease the production cost of a wide variety of nanofibers used, e.g., in smart clothing and disposable antimicrobial nonwoven textiles, in affinity chromatography for efficient protein purification, for affordable tissue engineering scaffolds (e.g. artificial skin), and for inexpensive photovoltaic semiconductor materials. It also opens an area for fundamental studies of the shear and phase-separation processes during fiber formation at the nanoscale.
Figure 3.15: SEM images of various polymeric fibers produced from fluid shear driven method.

3.4 References


Chapter 4 Ultrathin Fiber Formation from Liquid Shearing of Polymeric Oil in Oil Emulsions
4.1 Introduction

In Chapter 2 and Chapter 3, we demonstrated a simple, scalable and versatile technique for creating a few classes of polymer nanomaterials in the bulk of liquid by the combined action of shear extension in a viscous medium and phase separation. It is suggested that the judicious combination of the process parameters selection yields fibers, ribbons, sheets or thin sheets from diverse classes of polymers. This method is promising to expand nanomanufacturing as it takes place in the bulk of liquid and is readily scalable. Among all the formed structures, nanofibers have evoked the widest research interest due to their unique properties including high surface area to volume ratio, high porosity and length. Additionally, the long fibers can be assembled into a three-dimensional porous mat. To enable wider application of nanofibers in filters, tissue engineering scaffolds, protein purification, smart textiles, catalysts and photovoltaics, polymeric fiber synthesis has become a topic of great interest for the past few years.

The current available methods in the market for nanofibers synthesis are mainly mechanical drawing, electrospinning, phase separation, template synthesis and self-assembly.\textsuperscript{1,2} However, the yield of the last three is low and only the first two have shown potential for commercial scale production. The drawing methods including melt blowing and bicomponent spinning have very high productivity, but are not applicable for non-melt-processable polymers and the fiber diameters are limited with $d > \sim 0.5$ mm. Electrospinning, the most popular commercial one, produces fibers with uniform diameters in a wide range ($d = 20 – 2000$ nm). Although the productivity is higher than self-assembly,
phase separation and template synthesis, its production rate is still limited up to a few g/min for the largest commercial units due to the “one nozzle, one fiber” paradigm. Alternatively, the highest capacity electrospinning technology (Elmarco’s Nanospider) initiates the fibers formation from a polymer solution-coated rotating drum. However, the commercial yield still cannot satisfy the growing market need of market. To hurdle this issue, a liquid shear driven method was proposed by this thesis and it shows the potential of producing fibers with diameter from 200 nm to several microns from a wide range of polymers by either batch or continuous process (Xanoshear™ device). The throughput of fiber production for Xanoshear™ is up to 12 kg per hour while the yield of Elmarco is only \(0.171 \text{ kg h}^{-1}\).

Beside the production rate, the other crucial parameters to determine the applicability of fiber production technique is the size of the resultant smallest fibers. Solution based electrospinning typically synthesize fibers with diameters down to 100 nm.\(^3\) Liquid shearing has attracted much research interests for being the most productive nanofibers production method in the market. However, it typically results in fibers with diameter from 200 nm to several microns. The fibers with diameter around 200 nm can only be formed at the combination of a number of parameters including low polymer concentration, low polymer molecular weight and high shear stress (i.e. 10% w/w polymer solution, 6000 rpm shear, 30% v/v antisolvent concentration). However, low polymer concentration is responsible for the formation of irregular aggregates formation due to enhanced polymer precipitation process. Additionally high shear rate would induce liquid instability, which is the major reason for the wide polydispersity of fiber sizes. Shear medium containing low concentration of antisolvent and high ratio of viscous medium not only favors spheres than fibers due to the intensified
emulsification process but also imposes difficulty of sample washing.

Colloid science usually categorizes emulsions as oil in water (O/W) and water in oil emulsions (W/O). However, the actual case is more complicated since immiscible organic liquid pairs also exist and water is not a necessary phase to build stable emulsions. For example, polymeric non-aqueous emulsion is organic heterogeneous phases with polymers existing in dispersed or continuous phases or both phases. Non-aqueous emulsions were usually applied to conduct water sensitive reactions, high temperature reactions (>100 ºC) due to the high liquid boiling temperature and drug encapsulation formulation.

