Phase separation events induce the coexistence of distinct nanofeatures in electrospun fibres of poly(ethyl cyanoacrylate) and polycaprolactone

Wanwei Zhang, and Elisa Mele*

Department of Materials, Loughborough University, Epinal Way, Loughborough, LE11 3TU, UK.

E-mail: E.Mele2@lboro.ac.uk

Here we show that thermodynamic instabilities during electrospinning of polymer <u>blends of</u> poly(ethyl cyanoacrylate) (PECA) and polycaprolactone (PCL) in a ternary solvent system (acetone/chloroform/acetonitrile) induce the formation of hierarchical composite fibres with dual porosity. The analysis of the surface and cross-section of the PECA-PCL fibres reveals that, differently from previous works, the electrospun fibres are formed of two distinct morphologies: half of the fibre exhibits parallel and elongated grooves; whereas the other half has near-circular shaped pores. Porosity is present throughout the fibre volume with some regions being hollow. The occurrence of this novel architecture is investigated using different solvent systems and a dual phase separation mechanism is proposed. Porous fibres with a hierarchical porous structure are beneficial in many fields, including biomedical, environmental and energy related applications.

1. Introduction

Hierarchical porous structures over different length scales, from nano- to macro-level, are widely available in nature [1-3]. They are fundamental for adaptation and provide unique properties to biological systems. Examples are: the outstanding mechanical properties of bone [4], which is composed of a dense cortical shell and a porous, cancellous interior of mineralised collagen fibres [5, 6]; the efficient light harvesting and nutrient transport capabilities of the green leaves of most photosynthesising plants, which possess a porous network of veins and irregular-shaped, loosely-packed spongy mesophyll cells [7, 8].

The development of multi-scale hierarchical porous materials that mimic natural structures has drawn increasing research interest over the last decade, for application in catalysis, energy conversion and storage, tissue engineering and drug delivery [9-12]. Among the diverse fabrication methods proposed, electrospinning, namely the extrusion of polymeric fibres using an electric field [13, 14], has demonstrated the possibility of creating <u>a variety of hierarchical primary and secondary structures</u> with easy control over morphology, porosity and chemical composition [15-<u>18]</u>. Porous electrospun fibres have been obtained by several methods, such as co-axial electrospinning [15, 19-21], selective removal [22-26], self-assembly [27, 28], breath figure [29-31] and phase separation [29, 32-42]. The last one has been the most commonly utilised, because it does not require specifically designed electrospinning apparatuses or post processing steps. By manipulating the composition of polymer solutions and adjusting electrospinning parameters, thermally-induced phase separation (TIPS) [29-31, 38, 39] or non-solvent induced separation (NIPS) [30, 34, 40, 41] can be caused during fibres formation. TIPS usually involves solvents that rapidly evaporate during electrospinning, leading to temperature drop and thus thermodynamically instabilities [29-31, 39]. NIPS instead

takes place when a non-solvent for the polymer is added to the solution for electrospinning, resulting in phase separation [30, 34].

In the case of polycaprolactone (PCL), which is relevant to the present work, the NIPS process has been proposed to create fibres with different surface morphologies, using binary solvent systems where a good solvent for PCL (chloroform, dichloromethane, tetrahydrofuran or formic acid) was combined with a poor solvent (dimethyl sulfoxide, DMSO) [43]. Bead-free porous fibres were obtained for 12.5% w/v PCL in chloroform/DMSO solutions (10-20% v/v of DMSO). The fast evaporation of chloroform during electrospinning induced changes in the solution concentration (more DMSO remained in solution), leading to phase separation events and formation of irregularly shaped pores onto the fibres surface. In another work, NIPS was studied for PCL solutions (15% w/v) in chloroform/methanol (volume ratio of 18/2) and chloroform/DMSO (volume ratios of 19/1, 18/2 and 16/4) [44]. The use of methanol in the solvent mixture determined the appearance of surface roughness onto PCL fibres (relative humidity higher than 35%). Fibre produced from chloroform/DMSO (relative humidity higher than 35%). Fibre produced from chloroform/DMSO is provided surface porosity. This morphology was effective for the physical entrapment of a O₂-sensitive indicator dye to sense the oxygenation of cell cultures.

