Nanostructures Hot Paper

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Reactive Magnetospinning of Nano- and Microfibers

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Abstract: *Reactive spinning of nano- and microfibers that involves very fast chemical reactions and ion exchange is a challenge for the common methods for nanofiber formation. Herein, we introduce the reactive magnetospinning method. This procedure is based on the magnetic-field-directed collision of ferrofluid droplets with liquid droplets that contain complementary reactants. The collision, start of the chemical reaction, and the fiber drawing are self-synchronized. The method is used to synthesize, cross-link, and chemically modify fiber-forming polymers in the stage of fiber formation. The method provides new opportunities for the fabrication of nanofibers for biomedical applications.*

There has been a continuous increase in the use of nanofibers owing to the recent advances in the different fiber compositions that can be used and the sizes that can be achieved. The most common fiber fabrication techniques are spinning methods, such as electrospinning, force-spinning, and microfluidic spinning.[1] While these methods can be scaled up and have been commercialized,[2] they also have limitations, for example in the processability of the polymers, their solubility, dielectric properties, miscibility, and reactivity.[1a,d,3]

The physical limitation of many nanofiber formation methods is associated with reactive spinning, whereby polymers are synthesized or modified by a diffusion-limited chemical reaction.[1d] In cases when the reactions are fast (on the order of milliseconds), such as in ultrafast ionic and click-chemistry reactions, these methods are unable to draw the polymer solution fast enough before the reactions have taken place and the solution has solidified. In particular, reactive spinning plays an important role in the production of fibers made of biopolymers for biomedical and other applications that require biocompatibility and biodegradability of the fibers. Here the majority of biopolymers are water-soluble materials and the fibers are stabilized by cross-linking, which occurs on the same timescale as the common rates of fiber formation. As a result of the increasing number of applications, the development of new strategies for fiber spinning, in which the time of contact between two reactants is much smaller, are needed.[4]

One example of the reactive-spinning process is in the spinning of alginate nano- and microfibers. Here, an alginate solution is injected into a second solution bath containing Ca^{2+} ions, which cross-link the alginate.[1d] Although such fibers can be fabricated by microfluidic spinning, this process has limited productivity.[1d,5] The coaxial-spinning process, in which two fluids are mixed at the tip of a coaxial needle, offers higher productivity rates. However, such a method is not appropriate for reactive spinning because of the very long contact of two liquids at the needle tip (see the Supporting Information).

Recently, we introduced a new method of fiber spinning—magnetospinning.[6] This technique utilizes a setup in which a magnet is glued to a rotating stage (Figure 1 a–d). A polymer solution is mixed with magnetic nanoparticles and pushed through a needle facing the magnet. When the magnet approaches the droplet, the fluid is attracted towards the magnet and a liquid bridge is formed between them. Further motion of the magnet leads to the stretching of the liquid thread and a fiber is formed between the magnet and the needle.

Herein we report the concept of two-droplet reactive magnetospinning, in which two distinct fluids that emerge from separate needles interact with one another on a timescale of the order of milliseconds, and the process is limited by diffusion only. The time of contact of two liquids prior to spinning is then much shorter than the time of fiber spinning. We will show how this method can be used with droplets of two miscible liquids, to offer a route to realizing reactive spinning with fast kinetics, for example, in the aforementioned reactive magnetospinning of alginate, nylon, and polycaprolactone (PCL) nano- and microfibers. We also demonstrate how a similar strategy may be adopted using two immiscible liquids to enable polymer formation or postpolymerization modification in the spinning solution by exploiting interfacial reactions. Finally, an approach with two immiscible liquids can be used to transfer momentum from a droplet of magnetic liquid that experiences the attractive force exerted by the magnet to another droplet of non-magnetic polymer solution to produce fibers that are completely free of magnetic material.

The two-droplet magnetospinning process is shown in Figure 1. Two droplets are formed from two different fluids that are pushed through adjacent needles (Figure 1 a, e, i)—one droplet is filled with a Fe_3O_4 dispersion in an aqueous alginate solution, while the other droplet is filled with an aqueous $CaCl_2$ solution. The magnet approaches the droplets (Figure 1 b,f) and the magnetic droplet begins to move towards the magnet, passing through the droplet containing