Emulsions are generally used to fabricate core-sheath electrospun fibers which are traditionally produced by co-axial electrospinning. Emulsion electrospinning is preferred compared to co-axial electrospinning due to the simple experimental set up and a close control on the fiber structures. On one hand, hydrophilic drug loaded core-sheath fibers, with hydrophobic polymer as the sheath forming material and the drug as the core can be fabricated by dispersion of water drops containing hydrophilic molecules (W/O) in electrospun polymer solutions. This method is especially applicable for organic solvent sensitive drugs. On the other hand, oil in water emulsion provides a novel approach for producing core-shell nanofibers with a liquid core, which can be long continuous structures or discontinuous ones due to droplet breaking up, such as PVA nanofibers with hexadecane core. The embedded droplets can also be used as the templating agent to create the pores or cylindrical cavities inside the fibers. The only available publication describing the use of non-aqueous emulsions in fiber area is electrospinning of the emulsions consisting of PMMA/DMF as the disperse phase and PAN/DMF phase as the continuous phase to fabricate
PMMA-PAN core-shell fibers in an ordinary single nozzle set-up.\textsuperscript{11,18} The components of the emulsion adopted in the PMMA-PAN core-sheath fiber synthesis are two immiscible polymers and one solvent which is miscible with both polymers. Unlike the small solute molecules, the formulation of heterogeneous polymer emulsion can be realized by one polymer and one solvent based on the phase separation due to the large scale of polymer molecules. A large field of application of this kind of polymer emulsion for fiber formation is still unexplored.

Here we demonstrated a novel way to fabricate ultrathin PS nanofibers with size down to 100 nm by shearing the polystyrene-cyclohexane emulsion in the viscous medium. It is also proposed for the first time to fabricate nanofibers from phase separated polymer – solvent system.

4.2 Experimental Section

4.2.1 Materials

Polystyrene (PS) (Mw ~ 19,000 – 230,000, Mw/Mn = 1.6) was obtained from Sigma-Aldrich. Cyclohexane(99+%), chloroform(HPLC, 99.8%) and glycerol(99+%) were purchased from Fisher and used without further treatment.

4.2.2 Preparation of PS-cyclohexane emulsion

PS-cyclohexane emulsions of various concentrations were prepared by blending different amount of PS pellets with cyclohexane by weight. The polymer – solvent mixture was stirred at 2000 rpm for 24 hrs. To get fully emulsion coalescence for PS concentration measurement
on both top and bottom phases, stirring was stopped for at least one week.

4.2.3 PS concentration measurement

The concentration of PS in cyclohexane was measured using the colorimetric UV-vis method and the absorbance was measured at 269 nm using a UV-Vis spectrophotometer (V550, Jasco Corp., Japan). Light absorption is applicable to the dilute polymer solution due to neglectable interactions between polymer chains. The absorbance against concentration curve is linear at low concentration and curved at high polymer concentration due to interaction variation between polymer molecules and solvent. Standard curve was established to identify the linear regime by measuring the absorbance of known polymer concentration of PS-cyclohexane clear solution. All the samples are diluted to adjust the concentration in the established linear regime to guarantee the measurement accuracy. The procedure of calculating the concentration of PS in the disperse and continuous phases has the following four steps: 1) stop the stirring for at least one week until the liquid separated in top and bottom layer with clear phase interface; 2) get the height of top and bottom layer; 3) collect the clear solution from top layer without disturbing the bottom layer to measure the dissolved PS concentration via UV-Vis; 4) calculate the bottom layer PS concentration from the original bulk concentration and volume ratio between top layer and bottom layer.
Figure 4.1: Standard curve of absorbance at 269 nm against PS concentration in the PS-cyclohexane solution.

4.2.4 Fiber Synthesis

PS fibers were prepared as reported previously. At ambient temperature, a benchtop Couette flow apparatus with a 2.3 mm gap with a rotating cylindrical shaft (radius $r_i = 5.0$ mm) and a disposable, stationary polypropylene tube (ID = 14.6 mm, Evergreen Scientific) was constructed. Shaft rotation was digitally controlled (150 - 6000 rpm) by a Cole-Parmer Servodyne Mixer, Model #50003. 0.05 ml of PS-chloroform solution or PS-cyclohexane emulsion was injected into 6.5 ml of shearing medium composing of glycerol and polymer
antisolvent under shearing from 2000 to 6000 rpm for 2 min. The fibers were formed from the solidification of the elongated polymeric droplets and collected after being peeled off from the shaft for subsequent morphological analysis.

4.2.5 Characterization

Optical microscopy (Olympus BX-61 microscope with a DP-70 digital CCD camera) was used to characterize the emulsion structure and fiber existence. The JEOL 2000FX Scanning Transmission Electron Microscope (SEM) was used to study the fiber morphology and size. Each sample was coated with gold using a sputtering machine for 60 s prior to observation under the SEM. The average diameter and standard deviation of each sample were determined by at least 50 measurements of fibers from the SEM images. Measurements were conducted by an image-processing program named ImageJ (NIH).

4.3 Results and Discussion

To form long and uniform fibers under external shearing, the polymer solution concentration must be above a critical minimum value ($c_e$) to allow sufficient molecular chain entanglements, which would prevent the polymer droplets from breaking up under continuous shearing. Polymeric irregular aggregates or incipient fibers would be formed. 10% w/w is well above the critical value for PS (Mw= 190~230K), so at this concentration, uniform fibers are formed from PS- chloroform solutions.

