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Chapter 14

Electroconductive Nanocomposite Scaffolds: A New Strategy Into Tissue Engineering and Regenerative Medicine

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Additional information is available at the end of the chapter

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1. Introduction

Nanocomposites are a combination of a matrix and a filler, where at least one dimension of the system is on the nanoscale being less than or equal to 100 nm. Much work has focused on the construction of nanocomposites due to the structural enhancements in physico-chemical properties, and functionality for any given system [1-6]. The physico-chemical enhancements result from the interaction between the elements being near the molecular scale. Nanocomposite materials have also received interest for tissue engineering scaffolds by being able to replicate the extracellular matrix found *in vivo*. Currently, researchers have created composite materials for scaffold formation which incorporate two or more materials. Some of these materials consist of minerals for bone tissue engineering including calcium, hydroxyapatite, phosphate, or combinations of different polymers, such as poly (lactic acid), poly (ε-caprolactone), collagen and chitosan, and many other different combinations [7-9]. Other work has focused on doping the polymer scaffolds with specific growth hormones or adhesion sequences to influence how cells attach to the scaffold and cause the scaffold to become a drug delivery vehicle for different kind of tissue engineering applications [10]. Among different materials used in preparation of nanocomposits, conducting polymers are one of the effective materials that can be employed to facilitate communication with neural system for regenerative purposes.

However, the major obstacle concerning the electrically conducting polymers has been the difficulty associated with the processing of them [11]. To overcome this problem, most researchers have electrospun conducting polymers by blending them with other spinnable

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polymers, compromising the conductivity of the nanocomposite fibres [12-16]. Blending of conducting polymers with other polymers positively affects the properties of the resultant nanocomposite fibres. In addition, sometimes for making benefid from condicting polymers and the specific properties of them we can have just a small thib coating of the polymer on the surface of nanocomposite.

The term of "Tissue Inducible Biomaterials" has been recently applied based on the principles of biology and engineering to design nanocomposite scaffolds that restore, maintain or improve the general function of damaged tissues. To gain tissue induction activity and assist tissue regeneration, the nanocomposite scaffolds need to be designed based on nanostructural properties, surface modifications or incorporation of molecules into them. Among different approaches and materials for the preparation of scaffolds, get benefit from conducting polymers seems to be more interesting and promising. Electroconductive polymers exhibit excellent electrical properties and have been explored in the past few decades for a number of applications. In particular, due to the ease of synthesis, cytocompatibility, and good conductivity, some kind of conducting polymers have been extensively studied for biological and medical applications. Different forms of conducting polymers such as polypyrrole (PPy), polythiophene (PT), polyaniline (PANI), poly(3,4-ethylenedioxythiophene) (PEDOT) etc. are used in our daily life due to their uniqe properties which can be applied in different applications. These materials have a conjugated π electron system with "metal-like" electrical conductivity. Due to the rich chemistry of conducting polymers, they have attracted the attention of many researchers and leading to the publication of thousands of papers. The most important property of conducting polymers is their electrical conductivity, so the first approach is to study their electrical-related biological behaviors. Neurons are well known for the membrane-potential-wave style signal transduction. Hence, early studies were focused on the electrical stimulation to the neuron cells using conducting polymers as electrodes. The results showed that the electric conducting polymers can be used as biological electrodes and the neuron growth can be enhanced under an electrical field.

Using conducting polymers in nanocomposite scaffold design is relatively new in tissue engineering applications [17]. It has been demonstrated that these conducting nanocomposites are able to accept and modulate the growth of different cell types [18] including endothelial cells, [19] nerve cells [20] and chromaffin cells [21]. It has been demonstrated that using conducting nanocomposite scaffolds are most promissing in nerve tissue engineering. These electroconductive polymers have been recognized as potential nanocomposite scaffold materials to electrically stimulate tissues for therapeutic purposes in tissue engineering scaffolds. Based on the literature search within the last decade, the present chapter summarized the strategy of electroconductive nanocomposite scaffolds for tissue engineering and regenerative medicine purposes.

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2. Conductive polymers

2.1. General approaches and considerations

Conducting polymers are a special class of materials with electronic and ionic conductivity [22]. The structures of the widely used conducting polymers are depicted in Fig. 1 [23]. These polymers have immense applications in the fields of drug delivery, neuroprosthetic devices, cardiovascular applications, bioactuators, biosensors, the food industry and etc.

One of the first electrically conducting polymers, polypyrrole (PPy) was introduced in the 1960s, but little was understood about this polymer at that time [24]. In 1977, a research team reported a 10 million-fold increase in the conductivity of polyacetylene doped with iodine as the first inherently conducting polymer [25,26]. Unlike polyacetylene, polyphenylenes, are known to be thermally stable as a result of their aromaticity [27]. Polyheterocycles, such as PPy, polythiophene (PT), polyaniline (PANI), and poly(3,4-ethylenedioxythiophene) (PEDOT), developed in the 1980s, have since emerged as another class of aromatic conducting polymers that exhibit good stabilities, conductivities, and ease of synthesis [28]. Table 1 shows a list of different conducting polymers and their conductivities [29].

