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This is a post-review version of the following article:

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May 2014

The final published version of this article can be found at:

<http://dx.doi.org/10.1088/0960-1317/24/6/065009>

Citation for this paper:

Ko, J., Bhullar, S.K., Mohtaram, N.K., Willerth, S.M. & Jun, M.B.G. (2014). Using mathematical modeling to control topographical properties of poly (ϵ -caprolactone) melt electrospun scaffolds. *Journal of Micromechanics and Microengineering*, 24(6), 1-13.

Using Mathematical Modeling to Control Topographical Properties of Poly (ϵ -caprolactone) Melt Electrospun Scaffolds

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Abstract.

Melt electrospinning creates fibrous scaffolds using direct deposition. The main challenge of melt electrospinning is controlling the topography of the scaffolds for tissue engineering applications. Mathematical modeling enables a better understanding of the parameters that determine the topography of scaffolds. The objective of this study is to build two types of mathematical models. First, we modeled the melt electrospinning process by incorporating parameters such as nozzle size, counter electrode distance and applied voltage that influence fiber diameter and scaffold porosity. Our second model describes the accumulation of the extruded microfibers on flat and round surfaces using data from the microfiber modeling. These models were validated through the use of experimentally obtained data. Scanning electron microscopy (SEM) was used to image the scaffolds and the fiber diameters were measured using Quartz-PCI Image Management Systems® in SEM to measure scaffold porosity.

Key words

Melt electrospinning, Modeling, Topography, Microfibers, and Scaffolds.

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1. Introduction

As one of the most commonly used polymer processing techniques, electrospinning is currently used to fabricate nano to micro scale fibers as scaffolds for biomedical applications [1-3]. In the 1980s, the first melt electrospinning setup was built [4-6] and since then more than 50 polymers have been successfully spun into fibers through this technique [7-10]. In the melt electrospinning process, electric charges are applied to the polymer melt while providing a strong tensile force to stretch out fibers from the viscoelastic flow of polymer melt. Consequently, a jet of polymer melt is pulled from a meniscus formed

at nozzle tip. The polymer chain entanglements within the melt prevent the electrospinning jet from breaking up. The molten polymer cools and solidifies to yield fibers on a collector plate. To date, there have been a number of papers and experiments dedicated to produce fibers ranging in diameter from a few nanometers to several micrometers using this technique [2, 3, 11-17]. These nonwoven collected random fibrous structures can potentially be used in a variety of biomedical applications such as wound dressings, vascular grafts and tissue scaffolds [18, 19]. Compared to the other techniques of scaffold fabrication such as solution electrospinning, particulate leaching and solvent casting, virtues of melt electrospinning include an excellent degree of reproducibility for controlling topography and consequently tailoring the mechanical properties of electrospun scaffolds [1-3]. Further, melt electrospinning does not require the use of toxic solvents to produce biocompatible scaffolds. More interestingly, a variety of topographies can be implemented through melt electrospinning based on the desired application. For instance, Dalton *et al.* fabricated different structures to serve scaffolds and they could control the topographical properties in a reproducible and controlled way [1, 2, 20].

Recent studies have explored the effect of the nozzle diameter, nozzle temperature and spinning temperature on controlling topographical properties such as fiber diameter and porosity [1, 2, 20]. The parameters affecting electrospinning and the fibers are the rheological properties of polymer melt flow and processing conditions such as applied voltage, temperature and counter electrode distance, and ambient conditions. With the understanding of these parameters, it is possible to come out with setups to yield fibrous structures of various forms and arrangements and to create microfiber with different morphology by varying the parameters.

Melt electrospinning is an important polymer processing technique but a poorly understood one in terms of modelling. Most studies investigate phenomenological models of polymer behaviour through the process of melt electrospinning [11-13, 21-23]. Although brilliant results have been achieved in terms of microstructure physical properties such as crystallinity, there is a need to design more practical models to control the desired microstructure topographical properties of electrospun fibers. For instance, Zhmayev and Joo have a model which analyzes the polymer melt behaviour of nylon through its flow induced crystallization properties [22, 23]. In another work by Zhmayev, the stable jet region in melt electrospinning has been reported [22]. The results showed a good similarity when the comparison between the final jet diameter and the average thickness of collected fibers have been studied.