The working liquid was prepared by blending of PS pellets and cyclohexane emulsions of various concentrations by weight. After around 12 hours stirring at 2000 rpm, the polymer-solvent system decomposes into metastable emulsion. On one hand, the direct
evidence that emulsification happens is that the whitely opaque color of the mixture without any observable solid existence (Figure 4.2). On the other hand, after the 24 hours mixing, the emulsions consisted of droplets with diameter in the range of 20 – 100 µm (optical microscopy image in Figure 4.2). Since the interfacial tension between non aqueous liquid is usually lower than that between water and a solvent, it is more difficult to stabilize the O/O emulsions than O/W or W/O emulsions. The interfacial tension in PS-cyclohexane is much smaller since the disperse and continuous phases share the same solvent, which guarantee the Ostwald ripening existence in PS-cyclohexane emulsion. After one day without stirring, the emulsions separated into two distinct layers with the transparently low PS concentration layer on top and the opaquely high PS concentration layer on bottom. The thickness of the bottom PS-cyclohexane layer is about half of the top PS-cyclohexane layer. After calculation, polymer concentration is approximately 3.5% w/w on top layer and 23% w/w on bottom layer while the overall concentration is 10% w/w.

Polymer solubility in a given solvent is significantly affected by polymer concentration, polymer molecular weight, solvent property, temperature and other variables. Interactions between polymer and solvent determine the conformation of the polymer chain in the solution. A polymer solution with high polymer solubility prefers polymer - solvent interaction and the polymer chains would swell and expand to maximize intermolecular interaction with “globule” configuration while a polymer solution with poor polymer solubility favors polymer – polymer interaction and the polymer chains would contract and form “coil” to maximum the self-interaction.\textsuperscript{20}

Solvent quality is determined by the chemical compositions of the solvent and the
polymer at constant temperature. Three-component Hansen solubility parameters (HSP) are one commonly used theory to describe polymer solvent quality:

\[ E = E_D + E_P + E_H \]  \hspace{1cm} (4.1)

\[ \delta^2 = \frac{E}{V} = \delta_D^2 + \delta_P^2 + \delta_H^2 \]  \hspace{1cm} (4.2)

Error! Reference source not found.

\[ R^2 = 4 \cdot (\delta_{D2} - \delta_{D1})^2 + (\delta_{P2} - \delta_{P1})^2 + (\delta_{H2} - \delta_{H1})^2 \]  \hspace{1cm} (4.3)

\[ RED = \frac{R_a}{R_o} \]  \hspace{1cm} (4.4)

where cohesion energy \( E \) is the sum of the dispersion forces energy \( (E_D) \), permanent dipole–dipole forces energy \( (E_P) \), and hydrogen bonding energy \( (E_H) \). The Hildebrand solubility parameter Error! Reference source not found. is the square root of the cohesion energy density and \( V \) is the molar volume. Solubility parameter distance \( R_a \) is the sum of the weighted difference of the three HSP of the polymer and the solvent. RED is calculated by dividing \( R_a \) with interaction radius \( R_o \). A simple criterion is proposed that the value of RED should be below 1 for the solvent to form “good” polymer-solvent solution with globule molecular configuration. Besides RED, another way to predict solvent thermodynamic quality for a given polymer is based on the value of \( a \) from Mark-Houwink equation (Equation 4.5), which describes the relationship between intrinsic viscosity \( (\eta) \) of polymer solution and polymer molecular weight:

\[ \eta = KM^a \]  \hspace{1cm} (4.5)

where \( K \) and \( a \) are Mark-Houwink constants that can be determined empirically. For a good solvent, the value of \( a \) is between 0.65 and 0.85 while the value for a bad solvent is below
0.65. Both RED and a from Table 4.1 point to the same conclusion that chloroform is a good solvent for PS while cyclohexane is in the transition range of good and bad solvent. For PS (Mn=20 kDa, Mw/Mn= 1.30) in cyclohexane, the polymer favors coil than globule molecular conformation at 25ºC at 0.01% w/w. The contraction trend of polymer molecules from globule to coil is enhanced with higher polymer concentration or molecular weight. 21 If the concentration is above the thermodynamically stable value, phase separation is initiated and heterogeneous solutions consisting of one continuous phase and one disperse phase are formed under external shearing. Thus, without surfactant, polymeric emulsions are formed only from one polymer and one solvent. The phase separation phenomenon from blending of PS with cyclohexane has been investigated during the past few years (Figure 4.3). However, to date the application of this polymeric heterogeneous system with droplets in micron meter range is rare. Cyclohexane solely is generally considered as not electrospinnable due to its low conductivity22 or low dielectric constant23 and it is usually adopted as one component of polymer solvent mixture for fiber formation from electrospinning.