So far, it has been demonstrated that phase separation is a useful approach to create porous electrospun fibres [45, 46]. However, phase separation events have not been used yet to promote the coexistence of micro- and nano-features with distinct morphology on the same fibre. Here we show that each single electrospun fibre of poly ethyl cyanoacrylate (PECA) and PCL can be partitioned in one region with aligned micro-grooved and one with circular nanopores by blending the polymers in a selected mixture of solvents. In order to elucidate the formation of those structures, we investigated the role played by diverse solvents (acetone, chloroform and acetonitrile) and their mixtures. We described the results obtained using a

mechanism based on the simultaneous happening of diverse types of phase separation events. <u>The surface micro- and nanostructures and the internal porosity generated are of interest for</u> <u>biomedical applications as physical cues to locally influence cellular behaviour [47, 48] and to</u> <u>control the release of bioactive compounds [46].</u>

2. Experimental methods

2.1 Materials

Polycaprolactone (PCL, 80000 g/mol), poly ethyl cyanoacrylate (PECA, medium viscosity), dimethyl sulfoxide, acetone, chloroform and acetonitrile were purchased by Sigma Aldrich, and used as received without further purification.

2.2 Electrospinning process

We prepared solutions for electrospinning by dissolving PECA in acetone (10% v/v) and PCL in chloroform (10% w/v). PECA was first prepared by mixing ethyl cyanoacrylate and dimethyl sulfoxide at 1:1 ratio [49]. PECA/acetone and PCL/chloroform solutions were then mixed together at 2:1 volume ratio and diluted in acetonitrile to achieve a 7% w/v mixture. All solutions/mixtures were then electrospun by keeping the tip-to-collector distance fixed at 15 cm, solution injection rate between 2 and 3 mL/hour (pump system PHD ULTRA, Harvard Apparatus), needle gauge of 21, and applied voltage between 10 and 12 kV (Table S1 of the Supplementary Material). The electrospinning process was conducted at room temperature, usinga Linari srl. electrospinning system.

2.3 Morphological characterisations

The morphology of the electrospun fibres (<u>surface and cross section</u>) was observed using a scanning electron microscope (SEM), with a field emission gun system LEO1530VP. A

gold/palladium coating was deposited onto the fibrous mats before imaging using an Emitech SC7640 sputter coater (90 s sputter time). The fibres size, the distribution and alignment of the micro- and nanostructures presented onto the fibres surface were measured using ImageJ software (US National Institutes of Health). For each sample, ten SEM micrographs with different magnification were analysed and 50 measurements were used to perform statistical analysis.

3. Results and discussion

The SEM images of Figures 1a-1c show that the resulting PECA-PCL fibres were characterised by an average diameter of (4.5 ± 1.2) µm and, more interestingly, by two different types of porosity. Each single PECA-PCL fibre had one region with elongated and parallel grooves and one region with near-circular shape pores (Figure 1b and 1c). Although several researchers have worked on the electrospinning of polymer blends [22-26, 29-31, 34, 37-41], no accounts have been reported so far on electrospun fibres with dual morphology. SEM investigations revealed a net separation between the two regions along the whole length of the PECA-PCL fibres. The fibre portion with circular-shape pores (green area in the schematics of Figure 1d) had an average width (a) of (2.23 ± 0.30) µm, whereas the portion with elongated structures (orange area in Figure 1d) had an average width (a') of (2.26 ± 0.30) µm. Therefore, the a/a'ratio was of (1.01 ± 0.30) , indicating that half of each fibre was formed by pores and the other half by parallel micro-features. In particular, as shown in Figure 1e, the majority of the fibres population (60.5%) had a/a' values between 0.8 and 1.1; whereas a/a' was in the range of 0.5-0.8 and 1.1-1.6 for 15.8% and 23.7% of the fibres produced, respectively. Furthermore, both pores and grooves exhibited a degree of alignment to the main axis of the fibre. The polar diagram in Figure 1f (green symbols) shows that the angle (θ) formed by the main axis of the fibre and the main axis of the near-circular shape pore was in the range of 0-34°: <u>48% of the</u> values were between 1° and 7° (included), and 24% between 7° (excluded) and 14°. The statistical analysis of θ values can be described by a broad bell curve centred at 3.9° with a variance of 8.4° (Figure S1 of the Supplementary Material). On the contrary, the angle (θ ') formed by the main axis of the fibre and the main axis of the elongated structures (orange symbols in Figure 1f) ranged between 0 and 14°, with most of the values (90%) between 0° and 7°. The statistical distribution of the values had a mean of 3.0° and a variance of 2.1° (Figure S1 of the Supplementary Material). This denotes that the grooves were more aligned to the fibre direction than the pores. Alignment of both grooves and pores can be associated to the stretching of the polymer filaments during electrospinning, as previously reported in other studies [39-41].