Here, we present our geometrical model based on, key parameters of melt electrospinning to predict the topographical features of such scaffolds, including fiber diameter and porosity. To our knowledge, there is a lack of research for linking the prominent parameters of melt electrospinning, such as applied voltage and counter electrode distance to topographical properties. In our previous study, we could successfully control the poly (ϵ -caprolactone) (PCL) fiber diameter by varying the processing conditions such as temperature, the collecting distance, and applied high voltage between nozzle and counter electrode, and nozzle diameters [3]. PCL is tailorable in its rate of surface and bulk biodegradation, crystallinity, structure topography and mechanical properties [24]. In this study we will present a justification of our novel geometrical model to predict topographical features of electrospun melt fibers altered by temperature, collecting distance, applied voltage and nozzle diameter. For each set of

controlling parameters, numerical results are discussed in detail and compared to the experimental data. Finally, the results of fiber diameter and scaffolds porosity under random conditions without any experiments can be predicted.

2. Modeling procedure

As our objective is to develop a microfiber model to describe the melt electrospinning parameters that influence fiber diameter and scaffold porosity, including nozzle size, counter electrode distance and applied voltage. First we briefly discuss on melt electrospinning process and the next section describes relevant geometrical modeling.

2.1 Geometrical Modeling

In melt electrospinning process after the introduction of the electric field the shape of the jet continuously changes hence droplet is stretched into a Taylor cone and a straight jet as illustrated in Figure 1 then stretched into a helix movement jet. Initially, the extruded polymer melt at the tip of the nozzle is like a truncated spherical droplet which changes its shape after the introduction of the electric field. Though there are geometrical models for electrospinning process such as Taylor cone as a frustum and straight jet as a cylinder are discussed in literature [5, 8, 21, 22, 25]. In our modeling, the jet pulled out from droplet is geometrically defined as a funnel as shown in Figure 1 which consists of a cone whose tip is removed surmounted on a narrow cylinder is discussed. Also, our interest is to develop a geometrical modeling to optimize nozzle diameter through derivation of the relation between the nozzle diameter and fiber diameter.

First, we consider a droplet of melt polymer as a truncated spherical shape at the tip of the nozzle of a radius r_1 , height $h_0 = r_1$ having volume as:

$$V_0 = \frac{2\pi r_1^3}{3} \quad (1)$$

On exiting the nozzle, the tip droplet becomes exposed to all the forces acting on it and it is pulled into a Taylor cone with, the top radius r_1 (constant), bottom radius r_2 and height h_1 where both (r_2 , h_1) are function of time. The following are the initial conditions assumed in further development of the modeling:

$$t = \begin{cases} t = t_0, & r(t = t_0) \\ t = t_f, & r(t = t_f) \end{cases}$$

where, t_0 is the initial time and t_f is total time of electrospinning. Next, the volume of Taylor cone V_1 is given by:

$$V_1 = \frac{\pi h_1(t)}{3} [r_1^2 + r_1 r_2(t) + r_2^2(t)] \quad (2)$$

Further upon using the flow rate of the polymer melt the volume of the system at any time t , can be calculated [8]. Therefore, the volume of the melt polymer in the truncated cone Ω_1 is:

$$\Omega_1(t) = V_0 + Qt \quad (3)$$

where, Q , t and V_1 are the flow rate, time and volume of truncated cone given in Eq. (1). The whole system (jet or fiber) before it becomes unstable geometrically is assumed as funnel which means a cylinder surmounted by a truncated cone as illustrated in Figure 1.

Therefore, the radius of the top and bottom of the funnel are r_1 and r_2 respectively as illustrated in Figure 1. Further, the radius of straight jet r_2 is considered as a good approximation to estimate the fiber diameter. Also, r_2 is assumed as a constant in the further process of electrospinning. Now, the volume of cylinder V_2 and volume of polymer melt in cylinder Ω_2 , at time t are:

$$V_2 = \pi[r_2^2 h_2(t)] \quad (4)$$

$$\Omega_2(t) = V_1 + Qt \quad (5)$$

Furthermore, from our geometrical model shown in Figure 1 and upon using Eq. (2), (4) and (5), we have derived the relation between nozzle radius r_1 and straight jet radius r_2 , which is same everywhere within the straight jet as:

$$r_2(t) = \frac{-h_1(t)\pi r_1 \pm \sqrt{3\pi} \sqrt{-4(h_1(t)-3h_2(t))Qt - h_1(t)(h_1(t)-4h_2(t))\pi r_1^2}}{2(h_1(t)-3h_2(t))\pi} \quad (6)$$

In the beginning the height of droplet $h_0 = r_2$, the radius of the nozzle which is constant. After the introduction of electrical force polymer melt move toward collector the height of the jet changes with time. Therefore height of Taylor cone h_1 and straight jet h_2 can be calculated as:

$$h_n(t) = h_{n-1} + \int_0^t u_n(t) dt \quad (7)$$

where, $n = 1, 2$, and $u(t)$, the electrospinning velocity at any time t is:

$$u_n(t) = u_{n-1} + \int_0^t \frac{\sum F}{m} dt \quad (8)$$

where, $n = 1, 2$ represent Taylor cone and straight jet respectively, $\sum F$ is the sum of forces – surface tension F_s , viscoelastic F_v , gravity F_g and electrostatic F_e , and m the mass of polymer melt which are discussed in next sections.

