doi:10.2533/chimia.2022.229 Chimia 76 (2022) 229–235

Tailoring Fibre Structure Enabled by X-ray Analytics for Targeted Biomedical Applications

Jean Schoeller[§ab], Jonathan Avaro[§c], Anjani K. Maurya[ace], René M. Rossi[ab], and Antonia Neels*[cd]

Abstract: The rising interest in designing fibres *via* spinning techniques combining the properties of various polymeric materials into advanced functionalised materials is directed towards targeted biomedical applications such as drug delivery, wearable sensors or tissue engineering. Understanding how these functional polymers exhibit multiscale structures ranging from the molecular level to nano-, micro- and millimetre scale is a key prerequisite for their challenging applications that can be addressed by a non-destructive X-ray-based analytical approach. X-ray multimodalities combining X-ray imaging, scattering and diffraction allow the study of morphology, molecular structure, and the analysis of nano-domain size and shape, crystallinity and preferential orientation in 3D arrangements. The incorporation of X-ray analytics in the design process of polymeric fibres *via* their nanostructure under non-ambient conditions (*i.e.* temperature, mechanical load, humidity…) allows for efficient optimisation of the fabrication process as well as quality control along the product lifetime under operating environment conditions. Here, we demonstrate the successful collaboration between the laboratory of Biomimetic Textiles and Membranes and the Center for X-ray Analytics at Empa for the design, characterisation and optimisation of advanced functionalised polymeric fibrous material systems.

Keywords: Fibres · Functionality · Nano-structure · X-ray multi-modalities

Jean Schoeller studied Chemistry and Physics at the Graduate School of Chemistry and Physics of Bordeaux (ENSCBP) and is currently a doctoral student in the Laboratory of Biomimetic Membranes and Textiles at Empa and in the Institute for Biomechanics in the Department of Health Science and Technology at the ETHZ. His research focuses on the development of drug delivery systems using electrospun nanofibres.

Jonathan Avaro studied Geology and Oceanography from Bordeaux 1 University, France. He obtained his PhD in Geo-Science from Southern Cross University, Lismore, Australia working on nucleation and crystallisation questions using X-ray and neutron analytical techniques such as SAXS, SANS and EXAFS. He joined the physical-chemistry department of Konstanz University in 2016 as a postdoctoral fellow and in 2021, Empa Swiss Federal Laboratories for Materials Science and Technology as X-ray scientist specialising in Small and Wide-Angle X-ray Scattering. His research focuses on nucleation and crystallisation in inorganic and organic environments and the development of analytical tools to better understand materials organisation at the nano-scales.

Anjani K. Maurya studied applied and engineering physics at the Indian Institute of Technology Guwahati, India and Technical University of Munich, Germany. He worked in the Center for X-ray Analytics and the laboratory for Biomimetic Membranes and Textiles at Empa and obtained his PhD in Biomedical Engineering from the University of Bern, Switzerland. Currently, he is a postdoctoral research fellow at Stanford University and works at Stanford Synchrotron Radiation Lightsource, SLAC National Accelerator Laboratory, USA. His research focuses on the multiscale characterization of polymeric materials for biomedical, plastic recycling, and energy storage applications by using/developing modern X-ray scattering and spectroscopy techniques.

René M. Rossi studied applied physics at the University of Neuchâtel and obtained his PhD at ETH Zurich. Since 2003, he has been leading the Laboratory for Biomimetic Membranes and Textiles at Empa, a group developing novel smart fibres, textiles and membranes for body monitoring, drug delivery and tissue engineering applications. A special focus is to develop physical and numerical skin/body models for the analysis of the interactions between materials and the human skin to optimise the protection and ergonomics of systems. René Rossi is an adjunct

*Correspondence: Prof. Dr. A. Neels[cd], E-mail: antonia.neels@empa.ch

[a]Empa, Swiss Federal Laboratories for Materials Science and Technology, Laboratory for Biomimetic Membranes and Textiles, CH-9014 St. Gallen, Switzerland; [b]ETH Zürich, Department of Health Science and Technology, CH-8093 Zürich, Switzerland; [c]Empa, Swiss Federal Laboratories for Materials Science and Technology, Center for X-ray Analytics, CH-8600 Dübendorf, Switzerland; [d]University of Fribourg, Department of Chemistry, Chemin du Musée 9, CH-1700 Fribourg, Switzerland; [e]Current address: Stanford Synchrotron Radiation Lightsource, SLAC National Accelerator Laboratory, Menlo Park, CA, 94025 USA.

[§]These authors contributed equally

professor at the Department of Health Sciences and Technology at ETH Zurich and invited professor at the University of Haute-Alsace in Mulhouse/France.

Antonia Neels studied Chemistry at the Humboldt University of Berlin, Germany, and obtained her PhD in Science from the University of Neuchâtel, Switzerland. She led the XRD laboratory at CSEM/EPFL and heads today the Center for X-ray Analytics at Empa. She studies novel materials with fascinating structures leading to new physical properties and applications. Her interest in developing X-ray-based analytical concepts is directed towards strain and defect mobility in order/disorder materials especially for space and medical applications. She has published more than 270 papers and is active in national and international crystallographic associations and commissions. Antonia Neels is a Titular Professor at the University of Fribourg, Switzerland.