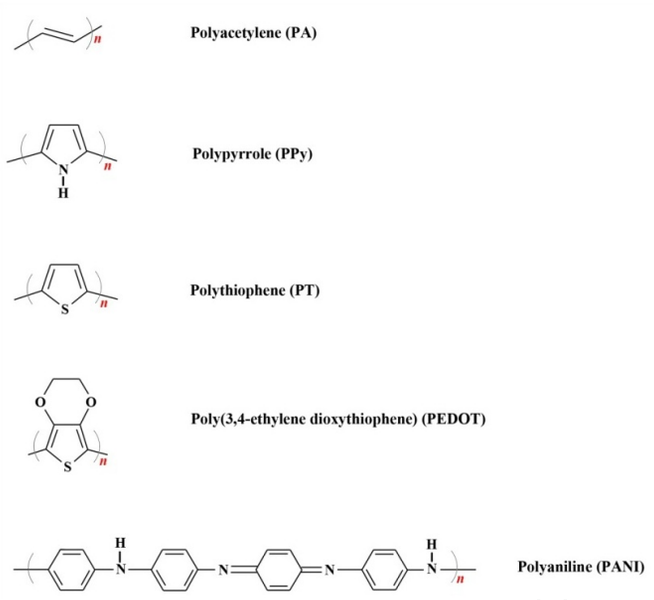
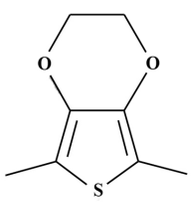


Figure 1. Chemical structures of various conducting polymers

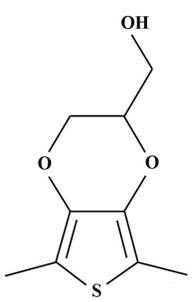
Conducting polymers have an inherently unstable backbone, resulting from the formation of alternate single and double bonds along with the monomer units during polymerization. The delocalized π bonding electrons, produced across the conjugated backbone, provide an electrical pathway for mobile charge carriers which are introduced through doping. Consequently, the electronic properties, as well as many other physicochemical properties, are determined by the structure of the polymer backbone and the nature and the concentration of the dopant ion [30].

Conducting polymer	Maximum Conductivity (Siemens/cm)	Type of doping
Polyacetlene (PA)	200-1000	n,p
Polyparaphenylene (PPP)	500	n,p
Polyparaphenylene sulfide (PPS)	3-300	p
Polyparavinylene (PPv)	1-1000	p
Polypyrrole (PPy)	40-200	p
Polythiophene (PT)	10-100	p
Polyisothionaphthene (PITN)	1-50	p
Polyaniline (PANI)	5	n,p

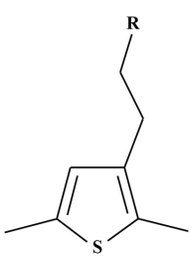
Table 1. Some of the common conducting polymers and their conductivity [29].



Poly(3,4-ethylene dioxythiophene)



Poly(hydroxymethyl-3,4-ethylenedioxythiophene)



Poly(3-alklythiophene)

Figure 2. Typical monomer structures used to fabricate Poly(3,4-ethylene dioxythiophene), Poly(hydroxymethyl- 3,4-ethylenedioxythiophene) and Poly(3-alklythiophene) [30]

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Conjugated aliphatics, including polyacetylene, and benzene derivatives such as PANI, have been largely ruled out for biomedical applications due to their oxidative degradation in air and the cytotoxic nature of their by-products. Although recent research has shown that the emeraldine salt of PANI (EPANI) can be successfully fabricated in a biocompatible form [31,32], modern biomedical conducting polymers are typically composed of heterocyclic aromatics, such as derivatives of thiophene and pyrrole [33,34]. Specifically, PEDOT and PPy have been widely studied for their superior environmental and electrochemical stability [35-37]. Fig. 2 shows the chemical structure of various thiophene derivatives including EDOT, EDOT-MeOH and 3-alkylthiophene [30].

2.2. Surface modification of conducting polymers

For biomedical approaches, sometimes we need to modify the outer surface of the materials to induce special features. Conducting polymers can be also modified to enhance the functionality of nanocomposites. The surface modifications of conducting polymers have some concerns including:

- Enhancement of the charge transport of carriers between the implant and tissue
- Mediating the large difference in mechanical modulus
- Improvement of biodegradation
- Decreasing the impedance to enhance the sensitivity of the recording site
- Cell response enhancement
- Bioactivity enhancement

Surface modification and functionalization of conducting polymers with different biomolecules or dopants has allowed us to modify them with biological sensing elements, and to turn on and off different signalling pathways required for cellular processes. In this way, conducting polymers can show significant enhancement in cell proliferation and differentiation. Thus, conducting polymers provides an excellent opportunity for fabrication of highly selective, biocompatible, specific and stable nanocomposite scaffolds for tissue engineering of different organs [39,40].

2.3. General use of conducting polymers

A range of applications for conducting polymers are currently being considered, such as the development of tissue-engineered organs [41], controlled drug release [42], repaire of nerve chanels [43], and the stimulation of nerve regeneration [44]. In addition, electrically active tissues (such as brain, heart and skeletal muscle) provide opportunities to couple electronic devices and computers with human or animal tissues to create therapeutic body–machine interfaces [45]. The conducting and semiconducting properties of this class of polymers make them important for a wide range of applications. The important properties of various conducting polymers and their potential applications are discussed in Table 2 [23].