2.2 The forces action on the straight jet

The forces acting on the straight jet are surface tension, viscoelastic, gravity and electrostatic. The surface tension on the droplet and the viscoelasticity within the droplet will be opposing the formation of an extended jet and will therefore result in a negative force. The surface tension force is given in [8] as:

$$F_s = \frac{-\gamma (a_{s_{n+1}}(t) - a_{s_n})}{h_n(t)} \quad (9)$$

where, surface tension γ , which is by definition work per change in surface area is given as:

$$\gamma = \int \frac{2 F_s r h_n(t)}{a_{s_n}} \quad (10)$$

and $a_{s_1}(t) = \pi(r_1 + r(t))\sqrt{(r_1 - r(t))^2 + (h(t))^2}$, $a_{s_2}(t) = 2\pi r(t)(r(t) + h(t))$ are surface area of Taylor cone and straight jet respectively at $n = 1, 2$. The viscoelastic force F_v which opposes the flow of the stream is:

$$F_v = -\sigma(t) \times A \quad (11)$$

where, A is the area of the jet top and the corresponding stress $\sigma(t)$ can be expressed through the relationship:

$$\sigma = Y\varepsilon + \eta_d \dot{\varepsilon} \quad (12)$$

where, Young's modulus Y , dynamic viscosity η_d [26], strain ε and strain rate $\dot{\varepsilon}$ are given by:

$$Y = \frac{\eta_d}{t_r} \quad (13)$$

$$\eta_d = e^{-\frac{E_\eta}{RT}} \quad (14)$$

$$\varepsilon = \frac{\text{Stretched length } (L_s)}{\text{Flow length of the melt polymer } (L_f)} \quad (15)$$

Flow length and stretch length are given by the relation

$$L_f = \frac{4 t Q}{2\pi(\frac{1}{3}r + \frac{2}{3}r_1)} \quad (16)$$

$$L_s = h + \int_0^t u_n dt - L_f \quad (17)$$

and

$$\dot{\varepsilon} = \frac{d\varepsilon}{dt} \quad (18)$$

where, u is the velocity of fiber and T , t_r , E_η , R are constant temperature, relaxation time, activation energy and gas constant are constants given in Table 1. In our model of straight jet polymer volume changes from a truncated cone to a straight jet having both elastic and viscous characteristics in hence some of the energy is returned to the system and some of the energy is converted into heat due to unloading. Further, the forces that act in the same direction of the flow of the jet gravity and electrostatic forces are:

$$F_g(t) = m\rho g = (V_1 + Qt_f)\rho g \quad (19)$$

$$F_e(t) = \frac{e(t)\psi}{z} \quad (20)$$

where, the density ρ of the material(PCL)[3], the jet mass m at time t , and the charge on the jet $e(t)$ [27] are given as :

$$\rho = \frac{0.9046 e^{0.0006392T}}{0.99868+0.0081076T+0.000070243 T^2} \quad (21)$$

$$m_n = (V_{n-1} + Q t_f)\rho \quad (22)$$

$$e(t) = 8\pi\sqrt{r_2^2(t)} \gamma \epsilon_o C \quad (23)$$

where, γ is surface tension given in Eq. (10) and ϵ_o , C , ψ is, z are primitivity of veccum feasibility factor of material, applied voltage and the collection plate distance from the tip of the jet, respectively given in Table 1.

Next, as we know from literature, both the voltage supplied and the resultant electric field have an influence in the stretching and the acceleration of the jet hence 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 melt due to the stronger electric field thus the effect of reducing the diameter of the fibers [7, 9]. Therefore, we have derived results for the effect of voltage and distance on electrospun fiber of polymer PCL based on Eq. (20) which are discussed in section of numerical and experimental results.

2.3 Scaffold modeling

The topology of scaffold is estimated using fiber diameter (r_2) and fiber velocity (u) calculated from the previous sections. Figure 2A shows loop pattern in melt electrospinning and Figure 2B represents schematic of position trajectory on a flat surface.