<table>
<thead>
<tr>
<th></th>
<th>Chloroform</th>
<th>Cyclohexane</th>
</tr>
</thead>
<tbody>
<tr>
<td>RED*</td>
<td>0.59</td>
<td>1.05</td>
</tr>
<tr>
<td>a</td>
<td>0.76</td>
<td>0.58</td>
</tr>
</tbody>
</table>

*RED is calculated based on the data from “Hansen Solubility Parameters: A User’s Handbook”
Figure 4.2: A) Schematic demonstration of PS-cyclohexane emulsion system formation. B) Image of PS-cyclohexane mixture and PS-chloroform mixture (left) and optical image of PS-cyclohexane emulsion.
Figure 4.3: PS concentration of solvent-rich phase and polymer-rich phase from phase separated PS-cyclohexane system dependence on A) bulk concentration (Mw= 41 KDa Mw/Mn= 1.06 at 298.85 K) B) temperature (Mw=143 KDa, Mw/Mn=1.09, bulk concentration= 11.787%). All plotted data are from CRC Handbook of Liquid-Liquid Equilibrium Data of Polymer Solutions (page 133 to page 149).
The scalable method that we introduced in Chapter 2 and Chapter 3 adopts shear force and antisolvent-induced phase separation. By adding polymer solution in the bulk containing a viscous medium which is chosen to be miscible with polymer solvent, fibers are synthesized with. The biggest innovation of this technique is that it can draw thin fibers in parallel from the polymeric droplet due to the ultra-low interfacial tension between the droplets and the medium, which allows high degree of stretching and generation of materials with high surface area. As the solvent diffuses out of the droplets, polymer fibers in the diameter range of 200 nm – several µm are left behind (Figure 4.3 left). As a result, the fibers are formed in the bulk liquid without the use of nozzles or spinnerets by the combined action of shear and phase separation.

Liquid shear of PS-cyclohexane emulsions produced a surprising outcome that the resultant fiber sizes was 10 times smaller than those from PS-chloroform solution under same condition (Figure 4.4). First, it is reasonable to believe that the interfacial tension between cyclohexane and ethanol is similar due to the high miscibility between polymer solutions and shear medium. Secondly, the shearing medium is the same which guarantees the shear stress is not different. The only difference is that the viscosity of PS-cyclohexane is higher (0.10 Pa·S) than that of PS-chloroform solution (0.03 Pa·S). However, the 3 times smaller viscosity difference is not likely to be completely responsible for the synthesis of 10 times smaller fibers. Using the date from Chapter 3 as an example, the fiber sizes remains in the same range even though the viscosity of PS in chloroform increases from 0.18 Pa·S to 0.68 Pa·S while the concentration increases from 10% to 15%. Thus, the droplet viscosity difference is not the main reason for fiber size reduction. The smaller emulsion droplets having
concentrated polymer in the polymer solution droplet is responsible for the reduced fiber size and the mechanism demonstration is drawn in Figure 4.5. While the droplets are shearing in the viscous medium which is also miscible with polymer solvent, the smaller emulsion droplet with higher polymer concentration inside the sheared liquid are stretched to form thinner fibers while the larger droplet from PS-chloroform are stretched to form fibers with larger diameters. By increasing the shear rate to 6000 rpm, the fiber sizes are reduced to around 100 nm, which is difficult to achieve by liquid shear driven method from the one phase PS-chloroform solution in stable Couette flow.
Figure 4.4: a) Schematic demonstration of shear driven of PS-cyclohexane emulsion. b) Image of PS-cyclohexane mixture and PS-chloroform mixture (left) and optical image of PS-cyclohexane emulsion.
Figure 4.5: Schematic illustration of nanofibers formation mechanism from PS-chloroform (left) and PS-cyclohexane (right).
Figure 4.6: A) PS Fiber diameter dependence on shear speed from PS-cyclohexane emulsion. B) Fiber diameter size and distribution at 6000 rpm.
Microfibers have large inter-fiber pore sizes while nanofibers have extreme high surface area to volume and strong mechanical property. The fiber mixture consisting both microfibers and nanofibers can only be prepared by sequential electrospinning or electrospinning with specific collect drum, which holds limited productivity. The combination of shearing O/O polymer emulsion and polymer solution provides a novel approach to prepare the nano/microfibrous structures by stretching droplets with various sizes simultaneously (Figure 4.7). Multilayer nano/microfibrous structures have wide application in tissue engineering since they combine large inter-fiber pore size which is crucially important for cell growth, and high surface area for cell invasion and penetration ascribed to nanofibers\textsuperscript{25,26}. The multilayer nano/microfibrous structures can be prepared by wet-laying from the Xanoshear device.

