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Magnetic Field-Assisted Electrospinning of Aligned Straight and Wavy Polymeric Nanofibers

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Electrospinning has emerged as a very attractive approach to the fabrication of nanometer (nm)- and submicron-sized fibers.[1–6] Nanofibers generated using the electrospinning technique have been explored for a wide range of applications such as tissue engineering and bioassay,[5,7–13] sensing,[14,15] textile,[16] filtration,[17] electrode,[18] and catalyst supports.[19] In many of these cases, the ability to control the alignment and arrangement of fibers is critical to achieve the designed functions, particularly for tissue engineering that requires the release of proteins and growth factors in a guided fashion.[20–22] Improvements in fiber quality has been achieved in recent year through the optimization of electrospinning conditions and oriented fiber arrays can be produced using either rotating collectors or patterned electrodes.[1,23–26] Furthermore, when magnetic nanoparticles are mixed with polymers, aligned fibers can also be fabricated.[27]

Despite these advancement, it is highly desirable to develop an approach that is able to not only generate well-aligned nanofibers, but also allow convenient deposition of the as-made fibrous matrices onto surfaces of solid substrates for device fabrication or subsequent uses. [28] To create aligned or patterned bundles of electrospun fibers, electrodes either in parallel and/or arranged at a particular angle with a gap have been used.[1,23,29,30] When these two techniques are combined, fibers can be spun with improved orders in the products.[24,31] Well-aligned thick fibrous layers in large areas are hard to produce using currently existing approaches. Control of fiber diameter, uniformity, and orientation without branching is also hard to achieve simultaneously. In this communication, we show that by introducing properly an external magnetic field at the collector region, electrospinning of well-ordered

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nanofibers can be achieved.[32–34] These ordered arrays of nanofibers can be made over large areas and as thick matrix films. Furthermore, the fibers fabricated using the magnetic field-assisted electrospinning (MFAES) method are substantially more uniform and with much less, if any, splitting than those without the field.

Figure 1 shows a schematic illustration of the setup used in the MFAES process. Two bar magnets ($2.5 \times 2.5 \times 15$ cm, Rochester Magnet Co., Part No.: RMC5B-522, non-conductive) was introduced to the conventional configuration at the collector region. Thick insulating sheets were placed between the magnets and the aluminium foil, the collector, to ensure that there was no direct contact between them. The magnetic field at the center of the gap was maintained at 0.2 Tesla (T) and the optimal distance between the two magnets was in the range of 0.5–4 cm. The field strength was determined using an F.W. Bell 9500 Series Gaussmeter. The charged jet would experience a radial Lorentz force during its movement in the magnetic field, and the jet direction and diameter were determined by the magnetic field gradient.[32–34] The charged fibers were spun onto the collector and stretched across the gap of two opposite magnetic poles along the directions normal to the surfaces of the magnets. As they were suspended over the gap between the two magnets, the fibers could easily be removed from the substrates and used as scaffolds or transferred onto other surfaces for subsequent treatment or characterization.

We used ester-terminated poly (D, L-lactic-co-glycolic acid) (PLGA) and poly(vinyl pyrrolidone) (PVP) as the polymers for this study. No magnetic nanoparticles were added or required in the polymer mixture for this MFAES method. In a typical procedure, PLGA with monomer ratio between lactic and glycolic acids of 50:50 (Inherent viscosity range: 0.55–0.75 dL/g in HFIP; Durect Corporation) was dissolved in 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP, 99%, Alfa Aesar) at a predetermined concentration, typically between 0.22 and 0.28 g/mL solvent. This polymer solution was loaded into a 10-mL plastic syringe (NORM-JECT[®] from Henke-Saas-Wolf) equipped with a 22-Gauge stainless steel needle (Precision Glide, Becton Dickinson and Company). The needle was connected to a high-voltage power supply (ES30P-10W, Gamma High Voltage Research Inc.) that is capable of generating DC voltage up to 30 kV and was operated at 15 kV. The distance between the tip of the needle and the collector was 14 cm. The solution was extruded using a syringe pump (Harvard Apparatus, Model: 55–4140) at a constant flow rate between 0.5 and 3.0 mL/h. PVP fibers were also fabricated under the 0.2-T external magnetic field using the MFAES. PVP (Sigma-Aldrich) used in this work has a molecular weight of 1300 kg/mol. A mixture of ethyl alcohol and distilled water at a volumetric ratio of 80:20 was used as the solvent. The optimal electrospinning conditions were 0.11 g PVP/mL solvent, applied voltage of 20 kV and needle-to-collector distance of 10 cm.