1. Introduction

Elucidating the impact of the processing parameters on the structure of fibrous materials allows for the development of tailored functional materials. A fibre is defined as a material with a significantly higher length compared to its width. The resulting fibrous structures present a high surface-to-volume ratio and high porosity. Due to these inherent properties, advanced fibrous materials have recently found applications as sensors, in biomedical and tissue engineering, filtration, energy harvesting and smart textiles.[1–8] Our emphasis and recent developments in X-ray-based analytical methods[9–12] and related structural findings, especially through small/wide-angle X-ray scattering (SAXS/WAXS) studies, enable us to tailor the fibre functions for advanced and smart applications. Non-destructive X-ray methods enable us to observe changes in the partially crystalline polymer structure depending on a change of experimental condition (temperature, mechanical load or humidity). The structure–property relationship is studied in realistic environmental conditions for fibre systems under load; *e.g.* during the degradation of biopolymer-based drug delivery systems[13] or heat degradation in wearables.[12]

Several techniques exist for the processing of polymers into fibrous materials (Fig. 1).[1] Solution spinning is one of the oldest techniques for the production of fibres. In this process, a natural or synthetic polymer is dissolved in an appropriate solvent to produce a viscous solution from which the fibres can be produced.[14] Among solution spinning, different techniques are available to produce fibres such as wet spinning, dry spinning and electrospinning.

Wet spinning is a technique where the polymer solution is extruded through a spinneret into a coagulation bath containing a non-solvent for the polymer. Dry spinning uses hot air to evaporate the solvent instead of a coagulation bath. The aforementioned methods produce fibres with diameters of a few microns up to the millimetre range. Electrospinning is a technique where the polymer solution is submitted to a high electric field by using the spinneret as a cathode and a grounded/negatively charged collector. Once the electric field overcomes the surface tension of the polymer solution a whipping jet is formed, which travels to the collector.[15,16] As the jet flies to the collector, the solvent evaporates and fibres with diameters in the nano/microscale are deposited onto the substrate of choice.

All the aforementioned processes produce fibres with different properties and the processing parameters influence the structure and morphology of the fibres. This has been an area of research for both laboratories and the source of many collaborations.[17–19] By deepening our understanding of the structure of fibres, one can expect to obtain better control on the fabrication in order to produce tailor-made materials. In fact, X-ray scattering allows for an in-depth characterisation of the materials nanometric structure with the versatility of such techniques being available for various sample environments. With the possibility to combine the characterisation of powders, fibres, biological or hybrid samples under variable experimental conditions such as temperature, tensile loading, or microfluidics enabling controlled humidity conditions, realistic working conditions can be probed for fibre systems. The uniqueness of Empa's approach in developing state-of-the-art advanced functional fibres is to combine multi-polar polymeric material production with structural characterisation using X-ray analytical concepts applying a variety of environmental parameters corresponding to realistic conditions for the respective systems in applications. Understanding how polymeric fibril material nano-domains react when exposed to environmental parameter changes such as strain,[9,11] humidity[13] to only cite a few, and, per translation, how the size and shape of amorphous, crystalline or lamellar domains emerge, change at different levels or self-assemble in 3D. Non-destructive X-ray analytical methods, by combining X-ray imaging, diffraction and scattering methods, provide a unique tool for the fine tailoring of structures and therefore properties of such materials on a laboratory scale as well as for industrial upscaling. With the ongoing effort of designing advanced functionalised fibres involving multi-polymeric materials, X-ray analysis provides an in-depth 4D understanding of a system (changes of 3D structure over time) and a unique possibility for establishing quality control measures for a product in service conditions. Furthermore, the non-destructiveness aspect of X-ray analytics makes it an attractive tool for quality control of a wide range of materials.[12]

In the present article, we review the work that has been the result of a successful collaboration between the laboratory of Biomimetic Membranes and Textiles and the Center for X-ray Analytics of Empa which have been working side by side to understand the structural properties of wetspun advanced fibrous materials using state-of-the-art X-ray analytical methods. First, the capacity of fibrous systems to be used as sensors for different applications is summarised. Then, the development of fibre-based drug delivery systems is presented. Finally, the development of fibres for tissue engineering is discussed and how X-ray analytical methods, especially SAXS, can accelerate the design of tailor-made cell scaffolds. We conclude with an outlook of today's challenges and the future of fibrous systems at Empa in light of these recent developments and modern applications.

2. Polymeric Sensors

Materials consisting of two or more types of finely phase-separated polymers often possess improved and novel properties due to a synergistic combination of the individual components in one nanostructured material. Amphiphilic polymer co-networks (APCNs) represent such a novel material in this field.

The uniqueness of APCNs comes from the combination of both hydrophobic and hydrophilic materials in a nano-phase separated system. Their nanostructure in small domains gives the material unique properties such as swelling abilities in various solvents, optical transparency and excellent mechanical properties. Also, these materials allow for the nanometre-precise embedding of hydrophilic/hydrophobic luminescent materials for ratiometric sensors as demonstrated in our previous work.[20] This remarkable versatility makes this material an ideal candidate for drug-delivery systems, anti-biofouling surfaces, separation membranes, lithium-ion conductor materials, sensors, self-sealing breathable membranes or matrices for catalysis.[21]

The challenge for the fabrication of APCNs lies in the necessity to combine two immiscible polymers into a macroscopically

