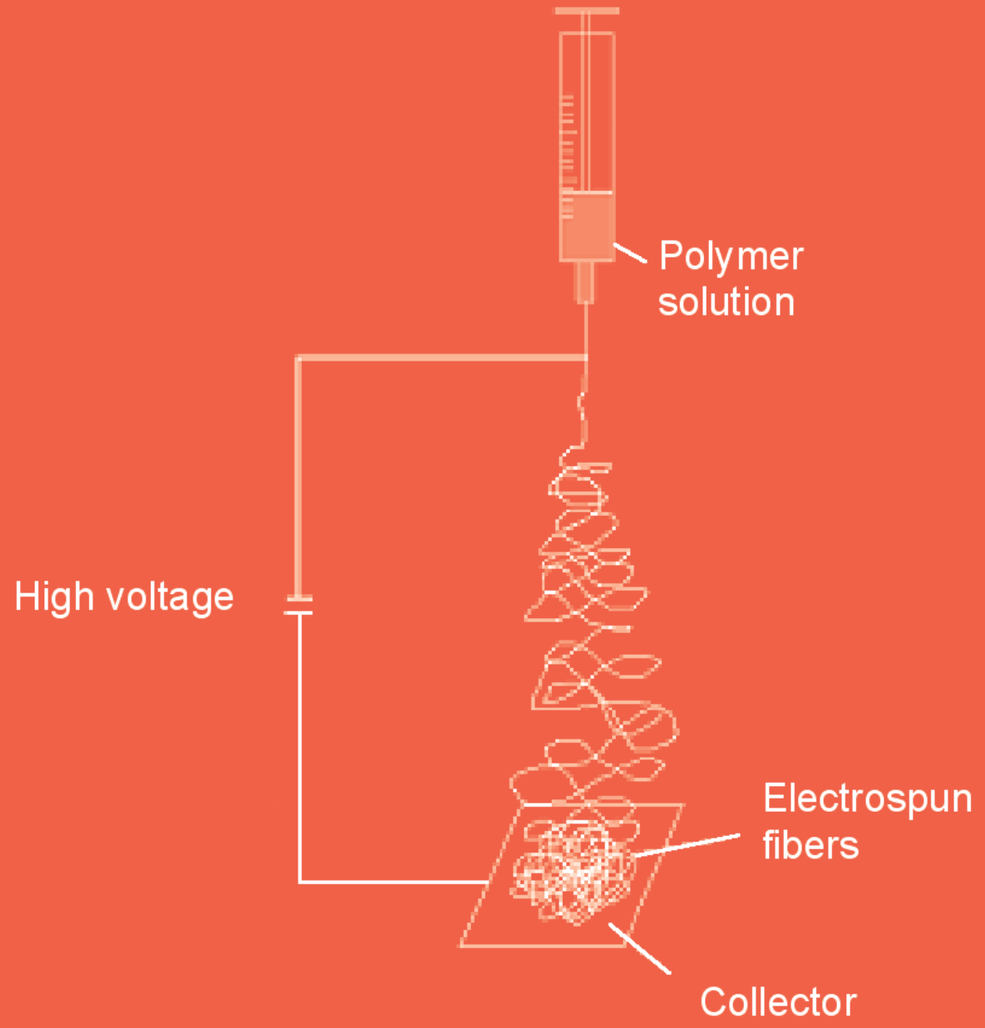

Figure 1: Illustration of equipment for electrospinning of nanofibers.

Electrospinning of nanofibers for biomedical applications

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Electrospinning of nanofibers

Electrospinning is a technique used to spin fibers with diameters less than 100nm up to micrometer level from a wide range of polymers. This electrostatic processing method uses a high-voltage electric field to form solid fibers from a polymeric fluid stream (solution or melt) delivered through a millimeter-scale nozzle. Reneker and co-workers have investigated the mechanism and theories of electrospinning in detail [1]. In Figure 1, an electrospinning set-up on laboratory scale is shown.

Nanofiber-based materials have several advantages compared to conventional textiles. In particular they represent a very large surface area; fibers with diameters around 100nm represent roughly 1000m^2/gram material. Other advantages are that the pore sizes of the materials are tunable, the surface functionality is possible to influence, various morphologies are achievable like nano tubes, etc. When used in applications, these advantages are utilized for adding technical surplus and uniqueness to products. Nanofibres are useful in the field of biomedicine, particularly in tissue engineering, wound healing and drug delivery applications.