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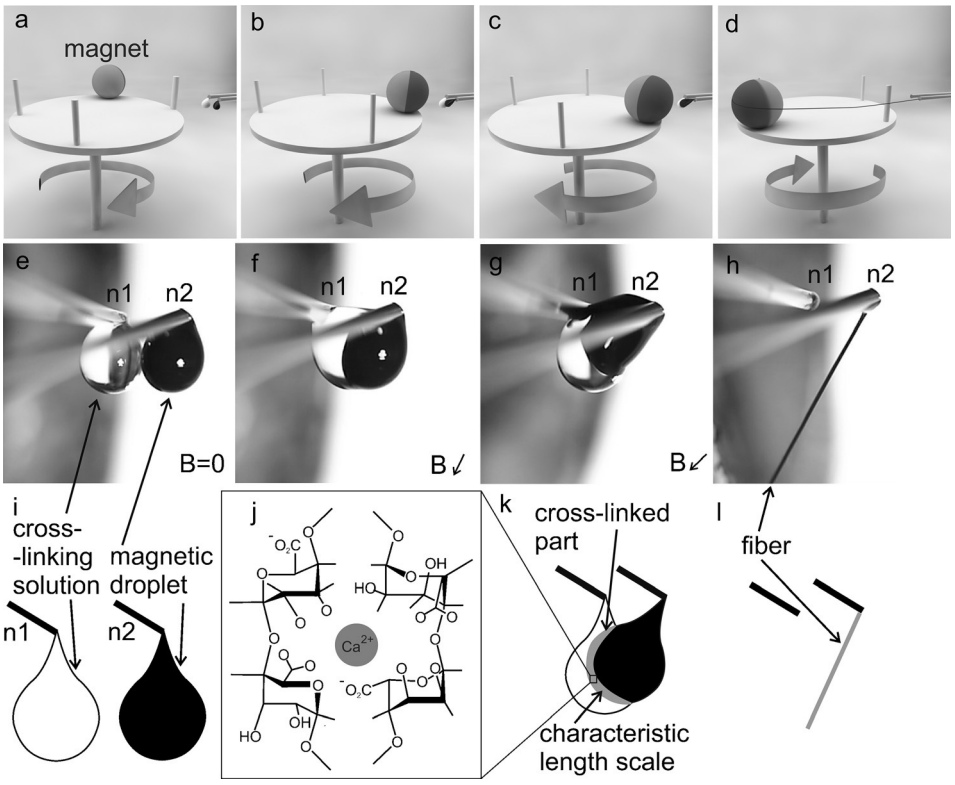

Figure 1. Magnetospinning of alginate fibers. a, e, i) Different fluids are pushed through adjacent needles n1 and n2 to form droplets at the tip—the droplet attached to needle n1 is filled with an aqueous solution of $CaCl_2$ and the droplet attached to n2 is filled with an Fe_3O_4 dispersion in alginate aqueous solution. b, f) As the magnet approaches the needle the magnetic droplet is attracted towards the magnet. c, g, k) The magnetic droplet moves towards the magnet and passes through the droplet containing the $CaCl_2$ solution. j) Ca^{2+} ions cross-link the alginate and the polymer droplet is stretched into a fiber (d, h, l).

The same setup was used to produce nylon 6,6 fibers by interfacial polymerization between hexamethylene diamine dissolved in a magnetic fluid and sebacoyl chloride dissolved in water (Figure 2e). Since the time of contact between the two liquids in our setup is less than 0.1 s for the typical magnet rotation rates we use, the characteristic length scale of the reaction (Figure 1g,k) is in the range of tens of micrometers. This length scale is comparable to the fiber diameter generated in magnetospinning, prior to evaporation. Thus, the operating conditions of magnetospinning offer a range of time and length scales where fast reactions in solutions and at interfaces can be utilized synergistically. The two-droplet method is also uniquely suited for magnetospinning since the magnetic field selectively attracts droplets of magnetic fluid while having no effect on nonmagnetic droplets.

The mechanism of two-droplet fiber drawing has additional advantages besides reactive spinning if two immiscible

the $CaCl_2$ solution that is positioned between the magnetic droplet and the magnet (Figure 1c, g, k). On contact, Ca^{2+} ions cross-link the alginate (Figure 1g, k, j) and at the same time, the polymer droplet is stretched into a fiber (Figure 1d, h, l). An SEM image of the resulting alginate fiber is shown in Figure 2d. For the two-droplet setup, an experimentally measured characteristic time of the interaction of the two liquids during the stage of the liquid bridge formation is approximately 3 ms. The fluids remain in contact during the fiber-drawing stage for a period of 0.1–0.02 s, for respective magnet rotation speeds in the range 500–2500 rpm. Assuming that the cross-linking is diffusion-limited, this timescale corresponds to a characteristic reaction length for Ca^{+2} ions in the micrometer range, which is comparable with the fiber diameter. Hence, the fiber-drawing process is in agreement with the chemical kinetics: the cross-linking takes place during the fiber-formation process. Consequently, the non-spinnable alginate solution becomes spinnable as a result of branching and cross-linking in the drawn fluid that ultimately forms the fiber. Our experiments demonstrate that the two-droplet setup provides the possibility for transport of the ferrofluid droplet through the droplet containing the cross-linking Ca^{2+} ions, which avoids any prior contact between the liquids.

