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Electrospinning of functional materials for biomedicine and tissue engineering

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Published data on nanostructured materials prepared by electrospinning are analyzed and generalized. Particular attention is devoted to the design and properties of nanocomposite fibrous materials and methods for modification and functionalization of fibre surface. The prospects for the application of non-woven materials for biotissue engineering and for the development of smart materials are considered.
The bibliography includes 330 references.

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I. Introduction

Nanocomposite materials are widely used in various fields of science and technology.[1, 2] By modify the characteristic size and chemical compositions and volume fractions of the components, it is possible to vary the physical properties of materials over a broad range.[3 – 5] The most promising applications of these materials are related to the design of biomimetic scaffolds for tissue engineering and to design of smart clothes.

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Today, there are virtually no methods for treating diseases and injuries that would allow complete restoration of the functions of lost or damaged organs and tissues of living organisms. Tissue engineering is a new interdisciplinary area with the objective to use the fundamental knowledge and innovations of biology, medicine and technology for the design of 3D physiological substitutes that can restore and maintain the functions of tissues and organs.

The prospects of using nanofibrous matrices as tissue engineering scaffolds and the methods for preparing them have been surveyed in reviews.[6,7] Electrospinning is of particular interest among the methods for fabrication of these matrices as it is technologically easy and suitable for the preparation of continuous micro- and nanofibres on an industrial scale.[6,8] Owing to some features such as the large surface area to volume ratio and the possibility of surface modification and control of mechanical properties, nanofibres find extensive use for tissue engineering, targeted drug delivery, filtering devices and membranes, as sensing elements in sensors, *etc*.[9–12]

Most of review articles on electrospinning are devoted either to problems of control over the fibre surface morphology, structure and functions[13] or to electrospinning conditions for various synthetic and natural polymers.[14] Some reviews consider the use of fibres for tissue engineering and targeted drug delivery.[8,15] Electrospinning perfectly suits tissue engineering owing to the possibility to provide the living cells with a matrix environment that structurally, chemically and mechanically mimics the original extracellular matrix. The similarity of the physical structure of a fibre with the extracellular matrix is ensured by the nanometre diameter and the porous structure of fibres. Some publications discuss the strategies of fibre surface functionalization.[16,17]

Currently the processes for manufacture of smart materials are being actively developed. The crucial role in this area belongs to the selection of substances sensitive to external impacts. Such materials can be used both as a dispersion medium and the dispersed phase. They can be produced by the electrospinning technique. The manufacture of fibres sensitive to various impacts, in particular, endowing the fibres with pH-, thermo-, magneto- and photosensitive behaviour, and sensor applications for determination of various chemicals such as water, glucose, alcohols, proteins and so on, has been reported.[18] No less important is the development of methods for fibre characterization, specifically, studies of molecular configurations and electrophysical and mechanical properties as well as simulation of the electrospinning process, properties and geometry of the fibres.[19]

Analysis of modern periodicals through the last decade demonstrated that, despite quite a number of publications devoted to electrospinning, there are no papers that would systematically consider the investigation results related to the design of composite fibrous nanomaterials including detailed discussion of the nanofibre properties as functions of the electrospinning parameters, methods of surface modification and functionalization of fibres and the prospects for their use in both biotissue engineering and the design of smart materials. This review may fill this gap to an extent.

II. Electrospinning of ultrathin polymer fibres

Electrospinning is a process for production of micro- and nanofibres of infinite length from polymer solutions and melts under the action of electric field.[19]

Most of the methods for the manufacture of nanomaterials with rather high length-to-diameter ratio (nanorods, nanotubes, nanowhiskers) are based on the bottom-up principle according to which an item is assembled from smaller particles, molecules or atoms. Conversely, electrospinning implements the top-down principle where nanosized objects are produced by macroscopic processes.

The advantages of this method include a relatively simple and flexible manufacturing process, low cost and the possibility to obtain continuous ultrathin fibres from virtually any soluble polymer. A typical image of electrospun fibres recorded by a scanning electron microscope (SEM) is shown in Fig. 1. The electrospun fibres have a number of advantages, in particular, high surface area to volume ratio, controlled porosity and the possibility of preparing fibres of diverse shapes and sizes. Continuous and homogeneous electrospun nanofibres are widely employed in macroscopic systems.[19]

Historically, capillary electrospinning in which the continuous supply of the polymer solution is performed using a capillary was the first to be developed. A typical schematic diagram of the electrospinning setup is shown in Fig. 2. It consists of three principal parts — a high-voltage source, a spinning electrode with the spinning solution supply system and a collecting electrode. A constant voltage of 50–100 kV is applied to a capillary through which a polymer solution or melt is supplied by a dispenser micropump. Due to the action of electric forces, the polymer solution or melt is drawn into a thin jet. Upon evaporation of the volatile solvent or cooling of the melt, the jets are transformed into fibres, which move to a grounded or oppositely charged screen.

The fundamentals of the method were laid back in the early 20th century. The most important achievements in the electrospinning of polymer fibres were reported by I V Petryanov and N D Rozenblyum, who, under the supervision of N A Fuks, were the first in the USSR to

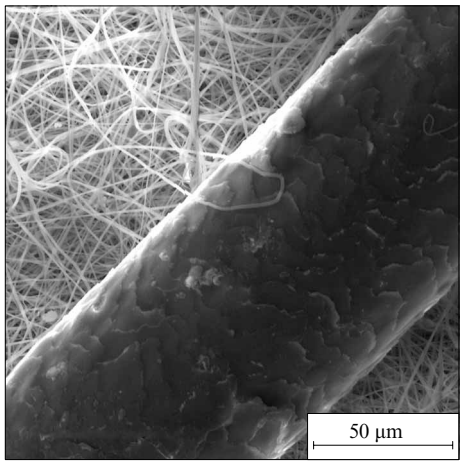


Figure 1. SEM image of polyamide nanofibres in comparison with a human hair.

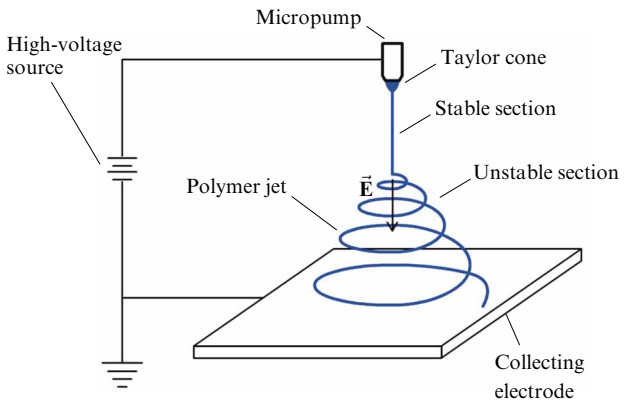


Figure 2. Schematic diagram of the capillary electrospinning setup depicting the stages of polymer jet movement.[20]

produce ultrathin polymer fibres by the electrocapillary method in 1938 and to organize, in the shortest time possible, the first industrial production of fibrous materials.[20]

Due to active development and commercialization of nanotechnologies, the interest in the method has markedly enhanced.[21] In the early 1990s, several research groups demonstrated the possibility of electrospinning of nanostructured non-woven materials from a number of synthetic and natural polymers. Since then, the number of publications related to electrospinning, one way or another, has annually increased,[22] and the range of applications is permanently extended. The growth of the number of publications dealing with electrospinning in the period from 2000 to 2012 is illustrated in Fig. 3.

A great contribution to the development of this area was made by the research team of the University of Akron (USA) headed by professor Reneker, engaged in thorough investigations of the details of electrospinning processes.[23,24] They demonstrated the possibility to prepare fibres of diameter ~30 nm based on various polymers (polybenzimidazole,[21] polystyrene,[25] styrene-butadiene-styrene triblock copolymer[26]) and also based on silk and DNA.[27,28]

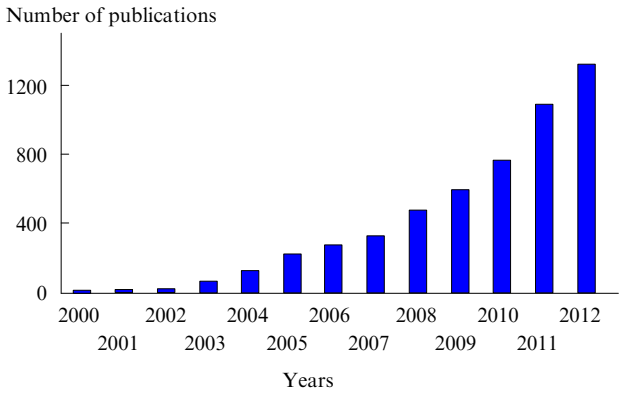


Figure 3. Variation of the number of publications dealing with electrospinning according to ScienceDirect data in the period from 2000 to 2012.

To date, there are more than 200 polymers, both synthetic and natural, that are known to possess fibre-forming properties and have been successfully tested in electrospinning.[29] Table 1 summarizes the polymers that are often electrospun and their applications.

Despite the fairly long history of the successful practical use of the electrospinning technique, theoretical description of the process has received little attention. However, with the advent of electrohydrodynamics, large progress has been achieved also in the related fields, in particular, in electrostatic atomization (electrospraying) of low-molecular-mass liquids. Several models for the formation and motion of a polymer jet in an electric field have been proposed; however, a unified theory of electrospinning has not yet been developed.

Electrospinning is a sophisticated process involving electrohydrodynamics of low-conductive non-Newtonian fluids and phase transformations — solvent evaporation and hardening of the polymer fibre. During electrospinning, the jet of the polymer solution (a mixture of the polymer and a volatile solvent) goes through several stages: appearance of the jet (Taylor cone), linear stationary flow, unstable motion and the final formation of a polymer fibre accompanied by deposition onto a substrate.

The electrohydrodynamic spraying of liquids in which a liquid having low electrical conductivity flows out of a dispensing nozzle that occurs under a constant high voltage and is sprayed into small drops due to the repulsion of like electric charges can be considered to be the predecessor of electrospinning. The electro- and hydrodynamics of charged jets have been studied in considerable detail.[73–76] The mechanism of jet formation from a drop of polymer solution has been described.[75,77] One-dimentional flow models for a steady-state jet were devised.[78,79] For unstable jets, discrete models have been proposed.[80–82]

The existence of a stable charged jet is a crucial condition for electrospinning to be possible. An approximate theoretical model for the conditions of existence of a steady-state jet has been developed. This model assumes that a Newtonian liquid with density ρ, viscosity η, relative dielectric permittivity ε, surface tension coefficient α and specific volume electrical conductivity γ flows at volumetric flow rate Q out of the lower end of a vertical capillary nozzle with external radius r_n into a space being under a uniform external electric field with the strength E.[83] It is assumed that after a certain maximum volume V_d has been reached, the liquid would be detached from the capillary at time intervals t_1, while the liquid bridge would be retained for some time,

$$t_1 = \frac{V_d}{Q} \tag{1}$$

The drops are considered to be spherical and the bridge is considered to be broken as the drop has displaced by the length equal to its radius r_d. In the equation of motion of the drop, the opposing electric and capillary forces are neglected, while the viscosity force is determined using the Stokes approximation

$$m\frac{dU}{dt} = mg - ar_n\eta U \tag{2}$$

$$U(0) = 0$$

Table 1. Polymers tested in electrospinning and their applications.