The morphology and size of the as-spun fibers were investigated using a field emission scanning electron microscope (FE-SEM, Carl ZEISS NTS GmbH; Model: SUPRA[™] 40VP) operated at an accelerating voltage of 10 kV. The samples were coated with a thin layer of gold deposited for 60 s using a sputter (DESK II, DENTON VACUUM) to reduce the surface-charging effect. The diameter of the fibers was measured directly from their high-magnification SEM images using Image J software based on at least 150 fibers on the different regions of the substrate. The specimen used for imaging the cross-sections of electrospun fiber matrices were made by freezing the sample in liquid nitrogen for 5 min, followed by cutting with a sharp knife.

To determine the suitability of using these matrices to support the attachment and survival of cells, we seeded pluripotent murine mesenchymal stem cell line (C3H10T1/2) on random or aligned PLGA fibers. PLGA fiber matrices were fixed to the culture surface by glue and sterilized by isopropanol, followed by extensive wash with phosphate-buffered saline (PBS)

solution. Cells were directly seeded on the PLGA matrices at a density of $1 \times 10^4/\text{cm}^2$ and cultured with basal medium eagle (BME) (Sigma-Aldrich) containing 10% fetal bovine serum (FBS), 1% penicillin/streptomycin and 1% glutamine at 37 °C with 5% CO₂. To facilitate the visualization of cell attachment and survival, the C3H10T1/2 cells were transduced with adenovirus expressing green fluorescent protein (Ad-GFP). The distinctive morphology of the cells can be visualized under a fluorescence microscope (Zeiss Axio).

Figure 2 shows the representative SEM images of aligned straight and wavy PLGA and PVP fibers fabricated using the MFAES method. The fibers fabricated from 0.24 g/mL PLGA in HFIP at a flow rate of 0.5 mL/h uniaxially aligned along the same direction varying in just a few degrees overall (Figure 2A). The average diameter of these PLGA fibers was 226 ± 75 nm and no obvious branching was observed. The branching of electrospun fibers is due to the electrostatic interactions between different segments of the charged jet. When the repulsive forces on the charged fiber jet generated by magnetic field surpassed the electrostatic interactions, straight fibers without branching were obtained. Interestingly, these aligned straight fibers could become wavy but maintain their overall alignment by increasing the flow rate from 0.5 to 3.0 mL/h (Figure 2B). Such oriented wavy morphology has not been observed so far and was the result of collective forces experienced by the electrospun jet under both the electric and external magnetic fields. The wavy nature favored the formation of void spaces between neighboring fibers that could facilitate the material transport in direction normal to the surface of fiber membranes. Similarly, aligned straight PVP fibers could be made from a 0.11 g/mL solution of ethanol and water at the feeding rate of 1.0 mL/h (Figure 2C), and wavy fibers at the feeding rate of 2.5 mL/h (Figure 2D). These results indicate that the generation of aligned straight and wavy polymeric fibers by the MFAES is independent of the material and solvent used, and does not require the electrospinning materials to be magnetically active.

The diameter and morphology of these aligned fibers could be readily controlled by changing the concentration of the polymer solution. Figure 3 shows SEM images and the diameter-concentration relationship for fibers made from solutions with the PLGA concentration ranging from 0.22 to 0.28 g/mL. In comparison with those fibers made without the external magnetic field (Figure 3, A–D), a significant drop in diameter could be observed for the fibers made using the MFAES method (Figure 3, E–H). The diameters were 140 ± 80 , 226 ± 75 , 324 ± 104 , and 369 ± 117 nm, respectively, for the aligned PLGA fibers made from 0.22, 0.24, 0.26 and 0.28 g/mL solutions (Figure 3I). The corresponding diameters were 279 ± 220 , 376 ± 169 , 650 ± 202 and 707 ± 218 nm for those fibers made under the same conditions but without the external magnetic field. The decreases in fiber diameter were at least 40%. The matrices of random fibers could clearly be observed at all four concentrations if no magnetic field was applied, while no branching and excellent alignment were both observed for those fabricated using the MFAES method. We observed that besides polymer concentration, feeding rate and applied voltage could also affect greatly the fiber diameter, uniformity and alignment using MFAES. The diameters of aligned fibers were especially sensitive to the applied voltage. The distribution of diameters also became narrower for fibers made with the magnetic field than those without. The large improvement in fiber uniformity could be attributed to the reducing of instability of spinning jet by applying magnetic field during the electrospinning. Under normal electrospinning condition, the spinning jet loses its stable linear motion within a short distance after it leaves the needle tip and reaches the substrate in a spiral motion. The instability can cause the branching and splitting of the jet. In a magnetic field, the polymeric jet experiences a magnetic force that superimposes onto the electrostatic force, gravity, surface tension and resistance force from shearing whose direction is opposite to that of jet movement.[35] The magnet field can balance off the force that creates the instability and reduce the possibility for the formation of branched fibers. The magnetic field, which generates additional force on the jet, also