![SEM images of fibrous mats composed of PS nanofibers and PLA microfibers.](image)

**Figure 4.7:** SEM images of fibrous mats composed of PS nanofibers and PLA microfibers.
In summary, the no-nozzle liquid shear driven method produces ultrathin PS fibers with diameters down to 100 nm from the PS-cyclohexane emulsions without any surfactant or other stabilization agents. The process not only simplifies the synthesis of fibers in nanometer scale from the shear driven method but also opens infinite possibilities for both batch and continuous shear driven devices. For example, the technique can be extended further to other polymer and solvent systems to produce a wide range of polymeric fibers. Instead of using only one solvent and one polymer, it introduces processes based on emulsions from two immiscible solvent and one polymer for the ultrathin fiber formation. The PS-cyclohexane emulsion also suggests a novel way for encapsulation a wide variety of drugs and particles inside the fiber matrix. Although shearing of non-aqueous emulsions is a powerful tool for synthesizing ultrathin fibers, the emulsions are destabilized rapidly due to Ostwald ripening and continuous external shearing is needed to stabilize the emulsion by preventing the droplets coalescence.
4.4 References


Chapter 5 Liquid Shear Driven Synthesis of Biodegradable Fibers for Controlled Drug Release Application
5.1 Introduction

A scalable and versatile technique to produce a few classes of polymeric nanomaterials in the liquid bulk is introduced thoroughly in Chapter 2-4. Adopting the simple experimental setup, fibers, ribbons, sheets or thin sheets can be produced by the combination of shear extension in the viscous medium and polymer precipitation. Nanofibers aroused the most wide research interest due to the high surface area to volume ratio, high porosity and extreme length and they are widely applied in various areas such as energy conversion devices, composites, catalysis, water desalination and other cutting-edge areas\(^1\). Liquid shear driven technique holds the superior advantage on commercial throughput compared to other existing methods in the market, such as electrospinning, melt blowing and melt spinning. Controlled release of drug combines the advantages of increased therapeutic efficacy reduced toxicity and administration frequency. Controlled drug release from fibrous polymers has been investigated for several years due to the useful properties of fibers including high surface to volume ratio, high porosity and the potential to form 3D matrix similar to ECM structure\(^2,3,4,5,6,7\). The nonwoven mats from fibers can be cut to or synthesized into any shape depending on the fabrication process. Biodegradable polymers have been used widely in pharmaceutical industry especially for drug delivery because, in addition to sustained release of encapsulated drug, they can degrade to nontoxic and low-molecular-weight compounds which are easily eliminated by the human body\(^8\). In particular, polylactic acid is one of the most popular candidates for drug loading because of its biocompatibility and the controllable degradation rate, as well as the appropriate mechanical and hydrophilic properties\(^9,10,11\).
In this study, liquid shear method is adopted to successfully encapsulate antibacterial drug in the biodegradable fibers. During the droplet shearing process, the majority of the drug is conveniently incorporated into the fiber matrix without any complicated preparation process. The encapsulation efficiency (up to 80% w/w) is determined by various parameters, such as polymer bulk concentration and fiber size. The initial burst release is determined by the drug located on surface, while the sustained release is mainly dependent on the fiber degradation which is determined by enzyme concentration in the release medium.

5.2 Experimental Section

5.2.1 Materials.

Rifampin (an antibiotic drug for tuberculosis, 99+%) of high purity, proteinase K and sodium azide were purchased from Sigma-Aldrich. Ingeo 6751D poly-(lactic acid) (Mw = 62,720, Mw/Mn = 2.880) was provided by NatureWorks Inc. Chloroform (HPLC, 99.8%) and glycerol (99+%) were purchased from Fisher and used without further treatment.

5.2.2 Preparation of Stock Solutions

10% PLA solutions were prepared by dissolving PLA pellet in chloroform. Rifampicin and PLA solution were then blended to obtain the mixture with 1% w/w rifampicin. The mixture was under ultrasonicated to disperse the drug evenly in the polymer solution prior to shearing process.

5.2.3 Fiber Synthesis

PLA fibers loaded with drug or without drug was synthesized followed the
aforementioned procedure. At ambient temperature, a benchtop Couette flow apparatus with a 2.3 mm gap was constructed with a rotating cylindrical shaft (radius $r_i = 5.0$ mm) and a disposable, stationary polypropylene tube (ID = 14.6 mm, Evergreen Scientific). Shaft rotation was digitally controlled (150 - 6000 rpm) by a Cole-Parmer Servodyne Mixer, Model # 50003. 0.05 ml of PLA-chloroform solution or PLA-chloroform-Rifampicin solution was injected into 6.5 ml of shearing medium composing of glycerol and polymer antisolvent under shearing from 2000 to 6000 rpm for 2 min. The fibers were formed from the solidification of the elongated polymeric droplets and collected after being peeled off from the shaft for subsequent morphological analysis.

5.2.4 Fiber Characterization

Optical microscopy (Olympus BX-61 microscope with a DP-70 digital CCD camera) was used to characterize fiber structure. The JEOL 2000FX Scanning Transmission Electron Microscope (SEM) was used to study the fiber morphology and size. Each sample was coated with gold using a sputtering device for 60 s prior to observation under the SEM. The average diameter and standard deviation of each sample were determined by at least 50 measurements of fibers from the SEM images. Measurements were conducted by an image-processing program named ImageJ (NIH).

