2.1 INTRODUCTION

Electrospinning is a unique technique of producing continuous polymer fibres. It has established a great deal of interest in recent times due to its flexibility in the spinning of a wide variety of polymeric fibres, and its consistency in producing polymer fibres with the fibre diameter on submicrometre to nanometre scales that depends on the kinds of polymer and processing conditions (Reneker et al. 1996). The term “electrospinning” is technically derived from “electrostatic spinning”, in which electrical charges are employed in the process to produce polymer nanomembrane. Electrospinning represents an attractive approach for polymer biomaterials processing, with the opportunity for control over morphology, porosity and composition using simple equipment.

Formhals (1934) introduced electrospinning methods and described fibre formation during the spinning process. Vonnegut et al. (1952) were able to produce streams of highly electrified even droplets of about 0.1 mm in diameter. Simons (1966) patented an apparatus for the production of non-woven fabrics of ultra thin and very light in weight with dissimilar patterns using electrical spinning. He found that the fibers from low viscosity solutions tended to be shorter and finer whereas those from more viscous solutions were relatively continuous. Taylor (1969) fundamentally studied the form of the polymer droplet at the tip of the needle and demonstrated that it is
a cone and the jet is ejected from the vertex of the cone, referred as the “Taylor Cone”. In subsequent years, most research focused on the structural morphology and characterization of nanomembranes. Baumgarten (1971) produced electrospun acrylic fibers with diameters in the range of 500-1100 nm. The spinning drop was suspended from a stainless steel capillary tube and maintained constant in size by adjusting the feed rate of an infusion pump. A high-voltage current was connected to the capillary tube whereas the fibers were collected on a grounded metal screen.

Since 1980s and particularly in recent years, the electrospinning process has regained more attention probably due in part to a surging importance in nanotechnology, as ultrafine fibers or fibrous structures of various polymers with diameters down to submicrons or nanometers can be easily fabricated with this process. Electrospun nanofibers are being considered for a variety of applications where their unique properties contribute to product functionality. Those properties include high surface area, small fiber diameter, potential to incorporate active chemistry, filtration properties, layer thinness, high permeability, and low basis weight.

Nanofiber researches in medical textiles consist of tissue engineering and wound dressing, and drug delivery. For tissue engineering and wound dressing, electrospun nanomembranes are treated as tissue scaffolds which improve cell growth and proliferation. The nanomembrane scaffolds with seeded cells can be fixed to patient's body to repair the damaged tissues. For drug delivery system, nanomembrane is considered as a potential drug carrier. Here, nanomembranes incorporated with drug component can be patched on wound of surgery or encapsulated into pharmaceutical capsules to deliver the drug through digestive system of patient.
2.2 FUNDAMENTAL ASPECTS OF ELECTROSPINNING PROCESS

Figure 2.1 shows a typical electrospinning apparatus. There are basically three components to fulfill the process: a high voltage supplier, a capillary tube with a pipette or needle of small diameter, and a metal collecting screen.

![Figure 2.1 Schematic diagram of electrospinning apparatus](image)

In the electrospinning process a high voltage is used to produce an electrically charged jet of polymer solution out of the pipette. Before reaching the collecting screen, the solution jet evaporates or solidifies, and is collected as an interconnected web of small fibers. One electrode is placed into the spinning solution and the other attached to the collector. In most cases, the collector is simply grounded. The electric field is subjected to the end of the capillary tube that contains the solution fluid held by its surface tension. This induces a charge on the surface of the liquid. Mutual charge repulsion and the contraction of the surface charges to the counter electrode cause a force directly opposite to the surface tension. As the voltage is increased the effect of the electric field becomes more prominent and as it approaches exerting a similar amount of force on the droplet as the surface tension does a cone (Taylor cone) as shown in Figure 2.2 shape begins to form with convex sides and a rounded tip. Further increasing the electric field, a critical value is
attained with which the repulsive electrostatic force overcomes the surface tension and the charged jet of the fluid is ejected from the tip of the Taylor cone. The discharged polymer solution jet undergoes an instability and elongation process, which allows the jet to become very long and thin. Meanwhile, the solvent evaporates, leaving behind a charged polymer fiber.

Fig 2.2 Taylor cone

2.3 PARAMETERS INVESTIGATION IN ELECTROSPINNING

It has been well established that both operating parameters and material properties affect the electrospinning process and the resulting fibre morphology. The operating parameters include the applied electrical field, the flow rate of the polymer solution, the distance between the tip and the collecting screen (spinning distance) and capillary tip diameter. A minute change in the operating parameters can lead to a considerable change in the fibre morphology. For example, finer nanofibres are electrospun from a nozzle of smaller diameter (Katti et al 2004); increasing the flow rate leads to larger fibre diameter; and a higher applied voltage results in the emergence of fibre beads, though reducing the fibre diameter (Deitzel et al 2001. Lee et al, 2004). The material properties that affect the electrospinning process and the fibre morphology include the polymer concentration, the solution viscosity, the solution conductivity, the surface tension and other properties concerning the solvent as well as the polymer itself. Among the material properties, the
solution concentration plays a most important role in stabilizing the fibrous structure because it also affects other solution properties, such as the solution viscosity, the surface tension and the conductivity. The solvent used is another important factor because it mainly determines the surface tension and the evaporation process. The volatility of the solvent affects the fibre surface morphology and the nanomembrane structure.

The solution bulk properties come from intermolecular interactions among the solvent molecules and the polymer macromolecules. Any factors that interfere with these interactions change the solution properties that affect the electrospinning process, and the fibre morphology is thus altered accordingly. For example, the solution viscosity is closely related to the entanglement of polymer macromolecules, in a good solvent, polymer chains with a higher molecular weight tangle with each other more easily, which leads to higher solution viscosity. Electrospinning such a polymer solution produces continuous and uniform fibres. However, when polymer of a low molecular weight is electrospun, even at the same polymer concentration, the resultant fibre could have a colloid bead or beaded fibre morphology (Koski et al 2003).

One of the most important quantities related with electrospinning is the fiber diameter. Since nanofibers are resulted from evaporation or solidification of polymer fluid jets, the fiber diameters will depend primarily on the jet sizes as well as on the polymer contents in the jets. It has been recognized that during the traveling of a solution jet from the pipette onto the metal collector, the primary jet may or may not be split into multiple jets, resulting in different fiber diameters (Figure. 2.3).
As long as no splitting is involved, one of the most significant parameters influencing the fiber diameter is the solution viscosity. A higher viscosity results in a larger fiber diameter. However, when a solid polymer is dissolved in a solvent, the solution viscosity is proportional to the polymer concentration. Thus, the higher the polymer concentration the larger the resulting nanofiber diameters will be. In fact, Deitzel et al (2001) pointed out that the fiber diameter increased with increasing polymer concentration according to a power law relationship. Demir et al (2002) found that the fiber diameter was proportional to the cube of the polymer concentration. Another parameter which affects the fiber diameter to a remarkable extent is the applied electrical voltage. In general, a higher applied voltage ejects more fluid in a jet, resulting in a larger fiber diameter.