The position P_s , the center of fiber, in 2D domain is defined by:

$$P_s(x, y) = \int V_A + \int V_L = \begin{bmatrix} r \cos(\omega t) \\ r \sin(\omega t) \end{bmatrix} + \begin{bmatrix} V_L t \\ 0 \end{bmatrix} \quad (24)$$

where, V_A is total angular velocity, V_L is linear velocity, R_T is experimental radius of torus and $\omega = u/R_T$ is angular velocity. If the extension is 3D domain, the position $P_s(x, y, z)$ can be obtained by following relation in zigzag movement:

$$P_s = \begin{bmatrix} x_1 \\ y_1 \\ z_1 \end{bmatrix} + \begin{bmatrix} V_L t \\ 0 \\ 0 \end{bmatrix} = \begin{bmatrix} R_T \cos(\omega t) + V_L t \\ R_T \sin(\omega t) \\ 2r_2(1 - \cos \omega t) \end{bmatrix} \quad 0 \leq t \leq t_1, 0 \leq z_1 \leq 2mm$$

$$P_s = \begin{bmatrix} x_1 \\ y_1 \\ z_1 \end{bmatrix} + \begin{bmatrix} 0 \\ V_L t \\ 0 \end{bmatrix} = \begin{bmatrix} R_T \cos(\omega t) \\ R_T \sin(\omega t) + V_L t \\ 2r_2(1 - \cos(\omega t)) \end{bmatrix} \quad t_1 \leq t \leq t_2, 0 \leq z_1 \leq 2mm$$

$$\begin{aligned}
P_s &= \begin{bmatrix} x_1 \\ y_1 \\ z_1 \end{bmatrix} + \begin{bmatrix} -V_L t \\ 0 \\ 0 \end{bmatrix} = \begin{bmatrix} R_T \cos(\omega t) - V_L t \\ R_T \sin(\omega t) \\ 2r_2(1 - \cos(\omega t)) \end{bmatrix} \quad t_2 \leq t \leq t_3, 0 \leq z_1 \leq 2mm \\
P_s &= \begin{bmatrix} x_1 \\ y_1 \\ z_1 \end{bmatrix} + \begin{bmatrix} 0 \\ V_L t \\ 0 \end{bmatrix} = \begin{bmatrix} R_T \cos(\omega t) \\ R_T \sin(\omega t) + V_L t \\ 2r_2(1 - \cos(\omega t)) \end{bmatrix} \quad t_3 \leq t \leq t_4, 0 \leq z_1 \leq 2mm
\end{aligned} \tag{25}$$

where, t_1, t_2, t_3 , and t_4 are arbitrary time to change directions.

The position P_d on a drum surface is defined by:

$$P_d = \begin{bmatrix} x_1 \\ y_1 \sin(\alpha t) \\ z_1 \cos(\alpha t) \end{bmatrix} + \begin{bmatrix} V_L t \\ d_r \cos(\alpha t) \\ d_r \sin(\alpha t) \end{bmatrix} = \begin{bmatrix} R_T \cos(\omega t) + V_L t \\ d_r \cos(\alpha t) + r \sin(\omega t) \sin(\alpha t) \\ d_r \sin(\alpha t) + 2r_2(1 - \cos(\omega t)) \cos(\alpha t) \end{bmatrix} \tag{26}$$

where, α is drum angular velocity, d_r is drum radius.

2.4 Porosity

The theoretical porosity was calculated based on estimation of fiber diameter, overlap area, and total volume of PCL microfibers. We have previously reported that we assumed the scaffolds were cuboid shaped, composed of perfect circular cylindrical microfibers called torus [3]. In addition, scaffold porosities on flat and drum surface are calculated in the same way.

The porosity of scaffold is defined by [10]

$$\phi_{mesh} = \left(1 - \frac{NV_t}{V_s}\right) \times 100\% \tag{27}$$

where, ϕ_{mesh} , V_t , V_s , N are respectively porosity of mesh, volume of torus, volume of whole scaffold, and number of torus. The torus volume is calculated by

$$V_t = 2\pi^2 R_T r_2^2 \tag{28}$$

where, R_T is distance from the center of the tube to the center of the torus and r_2 is the radius of the fiber. The volume of whole scaffold is determined by

$$V_s = w_1 w_2 H, w_1 = V_{tr} t_1, w_2 = V_{tr} t_2 \tag{29}$$

where, w_1, w_2, H, V_{tr} are respectively scaffold width, scaffold length, scaffold height, and transitional speed. t_1 and t_2 are arbitrary time. The number of torus and overlap percentage can be calculated by

$$N = \left\{ \frac{w_1}{2(R_T + r_2)} (1 + O_p) \right\} \left\{ \frac{w_2}{2(R_T + r_2)} (1 + O_p) \right\} \left\{ \frac{H}{4r_2} \right\}, O_p = \frac{A_2}{A_1} \times 100(\%) \tag{30}$$

where, O_p is overlap percentage [3].