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Tissue engineering

Artificial blood vessels, cartilage regeneration and artificial skin/skin models are all examples of interesting applications in the tissue engineering field. Difficulties in finding authentic replacements for, for example, small blood vessels push the search for artificial alternatives forward and the research in the area is extensive. Electrospun nanofibrous matrices are in this case of importance since they resemble the natural extra cellular matrix (ECM). The ECM is the fibrous network in the body along which the cells naturally grow and spread, hence a body-mimicking structure that imitates the ECM and can support cell growth is of great beneficence. The size range of electrospun nanofibers and the very large surface area of the constructs they form are two traits shared with natural ECM. Furthermore, the 3D structure of the electrospun scaffolds allows the cells to fully differentiate, in turn calling for a maintenance of normal biological activity of the cells that is not always possible in a 2D environment [2]. The flexibility of the electrospinning process is another great benefit, as different cells have different needs for optimal growth and by using electrospinning the morphology of both fibers and scaffolds can be easily varied and optimized. Also, a wide variety of materials can be electrospun and incorporation of particles and various agents, such as growth factors, is possible.

Nanofibers of poly(urethane urea) has been successfully electrospun and a detailed study has been published, involving fibroblast growth on the fibers [3]. The nanofibers are illustrated in the scanning electron microscopy (SEM) image shown in Figure 2a, which reveals a non-woven mat based on even fibers with a smooth impression. A bimodal fiber diameter distribution is noted in the image (Figure 2a), fiber diameters around 1000nm and around 100nm. In Figure 2b, the nanofiber web has been used as scaffold for fibroblast cell growth. A comparison with the pure nanofibers in Figure 2a, clearly shows that the fibroblasts have successfully adhered and spread on the scaffold material. A closer look at the image even allows interpretation about how the cells grow on the martial, which in this case seem to be by two mechanisms; the cells adhere to the surface of the fibers and attach mechanically to the scaffold by wrapping pseudopodia around the thin fibers.

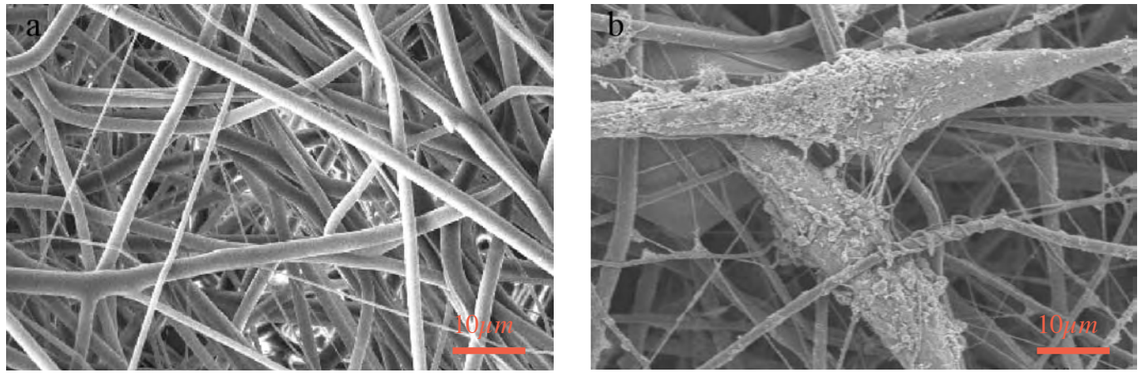


Figure 2: SEM-images of electrospun a) poly(urethane urea) nanofibers b) poly(urethane urea) nanofibers acted as scaffold for fibroblast cell growth.

