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Thick electrospun honeycomb scaffolds with controlled pore size

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ABSTRACT

A novel strategy to prepare thick nanofibrous scaffolds with controlled pore size and graded porosity by electrospinning was developed. Taking advantage of the self-assembling properties of bimodal nanofibers, it was possible to grow columns of pores with mm height. The use of a honeycomb microstructured collector allows the control of the pore diameter from 80 to 360 μm. With increasing sample thickness, the columns of pores begin to merge creating a gradient in pore diameter of up to several hundreds of microns. These scaffolds should be ideal for tissue engineering applications.

1. Introduction

Electrospun scaffolds are known to be good candidates for tissue engineering applications because of their ability to mimic the extra cellular matrix (ECM) of living tissues [1,2] mainly composed of collagen or elastin fibres, ranging from 10 to several hundreds of nanometres. Electrospinning usually produces 2D nonwoven nanofibrous scaffolds with interconnected pores in the range of a few microns. However, such densely packed scaffolds do not allow the migration of cells through the structure and present a barrier to the vascularization of the tissue. An ideal scaffold should be nanofibrous with pore sizes in the range of a few tens to a few hundreds of micrometers and thicknesses up to few millimeters, depending on the targeted tissue [3,4].

Recently, different strategies have emerged to approach this goal. Thicker scaffolds have been obtained by stacking 2D membranes [5–7], wet electrospinning [8,9] or using spherical dish collectors with needles [10,11]. Moreover, important efforts have also been made to increase the pore size of electrospun scaffolds. Increase of the nanofibrous diameters [12], addition of porogen agents [8,13,14], or cryoelectrospinning [15,16] leads to pore sizes ranging from tens to hundreds of microns. Bigger pores can also be burned into the scaffold by post-electrospinning femtosecond laser processing [17]. Yet, most of these strategies require special electrospinning set up or post processing operations.

A simpler method has been developed recently to create large pores and thick samples, based on the self-organization of nanofibers into honeycomb-like structures due to modulated electrical interactions [18]. The obtained cm-thick structures presented a gradient in pore sizes increasing from a few microns to a few hundreds of microns and good mechanical properties (compression modulus of 65 kPa with a porosity of 87%). However, pore sizes were not controlled and depended on nanofibers self-assembly, starting from very small pore sizes that could still prevent cells migration through one side of the scaffolds.

In this study, we have combined this approach with the use of honeycomb microstructured collectors in order to control the size of the honeycomb pattern and construct 3D scaffold with columns of pores of controlled sizes.

2. Materials and methods

2.1. Fabrication of honeycomb micropatterned collector

Honeycomb micropatterns of 60 μm height, internal diameter of 80, 160 or 360 μm and wall width of 20 μm (Fig. 1A) were obtained by photolithography on silicon wafers (mask aligner MJB3 SUSS Microtec) using SU-8 2050 photoresist (Microchem). A conductive layer (Al-150 nm and Au-20 nm) was then deposited on the collector by electron beam evaporation (Plassys MEB5505).

2.2. Electrospinning of 3D scaffold

15 wt.% poly(ε-caprolactone) (PCL, Mw = 80 kg.mol^{-1}, CAPA 6806, Perstorp) solutions in 60/40 V/V dichloromethane/N,N-dimethylformamide (Sigma-Aldrich, predistilled) and 10 wt.% poly(lactic acid) (PLA, Mw = 180 kg.mol^{-1}, 7000 D, NatureWorks) solution in 50/50 V/V dichloromethane/N,N-dimethylformamide, were prepared 24 h prior to electrospinning. The solutions were electrospun during 1 h