3. Experimental procedure

3.1 Fabrication of Microfibers

Poly (ϵ -caprolactone) (PCL) ($M_n \sim 45,000$) was purchased from (Sigma Aldrich, USA) with a melting point of 60°C . The detail of our custom-made melt electrospinning setup has been already published [28]. Previously, we reported that for the collection of randomly aligned scaffolds, a wood plate covered with aluminum foil has been used as the counter electrode [3]. Briefly, in order to fabricate microfibers, we have applied 10, 15 and 20kV to the molten PCL at 80°C using a high voltage power supply (Gamma High Voltage Research Inc., USA) with the working distance between the nozzle and aluminum foil collector ranging from 5 and 10cm. The PCL granules were dispensed into melting chamber with the nozzle attached and then heated to the desired temperature. The rheological properties of our PCL have been reported as well [3, 28]. To our knowledge, parameters related to fiber diameter and morphology of scaffold when melt electrospinning include nozzle diameter, processing temperature, collection distance, applied voltage, flow rate of syringe pump and linear velocity of x and y axis in CNC machine [2, 6, 11-13, 17]. As we previously reported, a syringe pump was used to inject the flow of PCL melt at a flow rate of 2 mL per hour [3]. To investigate the influence of electrical force, nozzle diameter and linear velocity were respectively fixed at 200 μm and 8.5 mm/sec. Based on our parameter analysis, the melt temperature was set at 80°C with an applied voltage of 20 kV and a collection distance of 5 cm. These conditions ensured proper fiber formation during the electrospinning process. Figure 3 shows two types of scaffold morphology on flat and drum surface. (A, B) and (C, D) respectively presents biaxial loop mesh on flat surface and uniaxial loop mesh on drum surface.

3.2 Analysis of microfiber topography

Prior to scanning electron microscopy (SEM) imaging, all PCL microfibers were coated using Cressington 208 carbon coater two times for 6 seconds at 10^{-4} mbar and consequently samples were transferred to loading stubs for Hitachi S-4800 field emission scanning electron microscope. High magnification images were captured at 1 kV with an 8 mm working distance. Using Quartz-PCI Image Management Systems® fibers were characterized in terms of fiber diameters, torus diameter and overlap measurements.

3.3 Image processing for porosity measurement

Due to an inability to collect data on the scaffold porosity directly, we used two software programs which are Adobe Photoshop CS5 and Matlab R2013a to determine porosity from SEM image. The Photoshop was used to clarify the boundaries between background and microfibers and change white microfibers as shown in Figure 4. Then the Matlab was used to count white pixels on microfibers and measure porosity of various scaffolds.

3.4 Spinning speed analysis

Speed of spinning fibers played a key role in controlling the morphology of scaffolds but directly measuring speed is one of challenging parts so two indirect methods are used: 1. Angular velocity analogy is that measuring angular velocity (ω) and distance from center of tube to the center of torus (R_T) from SEM images and then spinning velocity (V_{s1}) is calculated by .

$$V_{s1} = \omega R_T \quad (31)$$

2. Mass production analogy is that measuring accumulated weight (m_{t_s}) of fibers during a certain time (t_s) and then spinning velocity (V_{s2}) is defined by [3].

$$V_{s2} = \frac{m_{t_s}}{\pi r_2 D t_s} \quad (32)$$

where, D is density of PCL polymer.

3.5 Statistical analysis

Quantitative data are presented as mean $\pm$ standard deviation (SD). The processing parameter study were screened by one-way analysis of variance (ANOVA) with the assumption of normally distributed data using Microsoft Office Excel 2010, USA; significance was defined as $p < 0.05$.

