Preparation of Core−Shell Structured PCL-r-Gelatin Bi-Component Nanofibers by Coaxial Electrospinning

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There has been much recent research on production and control of fibers at the submicron or nanometer scale. Among the various processing methods used, electrostatic spinning or "electrospinning", which is a method of producing continuous ultrafine fibers with diameters ranging from a few nanometers to microns, has attracted much attention in the past decade.[1−10] To date, over a hundred different polymers have been electrospun into nanoscale fibers.[9] Due to the very high aspect ratio and specific surface area of electrospun nanofibers, more efforts have been seen in using them for a variety of applications including drug delivery,[6,11,12] tissue engineering,[13−15] conductive nanowires,[16] nanosensors,[5,17] biochemical protective clothing for the military,[4] and wound dressing.[18] Obviously, the electrospinning process provides a means to bridge the dimensional and property gap between nano- and macroscale engineering materials and structures.

Currently, nanofibers and nanostructures comprising single or blended materials have been widely produced. However, there is now an increasing need in producing coaxial compound nanofibers and core−shell types of nanostructures.[19] Potential applications of such core−shell nanostructures in biomedical areas include preserving an unstable biological agent from an aggressive environment, preventing the decomposition of a labile compound under a certain condition, delivering a biomolecular drug in a sustained way, and functionalizing the surface of nanostructures without affecting the core material. With regard to the ultrafine fibers configured in a core−shell structure, several fabrication techniques have been proposed, such as self-assembly,[20] laser ablation,[21] template synthesis,[22] and a TUFT process based on electrospinning.[23] The production of core−shell nanofibers from coaxial electrospinning was first demonstrated by Sun et al.[10] However, the processing details and the potential applications of those nanofibers have not been fully explored. Our interest is in creating bicomponent core−shell structured composite nanofibers via the coaxial electrospinning method for applications in controlled drug delivery as well as for use as tissue engineering scaffolds. This paper describes the technique of using coaxial electrospinning to generate bicomponent core−shell nanofibers from immiscible fluids with diameters in the submicron or nanometer range. The structure of composite nanofibers in the form of a core−shell structure was characterized using transmission electron microscopy (TEM) and X-ray photoelectron spectroscopy (XPS). Preliminary results on the effects of polymer concentrations on the diameter of the core, the overall dimensions of the as-spun fibers, and the wrapped amount of inner component relating to shell thickness are also reported.

The basic experimental setup is shown in Figure 1a. It is essentially the same as that of a conventional electrospinning setup[1], except for the introduction of an inner capillary tube or needle as shown in Figure 1b. To some extent, this simple setup is also similar to the one reported earlier.[10] The inner capillary tube, also acting as an electrode for the spinning dopes, is connected to an electrical potential of several to tens of kilovolts relative to a ground electrode, the collector. Two immiscible liquid solutions, schematically represented in different colors in the figure for an obvious contrast, are injected at appropriate flow rates through