Polymer	Application	Ref.
Polyglycolide	tissue engineering scaffolds	30
Copolymer of lactic and glycolic acids	biomedicine, wound coatings	31, 32
Polycaprolactone	tissue engineering (osteosynthesis)	33
Poly(L-lactide)	cell scaffold	34
Polyurethane	non-woven wound coating, electret filters, protective clothes	35–37
Copolymer of ethylene and vinyl alcohol	non-woven tissue engineering scaffold, drug delivery	38, 39
Polystyrene	skin tissue engineering, enzymatic biotransformation	40–43
Syndiotactic polybuta-1,2-diene	tissue engineering	44
Fibrinogen	wound coatings	45
Copolymer of vinyl alcohol and cellulose acetate	biomaterials	46
Cellulose acetate	sorbing membranes	47
Polyvinyl alcohol	wound coatings	48–50
Silk fibroin, silk/polyethylene oxide	nanostructured tissue engineering scaffold	51
Silk	biomedical applications	52
Silk fibroin	nanostructured wound coatings	53
Silk/chitosan	wound coatings	54
Chitosan/polyethylene oxide	cell engineering scaffolds, targeted drug delivery, wound healing	55
Gelatin	wound healing scaffolds	56
Hyaluronic acid	medical implants	57
Cellulose	affine membranes	58
Gelatin/polyaniline	tissue engineering scaffolds	59
Collagen/chitosan	biomaterials	60
Polyamide	protective garment	19
Polybenzimidazole	protective garment, reinforced nanofibrous materials	19
Polycarbonates	protective garment, sensors, filters	19, 36, 61
Polyacrylonitrile	carbon nanofibres	62, 63
Polylactide	sensors, filters, drug delivery	64–66
Collagen–polyethylene oxide	haemostatic agent, wound healing, tissue engineering	67, 68
Polyaniline	conducting fibres	69–71
Polyvinylcarbazole	sensors, filters	64
Polyvinylpyrrolidone	antimicrobial agent	70
Polyamide 4–6	transparent composites	71, 72
Polyacrylonitrile/TiO_2	light sensitive conducting fibres	66

where m is the drop weight, U is the drop velocity, g is the acceleration of gravity and a is a constant of the order of π.

The lifetime of the bridge is given by

$$t_2 = \frac{r_d}{U} = \frac{a r_d r_n \eta}{mg} \tag{3}$$

It is assumed that when $t_1 = t_2$, the drops have no time to separate and a continuous steady-state jet is established.

Then, having composed the balance of forces at the lower face of the nozzle, including
electric

$$F_{el} = \frac{9}{16} E^2 r_d \tag{4}$$

gravitational

$$F_g = \frac{4}{3} \pi r_n^3 \rho g \tag{5}$$

and surface forces

$$F_{suf} = 2\pi\alpha r_n \tag{6}$$

the fulfillment of which corresponds to the detachment of the drop, we get the set of equations describing the desired conditions for the transition of a flow of drops into steady-state jet

$$\begin{cases} F_{el} + F_g = F_{suf} \\ t_1 = t_2 \end{cases} \tag{7}$$

By substituting Eqns (1)–(6) into set (7) and excluding r_d, one can derive the desired conditions that also hold without an electric field in the dimensionless criterion form

$$\frac{3\mathrm{Eu_n}}{2\mathrm{We_n}} = \left(\frac{\mathrm{Re_n}}{4\pi\alpha\mathrm{Fr_n}}\right)^{2/5} \sqrt{1 - 2\left(\frac{3}{4\pi}\right)^{6/5} \frac{a^{3/5}}{3\mathrm{Fr_n We_n}} \left(\frac{4\pi\mathrm{Fr_n}}{\mathrm{Re_n}}\right)^{3/5}} \tag{8}$$

where

$$\mathrm{Eu_n} = \frac{\pi^2 E^2 r_n^4}{4\rho Q^2}$$

$$\mathrm{We_n} = \frac{2\pi^2 \alpha r_n^3}{\rho Q^2}$$

$$\mathrm{Re_n} = \frac{2\pi Q}{\pi r_\mathrm{n} \eta}$$

$$\mathrm{Fr_n} = \frac{Q^2}{2\pi^2 r_\mathrm{n}^3 g}$$

are the Euler, Weber, Froude and Reynolds numbers, respectively.

Thus, this theoretical model takes into account not only the effect of the surface tension coefficients but also the effects of density and viscosity of the liquid, specific volume electrical conductivity and the relative dielectric permittivity.

It was suggested that the pressure balance on the lower surface of the charged spherical drop that has not yet detached from the capillary is violated.[84]

$$P_\mathrm{suf} = P_\mathrm{el} + P_\mathrm{g} \tag{9}$$

In this case, the proposed model describes the ability of electric forces that oppose the capillary forces to form a unified stationary liquid surface comprising a drop not yet detached from the nozzle and the steady-state jet flowing from the drop.

The key drawback of most models is that they are one-dimensional, being based on the assumption of the invariable distribution of properties of the liquid and flow parameters across the the jet cross-section. Nevertheless, some publications describe three-dimensional flow models for a stable axially symmetrical jet in an electrostatic field that take into account mass transfer caused by solvent evaporation from the surfaces of thin jets, which may result in a substantial non-linearity of the rheological properties of the liquid across the jet and the flow parameters.[85]

Reneker *et al.*[86] modelled an unstable jet in an electric field by a system of charged points connected by viscoelastic interactions (Fig. 4).

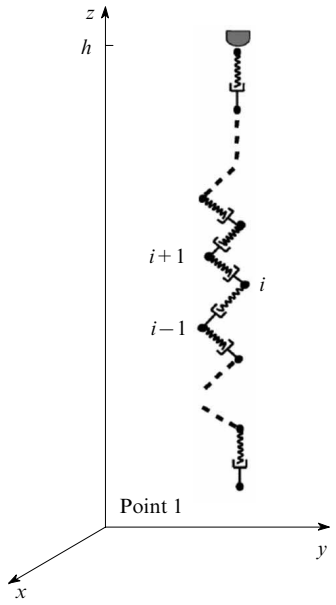


Figure 4. Unstable jet in an electric field presented as a set of charged point particles.[86]

The following forces act on each point (bead) of the model: viscoelastic force ($\vec{F}_\mathrm{ve}$), Coulomb force ($\vec{F}_\mathrm{c}$), external electric field ($\vec{F}_\mathrm{el}$), surface tension ($\vec{F}_\mathrm{suf}$) and gravitational force ($\vec{F}_\mathrm{g}$). The principal equation of dynamics of this system is written in the following way:

$$m\frac{\mathrm{d}^2\vec{r}}{\mathrm{d}t^2} = \vec{F}_\mathrm{ve} + \vec{F}_\mathrm{c} + \vec{F}_\mathrm{el} + \vec{F}_\mathrm{suf} + \vec{F}_\mathrm{g} \tag{10}$$

The following final expression was proposed as the principal equation of dynamics for the *i*th bead of the system:

$$m\frac{\mathrm{d}^2\vec{r}_i}{\mathrm{d}t^2} = \sum_{\substack{j=1,N \\ j\neq 1}} \frac{e}{R_{ij}^3}(\vec{r}_i - \vec{r}_j) - e\frac{V_0}{h}\vec{k} + \frac{\pi a_{ui}^2 \sigma_{ui}}{l_{ui}}(\vec{r}_{i+1} - \vec{r}_i) - \tag{11}$$

$$-\frac{\pi a_{di}^2 \sigma_{di}}{l_{di}}(\vec{r}_i - \vec{r}_{i-1}) - \frac{\alpha\pi a_{av}^2 k_i}{(x_i^2 + y_i^2)^{1/2}}(\vec{i}x_i + \vec{j}y_i)$$

where

$$\vec{r}_i = \vec{i}x_i + \vec{j}y_i + \vec{k}z_i$$

is the radius vector of bead i; $\vec{r}_j$ is the radius vector of bead j; e is the charge of the bead; R_{ij} is the distance between beads i and j; V_0 is the voltage between the spinning electrode and the substrate; h is the distance between the spinning electrode and the substrate; a_{ui} is the radius of the segment between beads i and $i+1$; a_{di} is the radius of the segment between beads i and $i-1$; σ_{ui} is the voltage between beads i and $i+1$; σ_{di} is the voltage between beads i and $i-1$; $\mathrm{l_{ui}}$ is the length of the segment between beads i and $i+1$; l_{di} is the length of the segment between beads i and $i-1$; α is the surface tension coefficient, k_i is the curvature of the circle that passes through bead i and neighbouring beads $i+1$ and $i-1$; and a_{av} is the average radius of the segments between the upper and lower beads.

The mathematical model (11) was used to study the process of jet deposition on the substrate depending on the configuration of the collecting electrodes and electric field parameters.[87] It is noteworthy that this model does not take into account the intense solvent evaporation from the jet surface. The modified model taking account for the effect of evaporation on the behaviour of the unstable jet and polymer diffusion inside the jet has been reported.[88]

These models were developed to study the flow of the polymer solution jet at early stages of jet formation and during unstable motion. The researchers studied the effect of rheological parameters of polymer solutions and process parameters on the character of motion and the structure of polymer jets in an electric field.

The modelling of the final stage of electrospinning in which the liquid polymer jet is converted to an air-dried thread deposited on the substrate as randomly oriented or partially ordered fibres has not been considered as yet. Now there is no complete mathematical model for electrospinning that would allow one to predict the final diameter and the properties of the obtained fibre based on the initial process parameters.

III. Electrospinning process parameters suitable for the control over the properties of fibres and non-woven materials based on them

III.1. Process parameters affecting the formation of fibres

The broad diversity of polymers and solvents used for electrospinning hampers determination of 'gold standard' parameters that would be suitable for any process (Fig. 5).

In the general case, for an arbitrary polymer–solvent system, a change in the electrospinning conditions may result in the formation of fibres with substantially different characteristics.[8]

The essential factor for preparing nano-sized fibres is the electric field strength during spinning. This follows not only from the experimental results but also from Eqn (11) presented above. For each spinning solution, there is the optimal range of variation of the field strength. The field strength also affects the diameter and morphology of the fibres by acting on the flow velocity of the polymer jet: the higher the field strength, the higher the flow velocity.[89] For high field strengths, beaded morphology tends to appear on the fibre.[90]

Yet another no less important factor of capillary electrospinning that affects not only the morphology but also the porosity of the fibrous material is the velocity of the polymer solution stream. As the flow velocity grows, the diameter and the pore size of the fibre increase.[42] When the velocity of the polymer solution is too high, the fibre cannot be completely dried before the collector is reached, which may give rise to the beaded morphology.[8]

The appearance of beaded morphology induced by viscoelastic effects in insufficiently dried polymer jets is also possible in the case where the distance between the capillary and the collector is too short.[42] The increase in this distance would result in a decrease in the fibre diameter, although, most often, this is not the limiting factors compared with the effects of variation of other parameters.[22]

The concentration of the polymer in the spinning solution is also a very important parameter determining the possibility of fibre formation. If the solution is too dilute, the polymer jet is disintegrated into drops without reaching the collector, due to high surface tension. A too high concentration of the polymer implies high viscosity of the solution, and this may prevent the formation of the thin polymer jet. Each fibre-forming polymer has an optimal concentration range in which the fibre can be successfully spun. A polymer concentration on the high side of the optimal range leads to higher fibre diameters.[8]

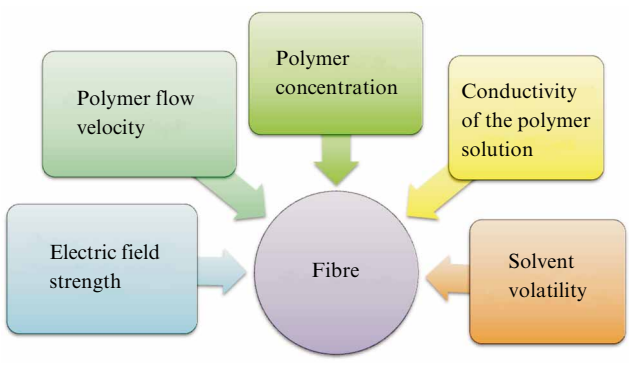


Figure 5. Process parameters affecting the electrospinning.