4. Numerical and experimental results

4.1 Effects of nozzle diameter

The effect of nozzle diameter on the fiber diameter is studied in simulation and experiment. All distance between nozzle and counter electrode, flow rate, voltage, and temperature are respectively fixed at 5cm, 2mL/h, 20kV and 80°C in order to restrict parameters related to fiber diameter. Nozzle diameter decides initial diameter of fibers by direct deposition and diameter of fibers is shrunk by electrical force and gravity force after spinning. Figure 5A and B present comparison of numerical and experimental fiber diameter and electrospinning velocity in various nozzle diameters. Numerically, when nozzle diameter changes, the Taylor cone V1 will be changed accordingly. Therefore, the increase in nozzle diameter would eventually affect the gravity force applied to the Taylor cone to stretch out fibers according to the equations (2) and (20). That eventually would lead to Experimentally the fiber diameter increased from $12 \pm 1 \mu\text{m}$ to $220 \pm 9 \mu\text{m}$ as the nozzle diameter increased from $150 \mu\text{m}$ to $1,700 \mu\text{m}$. Similarly, in simulation the fiber diameter increased from $18 \mu\text{m}$ to $212 \mu\text{m}$ as the nozzle diameter increased from $150 \mu\text{m}$ to $1,700 \mu\text{m}$. However, the velocity is decrease from 236.5 mm/s to 1.84 mm/s in simulation. Experimental velocity-1 and velocity-2 in Figure 5B respectively indicates angular velocity analogy and mass production analogy. Velocity-1 and Velocity-2 respectively are varied from $206.3 \pm 14.4 \text{ mm/s}$ to 4.2 ± 0.3 and from $210.4 \pm 14.7 \text{ mm/s}$ to $7.2 \pm 0.5 \text{ mm/s}$ when nozzle diameter increased from $150 \mu\text{m}$ to $1,700 \mu\text{m}$.

4.2 Effects of distance and voltage power on fiber diameter

Figure 6 shows the effects of collecting distance and voltage power on the resulting fiber diameter at 200 μm nozzle, 80°C temperature, and 2mL/h flow rate. According to Coulomb's law, magnitude of the electrical force was directly proportional to applied voltage and inversely proportional to the distance. Theoretically, the electrostatic force in melt electrospinning is a function of the net charge of fibers according to the equation (21). Since, $e(t)$ depends on the r_2 , any variation in the net charge coming from the electrostatic force would be affecting the fiber diameter as well. In experimental results, fiber diameter showed $49 \pm 5 \mu\text{m}$ at 10kV and $28 \pm 4 \mu\text{m}$ at 5cm and 20kV. Similarly, fiber diameter represented 44.44

μm at 10kV and 28 μm at 5cm and 20kV in numerical results. When distance was increased from 5cm to 10cm at 20kV, fiber diameter demonstrated $28 \pm 5 \mu\text{m}$ at 5cm and $37 \pm 7 \mu\text{m}$ at 10cm in experimental results. In numerical results, the fiber diameter showed 28 μm at 5cm to 44.44 μm at 10cm. Fiber diameters increased in size by approximately 1.4 times when the collecting distance was doubled at 20kV. Moreover, when applied voltage was doubled, the fiber diameters decreased to 1.6 times from their original size at 5cm.

4.3 Topology controlled by transitional speed

The fiber diameter (r_2) and electrospinning velocity (u) come from geometrical modeling becomes input parameters for scaffold modeling. The transitional speed (V_{tr}) in scaffold modeling is a significant parameter to determine topology of controlled scaffolds. Figure 7 shows (11mm x 11mm) numerical and experimental topology depended on various transitional speed at 200 μm nozzle, 20kV applied voltage, 5cm distance, 80°C temperature. (A, B), (C, D), and (E, F) in Figure 7 respectively represent 17mm/s, 8.5mm/s, and 7mm/s transitional speed. If V_{tr} is decreased, intervals between tori become more dense.

4.4 Porosity of controlled scaffolds

The porosity of scaffolds can be controlled by fiber diameter and transitional speed. Figure 8 shows results of numerical and experimental porosity depended on various nozzles at 20kV applied voltage, 5cm distance, 80°C temperature, and 8.5mm/s transitional speed. In numerical result, the porosity is varied from 95% to 85% when nozzle diameter is changed from 150 μm to 1,700 μm . Similarly in experimental result, the porosity is varied from 88% to 82% when nozzle diameter is changed from 150 μm to 1,700 μm . The significant factors to determine porosity in detail were torus volume (V_t) and number of torus (N). The increment of number of torus and the decrement of torus volume were very similar from 500 μm to 1,700 μm so Figure 8 shows flat in the section. Conversely, the decrease in torus volume occurred more rapidly than the increase in the number of torus from 150 μm to 500 μm so the porosity becomes increased.

Figure 9 shows the porosity controlled by transitional speed at 200 μm nozzle, 20kV applied voltage, 5cm distance, and 80°C temperature. The transitional direction is left to right on the figure and the speed is calculated by Eq. (27). The speeds of 7.2, 4.4, and 2.1mm/s represent respectively 80, 60 and 40% porosity. Figure 10 shows the result of porosity controlled by transitional speed. When aiming for 80, 60, and 40% porosity, the experimental porosity is respectively 74.8 ± 3.7 , 53.5 ± 2.7 , and $35.7 \pm 1.8\%$.