The formation of PECA-PCL fibres with dual morphology was likely to be determined by phase separation before and during the electrospinning process. In order to investigate this further, we firstly analysed the role played by solvent properties (boiling point and surface tension). PECA and PCL were separately electrospun using different solvents and solvent combinations: acetone, chloroform, acetonitrile, acetone/chloroform (2/1 volume ratio), acetone/acetonitrile (14/9 volume ratio), chloroform/acetonitrile (7/9 volume ratio), and acetone/chloroform/ acetonitrile (14/7/9 volume ratio). The polymer concentration was fixed at 7% w/v for all solutions to have a direct comparison with the PECA-PCL system. Solvent ratios of binary and ternary solvent systems were calculated based on the solvent ratio of the PECA-PCL blend: 10% w/v PCL in chloroform and 10% w/v PECA in acetone were mixed at 1:2 volume ratio, and then acetonitrile was added to achieve a 14/7/9 solvent volume ratio. Because PCL had a poor solubility in acetone and insolubility in acetonitrile, the following solvent studied for PCL: chloroform, chloroform/acetone, systems were chloroform/acetonitrile, and acetone/chloroform/acetonitrile. The SEM images of the PCL fibres produced revealed a beads-on-string morphology for all solvent combinations used

(Figure 2). The low polymer concentration was responsible for the formation of electrospun mats with beads, being widely accepted that a minimal concentration is required for producing uniform and defect-free fibres [41, 50-52]. For chloroform solutions, we observed spindle-like shape beads with micro-features (Figure 2a), similarly to golf-ball shaped particles discussed for the electrospray of PCL-chloroform at 1-4% w/v concentrations [53]. At these low polymer concentrations, a small amount of solvent was still present on the beads surface when they hit the collector. The successive evaporation of the solvent caused the formation of particles with a rough surface [54]. The effect of different solvents on the morphology of PCL electrospun mats is well documented in the literature [55, 56]. Katsogiannis et al. have reported on the electrospinning of PCL (molecular weight of 80000 g/mol) from chloroform solutions with a polymer concentration of 12.5% w/v [43]. When chloroform was used as a single solvent, they observed the presence of elongated beads, possibly due to the low dielectric constant of chloroform. The addition of dimethyl sulfoxide resulted in well-defined fibres but also in an increased fibre diameter. As shown in Figure 2b and 2d, for the binary (acetone/chloroform) and the ternary system (acetone/acetonitrile/chloroform), the beads presented a spindle-like shape along with a more rounded shape. They were also characterised by surface roughness, which could be caused by non-solvent induced phase separation (being PCL poorly soluble in acetone and not soluble in acetonitrile) and high vapour pressure of acetone and chloroform [36, 53, 57]. Bosworth and Downes have investigated the use of acetone in PCL solutions with polymer concentration of 5.0, 7.5 and 10.0 % w/v [58]. They observed that beads were formed for 7.5% w/v solutions, irrespective of the electrospinning parameters used (increase in applied voltage and needle-collector distance). The beading effect has been reported also by Nottelet et al. for PCL solutions of acetone/chloroform (3:7 volume ratio, 5-15% w/v polymer concentration) [50]. For acetonitrile/chloroform mixtures (Figure 2c), the beads appeared more

rounded in shape and with a smooth surface, which could be due to the relatively high boiling point (81.6 °C) and high surface tension (29.2 mN/m at 20 °C) of acetonitrile.

We investigated the effect of different solvent combinations (acetonitrile/chloroform, acetone/acetonitrile, and acetone/acetonitrile/chloroform) on the electrospinning of PECA. As shown in Figure 3, only acetone was suitable as single solvent for PECA, thanks to its high conductivity, which caused stretching of polymer solution with the electric field [59]. The fibres produced were well-defined and defect-free with a ribbon-like shape and a wrinkled surface (Figure 3a), in agreement with a previous study [49]. The wrinkled surface is expected to be due to the high volatility of acetone, which causes buckling instability during electrospinning [35, 36, 40]. Interestingly, although PECA could not be electrospun from acetonitrile and chloroform as single solvents, fibres were formed from the binary acetonitrile/chloroform system (Figure 3b), even if spindle-like beads were present along the fibre length. The combination of the two solvents could assist the formation of fibres by changing the conductivity, viscosity and evaporation rate of the system [60]. Beads along fibres were also observed for acetone/acetonitrile solutions of PECA (Figure 3c). The electrospinning of PECA from acetone/chloroform led to the formation of only beads. The ternary system (Figure 3d), instead, allowed us to obtain well-defined flat fibres decorated with near-circular nanopores.