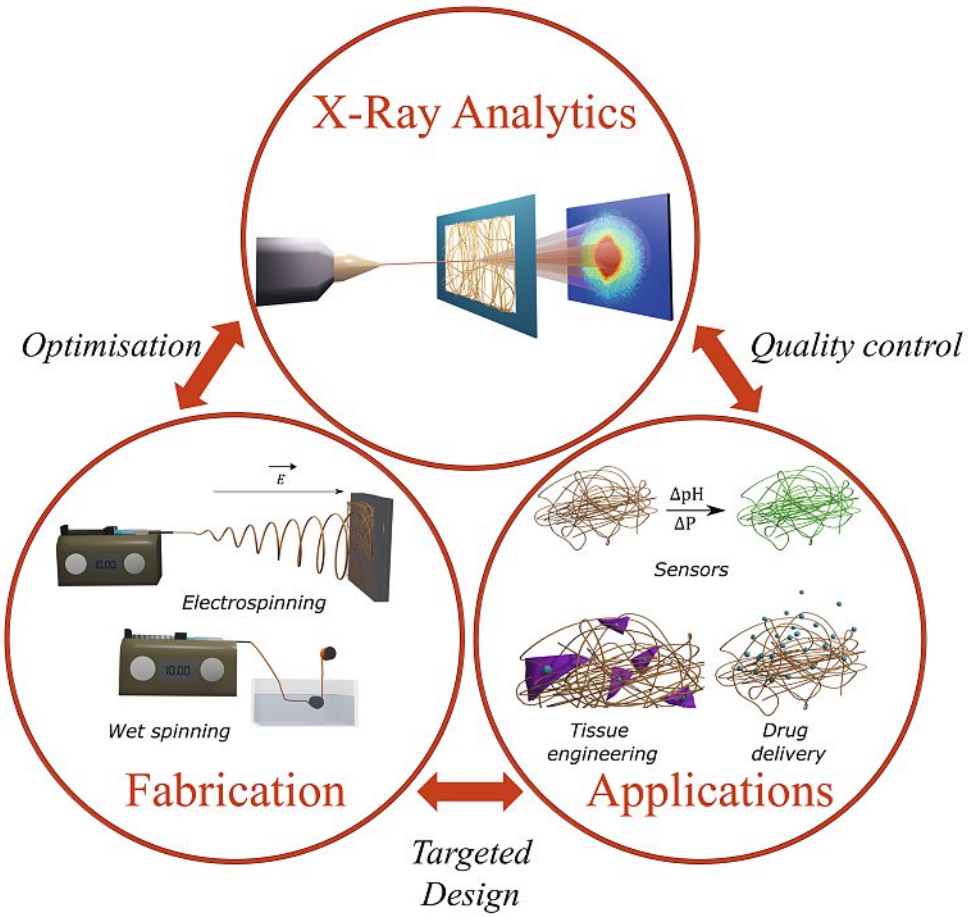

Fig. 1. Scope of the present review. The incorporation of X-ray analytics within the design and fabrication process of fibrous materials allows a tailored optimization of the fibre structures for state-of-the-art biomedical applications.

homogenous material and to characterise and control its internal structure. While several synthesis routes have already been proposed in the literature, Empa has developed its own recipe and included a wide range of functionalised groups rendering the material pH-sensible, fluorescent or as a preferential binder for protein in a drug delivery optic.[4]

The different morphologies arising for various mixing ratios have been characterised *via* Atomic Force Microscope (AFM), a surface-sensitive method, and revealed different nano-domain sizes.[22] However, direct quantification of the size of the domains *via* AFM is at best tedious, limited to the surface morphology and highly limited by the image resolution. By probing the bulk part of the material, scattering methods such as SAXS allow the direct characterisation of the average domain size within a large volume of the sample. The scattering curves presented in this study show a correlation peak (denoted q* in Fig. 2A) typical for recurring nanoscopic domains.

The use of a modelling approach to describe the form of these nano-domains and their interaction revealed that the use of different polymer materials in these APCNs allowed for fine-tuning of the nano-domain size for targeted functionalisation (Fig. 2B). This work done at Empa directly contributes to the fabrication of novel APCNs for drug delivery, smart contact lenses, sensors and self-healing materials.

Similar strategies, where the structural understanding of the polymer fibres material supports the optimisation of the manufacturing processes, are currently in development. One or several properties of a material can be fine-tuned, such as the size of amorphous or crystalline domains to tune for instance the opacity in optical fibre materials.

Another example of multi-material structures that are today widely used in our daily life is fibre optics. In telecommunication, optical fibres are preferentially utilised for sending information at high speed from point A to B. The information sent *via* light within an optical fibre follows the principle of total internal reflection where the light will bounce on the interface of a core-shell system in such a way that it will propagate down the core of the fibre. Historically the development of such fibres was made of drawn glass (single-crystalline glass) allowing for only very little loss of information over long distances. Similar geometries have been successfully developed with polymers but suffered from higher attenuation values averaging

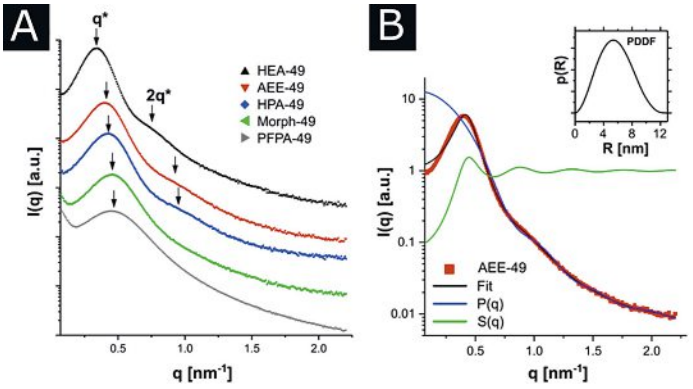

Fig. 2. (A) SAXS curves for the different APCNs materials showing a typical correlation peak from interdomain distances. (B) Fitting of the interdomain distance peak with a form factor describing the shape and size of the scattering objects and a structure factor describing their interaction. Adapted with authorisation from ref. [22].