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(1) Reneker, D. H.; Chun, I. *Nanotechnology* **1996**, *7*, 216−223.
(2) Theron, A.; Zussman, E.; Yarin, A. L. *Nanotechnology* **2001**, *12*, 384−390.
(3) Matthews, J. A.; Wnek, G. E.; Simpson, D. G.; Bowlin, G. L. *Biomacromolecules* **2002**, *3* (2),232−238.
(4) Schreuder-Gibson, H.; Gibson, P.; Senecal, K.; Sennett, M.; Walker, J.; Yeomans, W.; Ziegler, D.; Tsai, P. P. *J. Adv. Mater.* **2002**, *34* (4), 44−55.
(5) Wang, X.; Drew, C.; Lee, S.−H.; Senecal, K. J.; Kuma, J.; Samuelson, L. A. *Nano Lett.* **2002**, *2* (11), 1273−1275.
(6) Zong, X.; Kim, K.; Fang, D.; Ran, S.; Hsiao, B. S.; Chu, B. *Polymer* **2002**, *43* (16), 4403−4412.
(7) Li, D.; Wang, Y.; Xia, Y. *Nano Lett.* **2003**, *3* (8), 1167−1171.
(8) Ko, F.; Gogotsi, Y.; Ali, A.; Naguib, N.; Ye, H.; Yang, G.; Li, C.; Willis, P. *Adv. Mater.* **2003**, *15* (14), 1161−1165.
(9) Huang, Z. M.; Zhang, Y. Z.; Kotaki, M.; Ramakrishna, S. *Compos. Sci. Technol.* **2003**, *63*, 2223−2253.
(10) Sun, Z.; Zussman, E.; Yarin, A. L.; Wendorff, J. H.; Greiner, A. *Adv. Mat.* **2003**, *15* (22), 1929−1932.
(11) Kenawy, E.−R.; Bowlin, G. L.; Mansfield, K.; Layman, J.; Simpson, D. G.; Sanders, E. H.; Wnek, G. E. *J. Controlled Release* **2002**, *81*, 57−64.
(12) Zeng, J.; Xu, X.; Chen, X.; Liang, Q.; Bian, X.; Yang, L.; Jing, X. *J. Controlled Release* **2003**, *92*, 227−231.
(13) Li, W. J.; Laurencin, C. T.; Caterson, E. J.; Tuan, R. S.; Ko, F. K. *J. Biomed. Mater. Res.* **2002**, *60* (4), 613−621.
(14) Yoshimoto, H.; Shin, Y. M.; Terai, H.; Vacanti, J. P. *Biomaterials* **2003**, *24*, 2077−2082.
(15) Xu, C. Y.; Inai, R.; Kotaki, M.; Ramakrishna, S. *Biomaterials* **2004**, *25*, 877−886.
(16) MacDiarmid, A. G.; Jones, W. E.; Norris, I. D.; Gao, J.; Johnson, A. T.; Pinto, N. J.; Hone, J.; Han, B.; Ko, F. K.; Okuzaki, H.; Llaguno, M. *Synth. Met.* **2001**, *119*, 27−30.
(17) Drew, C.; Liu, X.; Ziegler, D.; Wang, X.; Bruno, F. F.; Whitten, J.; Samuelson, L. A.; Kumar, J. *Nano Lett.* **2003**, *3* (2), 143−147.
(18) Khil, M.−S.; Cha, D.−I.; Kim, H.−Y.; Kim, I.−S.; Bhattarai, N. *J. Biomed. Mater. Res. Part B: Appl. Biomater.* **2003**, *67B*, 675−679.
(19) Loscertales, I. G.; Barrero, A.; Guerrero, I.; Cortijo, R.; Marquez, M.; Ganan-Calvo, A. M. *Science* **2002**, *295*, 1695−1698.
(20) Liu, G.; Qiao, L.; Guo, A.*Macromolecules* **1996**, *29*, 5508−5510.
(21) Morales, A. M.; Lieber, C. M. *Science* **1998**, *279*, 208−211.
(22) Jang, J.; Lim, B.; Lee, J.; Hyeon, T. *Chem. Commun.* **2001**, *1*, 83−84.
(23) Bognitzki, M.; Hou, H.; Ishaque, M.; Frese, T.; Hellwig, M.; Schwarte, C.; Schaper, A.; Wendorff, J. H.; Greiner, W. *Adv. Mater.* **2000**, *12* (9), 637−640.

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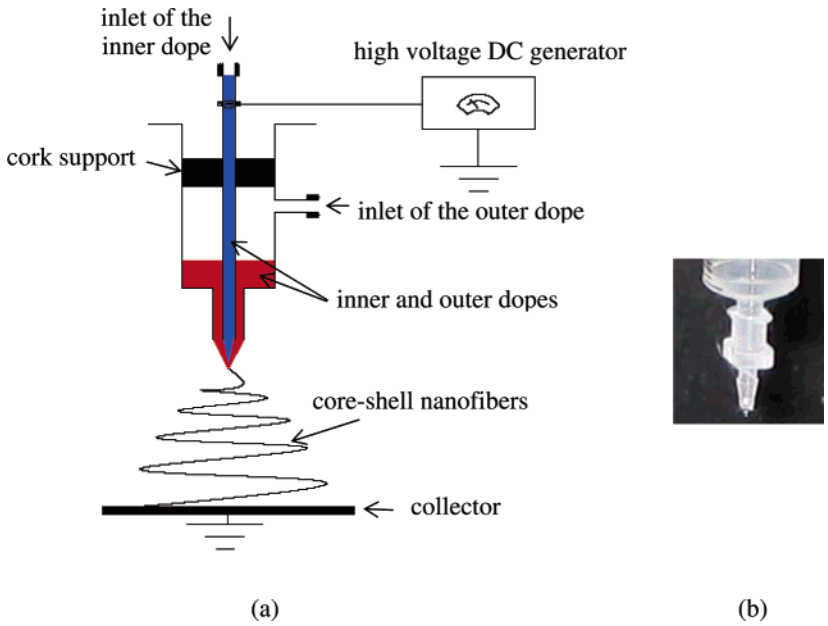