The investigations conducted on the diverse solvent combinations revealed that chloroform and acetone were necessary to produce electrospun fibres with increased surface roughness, both for PCL and PECA. A direct comparison between PCL and PECA mats, separately electrospun from the ternary system, showed that PCL fibres were characterised by a rough surface (Figure 4a), whereas PECA fibres exhibited a wrinkled surface with circular nanopores (Figure 4b). The composite PECA-PCL fibres were much bigger in size than PCL and PECA fibres, and they consisted of elongated grooves and near-circular pores (Figure 4c). Investigations of the

fibres cross section revealed that some PECA-PCL fibres possessed a cylindrical shape whereas others had a collapsed ribbon-like structure (Figure 5a). In both case, the porosity was not limited to the surface of the fibres, but cavities were visible throughout the fibre cross section. The fibres with a cylindrical shape were more likely to be hollow in some regions, as shown in Figure 5b. Li et al. have demonstrated the possibility to produce hollow electrospun fibres using a single nozzle instead of a coaxial needle (conventionally used to create core-shell and hollow fibres) [61]. The process was based on the electrospinning of phase-separated solutions of poly(vinyl pyrrolidone) (PVP), ethanol and tetraethyl orthosilicate (TEOS) in ethanol. During the fast ethanol evaporation, a concentration gradient was created along the fibre diameter: high concentration of TEOS, highly soluble in ethanol, in the core of the fibres; high concentration of PVP, immiscible with TEOS, at the edges of the fibres. After the complete evaporation of ethanol and TEOS, PVP nanotubes were formed. A similar approach has been reported also by Bazilevsky et al. for the fabrication of poly(methyl methacrylate) (PMMA)/polyacrylonitrile (PAN) core-shell fibres [62]. They electrospun emulsions of 100-200 µm-diameter drops of PMMA/DMF in a continuous phase of PAN/DMF. During electrospinning of the polymer blend, occasionally one PMMA/DMF drop (embedded in the PAN/DMF solution) reached the Taylor cone and a jet was formed at the drop edge. This resulted in core-shell fibres (PMMA core and PAN shell), whose structure was maintained until the drop was completely consumed.

In our case, phase separation occurred in the PECA-PCL solution (ternary system) mainly between PECA-acetone and PCL-chloroform, due to the immiscibility of PECA and PCL (hydrophilic and hydrophobic polymer, respectively) [63], the limited solubility of PECA in chloroform and acetonitrile, the poor solubility of PCL in acetone and its insolubility in acetonitrile [56, 44]. During fibre formation, solvents evaporation, mainly acetone and chloroform, determined a gradient in PECA and PCL concentration from the outer fibre surface (high concentration) to the inner core (low concentration) [61, 64, 65]. The acetonitrile concentration (being this a solvent with low evaporation rate) instead increased in the core of the fibres. Eventually, acetonitrile evaporated leading to fibres with a skin-core morphology. Some PECA-PCL fibres exhibited a ribbon-like structure with a peanut-shaped cross-section (Figure 5c), due to the collapse of the outer porous shell. This morphology has been previously reported in the literature and it has been related to buckling instability: a thin skin layer is formed around the fibres due to solvent evaporation; when the solvent continues to evaporate from the core of the fibres, the skin collapses under atmospheric pressure and cohesive forces stick together the skin from opposite sides of the fibres [35, 66, 67]. This phenomenon tends to be observed for fibres with large diameter (microfibres) due to the long drying time [67]. The unique morphology of the skin layer of the PECA-PCL fibres (grooves and pores) can be described by considering phase separation events occurring during the electrospinning process, namely a complex interplay between nucleation and growth and/or spinodal decomposition [16, 35, 39, 68, 69]. If a ternary system is considered, its phase diagram consists of three regions: one region where only one phase exists (good miscibility), one metastable region where phase separation proceeds via nucleation and growth, and one unstable region where phase separation proceeds via spinodal decomposition. The three regions are divided by the binodal and spinodal curves. When the system passes the binodal curve and enters the metastable region, nucleation and growth take place and the formation of isolated circular pores has been observed during electrospinning [35, 68-71]. In case of spinodal decomposition (transition through the spinodal curve into the unstable region), instead, fibres with bi-continuous morphology and wrinkled/grooved surface have been produced [35, 40, 70-72].