5.2.5 In vitro Drug Release Characterization

Fibers were immersed in ethanol solution to remove the residual glycerol and drug located on surface. Approximately 0.5 mg of the obtained fiber mats loaded with drugs were measured and exposed to release medium. The fiber sample was incubated at 37 °C in 10 ml
of PBS buffer solution at pH 8.6 containing 15 mg/ml proteinase K. After a certain time length, 1 ml of buffer solution was taken out and equal amount of fresh buffer solution was added to the incubation solution. The released amount of model drugs from the fibers was determined by UV-Visible spectrophotometer at the same wavelengths (473 nm) as the one was used for collecting for the calibration curve. The UV-Vis absorbance was detected and converted to the concentration of rifampin according to the calibration curve of rifampin in the same buffer. The calibration curve for the model drug was measured in the range of 0.001 to 0.1 mg/ml and a liner relationship between the UV absorbance and the drug concentration was obtained following Beer’s Law. Then the accumulative amount of the released rifampin was calculated and plotted against the immersion time. The measurements were all conducted three times and the results were used as the average ± standard deviation.

5.3 Results and Discussions

5.3.1 Drug loading

It is shown in Figure 5.1 that addition of rifampicin plays no role in the fiber sizes and the fiber color turns slightly yellow from white. This yellow color is a direct indication of fiber encapsulation inside the fiber instead of on the surface, which can be further confirmed by the confocal images (Figure 5.2). The drug concentration on surface is lower than that in the fiber core due to the washing procedure to remove the drug left on the surface. The surface drug on fiber matrix leads to a rapid initial burst release. The loaded drug amount and drug encapsulation efficiency are calculated by the following equations:

\[
m_{\text{drug (encapsulation)}} = m_{\text{drug (added)}} - m_{\text{drug (medium)}} - m_{\text{ethanol}}
\]  

(5.1)
\[ \theta = \frac{m_{\text{drug}}(\text{encapsulation})}{m_{\text{drug added}}} \]  \hspace{1cm} (5.2)

where \( m_{\text{drug}}(\text{medium}) \) and \( m(\text{ethanol}) \) are measured by UV-Vis spectroscopy and \( \theta \) is the drug encapsulation efficiency.

The drug encapsulation efficiency is determined by several parameters, including bulk polymer concentration and shear rate (Figure 5.3). For higher polymer concentration, larger amount of drugs are embedded inside the fiber matrix due to the molecular affinity between polymer and drug. The highest encapsulation efficiency is around 80%. The other phenomena is that more drugs are encapsulated in the fiber if the shear rate increases due to the higher surface area to volume from smaller fibers.

*Figure 5.1: Optical images of PLA fibers loaded without (A) and with rifampicin (B).*
Figure 5.2: Confocal snapshots of single PLA fiber loaded with rifampicin.
Figure 5.3: RIF loading efficiency dependent on A) polymer concentration and B) shear rate.
5.3.2 Release of Encapsulated Model Drugs

The release profile of the drug from the polymer matrix is determined by many factors, such as the solubility of the drug in the immersion medium, the solubility of the drug with the polymer, the solubility as well as the swelling behavior of the polymer fiber mats in the release medium, the diffusion of the drug from the polymer matrix to the medium, the degradation rate of the polymer matrix in the medium, all of which play an important role in the release rate and profile of the model drug from the polymeric fiber mats.

The release characteristics of the model drugs from both the drug-loaded CA mats were carried out after being immersed in the DI-water as the transferring medium at 37°C. Erythrosin B and Rifampicin released from the CA fiber mat showed a burst release during the first few hours, and the release immediately stopped after the burst release. The released amount of Erythrosin B is close to the amount left in the polymer matrix, which verified that Erythrosin B only aggregate on the cellulose acetate fiber surface again, while only 10% of encapsulated Rifampicin is dissolved, suggesting that around 90% of the drug is encapsulated inside the polymer matrix. The 100% burst release of Erythrosin B in the beginning is because of the high solubility of the drug in water and its low affinity with cellulose acetate. Due to the good miscibility between polymer and Rifampicin and really low affinity between the drug and the medium, most of the drug would disperse inside the polymer matrix instead of on the surface, which leads to the 10% burst release in the beginning.