Figure 1. Schematic of the coaxial electrospinning setup used in our experiment to generate core−shell structured PCL-r-gelatin bi-component nanofibers (a), and the coaxial spinneret consisting of one syringe needle and a fitting attached to a syringe (b).

the two concentrically arranged capillary tubes. The inner flow rate was adjusted by a syringe pump, whereas the outer tube was opened to the atmosphere. At a certain range of applied electrical potential and flow rate, a structured Taylor cone is formed at the exit of the coaxial tubes with an outer meniscus surrounding the inner one. A liquid thread is issued from the vertex of each one of the two menisci, giving rise to a compound jet. After evaporation of the solvents during the course of jet flying, a core−shell structured bi-component composite nanofiber is produced. In Figure 1b, the compound spinneret is formed by attaching a syringe PP Luer fitting (o.d. 2.5 mm, i.d. 1.5 mm) to a 10-mL medical plastic syringe which contains an 18G stainless steel needle (o.d. 1.2 mm, i.d. 0.84 mm). The stainless steel needle is connected to a 30-cm long Teflon tube (i.d. 1.0 mm) for feeding the inner dope using the syringe pump.

We used gelatin type A (approximately 300 Bloom, Sigma, St. Louis, MO) and PCL (M_n 80 000, Aldrich, Milwaukee, WI) as the core and the shell polymers, respectively, to construct our bi-component biodegradable nanofibers. Gelatin (a protein) is a natural biopolymer derived from collagens. It has the advantages of having compositions and biological properties almost identical to those of collagens, is low in cost, and is easily available. These features make gelatin widely used in a variety of biomedical applications. In our earlier study, using 2,2,2-trifluoroethanol (TFE) (purity ≥99.0%, Fluka, Buchs, Switzerland) as a dissolving solvent, we successfully electrospun this biopolymer into ultrafine fibers for use as a tissue engineering scaffold.[24] In this study, we used TFE as the solvent for both gelatin and PCL to prepare 10 w/v % concentration spinning dopes by stirring them for 6 h at room temperature. The core−shell structured PCL-r-gelatin bi-component nanofibers were obtained by using the following processing conditions: the distance between the tube exits and collector was 12 cm, the electrical voltage was set at 14.8 kV, the inner dope flow rate was at 0.4 mL/h, the ambient temperature was 20.9 °C, and the relative humidity was 73%.

Verification of the core−shell structure was conducted using a JEOL JEM-2010F FasTEM field emission electron microscope operated at 100 keV. The coaxially electrospun nanofiber samples for the TEM observation were prepared by directly depositing the as-spun fibers onto copper grids which had been coated with a supportive Formvar film. The samples were dried in a vacuum oven for 48 h at room temperature prior to TEM imaging. Typical TEM images of the bi-component nanofibers are shown in Figure 2. Sharp boundaries of the core−shell structure along the length of the fiber can be clearly seen in Figure 2 b, c, and d. The strong contrasts in these TEM photographs can be attributed to the following three reasons: (1) the presence of nitrogen in gelatin could enhance the TEM contrast over that of PCL, (2) the inherent dynamically thermal immiscible feature between PCL and gelatin made the mutual diffusion of macromolecules impossible, and (3) as explained in the Sun et al. work,[10] the characteristic time of the bending instability during electrospinning was much shorter than that of diffusion spreading so that the sharp boundaries could be formed. The TEM photographs also indicated that the composite nanofibers had an overall diameter between 100 and 300 nm, with a core diameter below 100 nm. The extremely fine size and variation of core diameters along the fiber axis indicated that the effect of the inner fluid in terms of thinning a compound fluid jet to submicron or nanoscale size during the coaxial electrospinning was dominant. Occasionally, we also found there were cases where the inner component skewed to the extent of a half-by-half morphology (Figure 2d). This phenomenon may be attributed to the flow instability of the inner dope and the bending instability during the electrospinning process.[25,26] The interfacial instability was also demonstrated in the work of Sun et al.[10]

(24) Zhang, Y. Z.; Ouyang, H. W.; Lim, C. T.; Ramakrishna, S.; Huang, Z. M. *J. Biomed. Mater. Res. Part B: Appl. Biomater.* **2004**, in press.