Further challenge with current electrospinning lies in the fact that the fiber diameters obtained are seldom uniform. Not many reports have been given towards resolving this problem. Another problem encountered in electrospinning is that defects such as beads Figure 2.4, and pores Figure 2.3 may occur in polymer nanofibers. It has been found that the polymer concentration also affects the formation of the beads.
2.3.1 Polymer Solution Concentration

As the polymer solution concentration plays a major role in the electrospinning process, it is not surprising that the polymer solution concentration has been extensively exploited to change and control fibre morphology in electrospinning. Under the same electropinning conditions, increasing the polymer concentration will increase the diameter of the electrospun fibres. However, a non-linear relationship between the solution concentration and the fibre diameter usually forms (Deitzel et al 2001). The reason for this non-linear relationship can be attributed to the non-linear relationship between the polymer solution concentration and the solution viscosity. As the polymer solution concentration increases, the viscosity increases gradually until the concentration reaches a specific value, after which the viscosity increases considerably (Lin et al 2004).

In the electrospinning process, the solvent evaporates from the jet/filament continuously until the jet becomes dry. Stretching the jet increases the surface area, which accelerates the solvent evaporation. From the initial jet to dry fibres, the fibre stretching process is quick, taking only tens of milliseconds (Shin et al 2001). If the strength of the stretch filaments remains the same, electrospinning a polymer solution of higher velocity could be much harder than that with a lower viscosity, because the concentration

Figure 2.4 AFM image of electrospun PEO nanofibers with beads
has a larger influence on the viscosity when the concentration is high. On the other hand the polymer solution concentration affects the solution conductivity, which further influences the solution charge density. This could compensate to some extent for the difficulty in stretching a solution of high polymer solution concentration. In certain cases, the strength is improved to such an extent that it neutralizes the effect of the viscosity, which results in a similarly linear relationship between the concentration and the fibre diameter. The relationship between the solution viscosity and the polymer concentration is highly dependent on the nature of the polymer and the intermolecular interactions within the polymer solution. Although reducing the polymer concentration is a straightforward way to produce finer nanofibres, electrospinning a dilute polymer solution usually leads to the emergence of colloid beads. These defectives even become the main products when the polymer concentration is very low. Because of this, the electrospinning of bead-free and uniform nanofibres particularly for the fibre diameters less than 100 nm still remains a great challenge.

Generally, when a polymer of higher molecular weight is dissolved in a solvent, its viscosity will be higher than solution of the same polymer but of a lower molecular weight. One of the conditions necessary for electrospinning to occur where fibers are formed is that the solution must consists of polymer of sufficient molecular weight and the solution must be of sufficient viscosity. As the jet leaves the needle tip during electrospinning, the polymer solution is stretched as it travels towards the collection plate. During the stretching of the polymer solution, it is the entanglement of the molecule chains that prevents the electrically driven jet from breaking up thus maintaining a continuous solution jet. As a result, monomeric polymer solution does not form fibers when electrospun (Buchko et al 1999).
The polymer chain entanglements were found to have a significant impact on whether the electrospinning jet breaks up into small droplets or whether resultant electrospun fibers contain beads (Shenoy et al 2005). Although a minimum amount of polymer chain entanglements and thus, viscosity is necessary for electrospinning, a viscosity that is too high will make it very difficult to pump the solution through the syringe needle (Kameoka et al 2003). Moreover, when the viscosity is too high, the solution may dry at the tip of the needle before electrospinning can be initiated (Zhong et al 2002). Many experiments have shown that a minimum viscosity for each polymer solution is required to yield fibers without beads (Fong et al 1999). At a low viscosity, it is common to find beads along the fibers deposited on the collection plate. At a lower viscosity, the higher amount of solvent molecules and fewer chain entanglements will mean that surface tension has a dominant influence along the electrospinning jet causing beads to form along the fiber. When the viscosity is increased which means that there is a higher amount of polymer chains entanglement in the solution, the charges on the electrospinning jet will be able to fully stretch the solution with the solvent molecules distributed among the polymer chains. With increased viscosity, the diameter of the fiber also increases (Jarusuwannapoom et al 2005). This is probably due to the greater resistance of the solution to be stretched by the charges on the jet.

2.3.2 Applied Voltage

A crucial element in electrospinning is the application of a high voltage to the polymer solution. The high voltage will induce the necessary charges on the solution and together with the external electric field, will initiate the electrospinning process when the electrostatic force in the solution overcomes the surface tension of the solution. Generally, both high negative or positive voltage of more than 6kV is able to cause the solution drop at the
tip of the needle to distort into the shape of a Taylor Cone during jet initiation (Taylor 1964). Depending on the feedrate of the solution, a higher voltage may be required so that the Taylor Cone is stable. The columbic repulsive force in the jet will then stretch the viscoelastic solution. If the applied voltage is higher, the greater amount of charges will cause the jet to accelerate faster and more volume of solution will be drawn from the tip of the needle. This may result in a smaller and less stable Taylor Cone (Zhong et al 2002). When the drawing of the solution to the collection plate is faster than the supply from the source, the Taylor Cone may recede into the needle (Deitzel et al 2001).

As both the voltage supplied and the resultant electric field have an influence in the stretching and the acceleration of the jet, they will have an influence on the morphology of the fibers obtained. In most cases, a higher voltage will lead to greater stretching of the solution due to the greater columbic forces in the jet as well as the stronger electric field. These have the effect of reducing the diameter of the fibers (Lee et al 2004) and also encourage faster solvent evaporation to yield drier fibers (Pawlowski et al 2005). When a solution of lower viscosity is used, a higher voltage may favor the formation of secondary jets during electrospinning. This has the effect of reducing the fiber diameter (Demir et al 2002). Another factor that may influence the diameter of the fiber is the flight time of the electrospinning jet. A longer flight time will allow more time for the fibers to stretch and elongate before it is deposited on the collection plate. Thus, at a lower voltage, the reduced acceleration of the jet and the weaker electric field may increase the flight time of the electrospinning jet which may favor the formation of finer fibers. In this case, a voltage close to the critical voltage for electrospinning may be favorable to obtain finer fibers (Zhao et al 2004). At a higher voltage, it was found that there is a greater tendency for beads formation (Zhong et al 2002). The increased in beads density due to increased
voltage may be the result of increased instability of the jet as the Taylor Cone recedes into the syringe needle. In an interesting observation, Krishnappa et al (2002) reported that increasing voltage will increased the beads density, which at an even higher voltage; the beads will join to form a thicker diameter fiber. The effect of high voltage is not only on the physical appearance of the fiber, it also affects the crystallinity of the polymer fiber.

The electrostatic field may cause the polymer molecules to be more ordered during electrospinning thus induces a greater crystallinity in the fiber. However, above a certain voltage, the crystallinity of the fiber is reduced. With increased voltage, the acceleration of the fibers also increases. This reduces the flight time of the electrospinning jet. Since the orientation of the polymer molecules will take some time, the reduced flight time means that the fibers will be deposited before the polymer molecules have sufficient time to align itself. Thus, given sufficient flight time, the crystallinity of the fiber will improve with higher voltage (Zhao et al 2004).