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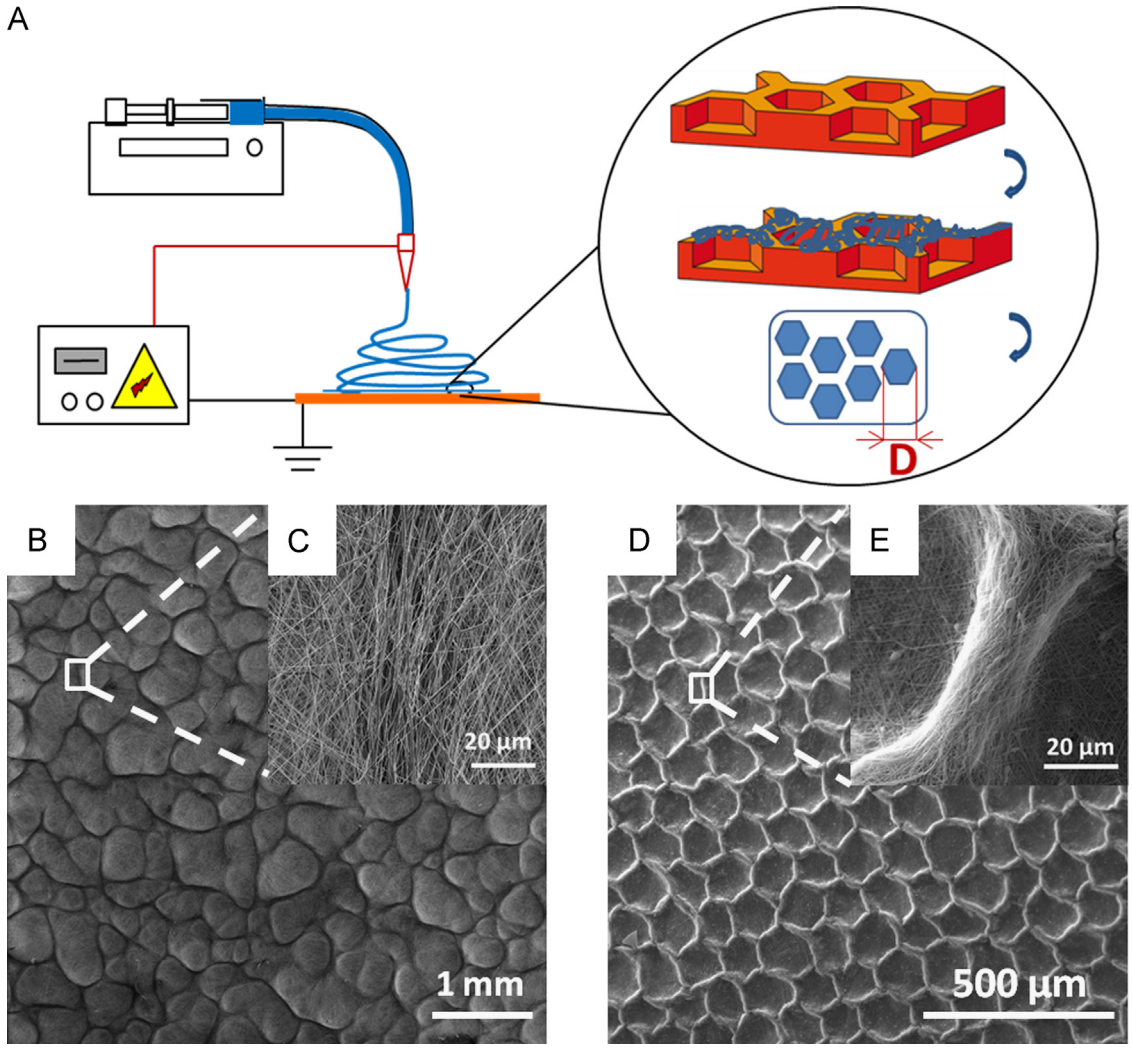

Fig. 1. A) Electrospinning setup using a honeycomb collector. B) SEM image of a PCL honeycomb-like self-assembled structure on a flat collector (10 min). C) SEM image of a wall of the honeycomb-like pattern. D) SEM images of PCL honeycomb structure on a honeycomb microstructured collector (10 min, $D = 160$ µm). E) SEM image of a wall of the honeycomb pattern.

using a homemade vertical set-up [18,19] (Fig. 1A, electrospinning conditions: PCL: needle/collector voltage = +15/−15 kV, distance = 15 cm, 1.4 mL/h; PLA: needle/collector voltage = +12/−5 kV, distance = 18 cm, 1.6 mL/h, temperature = 21 ± 1 °C, humidity = 44 ± 3%). Additionally, a 3 mm thick poly(methyl methacrylate) plate with a 25 mm diameter circular hole was placed onto the collector during electrospinning in order to concentrate the fiber deposition.

2.3. *Scanning electron microscopy (SEM) and X-ray microcomputed tomography*

Samples were peeled off from the collector by immersion in ethanol for PCL or isopropanol for PLA, dried, cut with a rasor blade in liquid nitrogen and characterized by SEM and X-ray microcomputed tomography as described in the Supplementary Data.

3. Results and discussions

A PCL solution was first electrospun for 10 min onto a flat aluminium collector. As described by Ahirwal et al. [18], nanofibers self-assembling occurs, leading to honeycomb-like patterns with a polydispersity in the pattern size (Fig. 1B). This phenomenon is due to a heterogeneous dissipation of the electric charges induced by the bimodal size distribution of PCL nanofibers diameter showing thick and thin domains [18] (Supp. Data. Fig. S1 and S2). Aggregates of thick fibers formed in the first seconds of the deposition are in good contact with the collector while thin fibers suspended in-between remain electrically charged, thus forming an electrostatic template of attractive and repulsive domains to the upcoming charged fiber. The electrostatic template mainly affects the thick portions of fibers that carry a higher linear charge density λ [20]. It results in the construction of a honeycomb-like structure with thick fibers, still slightly wet, merging to form the walls of the patterns and thin fibers crossing them (Fig. 1C).

To control the size and polydispersity of the self-assembled fibers patterns, a honeycomb micropatterned collector was used (Fig. 1A) with internal diameter D of the honeycomb patterns of 160 µm. The organization of the fibers and the formation of the patterns are then guided by the collector, leading to a more regular honeycomb structure (Fig. 1D). Once again, an electrostatic template is formed at the first deposition times, with attractive domains over the pattern walls and repulsive domains over the pattern nests leading to preferential deposition of the thick fibers over the walls in a self-sustained process (Fig. 1E). This phenomenon allows for the vertical growth of the patterns walls and the formation of columns of pores with diameters corresponding to the internal diameter D of the honeycomb pattern of the collector