Conducting polymer	properties	applications
polypyrrole (PPy)	Highly conductive Opaque Brittle Amorphous structure	biosensors drug delivery bioactuators Nerve tissue engineering Cardiac tissue engineering Bone tissue engineering
polythiophenes (PT)	Good electrical conductivity Good optical property	Biosensors Food industry
polyaniline (PANI)	A semiflexible rod polymer Requires simple doping/dedoping chemistry Exists as bulk films or dispersions High conductivity up to 100 S/cm	Biosensors Drug delivery Bioactuators Nerve tissue engineering Cardiac tissue engineering
poly(3,4-ethylenedioxythiophene) (PEDOT)	High temperature stability Transparent conductor Moderate band gap Low redoxpotential conductivity up to 210 S/cm	Biosensors Antioxidants Drug delivery neural prosthetics

Table 2. Properties and applications of some common conducting polymer [23]

2.4. Conductivity mechanism

Generally, polymers with loosely held electrons in their backbones can be called conducting polymers. Each atom on the backbone has connection with a π bond, which is much weaker than the σ bonds in the backbone. These atoms have allways a conjugated backbone with a high degree of π-orbital overlap [46]. It is known that the neutral polymer chain can be oxidized or reduced to become either positively or negatively charged through doping process [47]. It is also known that conducting polymers could not be perfectly conductive without using dopants, and doping of π-conjugated polymers results in high conductivity [24]. The doping process is influenced by different factors such as polaron length, chain length, charge transfer to adjacent molecules and conjugation length [46]. There have been different dopants for the addition of H^+ (protonation) to the polymers. For example, strong inorganic hydrochloric acid (HCl), organic and aromatic acids containing different aromatic substitution have been used as dopants for PANI. It is also reported that the surface energies of the doped conducting polymers vary greatly, depending on the choice of the dopants and doping level. Recently, PPy doped with nonbiologically active dopants (tosylate) and it has been

characterized for biological interactions as they can trigger cellular responses in biological applications. However, the incorporation of more biologically active dopants can significantly modify PPy-based nanocomposites for biomedical applications [48].

One of the most important challenges of nanocomposite scaffolds based on conducting polymers is their inherent inability to degrade in the body, which may induce chronic inflammation [49]. Hence, belending of conducting polymers with biodegradable polymers seems to solve the problem. PPy and PANI are the most importan conducting polymers for tissue engineering, and they are important in terms of their biocompatibility and cell signaling especially for nerve tissue engineering [24].

2.5. Polypyrrole

PPy is among one of the first conducting polymers that studied a lot for its effect on the behaviour of cells. This material has been reported to support cell adhesion and growth of different cells [50]. This conducting synthetic polymer has numerous applications in tissue engineering and drug delivery. Recently, Moroder *et al.* [51] studied the properties of polycaprolactone fumarate–polypyrrole (PCLF–PPy) nanocomposite scaffolds under physiological conditions for application as conductive nerve conduits. In their study, PC12 cells cultured on PCLF–PPy nanocomposite scaffolds were stimulated with regimens of 10 μA of either a constant or a 20 Hz frequency current passed through the scaffolds for 1 h per day. The surface resistivity of the scaffolds was 2 kΩ and the nanocomposite scaffolds were electrically stable during the application of electrical stimulation. As can be seen in Fig. 3, *in vitro* studies showed significant increases in the percentage of neurite bearing cells, number of neurites per cell and neurite length in the presence of electrical stimulation compared with no electrical stimulation. They concluded that the electrically conductive PCLF–PPy nanocomposite scaffolds possed the material properties necessary for application in nerve tissue engineering.

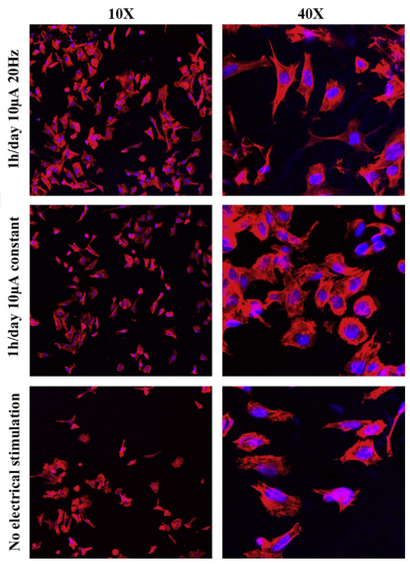


Figure 3. Fluorescence microscopy of PC12 cells at 10× and 40× magnification after undergoing different electrical stimuli treatment regimens for 48h

2.6. Polyaniline

PANI is an oxidative polymeric product of aniline under acidic conditions and is commonly known as aniline black [52]. The exploration of PANI for tissue-engineering applications has progressed more slowly than the development of PPy for similar applications. However, recently there has been more evidence of the ability of PANI and PANI variants to support cell growth [53]. Recently, Fryczkowski *et al.* [54] synthesized three-dimensional nanocomposite fibres of poly(3-hydroxybutyric acid) (PHB) and dodecylbenzene sulfonic acid (DBSA) doped polyaniline in chlorophorm/trifluoroethanol mixture, using electrospinning method. The morphology, electro-active properties and supermolecular structure of nanofibres webs have been analyzed and discussed. Obtained nanofibres are potentially applicable as nanocomposite scaffolds for tissue engineering. According to their results, there were limitations in composition of blended system and the PHB:PANI:solvent ratio needed to be optimized in order to obtain reasonable spinnability of compositions, and even small amount of PANI caused changes in super molecular structure of PHB/PANI nanofibres.