125 dB/km - loss of intensity over long distances when compared to the 1dB/km putting them aside for long-range communication.[23]

However, with the recent development of local digital networks (exchange of data over short distances), the interest in polymer optic fibres grew in the mid 20th century. Their low-temperature processing, allowing the tuning of their properties by the addition of photoluminescent dyes, revived this research field. Today, such fibres are used in a large variety of domains for short-range communication, sensing, light-harvesting, or smart textiles. The last-mentioned applications have been of special interest for Empa within its strategy to develop non-invasive materials for monitoring body vital signs as well as for light-harvesting applications. However, the production of such fibres for the textile industry is very demanding with respect to mechanical flexibility and toughness, combined with low light attenuation.[5]

To match these expectations, Empa scientists have developed thin bi-component polymer optical fibres with cyclo-olefin polymers (COP) within its core and THV fluoropolymer as the sheath material using melt spinning techniques. These two materials were chosen for high transparency, low water absorbency and high heat resistance for the core and the moisture repellent, high flexibility and good chemical resistance for the sheath. In addition, the materials are of low cost and the process allows for upscaling and industrial implementation.[5]

The refractive index of these two materials differs significantly (1.35 for COP and 1.5 THV for fluoro-polymer) to be combined in optical fibres. While several tests were made to optimise the opacity variation of the fibres, the characterisation of the fibres nanostructure was carried out using wide-angle X-ray diffraction (WAXD). WAXD provides information about crystal structure, crystallite size and preferred orientation formed by the arrangement of the polymeric chains.

The understanding of the internal structure given by WAXD characterisation is critical to the optimisation of the manufacturing processes. Upon changing the drawing ratio (ratio of the speed of the first godet and winder in the spinning setup), we observe a gradual change of the internal polymeric structure and crystallinity. First, the orientation of the preferred inter-chain distance rotates from a longitudinaly to a normal orientation with respect to the fibre direction. Simultaneously, the amorphous phase initially present in the fibre started to crystallise (Fig. 3). Such changes of orientation and degree of crystallisation combined with our visible red light propagation study within the bicomponent fibres allow the potential integration in a fully textile-based reflectance

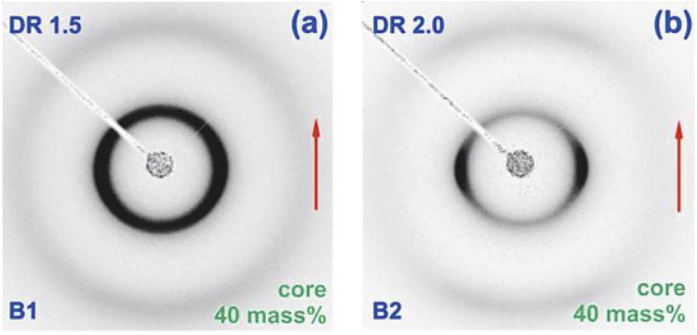

Fig. 3. WAXD pattern of the bi-component COP/THV fibres. The arrow indicates the fibre direction. While the diffuse spherical halo (a) indicates a homogeneously oriented structure, an angle-dependent change of intensity (b) accounts for an anisotropic orientation of the scattering objects. Adapted with authorisation from ref. [5].

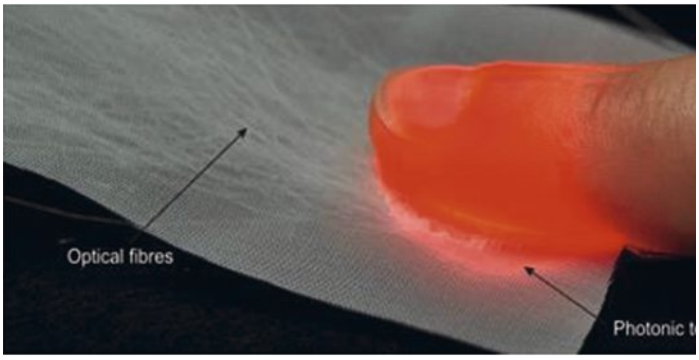

Fig 4. Example of measurement conditions of the heart rate and the oxygen saturation recording using the photonic textile developed based on COP/THV polymer optical fibres. Adapted with authorisation from ref. [25].

pulse-oximeter for non-invasive monitoring of heart rate and oxygen saturation values of humans (Fig. 4).[24]

3. Drug Delivery

The high porosity and surface-to-volume ratio of fibrous materials make them ideal candidates for the design of drug delivery systems with targeted delivery kinetics.[25] Solution spinning processes allow for an easy incorporation of pharmaceutics (drugs) within the polymer matrix of the fibres which leads to high loading efficiency and homogeneous loading throughout the fibres. Furthermore, steering the bulk and surface properties of fibrous constructs can help to obtain control over the release kinetics.[3] Several studies were done in our laboratories to elucidate fibre's structure to gain control over the release kinetics of fibrous materials for different applications.[25–27]

In electrospinning, many process parameters can be tuned to specifically tailor the structure or the surface of fibres. Yagzan *et al.* have steered the release rates of hydrophilic compounds (fluorescein sodium salt (FLU)) by changing the porosity of the fibres when electrospinning poly(vinyl pyrrolidone)/polystyrene emulsions in different humidity conditions. It was demonstrated that fibres with higher porosity led to a faster release of FLU in phosphate buffer saline (PBS) when compared to fibres of lower porosity. This study paved the way to understanding how the structure of electrospun nanofibres can tailor the release rates of pharmaceutics encapsulated within the polymeric matrix.