Table 2. Electrospinning parameters affecting the properties of the obtained fibres.[8]

Change in the electrospinning parameters	Change in the properties of fibres
Increase in the applied stress	fibre diameter decreases and then non-monotonically increases
Increase in the polymer volume flow rate	fibre diameter increases (if the flow velocity is too high, bead morphology is observed)
Increase in the distance between the capillary and the collector	fibre diameter decreases (if the distance between the capillary and the collector is too small, beads may form on the fibre)
Increase in the polymer concentration (viscosity)	fibre diameter increases (if the viscosity is too high fibre formation stops)
Increase in the electrical conductivity of the solution	fibre diameter decreases (if the electrical conductivity is too high fibre formation stops)
Increase in the saturated vapour pressure of the solvent	fibre diameter decreases, the fibre surface becomes porous

The solution conductivity also affects the fibre diameter. Highly conductive solutions are very unstable in strong electric fields, and this gives rise to fibres with substantial deviations from the mean diameter. Materials with monodisperse diameter distribution of fibres are usually produced from low-conductivity solutions.[91]

The volatility of the solvent determines the possibility of electrospinning of air-dry fibres from the solution and also affects the fibre porosity. Volatile solvents are preferred as the whole amount of the solvent should be evaporated on the way from the capillary to the collector to give dry fibres with homogeneous morphology. When highly volatile solvents are used, the fibres are saturated by the vapour from the adjoining atmosphere, which promotes the formation of a porous surface.[8]

The parameters that affect the properties of the materials are summarized in Table 2.

III.2. Process parameters affecting the mechanical properties of nanofibrous materials

Mechanical properties are highly important for applications of materials manufactured by the electrospinning technique. Studies of the influence of various polymer mixtures and parameters characterizing the manufacturing process on the mechanical properties of the fibres have been reported.[92–95] It was shown[96] that the mechanical properties of non-woven electrospun materials depend appreciably on the orientation of fibres and bonds between them. For example, the tensile strength of polycaprolactone fibres considerably increases when the fibre diameter is < 700 nm.[97] The decrease in the diameter is accompanied by an increase in the degree of molecular orientation, and this accounts for

the increase in the tensile strength for the fibres of smaller diameter.

By electrospinning, it is possible to incorporate disperse fillers into the nanofibres, in particular, inorganic nanoparticles, ordered carbon structures or dyes. The content of the filler substantially affects the mechanical properties of these composite fibres. For instance, the effect of the volume fraction of hydroxyapatite on the mechanical properties of composite fibres based on the poly(D,L-lactide-co-ε-caprolactone) copolymer has been studied.[98] It was shown that the Young's modulus of the composites increases, while the ultimate elongation decreases following an increase in the content of hydroxyapatite (Table 3). Apparently, underestimation of the parameters characterizing the mechanical properties (such as Young's modulus) is due to neglecting by the researchers cited [98] of the fact that such material is not a continuous medium even at the submicrometre level; therefore, the cross-sections of the fibrous materials used to calculate stresses did not correspond to real values (were overestimated).

Table 3. Mechanical properties of composite fibres based on poly(D,L-lactide-co-ε-caprolactone) with hydroxyapatite inclusions.[98]

Hydroxyapatite: poly(D,L-lactide-co-ε-caprolactone) mass ratio	Young's modulus /MPa	Ultimate elongation (%)
0 : 100	1.679 ± 0.503	396.0 ± 108.5
20 : 80	2.323 ± 0.347	389.2 ± 29.1
40 : 60	2.894 ± 0.292	255.0 ± 18.8
80 : 20	3.857 ± 0.790	60.3 ± 12.4

The effect of the concentration of multiwalled carbon nanotubes on the mechanical properties of polyvinyl alcohol nanofibres has been studied.[99] The tensile yield strength of the composite based on polyvinyl alcohol containing only 1 mass % of MWCNTs increased by ~15% (from 105 to 133 MPa) and the tensile modulus increased by ~2% (from 175 to 178 MPa) with respect to analogous characteristics of polyvinyl alcohol nanofibres. Moreover, if the content of the tubes increases from 1 mass % to 2.5 mass %, the tensile modulus increases by 5% (from 175 to 184 MPa). However, on further increase in the content of the filler (carbon nanotubes), both the tensile stress and the tensile modulus decrease. The load distribution was found to depend on the shearing stress at the interface between the filler and the polymer matrix.[100, 101]

There exist three key mechanisms of load transfer from the isolating polymer matrix to the nanotube filler:

— micromechanical interaction, which is difficult to implement for such composites due to the atomically smooth surface of carbon nanotubes;

— chemical bonds between the nanotube and the matrix; it was shown that the shear pressure at the interface can increase due to these bonds by ~50 MPa;[102]

— weak van der Waals interaction between the filler (tubes) and the polymer matrix.

The initial increase in the tensile yield strength and the tensile modulus (for example, for composites containing 1 mass % and 2.5 mass % of the filler) is attributed to the high degree of orientation of the filler in nanofibres. On further increase in the concentration of the filler in nanofibres (up to 5% and 7.5%), respectively, the nanotubes are agglomerated, and the degree of anisotropy of the fibres diminishes.

The mechanical properties of the fibres depend on such an important process parameter as the rotation speed of the mobile collecting electrode. As the rotation speed increases, the prepared polycaprolactone fibres are more oriented within the non-woven fabric.[103] It was shown [103] that an increase in the rotation speed of the collector substantially affects the mechanical properties of both individual nanofibres and bulk fibrous mashes. The Young's modulus of single fibres decreases following increase in the rotation speed; the authors attributed this to the decrease in the degree of ordering inside a single fibre. However, owing to the increase of the fibre ordering inside the material, which occurs at high rotation speeds, the ultimate tensile strength and the tensile modulus of the scaffolds along the fibre alignment increase. Thus the maximum value of the ultimate tensile strength of the material increased from 2.21 ± 0.23 MPa for the collector rotation speed of 0 rpm to 9.58 ± 0.71 MPa for the rotation speed of 6000 rpm. Similarly, the tensile modulus of the material increased from 6.12 ± 0.80 MPa for the rotation speed of 0 rpm to 33.20 ± 1.98 MPa at a rotation speed of 6000 rpm.

Thus, it was shown that owing to ordering of fibres upon rotation of the collector, the mechanical characteristics of single fibres diminish but, at the same time, the mechanical properties of the non-woven fabric as a whole are improved as a result of fibre alignment.[103]

IV. Modification of the fibre surface

For biomedical applications of nanofibres, the fibre surface is preliminarily modified by various molecules and ligands that are recognized by cells of living organisms. In this way, fibres may acquire biomimetic properties to provide contact with cells and tissues. Below we consider various methods for immobilization of biologically active molecules on the surface of polymer nanofibres.

It is noteworthy that synthetic polymers are more easily electrospun and form fibres with more controlled morphology than natural polymers. The electrospinning of water-soluble natural polymers is often associated with additional difficulties, as fibres based on them are mechanically unstable and can degrade under conditions of treatment.[104, 105] Most natural polymers that perform unique biological functions can be immobilized on the surface of nanofibres of synthetic polymers. Electrospinning can be used to incorporate various hydrophobic and hydrophilic therapeutic agents into the bulk of nano-sized fibres. For example, nanofibrous materials based on a biodegradable polymer containing the hydrophobic anticancer agent paclitaxel were prepared.[106]

The hydrophilic agents including, in particular, proteins and nucleic acids, can be chemically (covalently) and physically immobilized on a modified surface of nanofibres for modulation of cell processes. The scaffold nanofibres have nanoporous structure with a high specific surface area, which are the ideal conditions for effective encapsulation and release of biologically active compounds.[107] The charts of main methods for the surface modification of synthetic polymer nanofibres to be used in tissue engineering and for targeted drug delivery are presented in Fig. 6. They include:

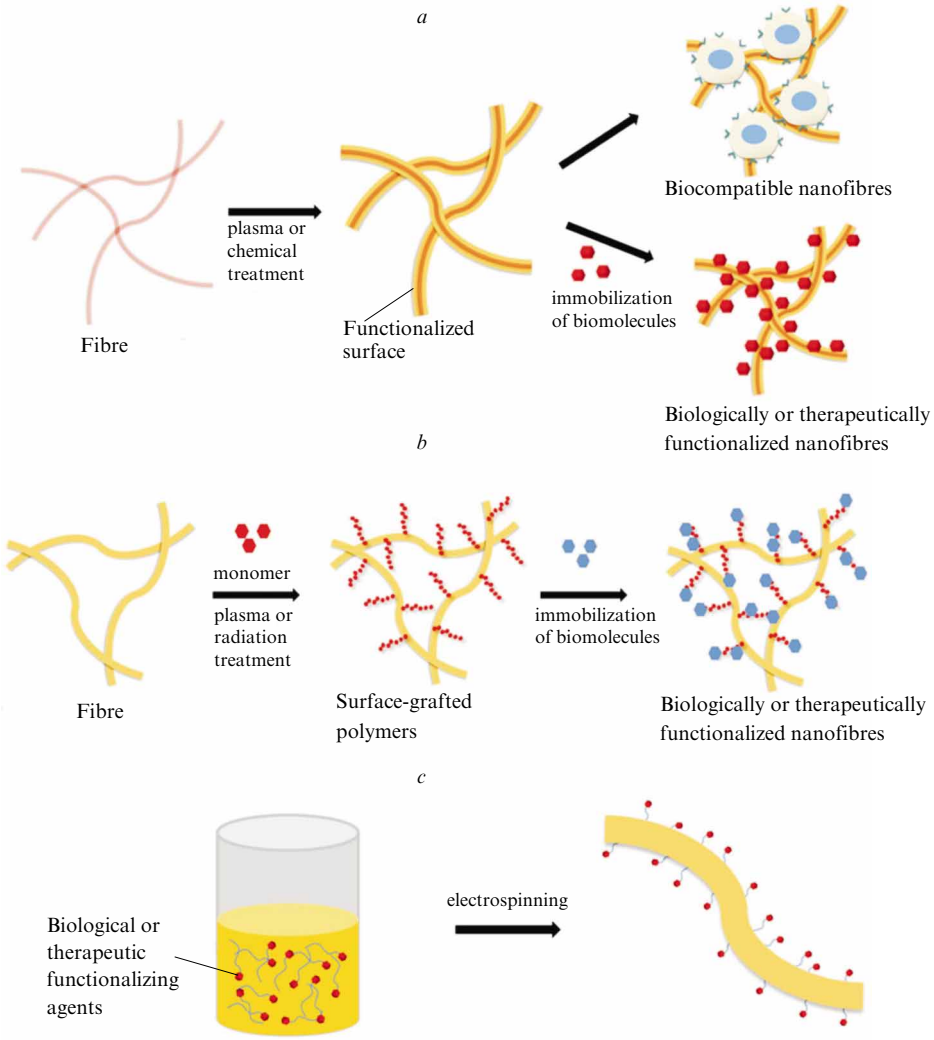


Figure 6. Approaches to surface modification of fibres.[108]
(*a*) Formation of surface functional groups upon plasma or chemical treatment of the fibre, (*b*) graft polymerization on the fibre surface, (*c*) co-electrospinning.