Poly (lactic acid) (PLA) is one kind of linear aliphatic polyester with biocompatible/biodegradable ability, which make it a highly promising candidate for drug
delivery system. It has been demonstrated that PLA will degrade under the catalysis of proteinase K in buffer solution and the degradation rate can be altered by changing the concentration of enzyme or surface charge\(^\text{11}\). The drug release experiment was conducted by incubating PLA fibers from shearing 10\% PLA -1\% rifampicin-chloroform solution is PBS buffer solution containing 15 \(\mu\text{g/ml}\) of proteinase K at 37 °C. The released amount of rifampicin as a function of time is measured the absorbance of supernatant from the solution at 472 nm after certain time length. It can be observed from Figure 5.4 that no initial burst release exists due to the ethanol washing before release experiment. Without proteinase K, little drug is released from the PLA fibers. Since PLA can be degraded by proteinase K under experimental condition, a conclusion can be drawn from Figure 5.4 that the drug release is mainly from the PLA degradation instead of the permeation of drug from the polymer matrix to the aqueous medium. The release rate is reduced with the bulk polymer concentration, which is due to the reduced surface area to volume ratio from resultant bigger fibers.
Figure 5.4: Release profiles of rifampicin from PLA nanofibers in PBS buffer solution with and without proteinase K. The data illustrates the critical role of proteinase K in fiber degradation.
Figure 5.5: Schematic of drug release mechanism of PLA fibers loaded with rifampicin in proteinase K solution.

Figure 5.6: Release profiles of rifampicin from PLA nanofibers produced from polymer solutions with various concentrations.
Fick’s first law of diffusion can be adopted to describe the drug release from the fiber mat (Equation 4.3). For the delivery system where the drug is uniformly dispersed throughout the matrix, unsteady–state drug diffusion in a one-dimensional slap – shaped matrix can be described by Fick’s second law of diffusion. Under proper initial and boundary conditions, the simplified form of the analytic solution is expressed in equation 5.4:

\[ J_A = -D \frac{dC_A}{dx} \]  
\[ \frac{dC_A}{dx} = D \frac{d^2C_A}{dx^2} \]  
\[ \frac{M_t}{M_0} = k t^n, \text{ for } \frac{M_t}{M_0} < 0.6 \]  

where \( J_A \) is the drug flux, \( D \) is the drug diffusion coefficient and is assumed constant to simplify the modelling, and \( C_A \) is the drug concentration, \( M_t \) is the calculated accumulative amount of drugs obtained at an arbitrary time \( t \), \( M_0 \) is the accumulative amount of drugs obtained at the infinite time, \( n \) is the exponent to describe the release kinetics, and \( k \) is the rate constant, which is determined by the related physical properties of the drug-delivery system. Since the release profile is linear in the first stage, \( n = 1 \) fits the experimental results in Figure 5.4 and 5.6, which indicates that dissolution of the released drug in the medium is a zero order kinetic process and the relative rate constants can be calculated in the future characterization of PLA nanofiber mat application.
5.4 Summary

By liquid shearing technique, drug loaded biodegradable fibers are synthesized and the drugs are trapped inside the fiber matrix instead of on the surface with highest encapsulation efficiency around 80%. The release rate of the drug is mainly controlled by the decomposing rate of PLA instead of drug permeation while the PLA degradation rate can be modulated by enzyme concentration. The model developed indicates a zero-order drug release process existence.
5.5 References


Chapter 6 Summary and Future Outlook


6.1 Summary

The main goal of my dissertation is to investigate the fabrication potential of the liquid shear driven process on synthesis of micro- and nanomaterials with controllable size, morphology and composition.

In Chapter 1, we introduced in details the liquid shear driven technique which is simple, scalable and versatile in details. By the combination of shear extension in a viscous medium and polymer phase separation, a few classes of polymer nanomaterials in the bulk of liquid are produced. The resultant micro- and nanostructures include fibers, ribbons, and thin sheets from a diverse class of polymers. Among all of these structures, nanofibers have attracted the most wide research interest due to the unique properties including high surface area to volume ratio, high porosity and extreme long length. The current leading fiber production approaches in the market all posses certain drawbacks. For example, the throughput of electrospinning is limited to around 2.5 kg/hr and the diameter of fiber produced by wet spinning cannot below micrometer while melt spinning is only applicable to melt-processable polymers. The breakthrough of liquid shear driven technique on fiber synthesis is that it produces fibers with diameter from 200 nm to several micrometers from a wide range of liquid- processable polymers with high commercial yield (up to 12 kg/hr). Thus in Chapter 2, the optimum parameters range for fiber formation is established and the effect on those parameters on fiber size, are investigated.

It is demonstrated that medium with high viscosity is necessary to stretch the droplets to infinite long strand. On the other hand, the viscous medium complicates the post sample
washing procedure and introduces the potential slippery danger in the working area. Thus non viscous medium shearing method is developed and it is the first time proposed that the synthesis of PLA or PS nanofibers can be completed in the aqueous ethanol medium, which extends the application potential of the liquid shear driven technique.

Colloid science usually categories emulsion as oil in water (O/W) emulsion and water in oil (W/O) emulsion. However, the non-miscible polymeric organic liquid pairs can form oil in oil emulsion. Phase separation happens in the mixture of PS and cyclohexane and emulsions are formed under continuous shearing while the continuous phase is solvent rich and the disperse phase is polymer rich. By shearing the emulsions, the fibers sizes are reduced around 10X due to the reduced initial polymer droplet size. The fiber sizes are further reduced to 100 nm to enhance the competitive advantages of liquid shear technique to other fiber product methods in the by adopting this non aqueous polymer emulsion.