Furthermore, Amarjargal *et al.* have electrospun Eudragit® RS100 blended with poly(methyl methacrylate) in different ratios to study the impact of the glass transition on the release kinetics of a model drug, namely Rhodamine B.[28] The authors have shown that by switching the temperature below the glass transition of the membranes, the release could be almost completely prevented (from 80% to 12% of drugs released when switching from 45 °C to 37 °C).

Such studies motivated a deeper investigation of the impact of the internal structure of fibres on drug release kinetics. Ongoing work involves the fabrication of fibrous membranes with tailored architectures for the design of advanced drug delivery systems.

The investigation of fibres designed for humidity responsive drug delivery systems was undertaken at Empa. In such a system, the successful design of a fibre relies on the change of lipid symmetry when exposed to humidity that will initialise the drug release process. For this purpose, hybrid electrospun membranes with a distinct structural hierarchy were synthesised. Submicrometre-sized self-assembled lipid nanoparticles were embedded into the PEO nanofibres by electrospinning to design a responsive membrane for controlled drug release applications.[13] SAXS analysis of the hybrid material reveals a re-organisation of

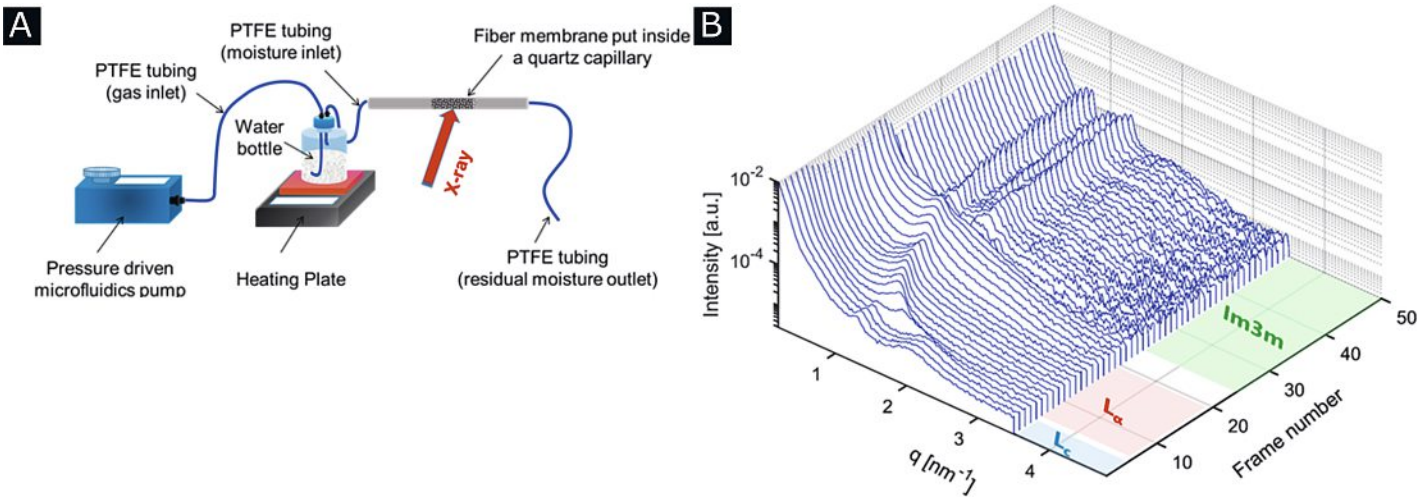

Fig. 5. (A) Schematic of the experimental setup of the humidity *in situ* SAXS instrument for probing the responsive behaviour of the membrane. (B) Scattering curves showing the structural change of the lipid nanoparticle embedded membrane transitioning from a lamellar (Lc) to an ($Im\bar{3}m$) cubic phase. Adapted with authorisation from ref. [20].

the lipid particles internal phase from the original ($Im\bar{3}m$) cubic (known as cubosomes) to mesosomes of crystalline lamellar phases (Lc) during the electrospinning process. Such internal transition, triggered by the electrospinning process, is associated with the interfacial curvature of lipid bilayers due to the low water content within the fibre.

While probing the internal structure of the lipid nanoparticles embedded into the nanofibres membrane *via in situ* SAXS measurements while exposed to different levels of humidity, the fibres showed gradual water uptake that directly translated to a change of the lipid nanoparticle structure (Fig. 5A). Gradually, the lamellar phase (Lc) transformed to a fluid lamellar phase (Lα) to finally regain the original ($Im\bar{3}m$) cubic phase of the lipid particle allowing drug release. Such change of nanodomain symmetry upon exposure to a specific environmental condition, here humidity (Fig. 5B), is a good example for the design of advanced functionalised hybrid fibres to tackle current challenges in biomedicine, tissue engineering and wearable health care devices.

Our studies motivated a deeper investigation of the impact of the internal structure of fibres on drug release kinetics. Ongoing work involves the fabrication of fibrous membranes with tailored architectures for the design of advanced drug delivery systems.

4. Tissue Engineering

Tissue engineering aims to replace diseased or damaged tissue by engineering *in vitro* bioartificial scaffolds. By adjusting the properties of the material, better control can be obtained over cell growth and biocompatibility. Therefore, fibre-based tissue engineering has emerged as a technique of choice for the design of biocompatible scaffolds.[2] Electrospinning is prioritised for tissue engineering due to the inherent high porosity and the surface-to-volume ratio of the membranes that mimic the structure of the extracellular matrix.