4.5 Predictions

In section 4.1 through 4.4, we compared numerical and experimental results and confirmed our modeling to be reliable. As the ultimate goal, the predictions of fiber diameter and porosity under ambiguous parameters are shown in Figure 11. The fiber diameter depended on diameter of nozzle can be predicted that move along the linear curve as shown in Figure 11A, with conditions (20kV applied voltage, 5cm distance, and 80°C temperature). We can anticipate that applied voltage and distance are inverse relationship and influences on fiber diameter inversely as well as shown in Figure 11B and C, with conditions (200 μm nozzle, (20kV applied voltage or 5cm distance), and 80°C temperature). Finally,

porosity of scaffold can be predicted as shown in Figure 11D, with conditions (200 μ m nozzle, 20kV applied voltage, 5cm distance, and 80°C temperature). The porosity is increased when transitional speed is increased but the porosity does not increase well after 10mm/s transitional speed.

5. Discussion

Fabrication of electrospun fibers can be accomplished either using solution or melt electrospinning. Even though there are numerous studies on the fabrication of fibers through the use of solution electrospinning, few studies focus on controlling topographical properties of melt electrospun fibers including the uniform distribution of fiber's diameter and also the architecture of scaffolds. Hohman *et al.* have worked on the modeling of electrospun polymeric fibers [3, 29, 30]. They have reported that the electrospinning jet is actually pulled along by surface stresses, electrical and elastic forces. Since in their modeling there has been no use of conservation of energy or momentum, here we have worked on calculation all forces in the process. In our work a mathematical modeling has been developed to obtain fine fibers through various nozzle diameter through the derivation of the relation between the nozzle diameter and fiber diameter. It has been observed that there was reduction in fiber diameter with small diameter nozzle as illustrated in Figure 5A. Additionally, it can be seen that due to the effect of the velocity as shown in Figure 5(B), the velocity decreased as the nozzle diameter was increased. Moreover, both the applied voltage supplied and the resultant electric field had significant influence on the topography of the fibers obtained. Furthermore, the influenced of the applied voltage and counter electrode distance on electrospun fiber of polymer PCL have been investigated numerically, experimentally and presented graphically in Figure 6. It can be clearly seen that fiber diameter decreased when the applied voltage has been increased.

Topography of scaffolds was also controlled by transitional speed at a fixed nozzle diameter. We took the data of the fiber diameter and electrospinning velocity from the aforementioned mathematical modeling. It can be seen from Figure 7, that the simulation and experiment conditions were kept to be consistent but the number of circles has been changed since CNC machine should follow trapezoidal velocity trajectory. The transitional speed was recognized as a prominent in controlling scaffold topography.

The porosity of scaffolds was highly influenced by nozzle diameter and transitional speed as well. Similar to our numerical data achieved from the mathematical modeling, the porosity of scaffolds have shown the same trend using experimental data controlled by fiber diameter and transitional speed. It can be seen clearly that the results of numerical and experimental porosity depended on various nozzles. For instance, numerical data have shown that when nozzle diameter was changed from 150 μ m to 1,700 μ m, consequently, the porosity was varied from 95% to 85%. Moreover, our work has shown that torus volume and number of torus are one of the most prominent factors to control and predict the porosity of melt electrospun fibers. Through the use of melt electrospinning, we could obtain fibers with the average diameter of $12 \pm 1 \mu$ m at 80°C when using the 150 μ m nozzle. We have been able to predict and control this fine fiber size distribution governed by different nozzles though the use of geometrical, mathematical modeling and image analysis as well. Fibers were fabricated with diameter in the range of $12 \pm 1 \mu$ m to $220 \pm 9 \mu$ m at 80°C. Moreover, the scaffolds with a specific porosity can be fabricated by transitional speed at fixed nozzle diameter. The transitional speed followed by trapezoidal velocity trajectory in

experiments has influenced to porosity control as shown in Figure 8, 9 and 10. When the porosity aims at 40%, 60%, and 80% porosity in Figure 10, the fabricated scaffold shows approximately 5% differences between numerical and experimental porosity. Thus, this excellent degree of predictability and controllability through the modeling approach would lead us to design and engineer melt electrospun fibers for different kind of tissue engineering application based on the desired topography.

The present model could capture melt electrospun PCL fiber topography and could present some topographical information (fiber diameter, topology and porosity). The model employed key parameters of melt electrospinning including nozzle diameter, counter electrode distance, applied voltage and transitional speed that have particular influences on scaffolds topography. As shown in Figure 11, the main goal of this research was to illustrate the feasibility of predicting fibers topography through the use of mathematical modeling and image analyses.