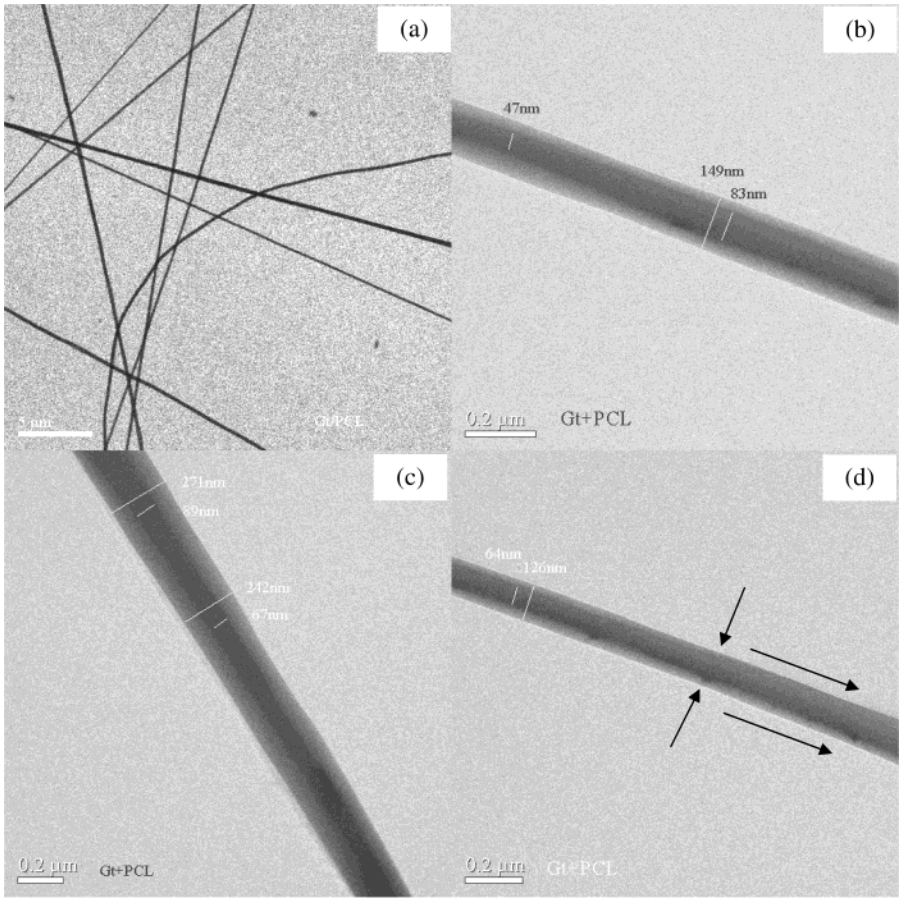

Figure 2. TEM images of core−shell structured PCL-r-gelatin bi-component nanofibers electrospun from 10 w/v % gelatin/TFE and 10 w/v % PCL/TFE. (a) Overview of nanofibers on a copper grid; (b) and (c) segments of the nanofibers with a sharp boundary; and (d) segment of the nanofibers with skewed inner component.

To further confirm the core−shell structure, an XPS experiment was performed to examine the chemical characteristics of the surface of PCL-r-gelatin bi-component nanofibers. Since gelatin possesses nitrogen-containing amino groups, an absence of N peak on the XPS spectra will facilitate illustration of the nanofiber structure. Figure 3 shows the XPS spectra of the electrospun nanofibers of pure gelatin and PCL-r-gelatin compound performed in a VG ESCALAB 220I-XL system. Apart from the presence of C 1s and O 1s peaks at ca. 290 eV and 540 eV, respectively, on the XPS spectra, one may notice there was indeed an absence of the N 1s signal at the binding energy of ca. 400 eV on the XPS spectrum of PCL-r-gelatin nanofibers (Figure 3 a). This implied that the gelatin component in the core was not contaminated with the PCL on the shell. Since XPS can detect elemental information in the uppermost ∼100 Å in depth of an analyzed specimen,[27] it is reasonable to draw a conclusion that the absence of traces of the N 1s signal in the PCL shell was at least thicker than 10 nm.