2.3.3 Capillary Tip–Collector Distance

The gap distance between the capillary tip and the collector influences the fiber deposition time, the evaporation rate, and the whipping or instability interval, which subsequently affect the fiber characteristics. In several cases, the flight time as well as the electric field strength will affect the electrospinning process and the resultant fibers. Varying the distance between the tip and the collector will have a direct influence in both the flight time and the electric field strength. For independent fibers to form, the electrospinning jet must be allowed time for most of the solvents to be evaporated. When the distance between the tip and the collector is reduced, the jet will have a shorter distance to travel before it reaches the collector plate. Moreover, the electric field strength will also increase at the same time and this will increase the acceleration of the jet to the collector. As a result,
there may not have enough time for the solvents to evaporate when it hits the collector. When the distance is too low, excess solvent may cause the fibers to merge where they contact to form junctions resulting in inter and intra layer bonding (Buchko et al 1999). Depending on the solution property, the effect of varying the distance may or may not have a significant effect on the fiber morphology. In some cases, changing the distance has no significant effect on the fiber diameter.

However, beads were observed to form when distance was too low (Megelski et al 2002). The formation of beads may be the result of increased field strength between the needle tip and the collector. Decreasing the distance has the same effect as increasing the voltage supplied and this will cause an increased in the field strength. As mentioned earlier, if the field strength is too high, the increased instability of the jet may encourage beads formation. However, if the distance is such that the field strength is at an optimal value, there is less beads formed as the electrostatic field provides sufficient stretching force to the jet (Jarusuwannapoom et al 2005). In other circumstances, increasing the distance results in a decrease in the average fiber diameter (Ayutsede et al 2005). The longer distance means that there is a longer flight time for the solution to be stretched before it is deposited on the collector. However, there are cases where at a longer distance, the fiber diameter increases. This is due to the decrease in the electrostatic field strength resulting in less stretching of the fibers (Lee et al 2004). When the distance is too large, no fibers are deposited on the collector. Therefore, it seems that there is an optimal electrostatic field strength below which the stretching of the solution will decrease resulting in increased fiber diameters.

2.3.4 Flow Rate

Megelski et al (2002) found that the flow rate of polymer solution affects the jet velocity and the material transfer rate with enhanced pore, fiber
sizes and beaded structures, as well with an increase in the polymer flow rate in case of polystyrene fibers. For a given voltage, there is a corresponding flow rate if a stable Taylor cone is to be maintained. When the flow rate is increased, there is a corresponding increase in the fiber diameter or beads size. This is apparent as there is a greater volume of solution that is drawn away from the needle tip (Rutledge et al 2000).

If the flow rate is at the same rate which the solution is carried away by the electrospinning jet, there must be a corresponding increased in charges when the flow rate is increased. Thus there is a corresponding increased in the stretching of the solution which counters the increased diameter due to increased volume. Due to the greater volume of solution drawn from the needle tip, the jet will takes a longer time to dry. As a result, the solvents in the deposited fibers may not have enough time to evaporate given the same flight time. The residual solvents may cause the fibers to fuse together where they make contact forming webs. A lower flow rate is more desirable as the solvent will have more time for evaporation (Yuan et. al. 2004).

2.3.5 Diameter of Pipette Orifice / Needle

The internal diameter of the needle or the pipette orifice has a certain effect on the electrospinning process. A smaller internal diameter was found to reduce the clogging as well as the amount of beads on the electrospun fibers (Mao et al 2004). The reduction in the clogging could be due to less exposure of the solution to the atmosphere during electrospinning. Decrease in the internal diameter of the orifice was also found to cause a reduction in the diameter of the electrospun fibers. When the size of the droplet at the tip of the orifice is decreased, such as in the case of a smaller internal diameter of the orifice, the surface tension of the droplet increases. For the same voltage supplied, a greater columbic force is required to cause
jet initiation. As a result, the acceleration of the jet decreases and this allows more time for the solution to be stretched and elongated before it is collected. However, if the diameter of the orifice is too small, it may not be possible to extrude a droplet of solution at the tip of the orifice (Zhao et al 2004).

2.4 PROPERTIES OF NANOFIBERS

Nanofibers possess significantly unique thermal and mechanical properties compared to normal fibers and bulk polymers due to their large specific surface areas and surface morphologies. These led to major research activities for advanced applications.

2.4.1 Thermal Properties

The relationship between nanostructure and thermal properties of various kinds of electrospun nanomembrane has been widely investigated. It was indicated that electrospun PLLA fibers had lower crystallinity, glass transition temperature (Tg), and melting temperature (Tm) than semicrystalline PLLA films (Zong et al 2002). The decrease in the Tg could be attributed to the large surface to volume ratio of nanomembrane whereas the high evaporation rate followed by rapid solidification of electrospun fibers during the electrospinning process is expected to be the reason for the low crystallinity. Kim et al (2000) proposed that the decreases in Tg and Tm, and the increase in the heat of melting of the electrospun polyethylene terephthalate (PET) and polyethylene naphthalate (PEN) were attributed to increase in the segmental mobility. They also found that the melting temperature of the PET and PEN electrospun fibers remained quite unchanged compared to regular fiber forms. Deitzel et al (2001) showed that PEO nanofibers had lower melting temperature and heat of fusion than powder PEO owing to the poor crystallinity of the electrospun fibers. From the WAXD patterns, it was determined that electrospun PLLA fibers were highly oriented, however the
crystallinity of the PLLA fibers was reduced by the electrospinning process. This behavior was observed in poly (meta-phe-nylene isophalamide), poly (glycolide), and polyacrylonitrile. Kim et al (2000) used the TGA technique to determine the thermal degradation of PET and PEN before and after electrospinning and found that the intrinsic viscosities of electrospun nanofibers of both materials decreased dramatically. They proposed that the low values of Tg and Tc were due to the reduction of molecular entanglements.

2.4.2 Mechanical Properties

Mechanical properties of electrospun nanofibers, including tensile strength and Young’s modulus are mainly affected by their nanostructured surface with small pores. Gibson et al (2002) showed that the Young’s modulus of electrospun pellethane thermoplastic elastomers was quite unchanged. On the other hand, a 40% reduction in tensile strength and 60% reduction in elongation were observed at maximum applied stress for pellethane electrospun elastomers compared with their cast film. Information on the mechanical properties of nanofibers and nanofiber composites has so far, been very limited.