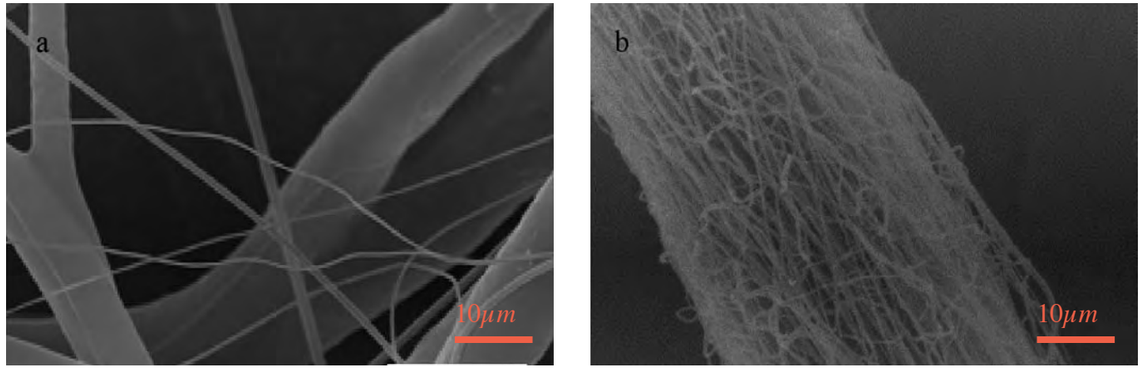
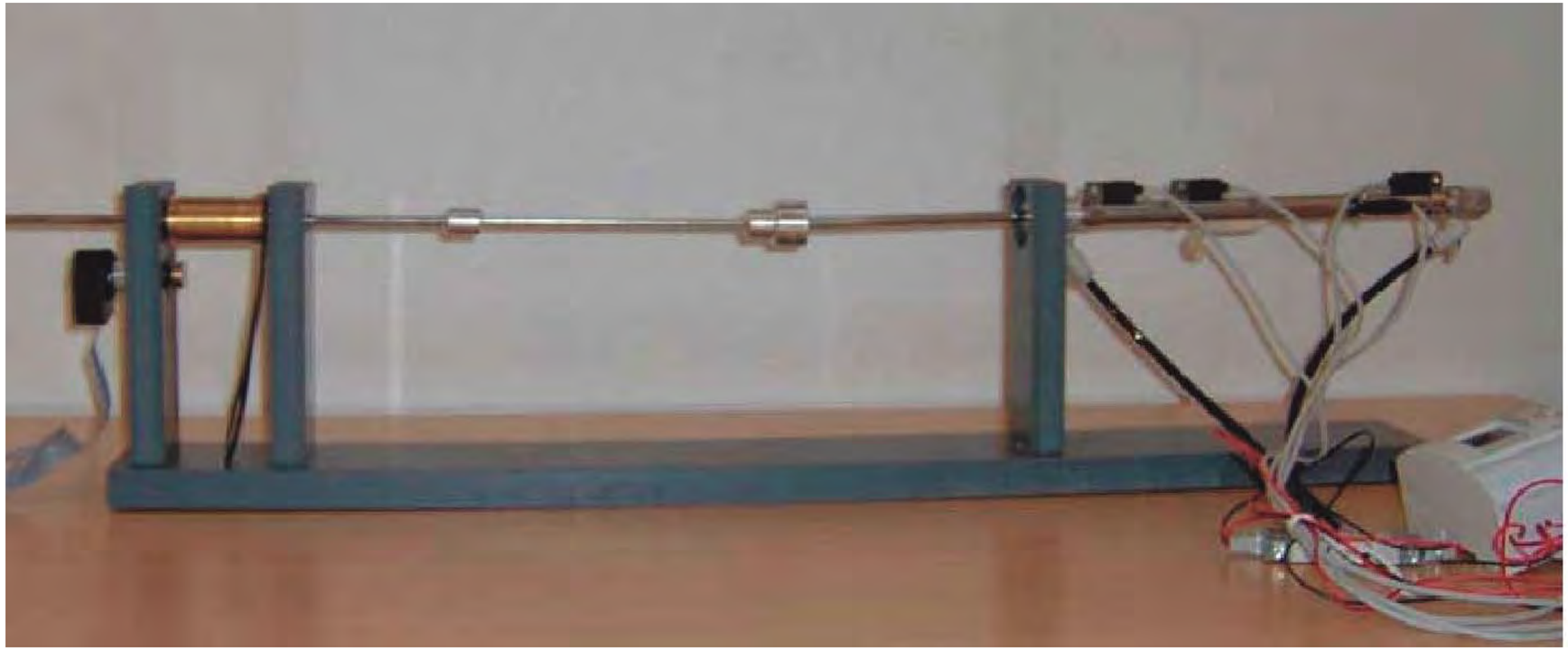


Figure 3: SEM-images of electrospun a) chitosan fibers b) polycaprolactone (PCL) fibers on micro fibers based on poly lactic acid (PLA).

IFP has during the last two years focused on possibilities to increase the porosity of nanofibrous scaffolds. The small pore size has so far been an obstacle in three-dimensional cell proliferation. Adequate cellular infiltration into the scaffold is crucial for development of a three-dimensional tissue construct, hence insufficient infiltration is a problem that must be solved before electrospun scaffolds can be utilized to their full potential. Several approaches are possible and trials have shown the potential in the approaches developed so far. In the selected SEM-images in Figure 3, some structures are shown, which allow for porosity and pore size manipulation by means of combination of fibres with different diameter scales (nano and micro).