We propose a dual phase separation mechanism for describing the hierarchical morphology and internal porosity of the PECA-PCL fibres, as schematically illustrated in Figure 6. When the two solutions, PCL in chloroform and PECA in acetone, were mixed together and then solubilised in acetonitrile, phase separation happened and caused the mixture to become partially cloudy. <u>During electrospinning, polymer-lean nuclei appeared on one portion of the ejected filament and they were embedded into a polymer-rich matrix (left-hand side path of Figure 6). Due to the rapid solvent evaporation, the polymer-rich matrix solidified, and limited time was given to the nuclei to grow. Therefore, isolated pores emerged onto the fibre surface. They represent one of the morphologies (near circular pores) observed for the PECA-PCL fibres (coloured in green in the SEM image of the inset of Figure 6) and often associated with the nucleation and growth mechanism [70, 71].</u>

Simultaneously, polymer-rich phase and polymer-lean domains appeared also onto the other portion of the electrospun filament due to solvent evaporation and changes in polymer concentration (right-hand side path in Figure 6). After complete solvent evaporation, grooves aligned along the fibre direction were formed. Those microstructures are attributed to spinodal decomposition [70, 73, 74] combined with stretching of the polymer filament by electric force [72]. Electrospun fibres with a grooved texture have been observed for polystyrene (PS) solutions of binary solvent systems with enough difference in evaporation rate between the two solvents [72]. Three different mechanisms of grooves formations have been proposed: voidbased elongation, wrinkle-based elongation, and collapsed jet-based elongation. In the case of the PECA-PCL fibres, the characteristic elongated and aligned structures (coloured in orange in the SEM image of the inset of Figure 6) were the result of the second mechanism. According to this mechanism (for a binary solvent system), a solvent with a low boiling point induces the formation of wrinkles at the fibre surface, while a solvent with high boiling point maintains the extruded filament wet and able to stretch because of the electric force [72]. The wrinkles then elongate and evolve into grooves upon fibre solidification. During the electrospinning of PECA-PCL fibres, we expect that the high evaporation rate of acetone (boiling point of 56 °C) and the slow one of acetonitrile (boiling point of 82 °C) influenced grooves formation. Since acetone and acetonitrile are a poor solvent and a non-solvent for PCL, respectively, while they solubilise PECA, we assume that the elongated microstructures consisted mainly of PECA. In order to verify this, we treated the PECA-PCL mats with acetonitrile: a 5µ drop acetonitrile was deposited onto the mat and let it dry at room temperature. SEM investigations of the treated mats (Figure S2) show that the regions with near-circular pores survived the acetonitrile treatment, while the other regions were solubilised. This indicates that it is most likely that the grooved surface and the porous one contained a high amount of PECA and PCL, respectively. The spatial separation of the two polymers within the electrospun fibres can be associated to the presence of PECA-rich and PCL-rich domains (emulsion) in the starting solution before electrospinning. Those domains further segregated during fibre formation due to changes in solvent concentration.

4. Conclusions

In conclusion, we demonstrated the formation of structured PECA-PCL fibres with dualporosity by inducing phase separation during the electrospinning process. The fibres were constituted by two distinct regions: one with elongated and parallel grooves, possibly caused by spinodal decomposition; the other one with near-circular nanopores as result of nucleation and growth phenomena. Compared with previous studies on hierarchical micro- and nanostructures, the method here discussed allows the easy and cost-effective production of fibres with a unique morphology. Those hierarchical, multi-scale electrospun mats can find potential applications as scaffolds for tissue engineering and devices for drug delivery.

Acknowledgements

The authors acknowledge the use of the facilities and the assistance of K. Yendall in the Loughborough Materials Characterisation Centre, Department of Materials, for SEM analysis.

The raw/processed data required to reproduce these findings are available from the corresponding author EM on request.