2.5 ALIGNMENT OF NANOFIBERS

There has been extensive work on making aligned electrospun nanofibers, since most nanofibers obtained so far are in non-woven form, which can be useful for number of applications such as filtration, tissue scaffold, implant coating film, and wound dressing. The following techniques have been attempted to align electrospun nanomembrane. It has been suggested that by rotating a cylinder collector at a high speed, electrospun nanofibers could be oriented circumferentially. Fennessey et al (2004) produced unidirectionally aligned carbon precursor fibers with diameters in
the nanoscale range using a rotating grounded wheel at speeds 0 to 2284 rpm as a collector. Bornat et al (1987) demonstrated the alignment method using an auxiliary electrode. For the production of tubular structures, it was reported that by asymmetrically placing rotating and charged mandrel between two charged plates, electrospun ultrafine fibers with larger diameter could be oriented circumferentially to the longitudinal axis of the tubular structure. A novel approach to position and align individual nanofibers on a tapered and grounded wheel like bobbin has been recently revealed. By this means, Yarin et al (2001) demonstrated that PEO nanofibers with diameters ranging from 100-400 nm and lengths of up to hundreds of microns were obtained in parallel arrays and with controllable average separation between the fibers. Later, he also used the rotating collector disk equipped with the rotating table to create layers of nanofiber arrays. Another method has recently been developed for fiber alignment by simply placing a rectangular frame structure under the spinning jet. Similarly, Li et al (2004) divided the typical collector electrode into two pieces and separated them with a void gap to produce the uniaxial alignment of nanofibers, which formed a parallel array across the void gap. A rotating multiframe structure was employed, on which the electrospun nanofibers could be continuously deposited. The shape and size of frame rods, the distance between the frame rods, and the inclination angle of a single frame were the key factors on the alignment characteristics of nanofibers.

2.6 EFFECT OF FIBER SIZE

Currently, there is tremendous interest in forming materials that are spatially organized on the nanometer length scale. According to the National Science Foundation (NSF), nanomaterials are matters that have at least one dimension equal to or less than 100 nanometers. Nanofibers are solid state linear nanomaterials characterized by an aspect ratio greater than 1000:1.
Materials in fiber form are of great practical and fundamental importance. Specifically, the role of fiber size has been recognized in significant increase in surface area; in bio-reactivity; in electronic properties; and in mechanical properties. The combination of high specific surface area, flexibility, and superior directional strength makes fiber a preferred material form for many applications ranging from clothing to reinforcements for aerospace structures.

2.7 APPLICATIONS OF NANOFIBERS

A large amount of effort has recently concentrated on nanofiber applications, because of the remarkable properties of nanofibers due to their high specific surface area and nanoporous structure. Potential applications in particular areas such as catalysis, filtration, nanocomposites, tissue scaffolds, drug delivery systems, protective textiles, storage cells for hydrogen fuel cells, etc. have been extensively investigated.

2.7.1 Filtration

Electrospun nanomembranes for filtration purpose have a long history. Electrospun nanomembrane provides dramatic increases in filtration efficiency at relatively small decreases in permeability. In comparison with conventional filter fibers at the same pressure drop, nanofibres with a diameter finer than half a micron have a much higher capability to collect the fine particles (Kosmider et al 2002). Both experimental measurements and theoretical calculations revealed that electrospun mats were extremely efficient at trapping airborne particles ranges from 0.5—200 μm (Gibson et al 2001). A very thin layer of electrospun nanofibres sprayed onto a porous substrate was sufficient to eliminate the particle penetration. The air flow resistance and aerosol filtration properties correlate with the add-on weight of the electrospun fiber coating. Also, electrospun layers present minimal impedance to moisture vapour diffusion, which is very important for
protection clothing in decontamination applications. A comparison study between a nylon-6 electrospun membrane of thickness 100 μm, pore size 0.24 μm and a commercial high μm, pore size 1.7 μm using 300 nm test particles indicated that the thin nanofiber membrane had a slightly higher filtration efficiency of 99.993% than the HEPA filter of 99.97% (Barhate et al 2007). Besides solid particles, tiny liquid droplets within a liquid-liquid immiscible system could also be removed by nanofiber membrane (liquid-liquid coalescence filtration). Polystyrene (PS) nanofibers (diameter about 600 nm) were electrospun from a recycled expanded polystyrene (EPS), and mixed with micro glass fibers to form a filter media for removal of water droplets from a water-in-oil emulsion (Shin et al 2004). In another work, electrospun nylon nanofibers were also blended with glass fibers (diameter 5 μm) for the coalescence filtration, and addition of an optimal amount of nanofibers (1.6 wt %) to the coalescence filter improved the capture efficiency, but did not cause excessive pressure drop (Wang et al 2005). Other works related to the filtration applications include effects of operating parameters in electrospinning on fiber morphology and pore structure for filter media (Barhate et al 2006).

2.7.2 Tissue Engineering

Tissue engineering is one of the most exciting inter disciplinary and multidisciplinary research areas today, and there has been exponential growth in the number of research publications in this area in recent years. It involves the use of living cells, manipulated through their extracellular environment or genetically to develop biological substitutes for implantation into the body and/or to foster remodeling of tissues in some active manners.

The core technologies intrinsic to this effort can be organized into three areas: cell technology, scaffold construct technology, and technologies for in vivo integration. The scaffold construct technology focuses on
designing, manufacturing and characterizing three-dimensional scaffolds for cell seeding and in vitro or in vivo culturing. For a scaffold to function effectively by assisting in the formation of neo-tissue, it must possess the correct design parameters. There are a few basic requirements that have been widely accepted for designing polymer scaffolds (Ma et al. 2004). First, a scaffold should possess a high porosity, with an appropriate pore size distribution. Second, a high surface area is needed. Third, biodegradability is often required, with the degradation rate matching the rate of neo-tissue formation. Fourth, the scaffold must possess the required structural integrity to prevent the pores of the scaffold from collapsing during neo-tissue formation, with the appropriate mechanical properties. Finally the scaffold should be non-toxic to cells and biocompatible, positively interacting with the cells to promote cell adhesion, proliferation, migration, and differentiated cell function. It is now well known that many biologically functional molecules, extracellular matrix (ECM) components, and cells interact on the nanoscale. Collagen is a major natural extracellular matrix component, and possesses a fibrous structure with fiber bundles varying in diameter from 50—500 nm (Hay et al. 1991). Many efforts have been made to search a suitable scaffold material, and an ideal scaffold should have similar physicochemical and biological characteristics to the ECM (Chiu et al. 2007).

In morphology, electrospun nanofiber mat is very similar to human native ECM (Wang et al. 2005), thus could be a promising scaffolding material for cell culture and tissue engineering application. The electrospinning process makes it possible to produce complex, seamless and three-dimensional (3D) nanofiber scaffolds that support diverse types of cells to grow into the artificial tissues. Nanofibers used come from different polymers including synthetic and natural polymers, biodegradable and non-biodegradable polymers. The cell culture has been conducted for potentially
engineering different tissues including muscles, bones and cartilages, skins, neural tissues, blood vessels, and others.

2.8 ELECTROSPUN NANOMEMBRANE WOUND DRESSINGS

2.8.1 Basic considerations

Wound healing is a native process of regenerating dermal and epidermal tissues. When an individual is wounded, a set of complex biochemical actions take place in a closely orchestrated cascade to repair the damage. These events can be classified into inflammatory, proliferative, and remodeling phases and epithelialization. Normally, body cannot heal a deep dermal injury. In full thickness burns or deep ulcers, there is no source of cells remaining for regeneration, except from the wound edges. As a result, complete re-epithelialization takes a long time and is complicated with scarring of the base (Marler et al 1998).