In making core−shell bi-component nanofibers by coaxial electrospinning, a key issue is to control the shell thickness and to estimate the amount of the wrapped

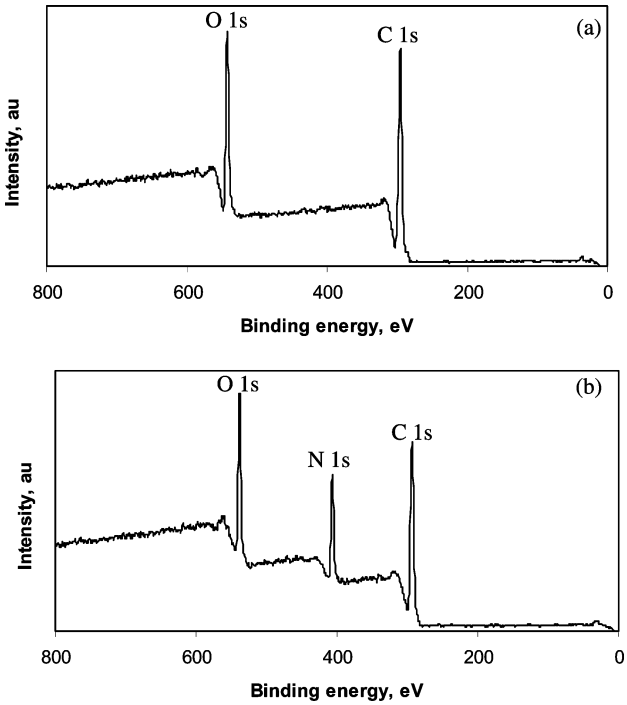

Figure 3. XPS spectra of the PCL-r-gelatin composite nanofibers (a), and pure gelatin nanofibers (b)

component. For this purpose, we investigated the influence of different mass concentrations in the inner dope, while maintaining a fixed one in the outer dope, on the geometry of the resultant bi-component nanofibers. This

(25) Reneker, D. H.; Yarin, A. L.; Fong, H.; Koombhongs, S. *J. Appl. Phys.* **2000**, *87* (9), 4531−4547.
(26) Shin, Y. M.; Hohman, M. M.; Brenner, M. P.; Rutledge, G. C. *Polymer* **2001**, *42*, 9955−9967.
(27) Ratner, B. D.; Chilkoti, A.; Castner, D. G. *Clin. Mater.* **1992**, *11*, 25−36.

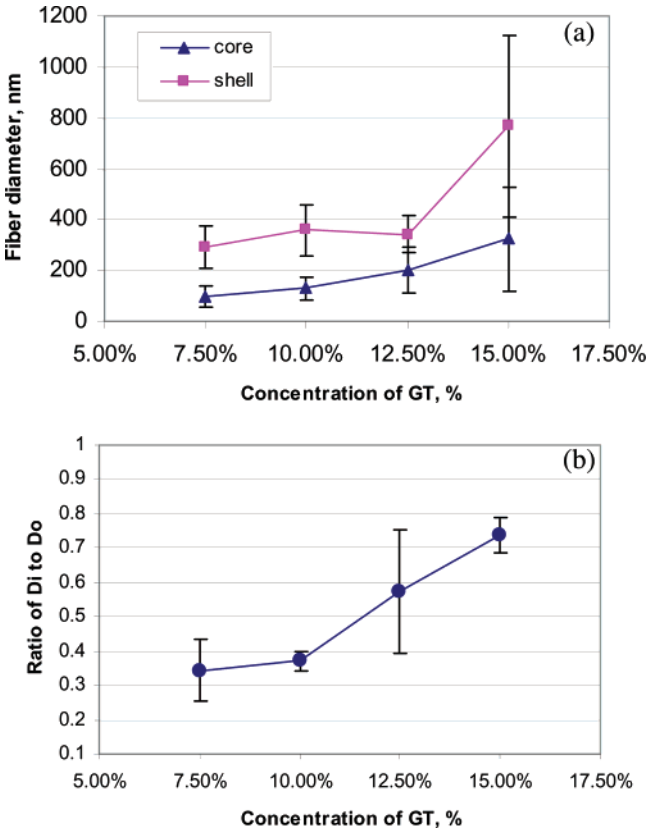

Figure 4. Effects of inner dope concentrations on the diameter of core component and total dimension of bi-component nanofibers (a), and on the content of the wrapped component (b).