References

- [1] P. Fratzl, R. Weinkamer, Prog. Mater. Sci. 52 (2007) 1263.
- [2] R. Lakes, Nature 361 (1993) 511.
- [3] F. Vollrath, D. P. Knight, Nature 410 (2001) 541.
- [4] D.-G. Yu, X.-Y. Li, X. Wang, J.-H. Yang, S. W. A. Bligh, G. R. Williams, ACS Appl.
- Mater. Interfaces 7 (2015) 18891.
- [5] J. Y. Rho, L. Kuhn-Spearing, P. Zioupos, Med. Eng. Phys. 20 (1998) 92.
- [6] N. Reznikov, R. Shahar, S. Weiner, Acta Biomater. 10 (2014) 3815.
- [7] H. Zhou, J. Guo, P. Li, T. Fan, D. Zhang, J. Ye, Sci. Rep. 3 (2013) 1667.
- [8] E. Shimoni, O. Rav-Hon, I. Ohad, V. Brumfeld, Z. Reich, Plant Cell 17 (2005) 2580.
- [9] J. Liu, S. Z. Qiao, S. B. Hartono, G. Qing, M. Lu, Angewande Chemie Int. Ed. 49(2010) 4981.
- [10] C. M. A. Parlett, K. Wilson, A. F. Lee, Chem. Soc. Rev. 42 (2013) 3876.
- [11] W. Huang, H. Zhang, Y. Huang, W. Wang, S. Wei, Carbon 49 (2011) 838.
- [12] Y. G. Ko, N. Kawazoe, T. Tateishi, G. Chen, J. Biomed. Mater. Res. Part B Appl.Biomater. 93 (2010) 341.
- [13] C.-L. Zhang, S.-H. Yu, Mater. Horizons 3 (2016) 266.
- [14] W. Zhang, S. Ronca, E. Mele, Nanomaterials 7 (2017) 42.
- [15] J. Wu, X. Qin, C. Miao, Y. He, G. Liang, D. Zhou, M. Liu, C. Han, B. Li, F. Kang, Carbon 98 (2016) 582.

[16] E. Rezabeigi, M. Sta, M. Swain, J. McDonald, N. R. Demarquette, R. A. L. Drew, P.M. Wood-Adams, J. Appl. Polym. Sci. 134 (2017) 44862.

[17] S. M. Bhaway, Y.-M. Chen, Y. Guo, P. Tangvijitsakul, M. D. Soucek, M. Cakmak, Y.Zhu, B. D. Vogt, ACS Appl. Mater. Interfaces 8 (2016) 19484.

[18] S. Sankar, C. S. Sharma, S. N. Rath, S. Ramakrishna, J. Tissue Eng. Regen. Med. 12(2018) e604.

[19] S. Zhan, D. Chen, X. Jiao, S. Liu, J. Colloid Interface Sci. 308 (2007) 265.

[20] D. Li, J. T. McCann, Y. Xia, Small 1 (2004) 83.

[21] Y. Z. Zhang, J. Venugopal, Z.-M. Huang, C. T. Lim, S. Ramakrishna,Biomacromolecules 6 (2005) 2583.

[22] A. Gupta, C. D. Saquing, M. Afshari, A. E. Tonelli, S. A. Khan, R. Kotek, Macromol.42 (2009) 709.

[23] Z. Wei, Q. Zhang, L. Wang, M. Peng, X. Wang, S. Long, J. Yang, Sep. Sci. Technol.48 (2013) 2287.

[24] S. O. Han, W. K. Son, D. Cho, J. H. Youk, W. H. Park, Polym. Degrad. Stab. 86(2004) 257.

[25] L. Jun, Y. Zhang, Y. Hao, L. Cheng, J. J. Zhang, J. Appl. Polym. Sci. 112 (2009)2247.

[26] W. S. Lyoo, J. H. Youk, S. W. Lee, W. H. Park, Mater. Lett. 59 (2005) 3558.

[27] T. Ruotsalainen, J. Turku, P. Heikkilä, J. Ruokolainen, A. Nykänen, T. Laitinen, M.Torkkeli, R. Serimaa, G. ten Brinke, A. Harlin, O. Ikkala, Adv. Mater. 17 (2005) 1048.

[28] T. Ruotsalainen, J. Turku, P. Hiekkataipale, U. Vainio, R. Serimaa, G. ten Brinke, A.Harlin, J. Ruokolainen, O. Ikkala, Soft Matter 3 (2007) 978.

[29] S. Megelski, J. S. Stephens, D. B. Chase, J. F. Rabolt, Macromolecules 35 (2002)456.

14

[30] C. L. Casper, J. S. Stephens, N. G. Tassi, D. B. Chase, J. F. Rabolt, Macromolecules 37 (2004) 573.