Dressings for wound healing function to protect the wound, exude extra body fluids from the wound area, decontaminate the exogenous microorganism, improve the appearance and sometimes accelerate the healing process. For these functions, a wound dressing material should provide a physical barrier to a wound, but be permeable to moisture and oxygen. For a full thickness dermal injury, the adhesion and integration of an “artificial dermal layer” consisting of a 3D tissue scaffold with well cultured dermal fibroblasts will considerably assist the re-epithelialization.

Electrospun nanomembrane is a good wound dressing candidate because of its unique properties: the highly porous membrane structure and well interconnected pores are particularly important for exuding fluid from the wound; the small pores and very high specific surface area not only inhibit the exogenous microorganism invasions, but also assist the control of
fluid drainage; in addition, the electrospinning process provides a simple way to add drugs into the nanofibers for any possible medical treatment and antibacterial purposes. Wound dressing with electrospun nanofibrous membrane can meet the requirements such as higher gas permeation and protection of wound from infection and dehydration. Electrospun nanomembranes for wound dressings usually have pore size in the range of 500 – 1000 nm which is small enough to protect the wound from bacterial penetration. High surface area of electrospun nanomembrane is extremely efficient for fluid absorption and dermal delivery (Huang et al 2003).

As stated by other researchers, the electrospun membrane kept exudate fluid from the wound area and inhibited the invasion of exogenous micro-organisms because of the fine pores (Khil et al 2003). In addition, electrospun nanofiber membranes have been used to deliver antibiotics to treat wounds. There is a particular advantage to this system because of the possibility of delivering uniform, highly controlled doses of bioactive agents at the wound area by taking advantage of the high surface-to-volume ratio of the nanofiber system (Qi et al 2006).

Wound dressing is a therapy to repair the skin damaged by ambustion and injury. So far electrospun nanofibrous membrane exhibited the potential in wound dressing field. The membrane attained uniform adherence at wet wound surface without any fluid accumulation (Bhattarai et. al. 2004). Wound dressing with electrospun nanofibrous membrane can meet the requirements such as higher gas permeation and protection of wound from infection and dehydration. The goal of wound dressing is the production of an ideal structure, which gives higher porosity and good barrier. To reach this goal, wound dressing materials must be selected carefully and the structure must be controlled to confirm that it has good barrier properties and oxygen permeability. The rate of epithelialization was increased and the dermis was
well organized in electrospun nanofibrous membrane and provided a good support for wound healing (Khil et. al. 2003). This wound dressing showed controlled evaporative water loss, excellent oxygen permeability and promoted fluid drainage ability due to the nanofibers with porosity and inherent property of polyurethane. The materials described here is to apply physical integration of natural and synthetic polymers to provide a favorable substrate for fibroblast (Venugopal et. al. 2005).

2.8.2 PVA nanomembrane

A PVA nanofibrous matrix was prepared by electrospinning an aqueous 10 wt % PVA solution. The mean diameter of the PVA nanofibers electrospun from the PVA aqueous solution was 240 nm. The water resistance of the as-spun PVA nanofibrous matrix was improved by physically crosslinking the PVA nanofibers by heat treatment at 150 degrees C for 10 min, which were found to be the optimal heat treatment conditions determined from chemical and morphological considerations. In addition, the heat-treated PVA (H-PVA) nanofibrous matrix was coated with a chitosan solution to construct biomimetic nanofibrous wound dressings. The chitosan-coated PVA (C-PVA) nanofibrous matrix showed less hydrophilic and better tensile properties than the H-PVA nanofibrous matrix. The effect of the chitosan coating on open wound healing in a mouse was examined. The C-PVA and H-PVA nanofibrous matrices showed faster wound healing than the control. The histological examination and mechanical stability revealed the C-PVA nanofibrous matrix to be more effective as a wound-healing accelerator in the early stages of wound healing than the H-PVA nanofibrous matrix (Kang et al 2010).

PVA nanofibers containing Ag+- loaded nanoparticles were prepared by electrospinning technique. The fibers were bactericidal to the testing microorganisms due to the strong antibacterial ability of silver ions
and the fibers can still maintain the white physical appearance. This novel Ag+-containing PVA electrospun nanofibers is believed to have great potential in the applications of wound dressings (JIA Jun et al 2007).

2.8.3 PCL, PU nanomembrane

Chong et al (2006) fabricated a composite comprising a semipermeable barrier and a scaffold filter layer for skin cells in wound healing by electrospinning. Tegaderm polyurethane (TG) was employed as a semi-permeable barrier which is permeable to oxygen and impermeable to moisture. PCL nanomembranes were electrospun on to the surface of TG to form a TG nanomembrane composite. TG nanomembrane was a suitable host substrate for human dermal fibroblast. Lee et al (2007) prepared chitosan containing nonwoven web that exhibited capacity to moisturize the skin. The chitosan was first electrospun into nanofibres with average diameter less than 1000 nm and then the nonwoven web was then treated in hyaluronic acid. The formed web was biocompatible and biodegradable and it is also showed quick antibacterial capability, excellent air permeability, and fast moisturizing performance. A multi layered anti-adhesion barrier was constructed by coating a hydrophilic, biooriginated polymer including PCL, PLA and hyaluronic acid on the electrospun nanofiborous base layer which comprised a hydrophobic, biodegradable, biocompatible polymer.

A study on using electrospun polyurethane membrane as wound dressing material revealed that the membrane effectively exuded fluid from the wound, without fluid accumulation under the membrane cover, and no wound desiccation occurred either (Khil et al 2003). Also the membrane showed a controlled water loss from evaporation, excellent oxygen permeability, and high fluid drainage ability, besides inhibiting the invasion of exogenous micro organism. Histological test also indicated that the rate of epithelialization was increased and the dermis became well organized when
the wounds were covered with the electrospun nanomembrane (Khil et al; 2003). However the combination with synthetic polymers (PU or PCL) is highly desirable to provide higher mechanical properties of scaffold. Some other natural polymers including silk fibroin, fibrinogen, or other blends have been electrospun as wound dressings or cellular matrix, and efficient cell attachment, growth or infiltration has been demonstrated in in-vitro culture, but limited clinical trial has been reported (Lee et al 2004).

Geun hyung kim et al (2008) introduced a direct-electrospinning apparatus that uses a guiding electrode and an air-blowing system to enable the fabrication of wound-dressing membranes consisting of biodegradable PCL micro/nanofibers. Stable, steady deposition of electrospun fibers on any substrate occurred without interrupting the charges on the substrate. The membrane had a highly reduced charge and sufficient removal of solvent. Moreover, the membrane had a broad range of small pores, which should prevent bacteria invasion, and sufficient mechanical properties to sustain internally/externally applied mechanical stress.