Controlled drug release combines the advantages of increased therapeutic efficacy, reduced toxicity and administration frequency. By dispersing model drugs in the spinning polymer solution, antibacterial model drugs are successfully encapsulated inside the biodegradable matrix and the encapsulation efficiency can be modulated by polymer concentration and fiber size while the release profile of the drug is determined by the degradation rate of the polymer matrix.

6.2 Future Outlook

6.2.1 Computation Modeling

During the PhD work, I conducted research to investigate the effect of various
parameters on resultant micron- and nanostructure morphology and size on liquid shear technique. However, the interpretation of the experimental results is mainly based on different theories proposed previously by other researchers and not a single theory is versatile enough to explain all the results in depth, for example, droplet breaking along the shear direction is reasonable for fiber formation from medium containing viscous solvent but not applicable for the fiber formation from the medium without viscous solvent. Thus to better investigate the mechanism for liquid shear process, numerical simulation by COMSOL interface will be a useful to model the flow type in Taylor-Couette device, the droplet breaking up and elongation and polymer phase separation. Initial attempt was performed to predict the time-dependent polymer droplet shape evolution in the Couette flow medium, which is miscible with the polymer antisolvent (Figure 6.1) \(^1\). These initial simulation results explain the immigration of droplet from the injection point to the center of the stream. However, the fiber collection in the center is not well demonstrated, which makes the modeling results inconclusive. The next step in Comsol simulation is to further optimize the initial model to better illustrate the experimental results. The modified simulation procedure will be extended to other fiber formation process by varying the Reynolds number, Capillary number as well as the Elastocapillay number.
6.2.2 Formation of Hierarchical Structured Functional Micro-/Nanofibers

A nanofiber is defined as a long cylindrical solid object with high surface area to volume ratio while hierarchical nanofiber materials provide additional heterogeneous interface which is promising for various applications due to enhanced nano-sized effect. The application spectrum of hierarchical structure is significantly broad, including sensor, energy storage,
catalysis, tissue engineering, filtration as well microreactor due to the numerous variations on structures and functions (Figure 6.2). Preliminary experiments are conducted to expand the liquid shear driven method to synthesize surface hierarchical and inner hierarchical structures.

Figure 6.2: Schematic illustration of hierarchical micro-/nanostructures and related applications.

6.2.2.1 Strategy 1: Inner hierarchical structure

Nanopeapod structures are defined as the spherical pores or nanoparticles acting as the peas encapsulated in and aligned along in the axial direction of the nanofibers or nanorods
However, no easy and scalable strategy was proposed to produce those structures. Our research showed that by shearing the O/W emulsion, the water droplets may be encapsulated inside the fiber matrix and the peapod structures could be formed after water evaporation (Figure 6.3).

6.2.2.2 Strategy 2: Surface multilevel structure

As it is discussed in previous chapters, during the liquid shear driven process, the stretched and not fully solidified polymeric droplet is in continuous contact with the liquid medium. So introducing functional molecules or particles to the medium provides a novel strategy to control the fiber surface structure. The solubility of zein, a prolamine protein, reduces with the increased water concentration in the aqueous ethanol solution. After precipitating zein particles inside the medium, PS-chloroform solutions are injected into the same medium containing zein nanoparticles. The zein particles aggregate on the PS fibers surface to enhance the fiber surface roughness (Figure 6.4 A). After immersion the fiber mat in the pure ethanol solutions, the zein particle on fiber surface disappears due to dissolution (Figure 6.4 B). The experimental result of successfully attaching zein particle on fiber surface expands the liquid shear driven method to synthesize surface multilevel structures. Besides fiber surface roughness enhancement, it is also applicable to grow stimulus-responsive or conductive molecular layer on fiber surface, which play an important role in sensor or energy related device fabrication.
Figure 6.3: A) Fluorescence optical image of water in oil droplet while fluorescent dye is dissolved in water; B) Fluorescence and non-fluorescence optical images of fibers embedded with water droplet; C) SEM images of peapod nanofibers after water evaporation.
In summary, liquid shear driven method has now emerged as a technique capable of produce a wide range of polymeric micro- and nanostructures. Firstly, the size, chemical composition, and inner/surface morphology can be modulated by the experimental parameters. Secondly, the setup of the liquid shear driven method is simple and easy to operate, which can be further modified to produce nanofibers (100 nm to several microns) in continuous device at high commercial yield. Thirdly, the diversity and scope of the materials that can be utilized is broad, which provides infinite application potential in a number of areas. It is expected that liquid shear method will become more and more dominating in the market in the near future.
6.3 References