2.7. Poly (3, 4-ethylenedioxythiophene)

Although PPy and PANI have been the most extensively conductive polymers for tissue engineering and regenerative medicine, recently the potential of polythiophene conductive polymer for tissue engineering have been approved. This polymer has received significant attention due to a wide range of promising electronic and electrochemical applications [55,56]. PEDOT can be considered as the most successful polythiophene due to its specific characteristics [57-65]. PEDOT can also be considered as the most stable conducting polymer currently available because of not only high conductivity but also unusual environmental and electrochemical stabilities in the oxidized state [57-60]. Recently, Bolin *et al.* [66] reported electronically conductive and electrochemically active 3D-nanocomposite scaffolds based on electrospun poly(ethylene terephthalate) (PET) nanocomposite fibers. They employed vapour phase polymerization to achieve a uniform and conformal coating of PEDOT doped with tosylate on the nano-fibers. They observed that the PEDOT coatings had a large impact on the wettability, turning the hydrophobic PET fibers super-hydrophilic. According to Fig. 4, the SH-SY5Y cells adhered well and showed healthy morphology. These electrically active nanocomposite scaffolds were used to induce Ca^{2+} signalling in SH-SY5Y neuroblastoma cells. Their reported nanocomposite fibers represented a class of 3D host environments that combined excellent adhesion and proliferation for neuronal cells with the possibility to regulate their signalling.

2.8. Piezoelectric polymeric nanocomposites

Recent studies on the application of conductive materials showed that piezoelectric polymeric materials can also be considered for tissue engineering applications. Piezoelectric polymeric materials can generate surface charges by even small mechanical deformations [67]. Poly(vinylidenefluoride) (PVDF) is a synthetic, semicrystalline polymer with piezoelectric properties that can be potentially used for biomedical application due to their unique molecular structure [107]. An electrical charged porous nanocomposite could be a promising ap-

proach for a number of tissue engineering applications. Reported data on piezoelectric polymeric nanocomposites showed that after electrical stimulation, cellular interaction and tissue growth might be improved [68].

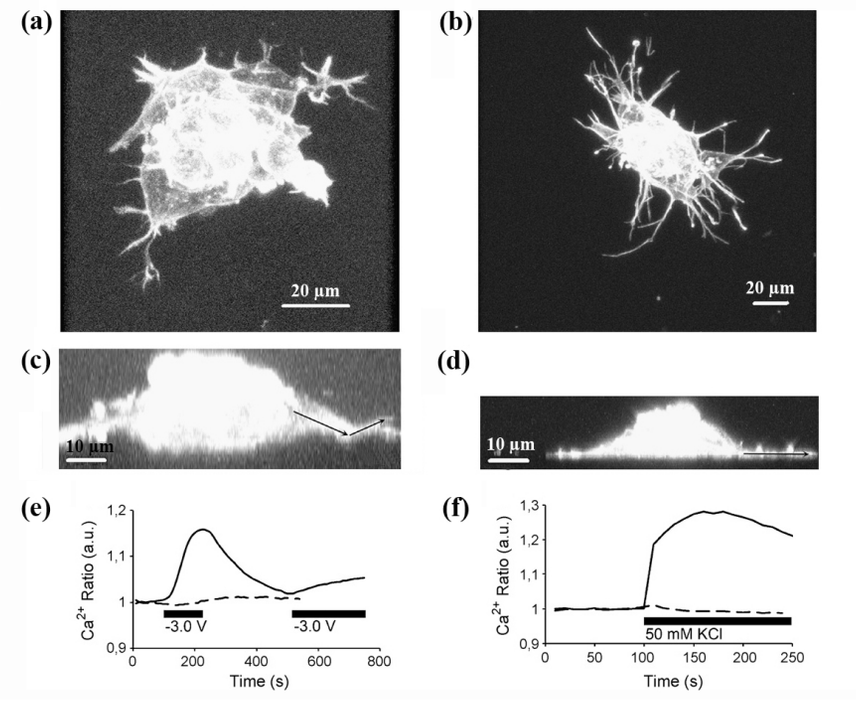


Figure 4. Confocal micrograph top view *Y*-axis projection of Tritc-phalloidin stained cluster of SH-SY5Y cells growing on (a) VPP-PEDOT coated nano-fiber (b) cell culture treated glass. Confocal micrograph side view Z-projection of Tritc-phalloidin stained cluster of SH-SY5Y cells growing on (c) VPP-PEDOT coated nano-fiber surface and (d) cell culture treated glass. Arrows indicate the direction of neurites. (e) Solid line shows intracellular Ca^{2+} flux in FURA-2-AM loaded SH-SY5Y cells cultured on nano-fiber surface. A potential of -3.0V is applied at 100 s. The potential is turned off at 250 s and turned on again at 500 s. Dashed line shows cell treated with 50µM nifedipine in order to block the VOCCs and stimulated with -3.0V at 100 s until 380 s. (f) Solid line shows intracellular Ca^{2+} flux in FURA-2-AM loaded SH-SY5Y cells cultured in cell culture dish 50mM KCl was added at 100 s. Dashed line shows cell treated with 50µM nifedipine in order to block the VOCCs and stimulated in the same way [66].

3. Applications of conducting polymers

3.1. Applications of conducting polymers: general view

Conductive polymers exhibit attractive properties such as ease of synthesis and processing [69]. The unique properties of this type of materials have recently given a wide range of applications in the biological field. Research on conductive polymers for biomedical applications expanded extrimly in the 1980s, and they were shown via electrical stimulation, to modulate cellular activities (e.g. cell adhesion, migration, DNA synthesis and protein secretion) [70-73]. Since then many studies have been done on nerve, bone, muscle, and cardiac cells. The unique characteristics of conducting polymers have been shown to be useful in

many biomedical applications, specially tissue engineering nanocomposite scaffolds and drug delivery devices [74]. In comparison to other conductive materials for biological applications, conducting polymers are inexpensive, easy to synthesize, and versatile. In addition, conducting polymers permit control over the level and duration of electrical stimulation for tissue engineering applications.