— plasma or chemical treatment of fibres to form surface functional groups;
— graft polymerization on the fibre surface;
— co-electrospinning of the polymer solution and the solution containing functional molecules.[108]

IV.1. Plasma treatment

The plasma treatment of polymeric substrates is usually employed to control adhesion to the surface and the wetting properties by changing the chemical composition of the surface.[17,109,110] By appropriate choice of the plasma source (oxygen, ammonia, air), various functional groups can be formed (for example, carboxy or amino groups) on the surface of the target for improving the biocompatibility or for the subsequent covalent immobilization of various biologically active molecules.[111–114]

Various protein components of the extracellular matrix such as collagen, laminin and fibronectin can be immobilized on the surface after plasma treatment to increase cell adhesion and proliferation.[115–118] Treatment with air or argon plasma is widely used to modify the surfaces of many biomaterials, as this sharply increases the hydrophilicity and simultaneously removes the undesirable surface impurities.[119–121]

IV.2. Chemical modification

The partial surface hydrolysis of biodegradable aliphatic polyester films in acidic or alkaline media is widely used to change the surface wettability or to create other functional possibilities.[122–124] This approach is based on the cleavage of ester bonds of surface macromolecules, resulting in the formation of carboxy and hydroxy groups on the fibre surface, and, consequently, markedly increasing the solubility of the polymer fragments in water. Chemical etching methods are more flexible than plasma treatment (the latter cannot efficiently modify deep-lying layers due to limited penetration of plasma into nanopores).[125]

In the case of hydrolysis of biodegradable polymer nanofibres, special attention should be devoted to process parameters such as duration of the hydrolysis and the

concentration of hydrolyzing agents, which are important for the optimal selection of the surface functional groups with only a minor change in the bulk properties of the fibre.[125] For example, surface-mineralized nanofibres based on polylactic acid were prepared by treatment with sodium hydroxide for hydroxyapatite mineralization[126] (carboxy groups chelate calcium ions, which initiates the surface nucleation and growth of the crystal phase).

IV.3. Surface graft polymerization

Virtually all types of synthetic biodegradable polymers retain the hydrophobic nature of the surface; therefore, hydrophilic modification is needed for the desired cell-mediated response. Surface polymerization is used not only to impart hydrophilicity to the surface but also to introduce surface functional groups for covalent immobilization of biologically active molecules to enhance cell adhesion, proliferation and differentiation.[127–130]

Surface polymerization is often started from plasma treatment or UV irradiation in order to generate free radicals. For example, polyethylene terephthalate nanofibres were modified by polymethacrylic acid *via* graft polymerization under mild conditions without structural damage in the bulk phase.[131] The carboxylic acid fragments formed on the surface were then conjugated with gelatin. It was shown that the surface density of carboxy groups increases with increase in the reaction time and concentration of the monomer. For the antibacterial application, the surface of the polyurethane nanofibres was modified by poly(4-vinyl-*N*-hexylpyridinium) bromide.[132] The antibacterial efficiency of the modified fibre with respect to *Staphylococcus aureus* and *Escherichia coli* was 99.999% and 99.9%, respectively, after a four-hour contact, which attests to very high antibacterial action.

IV.4. Electrospinning of polymers with bioactive components

The above methods for altering the surface properties are meant for modification of fibres prepared beforehand. However, nanoparticles and functional polymer segments can also be placed on the surface of nanofibres by means of co-electrospinning.[133–135] For example, composite fibres containing hydroxyapatite were obtained by electrospinning of a mixture of a solution of polylactic acid and hydroxyapatite nanocrystals, which diminished the degradation (with respect to that for neat polylactic acid fibre) owing to the reaction between the ester groups of the acid and calcium ions as counter-ions.[136]

V. Immobilization of bioactive molecules on the fibre surface

To date, methods providing prolonged release of medicines through controlled desorption from the nanofibre surface have been developed. These methods are demanded, for example, for preventing bacterial infections during the first several hours after the surgery.[137]

In the case of encapsulation of biomolecules into the nanofibre bulk by co-electrospinning with the polymers, their activity can substantially decrease. In addition, it is very difficult to obtain a homogeneous solution of so large charged macromolecules in the spinning solution. The biologically active charged macromolecules are adsorbed on the surface of modified nanofibres *via* specific and non-specific interactions.

V.1. Physical adsorption

Physical adsorption is the simplest method for immobilization of a substance on the surface of the nanofibre network (Fig. 7). As a rule, the surface adsorption can be driven by electrostatic interactions, hydrogen bonds, hydrophobic interactions and van-der-Waals forces.[138]

As a typical example, consider the specific interactions of heparin and growth factors.[139–142] Heparin, a sulfated glycosaminoglycan, can specifically bind to various growth factors such as fibroblast growth factor (FGF), vascular endothelial growth factor (VEGF), heparin-binding epidermal growth factor (HBEGF) and transforming growth factor β (TGF-β), which ensures retention of their biological activity. Attachment of growth factors to heparin molecules immobilized on the fibre surface is a highly efficient method for local growth factor delivery.[143, 144] Low-molecular-mass heparin was embedded in the fibres based on polyethylene oxide or copolymer of glycolic and lactic acids. Thus, these surface-functionalized matrices can be used as the means for delivery of growth factors to stimulate local angiogenesis.

Nanofibres with nanoparticles adsorbed on the surface are used in various fields — in electronics, catalysis, sensing elements and sensor devices.[145–148] Nanostructures of this type can be constructed using therapeutic or biological functional nanoparticles (*e.g.*, silver or hydroxyapatite nanoparticles).[149]

Of special note is layer-by-layer adsorption of polyelectrolytes as a versatile method for surface modification, which can be used to manufacture multilayer coatings with controlled thickness ranging from several nanometres to several micrometres.[150–154] The method comprises successive (layer after layer) adsorption of polyanions and polycations on a charged substrate surface, giving rise to a multilayer coating.[155] This method is attractive owing to its easy implementation, universality (no dependence on the type of the chosen substrate) and the possibility of using

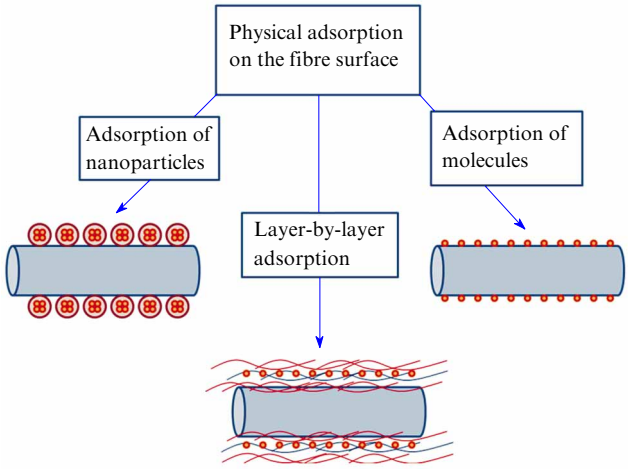


Figure 7. Diagram illustrating the methods of physical adsorption of biomolecules on the fibre surface including molecular adsorption of biomolecules on the fibre, adsorption of nanoparticles with encapsulated biomolecules and layer-by-layer method in which biomolecules are embedded into the multilayer coating on the fibre surface.

diverse components to form the coating. Other types of intermolecular interactions (hydrogen bonds, metal–ligand complex formation, covalent bonds, hydrophobic interactions, molecular recognition) can also be involved in the layer-by-layer adsorption process.[156]

Apart from the advantages noted above, one more important benefit of this method when used for immobilization of biologically active molecules on the surface of fibrous materials is the absence of chemical interaction that can lead to partial loss of activity. Multilayer coatings based on polyelectrolytes were deposited on the surface of preformed polystyrene fibres,[157] in which some of the surface groups were sulfonated and, hence, negatively charged. It was argued that modification of the fibre surface with synthetic (polyallylamine hydrochloride, sodium polystyrenesulfonate) and natural (DNA) polyelectrolytes can serve as the base for the design of non-woven materials that release encapsulated drugs for biomedical applications. Synthetic fibres coated by polyelectrolytes and sensitive to various external treatment are promising for the design of drug delivery systems in which the release of the agent is initiated by this type of treatment.

V.2. Chemical immobilization

As applied to tissue engineering, chemical immobilization of biologically active molecules on the surface of nanofibres should be preferred over physical adsorption, as the immobilized molecules are attached to the nanofibres by covalent bonds. Nevertheless, it should be noted that there is a risk of partial inactivation of immobilized molecules because they may be chemically modified. Primary amino and carboxy groups are used most widely for immobilization of biologically active molecules on the nanofibre surface. For example, after activation of carboxy groups by 3-(3-dimethylaminopropyl)-1-ethylcarbodiimide and *N*-hydroxysuccinimide, nanofibres were conjugated with the primary amino groups of bioactive molecules.[113, 158] The carboxy groups on the surface of polyacrylic acid nanofibres were used for conjugation with collagen.[159] The fibres modified by acrylic acid were conjugated with amino groups for the preparation of aminated nanofibres.[160]

The carboxy groups of the monomeric units of acrylic acid react with the amino groups of lipase; as a result, lipase demonstrated a decrease in the enzymatic activity with respect to the native lipase. Direct covalent binding of bioactive molecules to the nanofibre surface imposes some limitations on the cell adhesion and proliferation: cells cannot easily recognize these biological ligands because immobilized ligands are not entirely exposed on the surface but are partially submerged into the fibre structure. In order to enhance the cell recognition, hydrophilic linkers are introduced between bioactive molecules and nanofibres. Polyethylene glycol is often used as the hydrophilic linker; it is chemically conjugated with various hydrophobic polymer segments for further electrospinning.[161, 162] Chitosan is also suitable as a hydrophilic linker (owing to the presence of amino groups); it is subject to electrospinning for chemical immobilization of biologically active molecules on the surface of the chitosan fibre.[163] The surface functionalization based on co-electrospinning of amphiphilic diblock copolymers has several advantages. Indeed, upon enzyme immobilization directly on nanofibres, without the use of a polyethylene glycol spacer, the initial enzyme activity is not retained. For example, lipase immobilized on a nanofibre modified with acrylic acid showed an activity decrease of up to 37.6%.[164]

The above-described methods for modification of the fibre surface do not exhaust all of the options for the control of physicochemical properties of non-woven materials. An alternative approach is to change both the surface and bulk properties of the material, which can be achieved by introducing inorganic additives or by the selection of the polymer matrix, not only enabling a targeted change in the physicochemical properties of the material but also providing its sensitivity to external action, which can be utilized to design sensor systems.