2.8.4 Collagen nanomembrane

An open wound healing test for an electrospun collagen nanomembrane showed that the early-stage healing using collagen nanofiber mat was faster than that of using normal cotton gauze (Rho et al 2006). In the first week, the wound surface for the cotton group was covered by fibrinous tissue debris, below which dense infiltration of polymorphonuclear leukocytes and the proliferation of fibroblasts were formed. By comparison, the surface tissue debris in the collagen nanofiber group disappeared, and prominent proliferation of young capillaries and fibroblasts was found. Later stage healing processes were similar for both groups.
2.8.5 Chitosan nanomembrane

Chitosan is an excellent material for medical use because it is nontoxic, has good biocompatibility, exhibits antimicrobial activity, supports the healing of wounds, etc. Electrospinning yields nanofibers which have wide applications, such as high-performance filters, biomaterial scaffolds for wound dressings, etc (Ching et al 2008).

2.8.6 Gelatin nanomembrane

Gelatin was successfully electrospun into nanofibres using several solvents such as TFE, HFP, and formic acid. Potential application of electrospun gelatin as wound dressings and optimal fibre density to provide high cell viability, and optimal cell organization, and excellent barrier desirable for wound healing (Gu et al 2009).

2.8.7 PVA/Silver nitrate nanomembranes

The Ag ions were incorporated into electrospun nanofibers via adding AgNO₃ into the polymer solution for electrospinning. To maintain a long term antibacterial activity and control the release of Ag ions, the Ag was embedded in the form of elementary state by a post-electrospinning treatment of Ag ions incorporated. Ag nanoparticles can also be directly incorporated into electrospun nanofibers via the electrospinning process. An Ag/PVA nanofiber membrane exhibited excellent antimicrobial ability and good stability in moisture environment, as well as quick and continuous release with good effectiveness (Hong et al 2007). Besides adding antibacterial additives, antimicrobial nanofibers can also be prepared by directly using antimicrobial polymers. For instance, polyurethanes containing different amounts of quaternary ammonium groups were electrospun into nanofiber nonwovens, and the nanofibers showed very strong antimicrobial activities.
against Staphylococcus aureus and Escherichia coli (Jeong et al 2007). Polyvinyl alcohol (PVA) nanofibers containing Ag nanoparticles were prepared by electrospinning PVA/silver nitrate (AgNO3) aqueous solutions, followed by short heat treatment, and their antimicrobial activity was investigated for wound dressing applications. Since PVA is a water soluble and biocompatible polymer, it is one of the best materials for the preparation of wound dressing nanofibers. The PVA nanofibres containing Ag nanoparticles showed very strong antimicrobial activity.

2.8.8 PVA/Chitosan nanomembranes

Ultrafine chitosan fibers could be produced by electrospinning via the addition of PVA in the chitosan/dilute acetic acid solutions. The polymer concentration and the chitosan/PVA mass ratio were two important factors influencing the electrospinnability of the chitosan/PVA solutions as well as the morphology of the electrospun membranes. Uniform chitosan/PVA fibers with an average diameter of 99±21 nm were prepared from a 7% chitosan/PVA solution in 40:60 mass ratio. The electrospun chitosan/PVA membranes could have potential applications in wound dressings because of their higher water uptake (Yuanyuan Zhang et al 2007).

2.8.9 PCL/Collagen nanomembranes

Biodegradable polycaprolactone (PCL) is potentially useful for the replacement of implanted material by the repair of tissues by coating collagen and improves the mechanical integrity of the matrix. The PCL and collagen nanofiber structure provides a high level of surface area for cells to attach due to its 3D feature and its high surface area to volume ratio. This approach exploits the cell binding properties of PCL whilst avoiding the toxicological concerns associated with chemical crosslinking of collagen to impart stability. Tissue engineering scaffolds are required to exhibit a
residence time but do not compromise complete space filling by new tissue at the wound site. Cell interaction study proves fibroblasts that migrated inside the collagen nano fibrous matrices showed morphologically similar to dermal substitute. The collagen synthesized by the fibroblast enhanced the attachment of keratinocytes to the surface of artificial dermis in serum free medium. It is assumed that the presence of fibroblasts invade the wound tissue by early synthesis of new skin tissue because the fibroblasts on the artificial dermis can release biologically active substance cytokines. The dermal fibroblasts entering into the matrix through small pores in an electrospun structure by differently oriented fibers lay loosely upon each other. When cells perform amoeboid movement to migrate through the pores, they can push the surrounding fibers aside to expand the hole as small fibers offer little resistance to cell movement. This dynamic architecture of the fibers provides the cells to adjust according to the pore size and grow into the nanofiber matrices to form a dermal substitute for many types of wound healing. The nanofiber based cultured dermal fibroblast maintains the moist environment on the wound surface and thereby to promote wound healing. Gelatin, as an alternative protein to collagen, is commercially available at significantly lower cost preserves many merits of collagen such as a biological origin, biodegradability, and biocompatibility. Composite polymeric nanofibers can be electrospun using mixed solution, using dual or co-electrospinning method in separate solvent systems or coaxial core/shell electrospinning. Nanofibrous composite of PCL/collagen was electrospun, as the one in early model of composite used to support dermal fibroblasts.

Heather et al (2007) investigated the association of mechanical strength and biological affinity of blended PCL/collagen scaffolds with various ratios of PCL/collagen. Minimal addition of PCL (10%) to collagen produces the scaffolds suitable for tissue engineering skin with a good balance of mechanical strength and biological properties.
Composite films comprising non-crosslinked collagen mats stabilized by PCL were found previously to support a higher number of human osteoblasts in cell culture in comparison with PCL films. The preparation and characterization of collagen: PCL blended biocomposite and nanofibre membranes for support of human dermal fibroblast and keratinocytes in tissue-engineered skin in regenerative medicine. The PCL nanofibres support the fibroblast cell culture compared with PCL films. PCL is characterized by a resorption time in excess one year but known to be susceptible to enzymatic degradation. A variety of collagenase enzymes are secreted by macrophages, epidermal cells, and fibroblasts during wound healing, including matrix metalloproteinases, gelatinase-A, and stromelysin-1, which are implicated in the process of cell migration and repair.

2.8.10 PEO/Chitosan nanomembranes

Chitosan electrospun nanomembrane is an excellent material for medical use because it is nontoxic, has good biocompatibility, exhibits antimicrobial activity and supports the healing of wounds, etc (Lou et al 2008). Electrospun hyperbranched polyglycerol nanofibers capable of providing an active agent delivery for wound dressing applications. PEO/chitosan nanomembrane exhibited biotoxicity; chitosan promoted cell proliferation, helping cells generate pseudopods. This experiment verified that PEO/chitosan membranes enhanced the proliferation of cells and biocompatibility and this nanomembrane is successfully used in wound dressings applications. A blended chitosan nanofibers with electrospinnable PEO polymer encourages the formation of electrospun membranes. Mixture of weak acidic solution with volatile solvent improves the capacity of electrospun nanofibers. Various concentration ratios of PEO-Chitosan nanofiber membranes exhibited no biotoxicity (Valencia Jacobs et al 2010).
2.8.11 PCL/Gelatin nanomembranes

More recently, PCL/gelatin nanofibrous scaffold and layered dermal reconstitution were evaluated for wound healing. Significant cell adhesion, growth, and infiltration achieved on the PCL/gelatin produced a fibroblast-populated three-dimensional dermal analog. This cost-effective composite could be promising wound dressing or tissue scaffolds for skin construct. The potential application for PLGA/dextran was investigated as tissue scaffolds for skin tissue engineering (Pan et al 2006). A complete cell biological response of dermal fibroblasts was tested on electrospun PLGA/dextran nanofibers. The results showed that favorable fibroblasts interacted with the scaffolds and resembled a dermal-like architecture. Aimed to overcome poor infiltration of fibroblasts into electrospun mats, a novel threedimensional multilayered cell–nanofiber constructs of dermis was fabricated by architecting layer-by-layer of nanofibers–cells alternated using electrospinning nanofibers of PCL/collagen and seeding human dermal fibroblasts. Dermal tissue or bilayered skin equivalent was produced by continuous culturing of fibroblast/fiber-layered constructs or inclusion of keratinocytes seeded onto the dermal layer.