3.2. Use and modification of conducting polymers for drug delivery

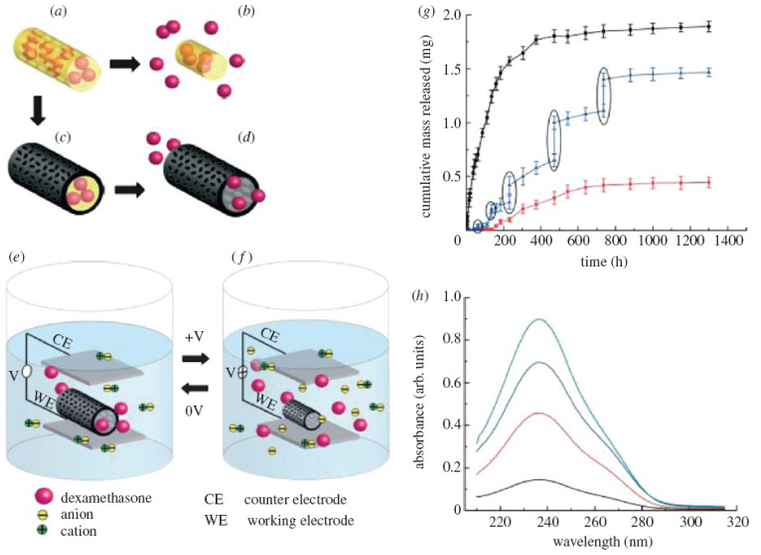


Figure 5. a) dexamethasone-loaded electrospun PLGA, (b) hydrolytic degradation of PLGA fibres leading to release of the drug and (c) and (d) electrochemical deposition of PEDOT around the dexamethasone-loaded PLGA fibre slows down the release of dexamethasone. (e) PEDOT nanotubes in a neutral electrical condition. (f) External electrical stimulation controls the release of dexamethasone from the PEDOT nanotubes. By applying a positive voltage, electrons are injected into the chains and positive charges in the polymer chains are compensated. (g) Cumulative mass release of dexamethasone from: PLGA nanoscale fibres (black squares), PEDOT-coated PLGA nanoscale fibres (red circles) without electrical stimulation and PEDOT-coated PLGA nanoscale fibres with electrical stimulation of 1 V applied at the five specific times indicated by the circled data points (blue triangles). (h) UV absorption of dexamethasone-loaded PEDOT nanotubes after 16 h (black), 87 h (red), 160 h (blue) and 730 h (green). [80]

Developing novel drug-delivery systems will open up new applications that were previously unsuited to traditional delivery systems. The use of conducting polymers in drug delivery is an excellent approach due to their biocompatibility and their possibility of using them in *in vivo* applications for real time monitoring of drugs in biological environments [75]. Controlled drug release can also be facilitated using a change in conductive polymer redox state to increase permeation of drugs such as dexamethasone [76]. Electrical stimulation of conductive polymers has been used to release a number of therapeutic proteins and drugs like nerve growth factor [77], dexamethasone [78] and heparin [79]. Another study demonstrated the use of PEDOT nanotubes polymerized on top of electrospun poly(lactic-co-glycolic acid) (PLGA) nanocomposite fibres for the potential release of the drug dexamethasone. Here, dexamethasone was incorporated within the PLGA nanocomposite fibres and then PEDOT was polymerized around the dexamethasone-loaded PLGA nanocomposite. As the PLGA fibres degraded, dexamethasone molecules remained inside the PEDOT nanotubes. These PEDOT

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nanotubes favoured controlled drug release upon electrical stimulation. Fig. 5 demonstrates the incorporation and release mechanism of dexamethasone from PEDOT nanotubes due to electrical stimulation. This drug-delivery system had the potential of immense interest for the treatment of cancer and tissue engineering and regenerative medicin [80].

3.3. Use and modification of conducting polymers for bioactuators

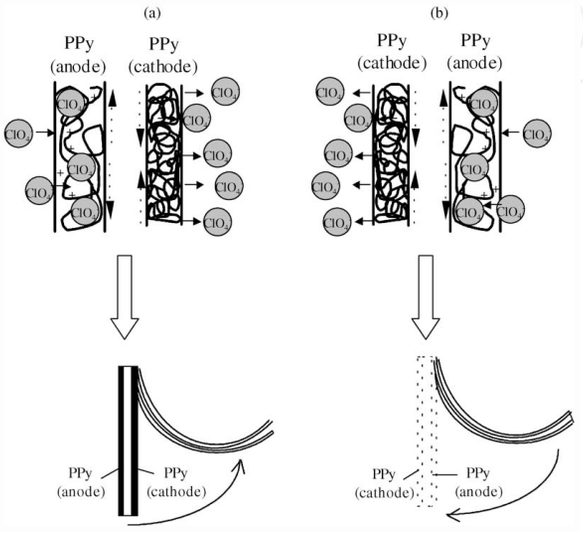


Figure 6. The triple layer device (polypyrrole(ClO_4^-)/non-conducting and adherent polymer/polypyrrole(ClO_4^-)) and its macroscopic movement produced as a consequence of volume change in the polypyrrole films. (a) A current flows and the left polypyrrole film acting as the anode is swelled by the entry of the hydrated counter ions (ClO_4^-). Simultaneously, the right film acting as the cathode contracts and shrinks because of the expulsion of the counter ions. These volume changes and the constant length of the non-conducting film promote the movement of the triple layer towards the polypyrrole film that is being contracted. (b) By changing the direction of the current, the movement takes place in the opposite direction. The muscle works in $LiClO_4$ aqueous solution [83]