VI. Fibres sensitive to external action

The sensitivity of a sensor is determined by diffusion and decreases with an increase in the thickness of the sensing element.[165] For geometrical reasons, fibres with a submicrometre diameter and rather high surface area to volume ratio (which stimulates the transfer of the stimulated signal) can provide the basis for fast-response materials. Furthermore, high porosity of fibres is important to enhance the mass transfer, for example, the transfer of ions and chemicals.[166]

VI.1. pH-Sensitive fibres

Polymers sensitive to the pH of the medium draw researchers' attention in regard to the controlled drug delivery, as the release of substances can be regulated by varying the pH.[167] As a rule, this feature is inherent in polymers containing carboxy or amino groups, as pH variation results in protonation or deprotonation and related changes in the hydrophilicity of the macromolecules. For example, polymers formed by acid-labile bonds (such as acetal groups) stimulate drug release at low pH. Cao *et al.*[165] demonstrated the possibility of preparing pH-sensitive fibres of styrene–maleic anhydride copolymer, which were subsequently spatially cross-linked in the presence of diethylene glycol to afford hydrogel nanofibres. As compared with classical hydrogels, these fibres were characterized by higher mechanical strength and pH-dependent swelling upon immersion into water.

Qi *et al.*[168] described pH-sensitive electrospun fibres containing ester groups suitable for drug release in weakly acidic medium. These fibres are stable at pH 7.4 but degrade at lower pH (5.6 and 4.0), which accelerates the release of encapsulated paracetamol (used as the model drug). It was shown[169] that the introduction of pH-sensitive acetal groups, which are hydrolyzed in acidic medium, into the poly(D,L-lactide)polyethylene glycol backbone, accelerates the release of paracetamol from the fibres of this coopolymer.

VI.2. Thermally sensitive fibres

Thermally sensitive polymers are promising for the design of sensors and systems for controlled delivery of biologically active compounds.[170] Thermally sensitive poly(*N*-isopropylacrylamide) with a lower critical solution temperature in the range of 31–35 °C has been vigorously investigated over the last 30 years.

In an aqueous solution of poly(*N*-isopropylacrylamide), a sharp reversible phase transition is known to occur upon a temperature change: at $T < 37$ °C, the polymer is readily soluble in water, while at $T > 37$ °C, it becomes insoluble

and precipitates. It is noteworthy that the rate of swelling of nanofibres based on this polymer is an order of magnitude higher than that of bulk gels due to great surface area and high porosity, which promote water diffusion. The lower critical solution temperature of the polymers can be changed by varying the length of the alkyl chain of hydrophobic monomers. This can be utilized for the development of thermally sensitive nanofibres. By electrospinning,[171] fibrous porous membranes based on copolymers of poly(*N*-isopropylacrylamide) with acrylic acid or hydroxyethyl methacrylate were produced and the thermal sensitivity of these materials was studied. It was noted that ionization of the carboxy groups of polyacrylic acid substantially accelerates the swelling and compression of the fibres at temperatures below and above the phase transition temperature, respectively.[171]

VI.3. Fluorescent fibres

As noted above, nanofibres with great surface area to volume ratio are the best candidates to be used as chemical sensors (the sensor sensitivity is believed to be correlated with this ratio). As compared with thin films, the surface area of submicrometre fibres can be 1–2 orders of magnitude higher.[172] Wang *et al.*[173] reported for the first time the application of thin fibres for the optical probing of metal ions and 2,4-dinitrotoluene. It was shown that in the presence of Fe^{3+}, Hg^{2+} or 2,4-dinitrotoluene, the fluorescence of the copolymer of polyacrylic acid with poly(pyrenemethanol), which was used as the matrix for electrospinning, is efficiently quenched, the fluorescence intensity being inversely proportional to the analyte concentration.

Membranes based on cellulose acetate nanofibres surface-modified by the fluorescence probe, poly[2-(3-thienyl)ethanolbutoxycarbonylmethylurethane], have been created.[174] The fibre diameter was varied from 100 to 400 nm; fluorescence quenching was observed in the presence of ppb amounts of an electron acceptor (methyl viologen) or donor (cytochrome c). The results demonstrate the importance of a high surface area to volume ratio, owing to which submicrometre fibres can function as highly sensitive optical sensors *via* effective interactions between the analyte and the fluorescent probe.

VII. Fibres sensitive to chemical agents

VII.1. Moisture-sensitive fibres

The principle of action of polymeric moisture sensors is variation of electric resistance and/or electric capacity of fibres upon water adsorption.[175] Determination of moisture by means of nanoporous polymer films is enabled by the change in the ionic conductivity; the total resistance of the sensor decreases depending on the amount of the bound water.[176] In the case of high surface area to volume ratio, the degree of water absorption by the fibres can increase and, hence, the system sensitivity would be substantially enhanced.

Quartz crystal microbalances the electrodes of which are coated by polymeric films in order to stabilize the analytical signal have been used as sensors for humidity measurements. The sensitivity of this sensor increases $\sim$2-fold as the electrode is coated by the composite fibres based on polyacrylic acid and polyvinyl alcohol instead of films.[177]

VII.2. Glucose-sensitive fibres

The extended surface of the fibres allows immobilization of a large number of enzyme units per polymer unit mass. For example, Aussawasathien *et al.*[178] demonstrated the potential applicability of fibres with surface-immobilized glucose oxidase for detection of glucose in the clinically significant concentration range (*i.e.*, 3.6 to 5.8 mmol litre^{-1}). However, despite the high sensitivity, this sensor has a considerable drawback, namely, limited stability due to enzyme denaturation.

As an alternative to this sensor, fibres containing boric acid have been proposed.[179] Borate ions form a complex with carbohydrates, and this can be used to detect glucose with high sensitivity. It is noteworthy that the selectivity of the fibres toward glucose can be achieved by modifying the fibres with the crown ether that selectively binds glucose in the presence of other monosaccharides. It was shown that $>90\%$ of the initial sensor activity was retained for more than 50 days, which attests to its high stability.

VII.3. Protein-sensitive fibres

The reliable detection of low concentrations of proteins is of primary importance for many biomedical applications, in particular, to detect the mutant proteins related to neurodegenerative diseases.[180] The sensitivity of protein detection is correlated with the presence of immobilized antibodies; considering the high surface area to volume ratio typical of fibres, it is possible to substantially decrease the limit of detection. Thus nanostructured membranes made of polyvinylpyrrolidone fibres demonstrated a $\sim$32-fold increase in the sensitivity compared to usual enzyme linked immunosorbent assay (ELISA) plates.[181] In addition, the time of similar analysis was reduced in this case to 1 h without the loss of sensitivity against 24 h required for classical ELISA. The increase in the sensitivity and a decrease in the time of analysis upon the use of fibres imply the possibility of development of an inexpensive sensitive high-throughput method for analysis of proteins.

VII.4. Fibres sensitive to reducing agents

The use of fibres in tissue engineering has acquired popularity due to high porosity, sufficient mechanical strength and high spatial interconnectivity of fibrous materials, which mimic the natural extracellular matrix supporting the cell growth in the body.[182–184] For preparation of scaffolds stable under physiological conditions, spatial cross-linking of the fibres is required. However, cross-linking can prevent degradation of the fibres in the body or even have a cytotoxic action, resulting in tissue inflammation upon decrease in the pH.[185] For solving these problems, biocompatible and biodegradable fibres cross-linked by disulfide bridges were prepared.[186, 187] These groups can serve to control the degree of cross-linking by varying the concentrations of non-toxic reducing agents such as glutathione or cysteine. The control over the number of cross-links is important, for example, for optimization of the cell growth process and provision for the controlled destruction of the fibres after transplantation. It is evident that these fibres can find wide use in tissue engineering, as they are able to efficiently degrade *in vivo* without inducing the cytotoxic effect in the body.

VII.5. Fibres sensitive to several types of treatment

The prospects of application of polymers sensitive simultaneously to two (or more) types of treatment are markedly more extensive than those for polymers sensitive to only one type of treatment. For example, for controlled drug delivery, the release of active agent stimulated by several types of treatment may increase the specificity. It was found, for example, that fibres based on the copolymer of poly(*N*-isopropylacrylamide) and polyvinyl alcohol are both pH- and thermally-sensitive.[188] At room temperature and at pH <4, the fibres almost do not swell, but they demonstrate considerable swelling at pH >4. Conversely, at elevated temperatures (70 °C) the swelling ratio of the fibres decreases from 15 to 2.6. Evidently, combination of unique properties of polyelectrolyte fibres would lead to the development of a flexible and versatile system for controlled release of the encapsulated substance.

VII.6. Sensor applications

The remodelling of the extracellular matrix by cells is the critical factor for wound healing or in the case of tumour cell metastasis.[189–191] In this connection, important tasks of tissue engineering are visualization and quantitative estimation of the cell interaction with the extracellular matrix and the environment and monitoring of the remodelling.

Most often, observations and quantitative estimations of changes in the matrix and the cells and their interactions are performed in the on-line mode using fluorescent labels, genetically encoded fluorescent proteins [192] or total internal reflection fluorescence microscopy.[193] As an alternative (without using the labels susceptible to bleaching), it is possible to utilize the surface plasmon resonance effect arising upon interaction of the light energy with the elecromagnetic field of metallic coating. The medium in which the metallic nanostructure is embedded substantially affects the refractive index of the directly adjoining region.[194–196] Plasmon effects may increase the intensity of the fluorescence signals from the molecules incorporated in bioobjects by more than an order of magnitude, and, hence, this substantially extends the possibility for their detection and identification and for diagnosis of their state. In view of the signal amplification effect, this visualization procedure can be accomplished with low-power lasers, and this is a necessary condition for the application of optical techniques of tissue and cell monitoring within living organisms.

Silver and gold nanoparticles are widely used for the design of biosensors owing to their unique optical,[197,198] electrical and catalytic properties.[199] Nanocomposites with metallic nanoparticles can serve for the elaboration of new multifunctional materials. There are two approaches to the development of these materials:

— dispersion of nanoparticles in a polymeric matrix; this method is simple but by this method it is difficult to achieve a uniform distribution of metallic nanoparticles in the matrix;

— chemical formation of nanoparticles by the reduction of metal ions that have been introduced into the polymeric matrix during its formation; in this technique, it is possible to control the nanoparticle size by varying the reaction conditions, for example, the concentration of ions in the initial solution (Fig. 8).[200–202]

Ultrathin polyamide fibres containing silver nanoparticles were prepared by electrospinning from a solution of polyimide and silver trifluoroacetylacetonate followed by heat treatment and reduction of silver on the fibre surface.

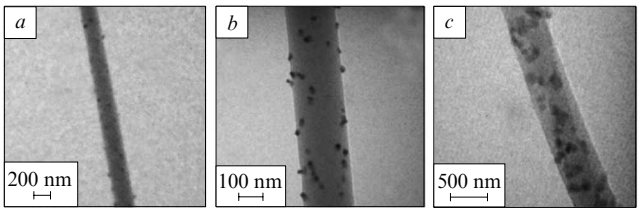


Figure 8. Transmission electron microscope images of nanofibres.[201]
Electrospinning was carried out using 10 mass % solutions of polyimide with 1 (*1*), 2 (*2*) and 7 mass % (*c*) of silver trifluoroacetylacetonate.