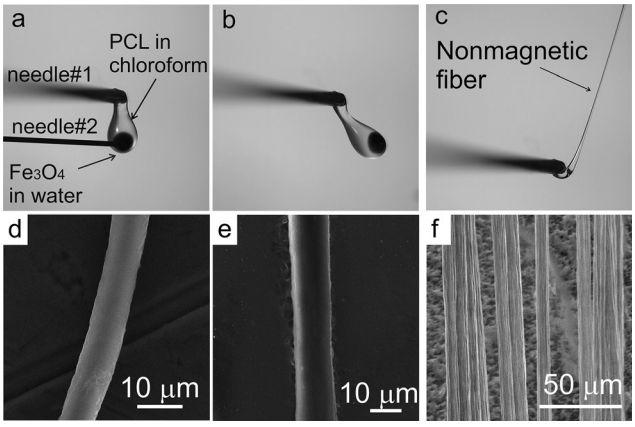

Figure 2. Magnetospinning of nonmagnetic fibers. a) A droplet of a solution of PCL in chloroform is pushed through the needle n1 using an automated pump. A droplet of Fe_3O_4 nanoparticles dispersed in water is placed on the PCL droplet using a second syringe with a needle n2 (needle n2 is shown schematically for illustration purposes because it is located out of focus on the photo). b) The magnetic droplet is attracted towards the magnet. c) The magnetic droplet jumps towards the magnet and a nonmagnetic fiber is produced. d, e, f) SEM images of alginate (d), nylon (e), and PCL (f) microfibers.

liquids are used. For example, if the presence of magnetic nanoparticles in the resulting fibers is detrimental to an application, the magnetospinning method can be modified to produce magnetic-particle-free nanofibers (Figure 2a–c). In this case, we employ the two-droplet magnetospinning technique using two droplets of immiscible liquids, such as water and an organic solvent. Depending on the polymer solution (water-based or organic-based), iron oxide nanoparticles can be dispersed in a second solution that is immiscible with the polymer solvent. For example, when the particles are stabilized with sodium citrate, we can disperse the nanoparticles in a water solution, while for a chloroform solvent the particles can be stabilized with oleic acid. In the example illustrated in Figure 2a–c, a solution of PCL in chloroform is pushed through needle n1 using an automated pump to create a droplet, while a droplet of Fe_3O_4 nanoparticles dispersed in water is added using a syringe connected to a second pump that pushes the fluid through needle n2. Since water and chloroform are immiscible, there is no intermixing of the ingredients dissolved in the droplets (Figure 2a). The coupled droplets are held together solely by surface forces on the liquid–liquid interface, which allow them to transition together towards the magnet (Figure 2b). This process results in stretching of the polymer solution droplet and production of a nonmagnetic fiber (Figure 2b,c,f and Figure 3b,c). High-speed imaging shows that after the magnetic droplet is attached to the magnet, a fiber is drawn as the stage undergoes four to five subsequent revolutions, until all of the fluid in the droplet is stretched out into fiber form. This method produces fibers of length 100–130 cm and diameters of (320 ± 42) nm (Figure 3b,c). The standard deviation of the fiber diameter over the whole fiber is 5%. We previously showed that the diameter of the fiber can be controlled by the concentration of polymer and by the speed of rotation of the magnet.[6] Since the magnetic fluid and polymer solution are immiscible, the magnetic liquid is also recyclable.

During two-droplet magnetospinning, nanofibers can be collected on a glass cover slide placed near the center of the rotating stage. The length of one nanofiber produced with a single rotation of the stage is 26 cm. Figure 3a shows a collection of approximately 1000 magnetic PCL nanofibers produced in one minute at a rotation rate of 1000 rpm. In the conventional (single-droplet) magnetospinning the nanofibers appear as a yellow-colored mesh because of the iron oxide particles embedded into the fibers (Figure 3a). In contrast, two-droplet magnetospinning is used to fabricate nanofibers free of magnetic particles as shown in the optical photograph (Figure 3b) and SEM image (Figure 3c). The PCL nanofibers can be used in a range of applications, such as scaffolds for cell growth and tissue engineering. We conducted reference experiments that demonstrated successful culturing of fibroblast cells on PCL nanofibers fabricated using two-droplet magnetospinning and showed that these fibers can be used for a production of scaffolds for fibroblast cells (Figure 3d).

We have introduced a two-droplet reactive magnetospinning method. This technique offers a new technique for spinning fibers when the polymer formation or postpolymerization modification is limited by diffusion. The two-droplet method can be realized for two miscible or two immiscible liquids, each with their own merits. The method can also be used for magnetospinning of fibers that are free of magnetic particles.