Bioactuators are devices that are used to create mechanical force, which in turn can be used as artificial muscles. The phenomenon of change in the volume of the conducting polymers scaffold upon electrical stimulation has been employed in the construction of bioactuators. In artificial muscle applications, two layers of conducting polymers are placed in a triple layer arrangement, where the middle layer comprises a non-conductive material [81]. When current is applied across the two conducting polymers films, one of the films is oxidized and the other is reduced. The oxidized film expands owing to the inflow of dopant ions, whereas the reduced film expels the dopant ions and in the process shrinks, as depicted in Fig. 6 [81]. Conducting actuators have many features that make them ideal candidates for artificial muscles, including that they:

- can be electrically controlled,
- have a large strain which is favourable for linear, volumetric or bending actuators,
- possess high strength,
- require low voltage for actuation (1 V or less),

- can be positioned continuously between minimum and maximum values,
- work at room/body temperature,
- can be readily microfabricated and are light weight, and
- can operate in body fluids [82].

3.4. Use and modification of conducting polymers for tissue engineering applications

The essential properties of conductive polymers desired for tissue engineering and regenerative medicine are conductivity, reversible oxidation, redox stability, biocompatibility, hydrophobicity, three-dimensional geometry and surface topography. Conductive polymers are widely used in tissue engineering due to their ability to subject cells to an electrical stimulation. Studies have addressed cell compatibility when a current or voltage is applied to PPy. An advantage offered by conducting polymers is that the electrochemical synthesis allows direct deposition of a polymer on the surface while simultaneously trapping the protein molecules [84].

In a recent study the release of NGF from PPy nanocomposites by using biotin as a co-dopant during the electrical polymerization was investigated [85]. In this research, NGF was biotinylated and immobilized to streptavidin entrapped within PPy nanocomposites doped with both biotin and dodecylbenzenesulfonate. The release of heparin from hydrogels immobilized onto PPy nanocomposites could also be triggered by electrical stimulation [86]. PVA hydrogels were covalently immobilized onto PPy via grafting of aldehyde groups to PPy and chemical reaction of these with hydroxyl groups from the hydrogel as shown in Fig. 7.

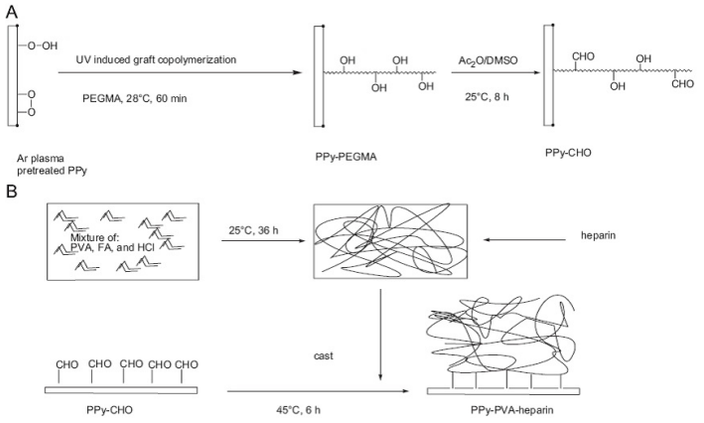


Figure 7. Controlled release of heparin from poly(vinyl alcohol) (PVA) hydrogels immobilized on PPy. (A) Post-polymerization of PPy to incorporate aldehyde groups. (B) Covalent immobilization of PVA hydrogels containing heparin on PPy substrates. Controlled release of heparin was obtained by electrical stimulation of PPy [148].

Electrically conducting polymers have attracted much interest for the construction of nerve guidance channels. The use of conducting polymers can help locally deliver electrical stimulus. It can also provide a physical template for cell growth and tissue repair and allow precise external control over the level and duration of stimulation [87,88]. The importance of

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conducting polymeric nanocomposites is based on the hypothesis that such composites can be used to host the growth of cells, so that electrical stimulation can be applied directly to the cells through the composite, proved to be beneficial in many regenerative medicine strategies, including neural and cardiac tissue engineering [89].

Recently, Li *et al.* [90] blended PANI with a natural protein, gelatin, and prepared nanocomposite fibrous scaffolds to investigate the potential application of such a blend as conductive scaffold for tissue engineering applications. As can be seen in Fig. 8, SEM analysis of the scaffolds containing less than 3% PANI in total weight, revealed uniform fibers with no evidence for phase egregation, as also confirmed by DSC.