increases the velocity of the jet reaching a substrate. In addition, the Lorenz force facilitates those charged polymeric chains to align within each fiber. Both high velocity and internal alignment of polymeric chains of the electrospinning jet can result in the reduction of fiber diameter.

Another advantage of using external magnetic field instead of parallel auxiliary electrodes to fabricate aligned nanofibers is that the alignment can maintain for thick fibrous membranes. Figure 4 shows SEM images of the top surfaces and the cross-sections of aligned fiber arrays made from a 0.24 g/mL PLGA solution in HFIP for collection times of 15, 60 and 120 min, respectively. While the thickness of the membrane changed from about 5.83 μm for 15 min collection to about 55.5 μm at 120 min, the fibers maintained excellent alignment and without obvious branching. On the contrary the alignment gradually disappeared and the fibers became increasingly randomly oriented with the increase of membrane thickness, when parallel auxiliary electrodes were used to prepare the electrospun fibers.[24,25]

Fiber alignment can greatly affect the morphology and direction of cell growth. Figure 5 shows fluorescence images of nonosteogenic mouse pluripotent (C3H10T1/2) mesenchymal stem cells cultured on the PLGA membranes consisting of random, aligned straight, and aligned wavy fibers. The random fibers were made using conventional electrospinning method without the external field. The stem cells were transduced with adenovirus expressing green fluorescent protein (Ad-GFP) to assist the imaging of the growth and morphology. The stem cells attached very well to the three PLGA fiber membranes. The cells on the random fibers had the pseudo-sphere like shapes (Figure 5A), while those on aligned fibers adapted the elongated morphologies and grew along the long axes of the fibers (Figure 5B). Noticeably, the morphology of the stem cells also followed the subtle wavy features of the fibers (Figure 5C).

In summary, we have developed a simple, effective strategy for electrospinning aligned straight and wavy fibers by introducing an external magnetic field to the collector region. This MFAES technique is versatile and can create uniaxially aligned fiber arrays of different materials with no magnetic particles added. Branching can be eliminated and the uniformity of fiber diameters also improves substantially. This method is capable of producing thick membranes without losing alignment for the fibers. A new type of aligned wavy fibers can also be fabricated by adjusting the conditions used for MFAES. We believe MFAES is a promising technique for making controllable fiber arrays for applications in tissue engineering, textile and other areas where the preferred organization, morphology, and uniformity of the fibers are important.

Acknowledgments

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Figure 1. Schematic illustration of the setup used in the magnetic field-assisted electrospinning (MFAES) method for making aligned nanofibers. The drawing is not to scale.

Figure 2.

SEM images of (A, B) PLGA and (C, D) PVP fiber arrays made using the MFAES method. The PLGA fiber arrays were electrospun from an HFIP solution at a polymer concentration of 0.24 g/mL and a constant feeding rate of (A) 0.5 and (B) 3.0 mL/h, respectively. The PVP fiber arrays were electrospun from an ethanol-water solution at a polymer concentration of 0.11 g/mL and a constant feeding rate of (C) 1.0 and (D) 2.5 mL/h, respectively.

Figure 3. (A–H) SEM images and (I) the diameter-concentration relationship for PLGA fibers made from polymeric solutions in HFIP at concentrations of (A, E) 0.22, (B, F) 0.24, (C, G) 0.26, and (D, H) 0.28 g/mL, respectively. The fibers were made (A–D) without and (E–H) with the external magnetic field. The field strength was 0.2 T at the center of the gap and the distance between the two magnets was 1 cm.

Figure 4. SEM images of the top surfaces and the corresponding cross-sections of membranes of aligned PLGA fibers collected with different electrospinning times: (A) 15, (B) 60, and (C, D) 120 min, respectively. Images in the insets of (A) and (B), and (D) show the cross-sections of the membranes.

Figure 5. Fluorescent microscope images of murine pluripotent mesenchymal stem cells (C3H10T1/2) cultured for two days on scaffolds consisting of (A) random, (B) aligned straight, and (C) aligned wavy PLGA fibers.