A separate study has been done, presenting the developed method for electrospinning nanofibers on micro fibers (Figure 3b), that is currently prepared for publication. By electrospinning nanofibers onto single microfibers one ends up with long fibers containing the best of two worlds. The nanofibers are present to enhance cell adhesion and spreading although by collecting them on a microfiber they can easily be formed into any shape, size and, most importantly, any porosity. It is indeed a new and innovative way of creating highly porous scaffolds with a suitable combination of nano- and microfibers and thus, opens up for possibilities to create structures of desired morphologies.



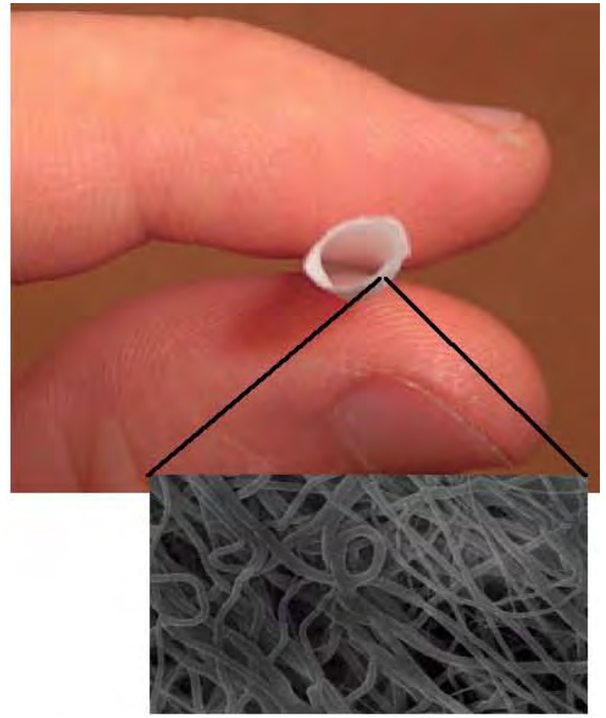


Figure 4: Equipment for tube production, an electrospun tube and a SEM-image of its microstructure.

IFP currently focuses on producing biosynthetic blood vessels, i.e. tubes, from electrospun biopolymer (gelatin and elastin) scaffolds with optimized porosity and mechanical properties. The latter is a pronounced bottleneck in the area today. The work is done in close collaboration with Professor Gatenholm at Chalmers, within the frames of the project *Biosynthetic Blood Vessels*, financed by Vetenskapsrådet/Stftelsen Strategisk Forskning/VINNOVA. In Figure 4, the equipment used for producing electrospun tubes is shown. The equipment has been developed within the frames of a Diploma work by Erik Borg, conducted at IFP and Chalmers, within the research group of Professor Gatenholm. Tubes based on biomaterials with elastic characteristics have been produced and the fibrous structure verified by SEM-microscopy (see Figure 4).

Wound care applications

There is a huge potential to use electrospun nanofibers in wound care applications. One of the main benefits is based on the possibilities with encapsulation of various agents (chemical substances like growth agents etc) in the nanofibers. If the “agent” dissolves in the solvent, together with the polymer, nanofibers with distribution of the “agent” similar to that in the solvent is feasible. Together with suitable degradation behaviour of the biopolymer matrix, unique wound healing applications can be designed.

In Figure 5, an SEM-image shows nanofibers with encapsulated, molecularly imprinted nanoparticles. The nanofibers show an appearance like a string of beads, since the diameter of the beads is slightly larger that that for the nanofibers.

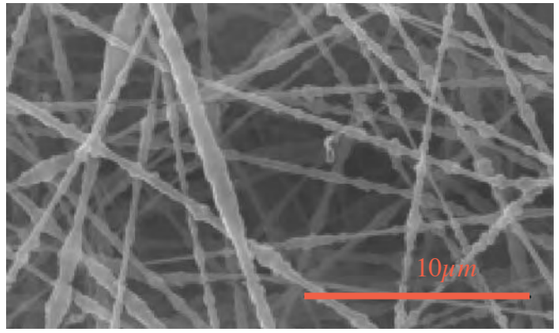


Figure 5: SEM-image of nanofibers based on poly(ethylene terephthalate) containing 5% Estradiol-molecularly imprinted nanoparticles [4].

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