Our laboratories have investigated the electrospinning process for the fabrication of biocompatible scaffolds for tissue engineering applications. X-ray analytical methods provide an indispensable tool to investigate the complex microstructure of electrospun nanofibres and thus to understand the relationship between processing parameters and the mechanics of single fibres and also fibre meshes. For example, cell growth and migration were elucidated through a multiscale analysis of poly(lactic acid) (PLA) electrospun nanofibres (Fig. 7A, B).[29–31] In a first study, a significant increase in mechanical strength of singular fibres was observed *via* AFM measurements when decreasing the fibre diameter.

Furthermore, fibres prepared from dichloromethane (DCM) were mechanically stronger than the fibres prepared from trifluoroacetic acid (TFA) due to the presence of nanofibrils oriented along the fibres' axis as revealed by SAXS measurement (Fig. 6).[30] This approach demonstrated how the evaporation of the solvent during the electrospinning process influences fibre stiffness by inducing the growth of either fibrillar or lamellar structures. All these insights about the fibre microstructure allowed for the design of tailored tissue engineering scaffolds.

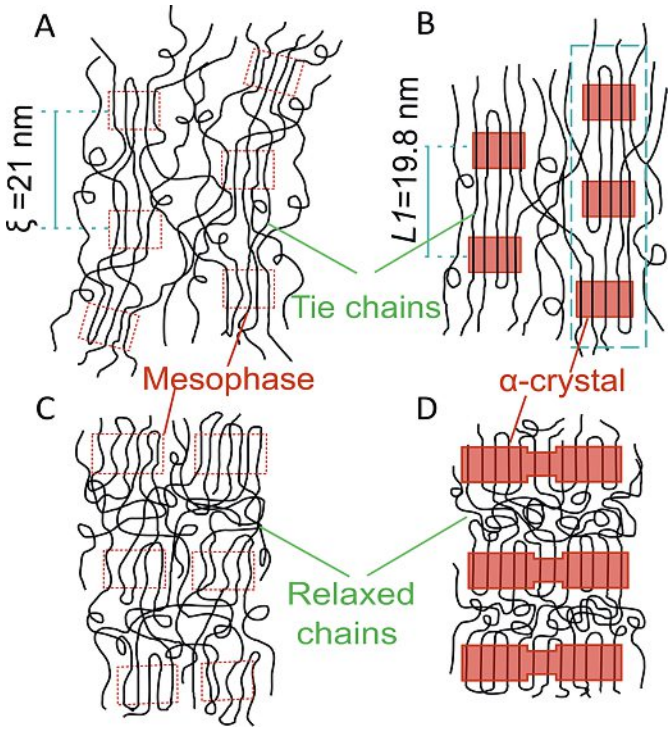

Fig. 6. Schematic representation of the mesophase within PLA nanofibres prepared in DCM (a) before and (b) after solvent induced crystallisation. PLA nanofibres prepared in TFA (c) before and (d) after solvent induced crystallisation. Adapted with authorisation from ref. [31].

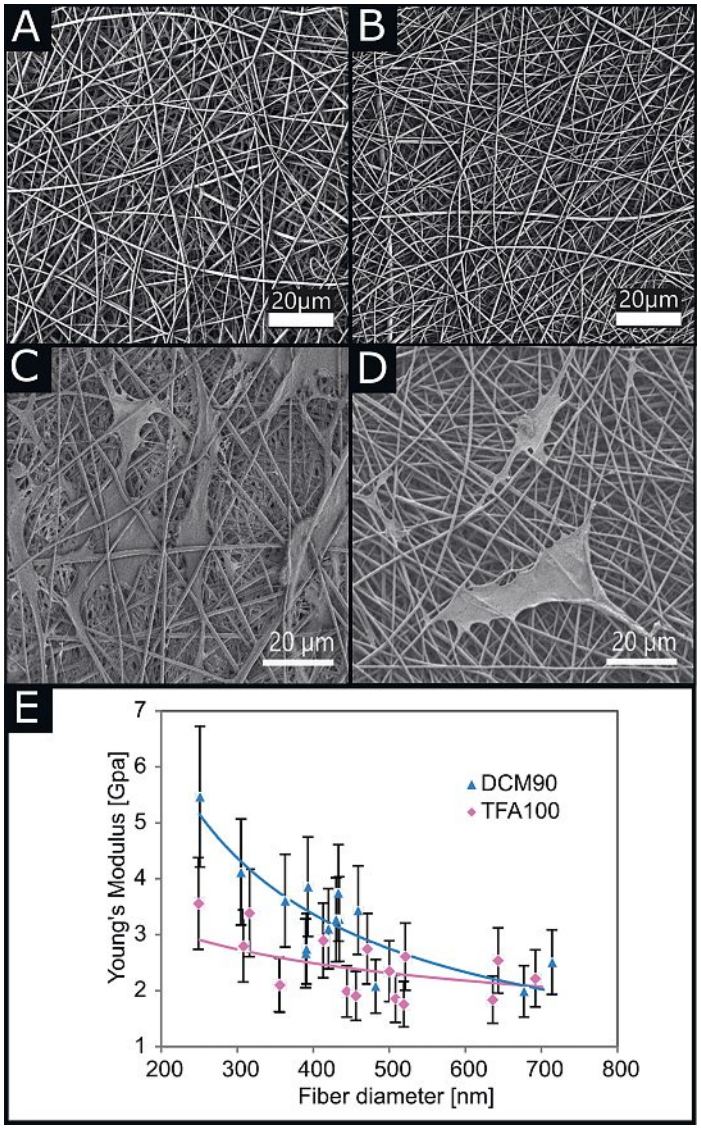

Fig. 7. (A) PLA nanofibres prepared in DCM, (B) PLA nanofibres prepared in TFA, (C) Young's modulus versus fibre diameter. Culture of normal human dermal fibroblast on PLA nanofibres prepared in (D) DCM and (E) TFA. Adapted with authorisation from ref. [32].