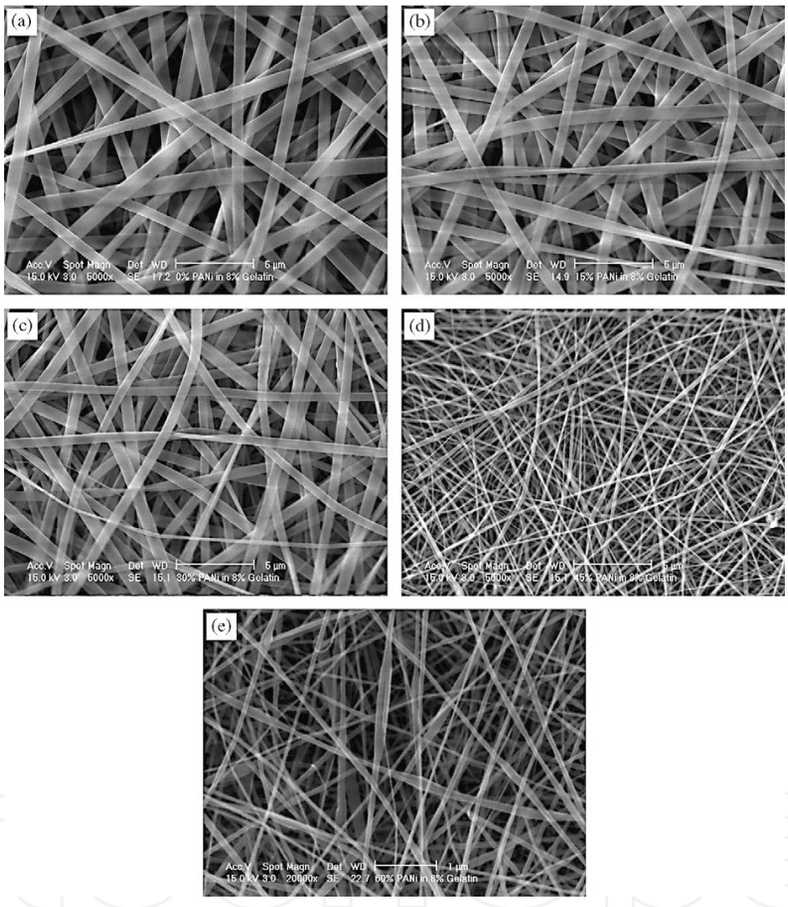


Figure 8. SEM micrographs of gelatin fibers (a) and PANi-gelatin blend fibers with ratios of (b) 15:85; (c) 30:70; (d) 45:55; and (e) 60:40. Original magnifications are 5000× for (a–d) and 20000× for (e). Figure shows the electrospun fibers were homogeneous while 60:40 fibers were electrospun with beads [90]

To test the usefulness of PANI/gelatin blends as a fibrous matrix for supporting cell growth, H9c2 rat cardiac myoblast cells were cultured on fiber-coated glass cover slips. Cell cultures were evaluated in terms of cell proliferation and morphology. According to Fig. 9, the results indicated that all PANI/gelatin blend fibers supported H9c2 cell attachment and proliferation to a similar degree as the control tissue culture-treated plastic (TCP) and smooth glass substrates.

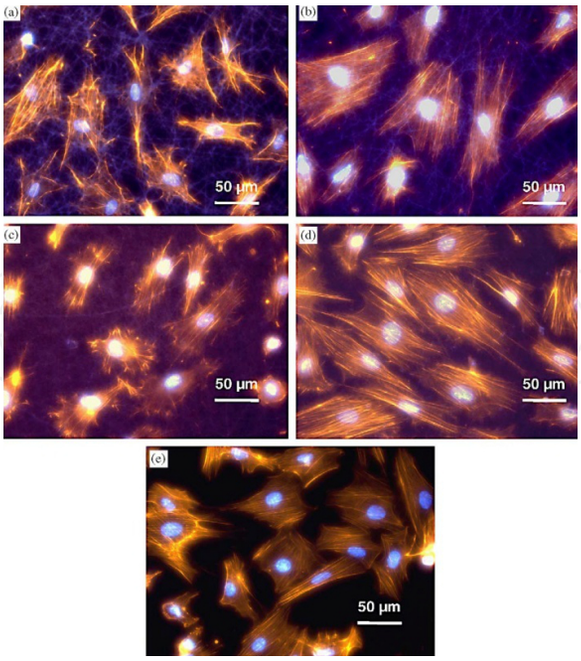


Figure 9. Morphology of H9c2 myoblast cells at 20 h of post-seeding on: (a) gelatin fiber; (b) 15:85 PANI/gelatin blend fiber; (c) 30:70 PANI/gelatin blend fiber; (d) 45:55 PANI/gelatin blend fibers; and (e) glass matrices. Staining for nuclei-bisbenzimide and actin cytoskeleton-phalloidin, fibersautofluorescence, original magnification 400× [90].

Depending on the concentrations of PANI, the cells initially displayed different morphologies on the fibrous substrates, but after 1week all cultures reached confluence of similar densities and morphology. Taken together they suggested that PANI/gelatin blend nanocomposite fibers could provide a novel conductive material well suited as biocompatible scaffolds for tissue engineering.

4. Conclusion

Tissue engineering is a new concept which is a growing area of research, in which cells are seeded on nanocomposite scaffolds and then implanted in defected part of body. Appropriate stimuli (chemical, biological, mechanical and electrical) can be applied and over a relatively short time new tissue can be formed to help restore function in the patient. The ideal scaffolds should have an appropriate surface chemistry and microstructures to facilitate cellular attachment, proliferation and differentiation. In addition, the scaffolds should possess adequate mechanical strength and biodegradation rate without any undesirable by-products. Among different materials, conducting polymers are one of the materials that can be employed to facilitate communication with neural system for regenerative purposes. In this chapter the recent methods of the synthesis of nanocomposite scaffolds using different conducting polymers was reviewed. The ability of conductive scaffolds to accept and modulate the growth of a few different cell types including endothelial, nerve, and chromaffin cells have shown a bright future in the field of tissue engineering and regenerative medicine.