In the studies of biological objects using various plasmon effects, fibres are modified, most often, by gold nanoparticles, which are less toxic and more stable in water and buffer solutions than silver particles. A method for the manufacture of hybrid nanofibrous matrices based on polyvinyl alcohol and gold nanoparticles was described and the possibility of using this system as an effective biosensor for glucose and hydrogen peroxide was demonstrated.[203]

Thus, by varying the composition of inclusions into nanofibres, it is possible to adjust the surface of the polymer matrix for solving particular tasks. The use of surface plasmon resonance for high-resolution imaging of proteins [194] and DNA [196] demonstrated that this visualization method is effective for cell imaging and its spatial resolution is sufficient for high-quality of the image.[204]

VIII. Chemical composition and physicochemical properties of composites with functional components

Nanomaterials, for example, semiconductor nanocrystals, carbon nanotubes and nanoclays, are used as coatings and fillers in order to achieve nano-size effects.[205,206] A topical recent trend is the manufacture of composites containing nano-sized inclusions (quantum dots, carbon nanostructures, metallic nanoparticles), as this allows the macrostructure to exhibit nano-size effects. Nanoobjects are embedded into ultrathin fibres by electrospinning of a mixture of nanoparticles and the polymer.

The design of nanocomposites is the most effective method for imparting unique nanomaterial properties to macrostructures. Electrospinning is a simple method for the preparation of ultrathin composite fibres.[19,207–210] Doping of neat polymeric fibres with inorganic nano-sized materials endows them with new properties and markedly extends the scope of application.

Magnetic nanoparticles, quantum dots, photocatalytic nanoparticles and carbon nanotubes can serve as excellent examples of nanoobjects promising for the electrospinning of composite fibres with specified properties. Iron oxide nanoparticles are widely used for biomedical applications, electromagnetic interference shielding and development of catalysts and sensors.[211] Quantum dots such as CdS, CdSe and ZnS can be used in semiconductor devices such as biological markers and optical switches.[212,213] The TiO_2

nanoparticles are known for their photocatalytic properties.[214] The unique mechanical and electric properties of carbon nanotubes have long attracted the attention of researchers. For example, the inclusion of carbon nanotubes improves the mechanical properties of nanocomposite fibres: a 4–5-fold increase in the Young's modulus is achieved by introducing nanotubes in an amount of < 1.5 mass %.[215]

Composite materials consist of at least two identified phases with interface(s) between them. The properties of composites are determined by both the properties of the filler (*e.g.*, shape and size) and the properties of the matrix (*e.g.*, the molecular mass) as well as by the filler distribution in the polymer matrix and the state of the filler/matrix interface. In the case of biocomposites, other factors should also be taken into account such as biocompatibility of the filler and the matrix, and degradation velocity and the absence of toxicity of the matrix.

VIII.1. Matrices loaded with ordered carbon structures

Nano-sized-filled polymer composites possess enhanced mechanical, electric and thermophysical properties. Electrospinning allows inclusion of ordered carbon structures (nanotubes, fullerenes, graphene) into the continuous nanosized fibre. Apart from functionalized graphene,[216,217] the fillers can represent graphite nanoplates,[218,219] carbon nanotubes[220,221] and graphite oxide.[222] These particular materials were selected due to their unique properties, in particular, mechanical strength, which opens up good prospects for practical application in various fields of science and technology. Grapene-functionalized polymers obtained to date are not inferior in the properties to composites containing single-walled carbon nanotubes.[223]

The inclusion of graphene into the polymer matrix gave rise to a new type of optical material combining the specific optical properties of graphene and the structural properties of the polymer. Furthermore, carbon structures absorb electromagnetic radiation over a broad spectral range, including the 'transparency window' of biological tissues,[224,225] which allows the composites based on them to be used for hyperthermia. In order to create macrostructures with unique mechanical, electric and thermal properties inherent in carbon nanotubes, various composite materials containing such tubes have been prepared.[226–229] Primary attention is paid to polymeric fibres containing carbon nanotubes.[230–232] Superstrong fibres were prepared by introducing a suspension of single-walled carbon tubes into polyvinyl alcohol during fibre drawing.[230,231] Ultrathin polyacrylonitrile fibres with single-walled and multiwalled carbon tubes are also fabricated by electrospinning.[215] The same method was used to prepare composite fibres from multiwalled carbon nanotubes and polyethylene oxide.[232] It was shown that by electrospinning, it is possible to align carbon nanotubes along the fibre axis.

Carbon nanotubes possess high stability and high electrical and thermal conductivity. Depending on the structure, they exhibit either metallic or semiconducting properties, which makes composites based on them promising materials for the design of various micro- and nanosensors. The semiconducting properties of nanotubes find use in electrochemical sensors that are sensitive to various biologically active substances in physiological concentrations.[233] However, although the conductivity of some carbon nanotubes is very high, the conductivity of composites based on them is mainly determined by the limitations of electron transfer on contacts of single tubes. The development of a composite exceeding the percolation threshold for conductivity, selection of the type of carbon material out of numerous options, appropriate treatment violating the perfect structure of the graphene layer and fullerene-like tube ends and inducing the appearance of delocalized electronic states on the surface, surface functionalization promoting delocalization of electron density, selection of the binding material for the composite that provides for the electric contact between the tubes — these are challenging research problems the optimal solutions to which are still to be found.

VIII.2. Hydroxyapatite-loaded matrices

The interfacial interaction strength at the filler/polymer interface and the interface wettability are important factors that should be taken into account in the development of composites. In the case of weak adhesion between the two phases, mechanical properties of the material, especially the tensile strength, are deteriorated.

The results of several studies demonstrated that inclusion of calcium carbonate or phosphates such as hydroxyapatite improves the osteoblast proliferation and differentiation[234–237] Hydroxyapatite-based ceramics have been widely used as bone tissue substitutes for ~ 30 years past, as its chemical composition is similar to the composition of the bone mineral phase.[238]

By electrospinning, composites of polylactic acid and hydroxyapatite have been obtained and the effect of the filler (hydroxyapatite) on the mechanical properties of the spun composite fibres have been studied.[239] The hydroxyapatite nanoparticles dispersed in polylactic acid interacted with the polymer matrix through hydrogen bonds, which enhanced the surface binding and improved the mechanical properties, namely, increased the ultimate tensile strength and increased the elastic modulus of the hybrid membrane (Table 4). For the hybrid membrane thus obtained, cell growth and adhesion characteristics were better than for the membrane made of pure polylactic acid. This demonstrates the prospects for the use of hybrid biomaterials for bone tissue regeneration.

Table 4. Mechanical properties of the fibres based on polylactic acid (I) and polylactic acid – hydroxyapatite hybrid system (II).[239]

Fibre	Elastic modulus /MPa	Ultimate tensile strength /MPa	Thickness /μm
I	12 ± 2	1.4 ± 0.11	0.040 ± 0.005
II	118 ± 10	2.86 ± 0.24	0.040 ± 0.005

A biodegradable scaffold system was formed using different concentrations of hydroxyapatite mixed with synthetic polycaprolactone and natural gelatin.[240] The effect of the concentration of hydroxyapatite particles on the mechanical behaviour of the nanocomposite material, which can be attributed to the interfacial adhesion between the hydroxyapatite particles and a mixture of polycaprolactone and gelatin, was studied. As the hydroxyapatite content in the polymer mixture increases, the mechanical

properties of the fibre are improved, for example, the ultimate tensile strength increases.

Hydroxyapatite content (%)	0	10	30	50
Tensile strength /MPa	1.4 ± 0.2	1.8 ± 0.1	3.2 ± 0.2	3.7 ± 0.2

VIII.3. Calcium carbonate-loaded matrices

Calcium carbonate is one of the most popular and inexpensive inorganic fillers used to produce nanocomposites. Calcium carbonate nanopowder of high purity degree is promising as a functional filler in polymeric systems based on polypropylene, poly(vinyl chloride), polyethylene terephthalate.[241–244]

The reinforcing effect of nano- and micro-sized calcium carbonate was studied using various polymers as matrices, including high density polyethylene, polyamide, polypropylene (PP), polylactide and thermoplastic polyurethane. In the presence of calcium carbonate nanoparticles, the mechanical properties of nanocomposites are improved.[245–248] The influence of the calcium carbonate particles on the mechanical, thermal and morphological properties of the polycaprolactone–chitosan nanocomposite has been studied.[249] As can be seen from the data presented in Table 5, the increase in the calcium carbonate content results in the increase in the elastic modulus, which is due to interactions between the polymer and the filler.

Table 5. Elastic properties of the composite based on polycaprolactone and chitosan with different contents of calcium carbonate.[249]

Content of $CaCO_3$ (mass %)	Elastic modulus /MPa	Ultimate tensile strength /MPa
0	15.05 ± 0.84	160.26 ± 4.15
0.5	17.31 ± 0.92	190.58 ± 3.20
1	20.18 ± 0.96	214.91 ± 3.53
3	14.65 ± 0.73	231.80 ± 3.89
5	12.16 ± 0.67	247.21 ± 5.36
7	9.18 ± 0.54	278.60 ± 4.53

An increase in the concentration of calcium carbonate in the nanocomposite entails the increase in the ultimate tensile strength, which reaches a maximum at 1 mass % of calcium carbonate particles (due to good dispersability of the powder in the matrix, the reinforcement effect is manifested). The particles act like stabilizing agents by enhancing the interfacial adhesion. On further increase in the mass fraction of nano-sized calcium carbonate particles, the ultimate tensile strength gradually decreases due to agglomeration of the filler particles.

VIII.4. Fibres loaded with semiconductor nanocrystals

The introduction of quantum dots into a polymer matrix is a challenging task, especially for submicrometre- and nanometre-sized fibres. Quantum dots tend to form aggregates, and their properties are highly sensitive to the change in the microenvironment; therefore, it is difficult to achieve a uniform distribution of quantum dots in the ultrathin polymeric fibres with retention of the optical properties of the latter.

The development of electrospinning methods for efficient inclusion of quantum dots into the fibre is considered in numerous publications. For example, semiconductor nanoparticles were formed *in situ* inside the fibre upon treatment with inorganic precursors.[19,250] The *in situ* formation of nanoparticles is used fairly successfully to control the particle size distribution and the particle distribution in the polymer matrix. However, due to the absence of stabilizing organic molecules that passivate the surface, these nanoparticles have surface defects resulting in unsatisfactory optical characteristics. For high-quality quantum dots with controlled size, which can be prepared as a colloid solution, direct mixing with a matrix polymer may become an alternative method for the manufacture of composite nanofibres.

Polyvinyl alcohol nanofibres with uniformly distributed CdTe quantum dots have been obtained.[251] Doping of the fibres was accomplished by water-soluble CdTe nanocrystals modified by mercapto derivatives, for example, by 3-mercaptopropionic or thioglycolic acid or 1-thioglycerol.[252,253] The uniform distribution of quantum dots without formation of aggregates makes it possible to avoid the fluorescence resonance energy transfer (or Förster energy transfer, FRET) and, hence, retain their initial fluorescence properties even upon inclusion of multicolour quantum dots. The subsequent studies demonstrated that the uniform distribution of quantum dots can be achieved upon fast solvent evaporation during electrospinning. Due to fast 'freezing' of polymer chains, the CdTe nanocrystals have no enough time to aggregate.