In an additional study, different solvents are used to produce scaffolds with different mechanical properties and similar morphologies.[31] While single fibres prepared with DCM exhibit a higher Young's modulus (Fig. 7E), the mechanical properties of the scaffold are the opposite, *i.e.* the scaffolds prepared with TFA exhibit higher stiffness compared to the one prepared in DCM. This is explained by the presence of more fibre-to-fibre junctions when compared to fibres prepared in DCM due to the solvent properties. Finally, the cell infiltration throughout the scaffold was demonstrated to be easier for fibres prepared with DCM compared to scaffolds prepared with TFA, which is explained by an easier migration throughout the scaffold due to less fibre-to-fibre junctions (Fig. 7C, D).

These studies show the importance of understanding the nanostructure of fibrous materials for the development and optimisation of tissue engineering scaffolds. Further work in our laboratories aims to tackle the challenges of fibre-based tissue engineering by revealing the impact of the internal structure on cell growth and proliferation.

5. Conclusion

Fibre developments, intimately linked to the history of St. Gallen and the research performed at Empa, keep pushing the boundaries of these industrial applications. The laboratory of Biomimetic Membranes and Textiles and the Center for X-ray analytics joined forces to achieve tailoring of fibre properties for novel applications, especially in the biomedical domain.

For the development of sensors, the analysis of the internal structure of fibres can allow for a higher sensitivity through a better understanding of the origins of the sensing properties. Such structural information is crucial for the optimisation of the properties of the fibres for drug delivery or tissue engineering applications. The optimisation of the structure–property relationship is established by utilising modern X-ray-based techniques through the continuous feedback loop from fabrication parameters of the fibres, and *in situ* structural investigation of the fibres when varying experimental conditions.

In the present review, we showed how X-ray-based technologies are a crucial tool to establish these correlations to be able to achieve tailoring of the fibre properties for the design of advanced materials for novel applications. Future studies within our laboratories aim to further investigate in multimodal X-ray analytical research for a better fundamental understanding of fibres' structure and to apply such knowledge for the design of functional multi-material systems for specific biomedical applications.

Received: January 18, 2022

[1] J. Hu, M. A. Jahid, N. H. Kumar, V. Harun, *Handb. Fibrous Mat*er. **2020**, *1*, https://doi.org/10.1002/9783527342587.CH1.
[2] A. Tamayol, M. Akbari, N. Annabi, A. Paul, A. Khademhosseini, D. Juncker, *Biotechnol. Adv*. **2013**, *31*, 669, https://doi.org/10.1016/J.BIOTECHADV.2012.11.007.
[3] J. Schoeller, F. Itel, K. Wuertz-Kozak, G. Fortunato, R. M. Rossi, *Polym. Rev*. **2021**, 1, https://doi.org/10.1080/15583724.2021.1939372.
[4] C. S. Huang, K. Jakubowski, S. Ulrich, S. Yakunin, M. Clerc, C. Toncelli, R. M. Rossi, M. V. Kovalenko, L. F. Boesel, *Nano Energy* **2020**, *76*, 105039, https://doi.org/10.1016/J.NANOEN.2020.105039.
[5] F. A. Reifler, R. Hufenus, M. Krehel, E. Zgraggen, R. M. Rossi, L. J. Scherer, *Polymer (Guildf)*. **2014**, *55*, 5695, https://doi.org/10.1016/J.POLYMER.2014.08.071.
[6] S. S. Ray, S. S. Chen, C. W. Li, N. C. Nguyen, H. T. Nguyen, *RSC Adv*. **2016**, *6*, 85495, https://doi.org/10.1039/C6RA14952A.
[7] B. Krause, M. Storr, T. Ertl, R. Buck, H. Hildwein, R. Deppisch, H. Göhl, *Chemie-Ingenieur-Technik* **2003**, *75*, 1725, https://doi.org/10.1002/CITE.200306149.
[8] M. Ulbricht, *Polymer (Guildf)*. **2006**, *47*, 2217, https://doi.org/10.1016/J.POLYMER.2006.01.084.
[9] A. K. Maurya, E. Mias, J. Schoeller, I. E. Collings, R. M. Rossi, A. Dommann, A. Neels, *Nanoscale Adv*. **2021**, https://doi.org/10.1039/D1NA00503K.
[10] A. K. Maurya, A. Parrilli, T. Kochetkova, J. Schwiedrzik, A. Dommann, A. Neels, *Acta Biomater*. **2021**, https://doi.org/10.1016/J.ACTBIO.2021.05.022.
[11] A. K. Maurya, L. Weidenbacher, F. Spano, G. Fortunato, R. M. Rossi, M. Frenz, A. Dommann, A. Neels, A. Sadeghpour, *Nanoscale* **2019**, *11*, 7176, https://doi.org/10.1039/C9NR00446G.
[12] A. K. Maurya, S. Mandal, D. E. Wheeldon, J. Schoeller, M. Schmid, S. Annaheim, M. Camenzind, G. Fortunato, A. Dommann, A. Neels, A. Sadeghpour, R. M. Rossi, *Polymer (Guildf)*. **2021**, *222*, https://doi.org/10.1016/J.POLYMER.2021.123634.
[13] N. D. Tien, A. K. Maurya, G. Fortunato, M. Rottmar, R. Zboray, R. Erni, A. Dommann, R. M. Rossi, A. Neels, A. Sadeghpour, *Langmuir* **2020**, *36*, 11787, https://doi.org/10.1021/ACS.LANGMUIR.0C01487.
[14] Kenry, C. T. Lim, *Prog. Polym. Sci*. **2017**, *70*, 1, https://doi.org/10.1016/J.PROGPOLYMSCI.2017.03.002.
[15] J. Doshi, D. H. Reneker, *J. Electrostat*. **1995**, *35*, 151, https://doi.org/10.1016/0304-3886(95)00041-8.
[16] D. H. Reneker, A. L. Yarin, H. Fong, S. Koombhongse, *J. Appl. Phys*. **2000**, *87*, 4531, https://doi.org/10.1063/1.373532.
[17] I. Richard, A. K. Maurya, S. Shadman, E. Masquelier, L. S. Marthey, A. Neels, F. Sorin, *Small* **2021**, 2101392, https://doi.org/10.1002/SMLL.202101392.
[18] A. Jain, A. K. Maurya, L. Ulrich, M. Jaeger, R. M. Rossi, A. Neels, P. Schucht, A. Dommann, M. Frenz, H. G. Akarçay, *Opt. Express* **2020**, *28*, 16673, https://doi.org/10.1364/OE.390303.