2.8.12 PLGA/Collagen, PLLA/Gelatin nanomembrane

Several other composites including PLGA/collagen, PLLA/gelatin, and PVA/chitosan have been electrospun and their characteristics oriented for the application in skin tissue engineering were discussed (Matthews et al 2002). These scaffolds showed their efficacy for wound coverage or cell growth biocompatibility, but further clinical studies are needed. Previous work using this nanofabrication technique already suggested great potential of applying nanofibrous scaffolds for wound dressing or skin tissue engineering. However, very limited in vivo applications for skin repair and regeneration have been reported. More effort is still needed to seek FDA approval for use
and to prove their effectiveness in repairing and regenerating skin. Electrospun scaffolds have been extensively used in vitro to study cell–scaffold interactions, and further understanding of the cellular response of nanofibrous scaffolds might ultimately lead to the success in tissue repair or regeneration of skin.

2.8.13 PVP/AgNP nanomembrane

Medical treatment of chronic wounds occurs, in the presence of pain causing great discomfort to the patient, especially when accompanied of infectious bacterial contamination (Roacha et al 2006). Hydrogel have been widely applied for biomedical and pharmaceutical purposes and/or crosslink density. A PVP/AgNP solution was produced by in situ reduction of AgNO$_3$. From this solution, a mat of nanofibres was produced using a typical electrospinning apparatus, under controlled temperature and humidity. After crosslinking a PVP/AgNP porous hydrogel was formed (Lopergolo et al 2003). The AgNP was successfully incorporated and the electrospun PVP/AgNP nanofibres exhibit smooth morphology, while producing a highly porous mat. The porosity remains after crosslinking process, originating pore diameters of a few microns, by partially keeping the original fibrous structure. The potential bactericidal effect of silver nanoparticles is already known, and the biological property of this hydrogel was improved by the large associations of these bactericidal nanoparticles maintained even after crosslinking and swelling. PVP/AgNP hydrogel electrospun nanomembrane was successfully used in wound care dressings.

2.8.14 PEO/sodium alginate

Su park et al (2010) has fabricated alginate-based nanofibers by electrospinning. Sodium alginate alone cannot be electrospun due to high viscosity and conductivity. Sodium alginate can be made to better nanofiber
by blending with PEO and improved by lecithin as natural surfactant to remove the bead of nanofiber. Fibrous morphology of sodium alginate/PEO blend nanofibers presented clear fiber with increasing alginate contents. Fine alginate nanofibers with smooth and uniform fiber were obtained in SA/PEO ratio of 1/2 and 2/2 during the electrospinning process. A combined crosslinking with CaCl2 can improve the fibrous morphology and uniform thickness of smooth fibers in SA/PEO 2/2 than SA/ PEO 1/2. The SA/PEO nanofibers exhibit good uniformity and water absorbance, and biocompatibility. Also, alginate fibers are cheap and easy to synthesize. Polymeric alginate nanofibers can be used for a biological and medical application as wound dressing.

PU and PCL nanofibres are frequently used in wound dressings because of their good barrier properties and oxygen permeability. Research has reported that semipermeable dressings, many of which are PU, enhance wound healing. The permeability to water is also important so that fluid from the wound does not build up between the wound and the dressing and wound desiccation does not occur. Researchers have tried to determine the effect of occlusive dressings on the healing of a wound prepared by PU. One of the drawbacks of the semiocclusive dressings is that significant fluid accumulation can occur under them, particularly after a few days of use. This may require aspiration of the wound to prevent leakage and infection. The electrospun nanofibrous membrane showed good and immediate adherence to a wet wound surface. The membrane attained uniform adherence to the wound surface without any fluid accumulation. The dermis of a wound covered with TegadermTM was inflammatory, whereas the rate of epithelialization was increased and the dermis was well organized in a electrospun nanofibrous membrane group. The nanofibrous membrane wound dressing showed controlled evaporative water loss, excellent oxygen permeability, and promoted fluid drainage ability owing to the porosity and
inherent property of PU. Histological examination confirmed that the epithelialization rate was increased and the exudates in the dermis was well controlled by covering the wound with the electrospun membrane. Thus, thenanofibrous PU and PPDO/PLLA-b-PEG (poly(pdioxanone- co-l-lactide)-block-poly(ethylene glycol))- membrane prepared by electrospinning could be properly employed as a wound dressing.

Various biodegradable and biocompatible polymeric materials have been electrospun into nanoscale fibers and demonstrated their potential as effective carriers for drug delivery. Delivery of tetracycline hydrochloride based on the fibrous delivery matrices of poly ethylene-co-vinyl acetate, polylactic acid and their blend were developed. In another work bioabsorbable nanofiber membranes of polylactic acid targeted for the prevention of surgery-induced adhesions, were also used for loading an antibiotic drug Mefoxin. Currently, many studies have been focused on incorporating drugs with blended polymer-based electrospun nanofibers. By adjusting the blending ratio of polymers, the property of the fiberous material and drug release behavior could be monitored.

2.8.15 Drug delivery nanomembrane

In some recent studies, the addition of drugs into nanofibers as controlled release system has been investigated for wound dressing to provide the required protection and pain management. Some antibiotic or antibacterial drugs/components such as cefazolin, lidocaine, mupirocin, or Ag particles have been electrospun into synthetic nanofibers in the blended form, and increased or controlled antimicrobial or antibiotic ability desirable for wound healing has been achieved with a sustained controlled release rate of drugs (Hong et al 2007). These drug delivery systems using electrospun nanofibers exhibit pain relief and extended antibacterial activity with great potential of the applications in wound healing. For the use of electrospun pure synthetic
polymer in skin tissue engineering, only limited synthetic polymers such as PLLA, PLGA, blended poly(ε-lactide), and poly(ethylene glycol) having acceptable hydrophilicity have been reported for the potential application in skin tissue scaffolding. It is widely accepted that the incorporation of natural polymer into electrospun synthetic nanofibers is desirable in skin tissue engineering to promote the biological activity of scaffolds.