[31] Y. Li, C. T. Lim, M. Kotaki, Polymer 56 (2015) 572.

[32] Y. Wang, H. Huang, G. Li, X. Zhao, L. Yu, C. Zou, Y. Xu, CrystEngComm 19 (2017)2673.

- [33] L. Natarajan, J. New, A. Dasari, S. Yu, M. A. Manan, RSC Adv. 4 (2014) 44082.
- [34] J. Lin, B. Ding, J. Yang, J. Yu, G. Sun, Nanoscale 4 (2012) 176.
- [35] L. Li, Z. Jiang, M. Li, R. Li, T. Fang, RSC Adv. 4 (2014) 52973.
- [36] J. Zheng, H. Zhang, Z. Zhao, C. C. Han, Polymer 53 (2012) 546.
- [37] M. Bognitzki, W. Czado, T. Frese, A. Schaper, M. Hellwig, M. Steinhart, A. Greiner,
- J. H. Wendorff, Adv. Mater. 13 (2001) 70.
- [38] J. T. Mccann, M. Marquez, Y. Xia, J. Am. Chem. Soc. 128 (2006) 1436.
- [39] P. Dayal, J. Liu, S. Kumar, T. Kyu, Macromolecules 40 (2007) 7689.
- [40] J. Lin, B. Ding, J. Yu, Y. Hsieh, ACS Appl. Mater. Interfaces 2 (2010) 521.
- [41] C.-M. Hsu, S. Shivkumar, J. Mater. Sci. 39 (2004) 3003.
- [42] Y. Z. Zhang, Y. Feng, Z.-M. Huang, S. Ramakrishna, C. T. Lim, Nanotechnology 17(2006) 901.
- [43] K. A. G. Katsogiannis, G. T. Vladisavljevic, S. Georgiadou, Eu. Polym. J. 69 (2015)284.
- [44] G. Yazgan, R. I. Dmitriev, V. Tyagi, J. Jenkins, G.-M. Rotaru, M. Rottmar, R. M. Rossi,
- C. Toncelli, D. B. Papkovsky, K. Maniura-Weber, G. Fortunato, Sci. Rep. 7 (2017) 158.
- [45] R. J. Wade, J. A. Burdick, Nano Today 9 (2014) 722.
- [46] H. Li, Y. Xu, H. Xu, J. Chang, J. Mater. Chem. B 2 (2014) 5492.
- [47] M. B. Taskin, D. Xia, F, Besenbacher, M. Dong, M. Chen, Nanoscale 9 (2017) 9218.
- [48] J. C. Rose, L. De Laporte, Adv. Healthcare Mater. 7 (2018) 1701067.

- [49] E. Mele, J. A. Heredia-Guerrero, I. S. Bayer, G. Ciofani, G. G. Genchi, L. Ceseracciu,
 A. Davis, E. L. Papadopoulou, M. J. Barthel, L. Marini, R. Ruffilli, A. Athanassiou, Sci. Rep. 5 (2015) 14019.
- [50] B. Nottelet, E. Pektok, D. Mandracchia, J.-C. Tille, B. Walpoth, R. Gurny, M. Möller,J. Biomed. Mater. Res. Part A 89A (2009) 865.
- [51] N. Bhardwaj, S. C. Kundu, Biotechnol. Adv. 28 (2010) 325.
- [52] S.-H. Tan, R. Inai, M. Kotaki, S. Ramakrishna, Polymer 46 (2005) 6128.
- [53] Y. Wu, R. L. Clark, J. Colloid Interface Sci. 310 (2007) 529.
- [54] R. V. N. Krishnappa, K. Desai, C. Sung, J. Mater. Sci. 38 (2003) 2357.
- [55] A. Cipitria, A. Skelton, T. R. Dargaville, P. D. Dalton, D. W. Hutmacher, J. Mater. Chem. 21 (2011) 9419.
- [56] C. J. Luo, E. Stride, M. Edirisinghe, Macromolecules 45 (2012) 4669-4680.
- [57] I. M. Smallwood, Handbook of organic solvent properties, Arnold, 1996.
- [58] L. A. Bosworth, S. Downes, J. Polym. Environ. 20 (2012) 879.
- [59] R. Casasola, N. L. Thomas, A. Trybala, S. Georgiadou, Polymer 55 (2014) 4728.
- [60] L. Van Der Schueren, B. De Schoenmaker, Ö. I. Kalaoglu, K. De Clerck, Eur. Polym.J. 47 (2011) 1256.
- [61] X. H. Li, C. L. Shao, Y. C. Liu, Langmuir 23 (2007) 10920.
- [62] A. V. Bazilevsky, A. L. Yarin, C. M. Megaridis, Langmuir 23 (2007) 2311.
- [63] S.-W. Choi, I. W. Cheong, J.-H. Kim, Y. Xia, Small 5 (2009) 454.
- [64] Q. Zhang, Y. Li, Z. Ren, Z. Ahmad, X. Li, G. Han, Mater. Lett. 152 (2015) 82.
- [65] D. Durgalakshmi, S. Balakumar, Phys. Chem. Chem. Phys. 17 (2015) 15316.
- [66] S. Koombhongse, W. Liu, D. H. Reneker, J. Polym. Sci. Part B: Polym. Phys 39 (2001)2598.
- [67] C.-L. Pai, M. C. Boyce, G. C. Rutledge, Macromol. 42 (2009) 2102.