was done by varying the gelatin concentration at increments of 2.5 w/v % from 7.5 to 15 w/v %. The resulting bi-component nanofibers were then characterized using the TEM. Based on the TEM images, the variation of the averaged diameters (for both core and overall diameters of the nanofiber) relative to the gelatin concentrations is shown in Figure 4a. These clearly show that increasing the gelatin concentration resulted in an increase not only in the core size, but also in the overall fiber diameter. When the concentration was below 12.5 w/v %, the core and the overall diameters were less than 200 and 400 nm, respectively.

A quantitative analysis on the effect of the gelatin concentration on the amount of the core component (which can also reflect an influence on the shell thickness) can be determined in terms of the ratio of inner to outer diameters (Di to Do). Results in Figure 4 b indicate that the higher the concentration in the inner dope, the thinner the shell thickness and the larger the amount of core component wrapped. In particular, when the concentration was greater than 12.5%, nearly 60% of the fiber volume was occupied by the core component. In some cases, the shell thickness of the core−shell structured nanofiber was so thin that it even resembled a coating of one substance over the other.[28] This kind of structure may greatly enhance the efficacy of the nanofibers in various fields of applications. For example, in the area of drug release application, this technology can help overcome the problem of burst release at an early stage. It was reported that by simply blending the drug with a carrier material, a burst release in an early stage could happen.[6,11] Core−shell structured nanofibers can be used to wrap bioactive molecules by using an appropriate polymer as shell so that the wrapped biomolecules can be retained till the moment the shell polymer has degraded. Obviously, this drug-wrapped nanofiber drug is suitable for situations where wrapped agents need to be preserved for a certain period of time prior to release. Similarly, in tissue engineering scaffold and biosensor applications, fully coated nanofibers at individual fiber level for improving cell-scaffold interactions can also be achieved instead of simply immersing a nanofibrous structure into a coating media,[14,17] which may give rise to poor coating of the surface of the nanofibrous structure due to high hydrophobicity of the fiber materials and the nanoscale size of the fibers.[29,30] Furthermore, using coaxial electrospinning, we believe that an incorporation of carbon nanotubes (or other nanoparticles) into the nanofibers can now be made easier and this can assist in the development of functional graded nanocomposite nanofibers.[8,31,32] This is expected to improve the thermal conductivity, electrical conductivity, and mechanical properties of the nanofibers.

Here, we have presented core−shell structured PCL-r-gelatin bi-component nanofibers produced via a coaxial electrospinning technique. The TEM observation and the XPS surface analysis confirmed the encapsulation of the gelatin within the PCL. By varying the concentration of the inner dope from 7.5 to 15w/v %, both the core and the overall diameters of the resulting nanofibers increased accordingly, while the core volume fraction also followed the same trend. The technique can be useful in producing different types of bi-component nanofibers, surface-modified nanofibers, functional graded nanocomposites, and continuous hollow nanofibers. The resulting core−shell structured bi-component nanofibers can be further applied for use in controlled drug release, bioactive tissue scaffolds, and highly sensitive biochemical sensors, just to name a few.

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Supporting Information Available: A typical TEM photograph of PCL-coated gelatin nanofibers coaxially electrospun at inner spinning dope concentrations above 12.5 w/v % (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(28) See Supporting Information.

(29) Feng, L.; Li, S.; Li, H.; Zhai, J.; Song, Y.; Jiang, L.; Zhu, D. *Angew Chem. Int. Ed.* **2002**, *41* (7), 1221−1223.
(30) Neimark, A. V.; Kornev, K. G.; Ravikovitch, P. I.; Ruetsch, S. *Polym. Prepr.* **2003**, *44* (2), 160.
(31) Zhang, Y. Z., Lim, C. T., Ramakrishna, S., Huang, Z. M. Coaxial Electrospinning Nanocomposite Nanofibers. In *Proceedings of ICMAT 2003 & IUMRS−ICA 2003*, Singapore, 2003; p 684.
(32) Dror, Y.; Salalha, W.; Khalfin, R. L.; Cohen, Y.; Yarin, A. L.; Zussman, E. *Langmuir* **2003**, *19* (17), 7012−7020.