Rifampin, encapsulated in PLLA during electrospinning, and incubated in a 0.05 M Tris-HCl buffer, was only released when proteinase K was added to the solution. This suggests that the release of rifampin was initiated by the degradation of PLLA and not by normal diffusion. In another experiment, doxorubicin hydrochloride and paclitaxil were encapsulated into PLLA nanofibers. Doxorubicin hydrochloride was detected on the surface of the nanofibers but paclitaxil remained encapsulated. Rifampin and paclitaxil were more soluble in the chloroform/acetone solvent compared to doxorubicin hydrochloride. The solubility of the molecule to be encapsulated in the polymer solvent plays an important role in its distribution throughout the nanofibers. Tetracycline hydrochloride (5%, w/w) encapsulated in poly-ethylene-co-vinyl acetate (PEVA), or in a blend of PEVA and PLLA, has a relatively slow and consistent release rate. The PEVA and PEVA/PLLA blend containing 5% (w/w) tetracycline hydrochloride had a similar release rate to Actisite, a commercial drug delivery system, following the initial high burst release. The antibiotic Mefoxin (cefoxitin sodium) was encapsulated in poly-lactate-co-glycolide (PLGA) fibers and in fibers consisting of a poly-lactate-co-glycolide/polyethylene glycol-block-poly(L-lactide) copolymer (PLGA/PEG-b-PLLA). Mefoxin released from the fibers inhibited the growth of S. aureus in culture and on an agar surface. PEG-b-PLLA prolonged the drug release for up to one week.
Controlled release is an efficient process of delivering drugs in wound dressings. It can balance the delivery kinetics, minimize the toxicity and side effects, and improve patient convenience (Yih et al 2006). In a controlled release system, the active substance is loaded into a carrier or device first, and then releases at a predictable rate in vivo when administered by an injected or non-injected route. As a potential drug delivery carrier, electrospun nanofibres have exhibited many advantages. The drug loading is very easy to implement via electrospinning process, and the high applied voltage used in the electrospinning process had little influence on the drug activity. The high specific surface area and short diffusion passage length give the nanofiber drug system higher overall release rate than the bulk material (e.g. film). The release profile can be finely controlled by modulation of nanofiber morphology, porosity and composition.

Nanofibers for drug release systems mainly come from biodegradable polymers, such as PLA, PCL, poly(D-lactide)(PDLA), PLLA,PLGA, and hydrophilic polymers, such as PVA, PEG and PEO. Non-biodegradable polymers, such as PEU, were also investigated. Model drugs that have been studied include water soluble, poor-water soluble and water insoluble drugs. The release of macro-molecules, such as DNA and bioactive proteins from nanofibers was also investigated. Many factors may influence the release performance, such as the type of polymers used, hydrophilicity and hydrophobicity of drugs and polymers, solubility, drug polymer comparability, additives, and the existence of enzyme in the buffer solution.

In most cases, water soluble drugs, including DNA and proteins, exhibited an early-stage burst (Zong et al 2002). For some applications, preventing post-surgery induced adhesion for instance, and such an early burst release will be an ideal profile because most infections occur within the first few hours after surgery. However, for a long-lasting release process, it
would be essential to maintain the release in an even and stable pace, and any early burst release should be avoided. For a water insoluble drug, the drug release from hydrophobic nanofibres into buffer solution is difficult. However, when an enzyme capable of degrading nanofibers exists in the buffer solution, the drug can be released in a constant rate because of the degradation of nanofibres (Zeng et al 2003). For example, when rifampin was encapsulated in PLA nanofibers, no drug release was detected from the nanofibers.

However, when the buffer solution contained proteinase K, the drug release took place nearly in zero-order kinetics, and no early burst release happened. Similarly, initial burst release did not occur for poor-water soluble drugs, but the release from a non-biodegradable nanofiber could follow different kinetics (Verreck et al 2003). In another example, blending a hydrophilic but water-insoluble polymer (PEG-g-CHN) with PLGA could assist the release of a poor-water soluble drug Iburprofen (Jiang et al 2004). However, when a water soluble polymer was used, the poor-soluble drug was released accompanied with dissolving of the nanofibers, leading to a low burst release. In another case, the burst release of ketoprofen from PVA nanofibers was eliminated when the PVA nanofibers were treated with methanol (Kenawy et al 2007).

The early burst release can be reduced when the drug is encapsulated within the nanofiber matrix. When an amphiphilic block copolymer, PEG-b-PLA was added into Mefoxin/PLGA nanofibers, the cumulative amount of the released drug at earlier time points was reduced and the drug release rate at longer time was prolonged (Kim et al 2004). The reason for the reduced burst release was attributed to that some drug molecules were encapsulated within the hydrophilic block of the PEG-b-PLA. Amphiphilic block copolymer also assisted the dispersion and encapsulation
of water-soluble drug into nanofibres when the polymer solution used an oleophilic solvent, such as chloroform, during electrospinning (Xu et al 2005). In this case, a water-in-oil emulation can be electrospun into uniform nanofibers, and drug molecules are trapped by hydrophilic chains. The swelling of the hydrophilic chains during releasing assists the diffusion of drug from nanofibres to the buffer. Coating nanofibers with a polymer shell could be an effective way to control the release profile. When a thin layer of hydrophobic polymer, such as poly (p-xylylene) (PPX), was coated on PVA nanofibers loaded with BSA/luciferase, the early burst release of the enzyme was prevented (Zeng et al 2005). The polymer shell can also be directly applied, via a coaxial co-electrospinning process, and the nanofibers produced are normally named “core-sheath” bicomponent nanofibers. In this case, even a pure drug can be entrapped into nanofiber as the core, and the release profile was less dependent on the solubility of drug released. The early burst release can also be lowered via encapsulating water soluble drugs into nanoparticles, followed by incorporating the drug-loaded nanoparticles into nanofibers. In addition, the rate of releasing water soluble drug could be slowed down when nanofiber matrix was crosslinked.

PCL and PLA fibers as well as bicomponent PCL–PLA fibers were electrospun at concentrations in the range of 9–15 wt.% and loaded with three different antibiotics. Chloroform proved to be the most suitable solvent for this purpose. Fiber properties were established by determining the viscosity, shear behavior, surface tension and the solvent evaporation behavior of the spinning solution. All fibers showed variations in surface morphology. Depending on the spinning system indentations of various sizes, depths and shapes were observed. The most uniform bicomponent PCL–PLA fibers with serrated surfaces and the least variation in diameter were obtained from 12 wt.% chloroform solutions at ratios of 1:1, 3:1 or 1:3. The fibers were exposed to a buffer solution of pH 7.35 to study the discharge rate of the
incorporated antibiotics. PCL released the drugs fairly fast and nearly completely, while PLA could hold the drugs much longer. Bicomponent fibers of PCL–PLA behaved in a similar manner as the dominant polymer in the bicomponent mat with release characteristics falling in-between pure PCL and pure PLA fibers. It seems very likely that their release behavior can be shaped by careful fiber design in which the effect of each component in the spinning system is taken into account (Gisela Buschle et al 2007).

2.8.16 Summary

Electrospun nanomembrane is a good wound dressing candidate because of its unique properties. Various types of polymers are produced into electrospun nanomembranes for wound care dressings applications. Drug can also incorporated in the electrospun nanomembrane for sustain delivery on the wound, several drug deliver electrospun nanomembrane wound care were also developed.