- [68] S. O. Han, W. K. Son, J. H. Youk, T. S. Lee, W. H. Park, Mater. Lett. 59 (2005) 2998.
- [69] H. Fashandi, M. Karimi, Thermochim. Acta 547 (2012) 38.
- [70] H. Fashandi, M. Karimi, Polymer 53 (2012) 5832.
- [71] Z. Qi, H. Yu, Y. Chen, M. Zhu, Mater. Lett. 63 (2009) 415.
- [72] W. Liu, C. Huang, X. Jin, Nanoscale Res. Lett. 10 (2015) 237.
- [73] L. Li, Z. Jiang, M. Li, R. Li, T. Fang, RSC Adv. 4 (2014) 52973.
- [74] L. Li, R. Li, M. Li, Z. Rong, T. Fang, RSC Adv. 4 (2014) 27914.

Figure captions

Figure 1. (a), (b) and (c) SEM images of electrospun PECA-PCL fibres at different magnifications. (d) Schematic diagram of one single fibre with dual porosity, where *a* is the size of the region with circular pores, *a'* is the size of the region with elongated structures, θ is the angle formed by the main axis of the fibres and the direction of the main diameter of the pores, and θ' is the angle formed by the main axis of the fibres and the fibres and the main direction of the structures. (e) Statistical distribution of *a/a'* ratio. (f) Polar diagrams of θ (green symbols) and θ' (orange symbols). Data were obtained by analysing 50 structures for each shape (circular pores and grooves).

Figure 2. SEM images of PCL electrospun fibres formed using different solvent systems: (a) chloroform, (b) acetone/chloroform, (c) acetonitrile/chloroform, and (d) acetone/acetonitrile/chloroform.

Figure 3. SEM images of PECA fibres electrospun from different solvent systems: (a) acetone, (b) acetonitrile/chloroform, (c) acetone/acetonitrile, and (d) acetone/acetonitrile/chloroform.

Figure 4. SEM images of (a) PCL (region of the mat without beads) and (b) PECA <u>and (c)</u> PECA-PCL fibres electrospun from the ternary system (acetone/acetonitrile/chloroform).

Figure 5. SEM images of the cross section of (a) PECA-PCL mats, (b) hollow PECA-PCL fibre with cylindrical shape, (c) PECA-PCL fibre with ribbon-like shape.

Figure 6. Schematic diagram (not in scale) of the dual phase separation process: green path shows nucleation and growth mechanism, while the orange path shows the spinodal decomposition mechanism. Central inset: Coloured SEM image of PECA-PCL fibres.



Figure 1



Figure 2



Figure 3







____ 1 μm



____ 1 μm

Figure 4



μ**m**

📕 1 μm





Figure 6

Supplementary Material

Table S1. Optimum conditions for the electrospinning process. All experiments were conducted at room temperature (20 °C) with a relative humidity of 33%. Solvent systems include: acetone, acetonitrile and chloroform, acetone and acetonitrile, and acetone, acetonitrile and chloroform.

Solutions	Flow rate (ml/h)	Applied voltage (kV)	Distance (cm)
PECA-PCL in acetonitrile	3	12	15
PECA in all solvent systems	2	10	15
PCL in all solvents systems	2	12	15

Figure S1: Statistical analysis of the distribution of θ (green histograms) and θ [•] (orange histograms). The continuous curves are the best fits with a Gaussian function.



Figure S2: SEM images of PECA-PCL electrospun mats after treatment with acetonitrile.