Upon dissolution in water, polyelectrolytes become charged at the side functional groups along the backbone, which makes them excellent platforms for the design of sensors sensitive to metal ions, pH change or moisture.[254,255] The nanocomposite fibres containing semiconductor nanoparticles tend to change optical properties owing to the additional influence of the microenvironment of the submicrometre-diameter fibre.[256,257] The optical sensors based on fluorescence enhancement or quenching in thin films and in ultrathin fibres were designed.[258,259] A composite fluorescence humidity sensor that combines an anionic polyelectrolyte with water-soluble carboxylated nanoparticles was obtained.[260] Composite fibres were prepared by electrospinning of aqueous solutions (6 mass %) of polyacrylic acid containing 0.15% to 0.20% (by volume) of CdSe/ZnS nanoparticles functionalized by carboxy groups. The fluorescent composite material thus obtained showed reversible quenching at high humidity. The sensor sensitivity to humidity is caused by the change in the local charges around the nanoparticle as a result of deprotonation of the carboxy groups in the nanoparticles and surrounding polymer matrix.

In recent years, efforts of researchers have been related to dispersion of the fluorescent quantum dots in polymers for the production of optical fibres.[251,261–263] These materials are promising for the manufacture of photonic devices.[264] The formation of composite fibres based on polyethylene oxide containing CdSe quantum dots has been reported.[265] The composites were prepared by dissolving 2%, 5% or 6% of CdSe in a polyethylene oxide solution with a 3 mass % concentration. The diameter of the fibres was found to increase with increase in the loading of CdSe nanocrystals.

VIII.5. Fibres loaded with iron oxide nanoparticles

Owing to the development of effective methods for the preparation and stabilization [266] of magnetic nanoparticles, the range of their applications was extended, in particular, for the design of planar nanocomposite coatings.[267–269] Doping with iron oxide nanoparticles allows targeted change of the physical properties of nanocomposites,[268–271] which are determined by the volume fraction,[270] size and chemical composition of magnetic nanoparticles.[271] Magnetic materials are widely used in biomedicine for delivery of drugs encapsulated in magnetic field-sensitive carriers;[272, 273] magnetic hyperthermia of cancer;[274, 275] and prolonged drug release from magnetically sensitive hydrogels.[276] Often, superparamagnetic nanoparticles are used for these purposes.[277] The polymeric fibre–magnetic nanoparticle composites can serve as examples of a functional structure, which finds wide use in biomedicine and in the design of sensor devices.[278, 279] The composite fibres containing magnetic nanoparticles can extend the potential scope of their application owing to the dependence of mechanical properties on the applied magnetic field.[280]

In a uniform external magnetic field, the magnetic moments of superparamagnetic nanoparticles embedded in the fibres are aligned along this field. In order to disturb this alignment, additional energy will be required for deformation of the fibre, *i.e.*, the strain characteristics of the fibres will be enhanced. In a non-uniform magnetic field, a magnetic fibre should also be deformed or bent in the field gradient direction, and the changes in the rigidity and shape should be fully reversible: upon the removal of the magnetic field, the particle magnetic moments and the fibre orientation should return to their initial distribution. The preparation of magnetic ceramic nanofibres containing nickel ferrite by annealing of polyvinylpyrrolidone fibres loaded with metal alkoxides as the precursors was reported.[208]

Superparamagnetic polymeric nanofibres of various diameters (140–400 nm) were obtained based on solutions of polyethylene oxide and polyvinyl alcohol containing polymer-stabilized magnetite nanoparticles.[277] Both fibre samples showed superparamagnetic properties at room temperature and responded to the external magnetic field (field gradient increased). The deformation testing of the composite fibres by the nanoindentation technique demonstrated that magnetite nanoparticles enhanced the mechanical properties of nanofibres, despite a large amount of short-chain polymer adsorbed on nanoparticles to ensure their suspension stability.

Loading of magnetic nanoparticles into tissue engineering scaffolds can increase the bone cell growth rate, promote cell proliferation and differentiation. Studies showed that mechanical stress arising in the bone tissue boosts the expression levels of many genes, growth factors and proteins.[18] These correlations could be utilized in tissue engineering by using magnetic nanoparticles. Considering the properties of these particles, non-invasive control over their behaviour can be provided by an external magnetic field.[281] By manipulating magnetic nanoparticles, mechanical stress is induced artificially within the bone tissue implant; this increases the rates of cell proliferation and subsequent differentiation. A study was carried out [282] to evaluate the possibility of using a polycaprolactone fibre composite containing magnetic nanoparticles for increasing the functionality of the tissue implant by enhancing the favourable cell–implant interactions, which finally results in bone tissue formation.

VIII.6. Fibres loaded with plasmon resonance nanoparticles

The polymeric biomaterials used for the manufacture of medical implants are often susceptible to bacterial colonization.[283] Three approaches are used to endow biomaterials with antibacterial properties — antiadhesion approach, release of biocidal substances and contact antibacterial modification.[284]

The dispersion of metallic nanoparticles in the polymer fibres to give metal/polymer composites opens up the way to new materials combining the properties of the base material and the dopant. Thus, the inclusion of silver nanoparticles as an antimicrobial agent into a polymer matrix gives systems that can be used as tissue engineering scaffolds, antimicrobial filters and in wound and protective dressings.[112, 285, 286]

A large number of studies are devoted to the development of antibacterial coatings.[285, 287, 288] For example, hollow fibres containing encapsulated silver nanoparticles were reported.[289] Ultrathin fibres based on polyvinylpyrrolidone with inclusions of silver nanoparticles were synthesized.[200] By electrospinning of a solution of a polymer containing silver nitrate followed by reduction to silver metal resulted in the preparation of biodegradable poly(L-lactide) fibres loaded with silver nanoparticles.[290] It was demonstrated that silver ions are released from the fibres and, as a consequence, the material shows high antimicrobial activity (98.5% and 94.2% against *Staphylococcus aureus* and *Escherichia coli*, respectively). It is expected that implementation of both the antimicrobial activity and a biodegradable matrix would allow these composites to find practical application in medicine.

Composite fibres based on polyethylene oxide loaded with dodecanethiol-stabilized gold nanoparticles were formed and investigated.[291] Non-stabilized gold nanoparticles were embedded into polyvinyl alcohol and polyvinylpyrrolidone fibres.[292, 293] Also, composite fibrous materials polystyrene/Au nanoparticles were synthesized by the electrospinning technique.[294] This was done using napthalenethiol-stabilized nanoparticles of 2–5 nm size with the adsorption maximum at 512 nm. The morphology of the nanocomposite fibres and distribution of the gold nanoparticles were examined by scanning and transmission electron microscopy. The Au nanoparticles incorporated in polymer networks can function as heating elements: photothermal effect is manifested upon the interaction of the nanoparticles with the electromagnetic radiation at the wavelength corresponding to the plasmon resonance peak. Researchers' attention was attracted by the ability of gold nanorods to absorb near-IR radiation.[295, 296] The near-IR electromagnetic radiation is scarcely absorbed by water and haemoglobin; therefore, it can penetrate deep into biological tissues.[297] Hence, it is possible to develop light-sensitive systems that can give-off encapsulated substances under the action of IR radiation. It was found that gold nanorods can be reliably embedded into nanofibre matrices obtained by spatial cross-linking of acryl-containing thermally sensitive polymers during electrospinning.[298] On exposure to IR radiation, these fibrous nanocomposites show a reversible collapse (the result of fibre aggregation and dehydration). This phase transition in the polymer was used to initiate the release of proteins encapsulated in nanocomposite fibres.

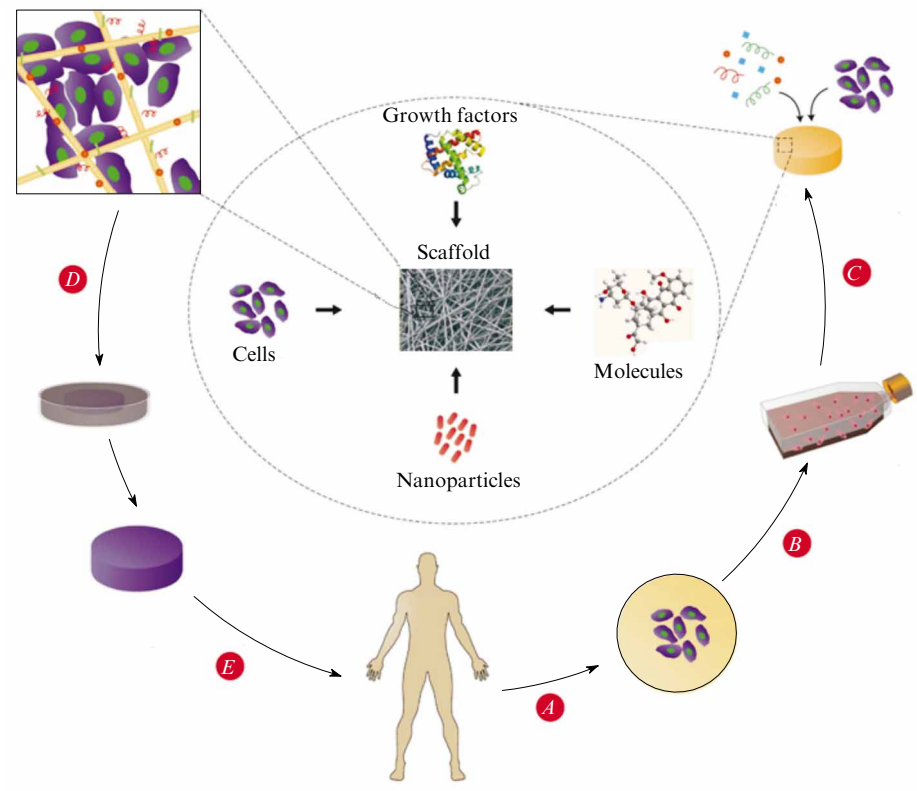


Figure 9. Illustration for the key concept of tissue engineering.[305]
Cells were inoculated on the surface of porous scaffolds from different biomaterials: (*A*) isolation of patient's cells; (*B*) cell growth *in vitro*; (*C*) cell culture inoculation together with growth factors and micro- and/or nanoparticles on the surface; (*D*) culturing of tissue engineered structures in bioreactors; (*E*) transplantation of the tissue engineered structures into patient's injured organ or tissue.

Validation of the concept proposed by the authors is the first step toward the development of functional smart nanofibrous systems with the remote control option.

IX. Applications of non-woven materials

Effective restoration of the structures and functions of injured organs and tissues is a topical problem of medicine. Currently, it is being successfully solved by specialists in regenerative medicine based on the use of molecular and cellular mechanisms of regeneration of the structures and functions of the body.[299, 300]

Tissue engineering is a biomedical technology, being formed now, aimed at the creation of new tissues and organs for the therapeutic reconstruction of injured ones by delivery into the required area of support structures, cells, and molecular and mechanical signals for regeneration (Fig. 9).[301] A tissue engineering structure is a complex biosystem consisting of functionally oriented biomaterial serving as the scaffold with cell cultures grown on its surface.[302]

The biomaterials used to manufacture the scaffolds have to comply with a number of requirements:

— biomaterials should be biologically inert and, after being transferred into the body, should ensure localization of the applied cell material in a particular site;

— most of tissue engineering biomaterials should be easily destroyed in the body to be replaced by its own tissues; however, no toxic intermediate products changing the tissue pH or deteriorating the cell culture growth or differentiation should be involved.

Tissues and organs are created using both synthetic materials and materials based on natural polymers (chitosan, alginate, collagen) (Fig. 10), as well as biocomposite materials.[303–305]

The architecture of tissue engineering scaffolds plays an important role in processes such as cell adhesion, migration, proliferation and differentiation (Fig. 11).