6. Conclusions

The aim of this research was to develop a reliable mathematical modeling to predict the effect of nozzle size, counter electrode distance and applied voltage on fiber diameter and consequently the topography of scaffolds. PCL microfiber scaffolds were fabricated using melt electrospinning technique with an excellent degree of reproducibility in terms of topographical properties. The effect of nozzle diameter on the fiber diameter was evaluated and the simulation results were compared with experimental data. For instance, according to our experimental data, the fiber diameter was increased from $12 \pm 1 \mu\text{m}$ to $220 \pm 9 \mu\text{m}$ as the nozzle diameter was increased from $150 \mu\text{m}$ to $1,700 \mu\text{m}$. Interestingly, the simulation results also showed that fiber diameter was increased from $18 \mu\text{m}$ to $212 \mu\text{m}$ as the nozzle diameter was increased from $150 \mu\text{m}$ to $1,700 \mu\text{m}$. Moreover, fiber diameter was increased in size by approximately 1.4 times when the counter electrode distance was doubled at 20kV. Additionally, when the applied voltage was doubled, the fiber diameters decreased to 1.6 times from their original size at 5cm. In terms of porosity characterization of scaffolds, we observed that porosity was varied from 95% to 85% when nozzle diameter was changed from $150 \mu\text{m}$ to $1,700 \mu\text{m}$. Similar to the numerical data, experimental results showed that porosity was varied from 88% to 82% while nozzle diameter was changed from $150 \mu\text{m}$ to $1,700 \mu\text{m}$. Moreover, the porosity of scaffold respectively showed $35.7 \pm 2.5\%$, $53.5 \pm 4.7\%$, and $74.8 \pm 5.1\%$ using $200 \mu\text{m}$ nozzle at 20kV and 5cm when the porosity aimed at 40%, 60%, and 80% porosity calculated by mathematical modeling. Overall, the ability of predicting topographical features of microfibrinous scaffolds fabricated by melt electrospinning, would hold a great promise in fabrication of scaffolds specifically for tissue engineering applications.

Acknowledgment

Funding support from Natural Sciences and Engineering Research Council (NSERC) Discovery Grants is acknowledged. The authors would also like to acknowledge the Advanced Microscopy Facility at the University of Victoria.

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Table1. Parameters used for numerical simulations.

Parameters	Experimental data	Literature & Standard data
Distance between nozzle and fiber collector, z	5 cm, 10cm	
Flow rate, Q	2mL/h	
Temperature, T	80 ⁰ C	
Ambient temperature, T_a	20 ⁰ C	
Activation energy, E_η		10.1 kcal/mol
Gas constant, R		1.9872 k ⁻¹ cal/ mol
Relaxation time , t_r	0.0001s	
Permittivity of vacuum, ϵ_o		8.854 187 817 x 10 ⁻¹² (F·m ⁻¹)
Feasibility factor of material, C	1	[6]

Figure 1. Geometry of different stages of electrospun fiber and the straight jet surmounted by a truncated cone.

Figure 2. (A) Loop pattern in SEM image, (B) schematic of position trajectory

Figure 3. Morphology of Scaffolds on (A, B) flat surface and (C, D) drum surface

Figure 4. (A) Original SEM image of microfibers using 150μm nozzle (Transitional speed: 8.5mm/s), (B) Image processing from SEM image

Figure 5. Effects of nozzle diameter in simulation and experiment at 20kV and 80°C, (A) fiber diameter depended on nozzle diameter, (B) velocity depended on nozzle diameter. (n=3), * and # indicates $p < 0.05$ versus all other nozzles.

Figure 6. Effects of collection distance and applied voltage on the resulting fiber diameter using 200 μm nozzle at 80°C (n=3). * indicates $p < 0.05$ versus all other voltage at 5cm distance. # indicates $p < 0.05$ versus all other voltage at 10cm distance.

Figure 7. Topology affected by transitional speed at 200 μ m nozzle, 20kV applied voltage, 5cm distance, 80°C temperature. A,C,E: Matlab image, B,D,F: microscope images. A-B: 17mm/s, C-D: 8.5mm/s, E-F: 7mm/s

Figure 8. Numerical and experimental porosity in various nozzle diameters at 20kV. (n=3) * indicates $p < 0.05$ versus all other nozzles.

Figure 9. The porosity controlled by transitional speed at 20kV: (A-B) 80%-7.2mm/s, (C-D) 60%-4.4mm/s, and (E-F) 40%-2.1mm/s

Figure 10. Result of porosity controlled by transitional speed at 200 μ m nozzle. (n=3), * indicates $p < 0.05$ versus all other transitional speed.

Figure 11. Predictions of fiber diameter and porosity under various conditions. (Marker X indicates experimental data)