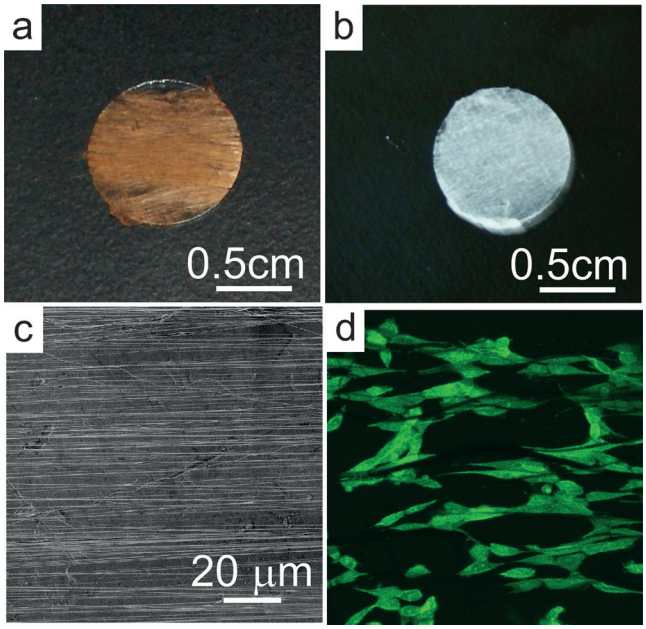

Figure 3. a) Glass slide covered with ca. 1000 PCL magnetic nanofibers produced by the regular magnetospinning method. b) Glass slide covered with ca. 1000 nonmagnetic PCL nanofibers produced by the two-droplet magnetospinning method. c) SEM image of nonmagnetic PCL nanofibers aligned in the horizontal direction. d) Confocal microscopy image of aligned fibroblast cells grown on aligned PCL nanofibers.

Experimental Section

Synthesis of nanoparticles: $FeCl_2 \cdot 4H_2O$ (1.625 g, 8 mmol) and $FeCl_3 \cdot 6H_2O$ (4.43 g, 16 mmol) were dissolved in water (190 mL) at room temperature while stirring. Then 25 wt% ammonia (10 mL) was added into the solution, which led to the formation of iron oxide nanoparticles. After ten minutes of stirring, the nanoparticles were magnetically separated from solution and washed five times with deionized water.

Magnetic nanoparticles stabilized in water: The nanoparticles were washed with HNO_3, diluted to 100 mL with water, and the pH raised to 2.5 with NaOH. A 0.5 M trisodium citrate dihydrate solution (5 mL) was added and the nanoparticles were stirred for 90 min while maintaining the pH close to 2.5 with hydrochloric acid. The nanoparticles were separated by applying an external magnetic field and the supernatant discarded. The precipitate was diluted to 50 mL with DI water and pH raised to 6. The concentration of the magnetite nanoparticles was 11.5 wt%.

Magnetic nanoparticles stabilized in chloroform: The nanoparticles were washed two times with ethanol and three times with chloroform. Following the final cycle of precipitation, in which the supernatant was removed, a few droplets of oleic acid were added to wet the precipitate and the mixture was sonicated for one minute with a high-power sonicator–homogenizer. The concentration of the magnetite nanoparticles was 11.5 wt%.

PCL in chloroform: Polycaprolactone (PCL, MW 80000 g mol^{-1}, Sigma Aldrich) was dissolved in in chloroform. The mixtures were used for spinning after 1–2 h of mixing. The stock solutions were used

to prepare formulations comprising 6 wt% polymer and 5.75 wt% nanoparticles.

Alginate in water: Sodium alginate (powder S-211, Fisher Scientific) was dissolved in an 11.5 wt% dispersion of magnetic nanoparticles in water at concentrations of 3 and 4%. A 0.5 M solution of $CaCl_2$ was used for the cross-linking of alginate during spinning.

Production of nylon 6,6 fibers: Hexamethylene diamine (98%, Sigma–Aldrich) was sonicated (Branson 3800 Ultrasonic Cleaner) in a water-based magnetic dispersion for 15 min to produce a solution with concentration of 4% w/v. Sebacoyl chloride (Sigma–Aldrich) was sonicated in hexane (>95%, Sigma–Aldrich) for 15 min to produce 4% w/v solution.

High-speed imaging: Videos of the magnetospinning process were recorded on an Olympus i-SPEED FS camera at 10000 fps and analyzed with VirtualDub software.

Cell culture: Mouse NIH-3T3 fibroblast cells were supplied by ATCC, USA. Dulbecco's Modified Eagle Medium (DMEM) with 10% (v/v) fetal bovine serum was used for cell growth. Experiments were conducted in an incubator at 7°C with a humidified atmosphere containing 5% CO_2. Cells were passaged at confluence using a standard trypsin protocol, and were washed twice and stored in PBS buffer. The cells were seeded and cultured on the collagen-coated PCL fibers in petri dish culture plates for 3 days. They were visualized using a Zeiss LSM 710 inverted confocal microscope.

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