[19] Y. Qu, T. Nguyen-Dang, A. G. Page, W. Yan, T. Das Gupta, G. M. Rotaru, R. M. Rossi, V. D. Favrod, N. Bartolomei, F. Sorin, Y. Qu, T. Nguyen-Dang, A. G. Page, W. Yan, T. Das Gupta, V. D. Favrod, N. Bartolomei, F. Sorin, *Adv. Mater*. **2018**, *30*, 1707251, https://doi.org/10.1002/ADMA.201707251.
[20] S. Ulrich, A. Osypova, G. Panzarasa, R. M. Rossi, N. Bruns, L. F. Boesel, *Macromol. Rapid Commun*. **2019**, *40*, 1900360, https://doi.org/10.1002/MARC.201900360.
[21] S. Ulrich, A. Sadeghpour, R. M. Rossi, N. Bruns, L. F. Boesel, *Macromolecules* **2018**, *51*, 5267, https://doi.org/10.1021/acs.macromol.8b00841.
[22] K. Schöller, S. Küpfer, L. Baumann, P. M. Hoyer, D. De Courten, R. M. Rossi, A. Vetushka, M. Wolf, N. Bruns, L. J. Scherer, *Adv. Funct. Mater*. **2014**, *24*, 5194, https://doi.org/10.1002/ADFM.201400671.
[23] K. Jakubowski, C. S. Huang, L. F. Boesel, R. Hufenus, M. Heuberger, *Curr. Opin. Solid State Mater. Sci*. **2021**, *25*, 100912, https://doi.org/10.1016/j.cossms.2021.100912.
[24] M. Krehel, M. Wolf, L. F. Boesel, R. M. Rossi, G.-L. Bona, L. J. Scherer, *Biomed. Opt. Express* **2014**, *5*, 2537, https://doi.org/10.1364/boe.5.002537.
[25] R. E. Ghitescu, A. M. Popa, A. Schipanski, C. Hirsch, G. Yazgan, V. I. Popa, R. M. Rossi, K. Maniura-Weber, G. Fortunato, *Eur. J. Pharm. Biopharm*. **2018**, *122*, 78, https://doi.org/10.1016/J.EJPB.2017.10.009.
[26] A. Camerlo, C. Vebert-Nardin, R. M. Rossi, A. M. Popa, *Eur. Polym. J.* **2013**, *49*, 3806, https://doi.org/10.1016/J.EURPOLYMJ.2013.08.028.
[27] A. Camerlo, A. M. Bühlmann-Popa, C. Vebert-Nardin, R. M. Rossi, G. Fortunato, *J. Mater. Sci.* **2014**, *49*, 8154, https://doi.org/10.1007/S10853-014-8524-5.
[28] A. Amarjargal, M. Brunelli, G. Fortunato, F. Spano, C. S. Kim, R. M. Rossi, *J. Drug Deliv. Sci. Technol*. **2019**, *52*, 8, https://doi.org/10.1016/J.JDDST.2019.04.004.
[29] A. Morel, S. Domaschke, V. Urundolil Kumaran, D. Alexeev, A. Sadeghpour, S. N. Ramakrishna, S. J. Ferguson, R. M. Rossi, E. Mazza, A. E. Ehret, G. Fortunato, *Acta Biomater.* **2018**, *81*, 169, https://doi.org/10.1016/J.ACTBIO.2018.09.055.
[30] A. Morel, S. C. Oberle, S. Ulrich, G. Yazgan, F. Spano, S. J. Ferguson, G. Fortunato, R. M. Rossi, *Nanoscale* **2019**, *11*, 16788, https://doi.org/10.1039/C9NR04432A.
[31] A. Morel, A. G. Guex, F. Itel, S. Domaschke, A. E. Ehret, S. J. Ferguson, G. Fortunato, R. M. Rossi, *Mater. Sci. Eng. C* **2021**, *130*, 112427, https://doi.org/10.1016/J.MSEC.2021.112427.