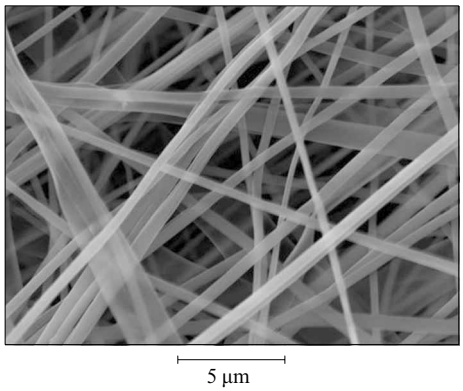


Figure 10. Photomicrograph of the non-woven scaffold based on chitosan fibres.

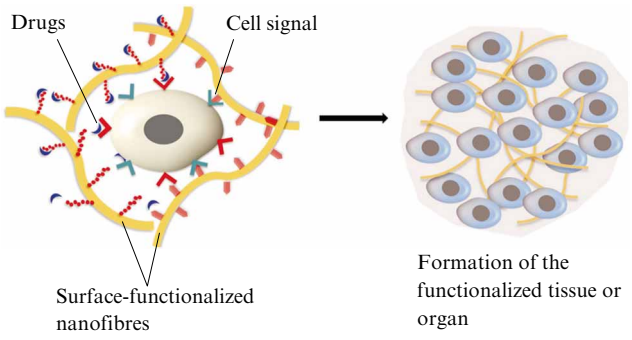


Figure 11. Illustration of the tissue engineering process based on polymeric fibres.[108]

Among various scaffolds used in tissue engineering, electrospun fibres are distinguished by two considerable advantages: first, they are easy to prepare and, second, they mimic to a larger extent the structure of the extracellular matrix.

IX.1. Application of fibres for the tissue engineering of skin

Skin performs a number of vital functions and extensive skin damage may cause, apart from local disorders, general pathological conditions that are life threatening to patients. The ideal tissue engineering structures for mimicking the skin architecture should have a moderately hydrophilic surface, a certain degree of contraction, microstructure and biodegradation-controlled porosity and appropriate mechanical properties. Necessary criteria are improved initial adhesion and increased proliferative activity of patient's own cells.

The initial materials for electrospinning include synthetic biodegradable polymers (such as polyglycolide, polycaprolactone, polylactide, copolymer of glycolic and lactic acids, *etc*.) and natural polymers (collagen, gelatin, chitosan, fibrin, *etc*.).[306, 307] It was shown[308] that electrospun fibres containing 30% of polyethylene glycol and 70% of polylactide have the optimal properties, including moderate hydrophilicity, minimum deviation of the fibre dimensions and coordinated biodegradation, and, furthermore, they can transmit cells into the scaffold and promote cell growth and division.

In addition, it was found that electrospun composites based on the glycolic and lactic acids copolymer mixed with collagen enhance cell adhesion and proliferation and mimic the functions of extracellular matrix.[309] High porosity and large pore size of the support allow the cells to migrate into the fibrous scaffold structure, and proliferative activity of the cells increases. Highly porous electrospun fibres based on the copolymer of glycolic and lactic acids have been obtained. On the surface of these fibres, human dermal fibroblasts showed high viability, and the production of collagen in high concentrations and the subsequent cell migration deep into the scaffold are observed.[310]

IX.2. Application of fibres for the tissue engineering of blood vessels

To date, scaffolds of different shape and size for mimicking blood vessels based on electrospinning using natural and synthetic biodegradable polymers have been developed. For example, mechanically active blood vessel grafts of small diameter from the elastic lactic acid copolymer with ε-caprolactone were produced by the electrospinning technique.[311]

An *in vivo* estimation of the stability of polycaprolactone–collagen structures during vascular reconstruction in rabbits demonstrated[312] that these structures are sufficiently mechanically strong for cell growth. Numerous investigations showed that the scaffolds containing electrospun fibres and endothelial cells can form an alternative to vascular implants in the reconstructive surgery.

Small-diameter fibres were obtained by electrospinning from the biodegradable polyurethane–urea elastomer. For this purpose, smooth muscle cells were simultaneously immobilized into an electrospun matrix to reach the maximum cell infiltration.[313] The ability of cells to migrate and be divided along the orientation of the electrospun fibres was demonstrated.[314, 315] In other words, the fibre orientation is favourable for the growth and subsequent division of the cells located on their surface. It was found that the coronary artery smooth muscle cell adhesion and proliferation were better on these scaffolds than on flat polymeric structures.[315] In addition, the protein molecules that form the cytoskeleton of the smooth muscle cells were aligned parallel to the scaffold fibres, which implies that cells tend to be arranged along the oriented fibre topography. These results indicate that the nano-size structured membranes described above containing fibres with equal diameters and distances from one another are favourable for directional cell division.

IX.3. Application of fibres for the tissue engineering of nerve channels

The nervous system performs an integrative function in the body, as it integrates the sensitivity, motion activity and functioning of other regulatory systems (endocrine and immune systems). However, the regenerative ability of the nervous system is quite limited. If direct surgical reconnection of nerve ends is impossible, artificial nerve conduits are used for the repair.[316, 317]

For the regeneration of nerve channels, thin fibrous scaffolds based on polyacrylonitrile methacrylate have been developed, which promote migration of the Schwann's cells (lemmocytes) and restoration of the critical gaps of nerve tissue without any exogenous imitations of the extracellular matrix or trophic proteins.[318] During the peripheral nerve regeneration, the oriented nanofibre structures are able to align and guide the axonal growth and to control the glial cell migration,[319] which is consistent with results for smooth muscle cells.[315]

The *in vitro* interaction of human nerve cells and oriented nanofibres has been studied. It was shown that the orientation of electrospun fibres substantially affects the growth rate, morphology and location of astrocytes. On the surface of the collagen-modified fibre, adhesion and migration of nerve cells are markedly improved. It was suggested[320] that functionalization of nanofibres and controlled inclusion of these structures into a three-dimensional scaffold are significant stages in the maintenance of axonal regeneration.

IX.4. Application of fibres for the bone tissue engineering

The bone matrix is the intercellular substance of the bone tissue of vertebrates with high concentration of calcium salts. The major component of the bone matrix of the vertebrates is the basic salt — hydroxyapatite $[Ca_{10}(PO_4)_6(OH)_2]$ — the crystals of which are deposited along the collagen fibres. The principal task of bone tissue engineering is to manufacture a biologically active bone transplant that mimics the extracellular matrix and provides efficient bone mineralization.

It was suggested [321] that biocomposite nanofibrous scaffolds based on polylactic acid and collagen and loaded with hydroxyapatite are able to enhance proliferation and mineralization of osteoblastic cells, which finally results in faster bone regeneration. The biocomposite polymeric nanofibres containing hydroxyapatite nanoparticles were prepared by electrospinning.

Recently, polycaprolactone fibre scaffolds with a stainless-steel mesh have appeared.[322] The electrospun polycaprolactone scaffolds with tailored architectures showed much higher level of osteoblastic cell proliferation in mice than the scaffolds with randomly oriented fibres. In addition, the cells grew and elongated along the electrospun fibres. These results indicate that the electrospun nanofibre scaffolds with tailored architectures hold potential for engineering of functional tissues or organs where an ordered cellular organization is essential. Thus, bone tissue regeneration requires an optimal combination of the cell cultures being grown and the scaffold material, on which the cells are mobilized or targeted delivery of the biological material occurs.

Dentists and oral surgeons often face the need to restore bone tissue defects in patients. One of the methods for defect restoration is the design and fabrication of the functional components that are used for bone tissue regeneration. Currently, this is done using the above-described two-component scaffold systems, various biocomposite and bioceramic materials, polymers and the highly purified bone matrix. The selection of the material depends on the size and position of the defect and the structure and architectonics of the surrounding tissues. A multipotent mesenchymal stem cell culture is frequently used as the cellular component.[323, 324]

IX.5. Creation of smart textile materials based on nanocomposite fibres

The creation of smart textiles — materials or structures capable of evaluating and responding to changes in the environment (mechanical, thermal, chemical, electric, magnetic and so on) — is a rapidly developing sector of innovative technologies that appeared at the junction of textile technologies, computer engineering and material science.

A separate area is the research and development of electronic textile. These fabrics are used to make up clothes with integrated functional electronic devices. The components and connections are parts of the fabric, they are invisible and attrition resistant. The so-called wearable electronics represents the second generation of smart fabrics — smart fabric and interactive textile (SFIT). These are textiles with a fully integrated electronic system; their advantages are the absence of necessity to install transducers by specialists and provision of reliable interaction with the body.[325] Sensors may be inserted into the fabric layers (*e.g.*, optical fibre), or the whole fabric can be a transducer or a transducer network (conducting or piezoresistive fabrics). An important application of SFIT systems is the monitoring of the state of health.[326] In the early 2000s, the first prototypes of SFIT systems for the monitoring of biological characteristics appeared.[327] They could monitor the state of the cardiovascular or respiratory system depending on the intent of the device. Thus, the design of wearable electronics is an important, rapidly developing branch of textile industry, which has aroused public interest.

Yet another important trend is the development of materials that mimic the functions and organization principles of living organisms. While designing smart textiles able to sense an external irritation and respond to it, researcher not only propose their own ideas but also utilize what has been made by Nature. Indeed, the light sensitive mechanism inherent in the eyespot apparatus of the flagellated algae inspired scientists to create clothes protecting from hazardous sun rays.[327] The chameleon camouflage effect could underlie the design of military outfit.[328] Yet another example are lotus leaves, which do not get dirty, as their surface consists of microprotrusions of $\sim$10 μm height coated by microfibres containing a layer of wax-like substance. Water is repelled from the lotus surface and flows down carrying away the dirt. The water- and dust-repelling fabric mimicking the lotus leave surface has been reported.[329] Advanced technologies make it possible to fabricate equipment for a human to move along a vertical surface like a gecko.[330] It is noteworthy that in the near future, transferring of the results obtained upon the design of smart clothes to tissue engineering is to be expected.

X. Conclusion

The electrospinning technique can be used to produce fibrous materials of various chemical composition, macro- and microstructure and morphology meant for tissue engineering and targeted drug delivery and for the development of smart materials. The nanofibrous structure mimics to some extent the extracellular matrix and, furthermore, it allows for easy encapsulation of bioactive molecules and drugs. Nevertheless, for effective application of nanofibres, it is important to determine a suitable cell pool and evaluate the consequence of cell interactions with the scaffold depending on its composition and fibre orientation and microstructure. A key factor is the precise control over the spinning process in order to achieve fibre diameter distribution in the nanometre range and mimic more closely the extracellular matrix.

Further development of this area is closely connected to the understanding of the mechanisms of nanofibre spinning and deposition, which may accelerate the advancement of the electrospinning technique and upgrading of the equipment and would provide for extension of potential applications of the fibrous materials in biomedicine.

Numerous studies demonstrating the potential of fibrous materials for biomedicine have been performed to date; however, only a minor part have been carried out *in vivo*. Such applications require the advent of more elaborate electrospinning procedures that would comply with biomedical requirements. For this purpose, interdisciplinary studies are required at the boundary of material science, biology and medicine with keen attention being given to the

implant/biological tissue biointerface. Non-invasive monitoring and control of the properties of this interface are highly important for the design and manufacture of smart composite materials for tissue engineering.

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