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References

[1] Mozafari, M., Moztarzadeh, F., Rabiee, M., Azami, M., Tahriri, M., Moztarzadeh, Z., & Nezafati, N. (2010). Development of Macroporous Nanocomposite Scaffolds of Gelatin/Bioactive Glass Prepared Through Layer Solvent Casting Combined with Lamination Technique for Bone Tissue Engineering. *Ceramics International*, 36, 2431-2439.

[2] Mozafari, M., Rabiee, M., Azami, M., & Maleknia, S. (2010). Biomimetic Formation of Apatite on the Surface of Porous Gelatin/Bioactive Glass Nanocomposite Scaffolds. *Applied Surface Science*, 257, 1740-1749.

[3] Mozafari, M., Moztarzadeh, F., Rabiee, M., Azami, M., Tahriri, M., & Moztarzadeh, Z. (2010). Development of 3D Bioactive Nanocomposite Scaffolds Made from Gelatin and Nano Bioactive Glass for Biomedical Applications. *Advanced Composites Letters*, 19, 91-96.

[4] Hamlekhan, A., Mozafari, M., Nezafati, N., Azami, M., & Hadipour, H. (2010). A Proposed Fabrication Method of Novel PCL-GEL-HAp Nanocomposite Scaffolds for Bone Tissue Engineering Applications. *Advanced Composites Letters*, 19, 123-130.

[5] Poursamar, S. A., Azami, M., & Mozafari, M. (2011). Controllable Synthesis and Characterization of Porous Polyvinyl Alcohol/Hydroxyapatite Nanocomposite Scaffolds via an in Situ Colloidal Technique. *Colloids and Surfaces B: Biointerfaces*, 84, 310-316.

[6] Hamlekhan, A., Moztarzadeh, F., Mozafari, M., Azami, M., & Nezafati, N. (2011). Preparation of Laminated Poly(ε-caprolactone)-Gelatin-Hydroxyapatite Nanocomposite Scaffold Bioengineered via Compound Techniques for Bone Substitution. *Biomatter*, 1, 1-11.

[7] Ghafari Nazari, A., & Mozafari, M. (2012). Simulation of Structural Features on Mechanochemical Synthesis of $Al_2O_3TiB_2$ Nanocomposite by Optimized Artificial Neural Network. *Advanced Powder Technology*, 23, 220-227.

[8] Hamlehkhan, A., Mozafari, M., Nezafati, N., Azami, M., & Samadikuchaksaraei, A. (2012). Novel Bioactive Poly(ε-caprolactone)-Gelatin-Hydroxyapatite Nanocomposite Scaffolds for Bone Regeneration. *Key Engineering Materials*, 493-494, 909-915.

[9] Baghbani, F., Moztarzadeh, F., Gafari Nazari, A., Razavi Kamran, A. H., Tondnevis, F., Nezafati, N., Gholipourmalekabadi, M., & Mozafari, M. (2012). Biological Response of Biphasic Hydroxyapatite/Tricalcium Phosphate Scaffolds Intended for Low Load-Bearing Orthopaedic Applications. *Advanced Composites Letters*, 21, 16-24.

[10] Jalali, N., Moztarzadeh, F., Mozafari, M., Asgari, S., Motevalian, M., & Naghavi Alhosseini, S. (2012). Surface Modification of Poly(lactide-co-glycolide) Nanoparticles by d-α-tocopheryl Polyethylene Glycol 1000 Succinate as Potential Carrier for the Delivery of Drugs to the Brain. *Colloids and Surfaces A: Physicochemical and Engineering Aspects*, 392, 335-342.

[11] Pomfret, S. J., Adams, P. N., Comfort, N. P., et al. (2000). Electrical and Mechanical Properties of Polyaniline Fibres Produced by a One-Step Wet Spinning. *Polymer*, 41, 2265-2269.

[12] Yu, Q. Z., Shi, M. M., Deng, M., et al. (2008). Morphology and Conductivity of Polyaniline Sub-Micron Fibers Prepared by Electrospinning. *Mater Sci Eng B*, 150, 70-76.

[13] Veluru, J. B., Satheesh, K. K., Trivedi, D. C., et al. (2007). Electrical Properties of Electrospun Fibers of PANI-PMMA Composites. *J Eng Fibers Fabrics*, 2, 25-31.

[14] Bishop, A., & Gouma, P. (2005). Leucoemeraldine Based Polyaniline-Poly-Vinylpyrrolidone Electrospun Composites and Bio-Composites: A Preliminary Study of Sensing Behavior. *Rev Adv Mater Sci*, 10, 209-214.

[15] Desai, K., Lee, J. S., & Sung, C. (2004). Nanocharacterization of Electrospun Nanofibers of Polyaniline/Poly Methyl Methacrylate Blends Using SEM, TEM and AFM. *Microsc Microanal*, 10, 556-557.

[16] Ju, Y. W., Park, J. H., Jung, H. R., et al. (2007). Electrochemical Properties of Polypyrrole/Sulfonated SEBS Composite Nanofibers Prepared by Electrospinning. *Electrochim Acta*, 52, 4841-4847.

[17] Schmidt, E., Shastri, V. R., Vacanti, J. P., & Langer, R. (1997). *Proc. Natl. Acad. Sci. Usa*, 94, 8948.

[18] De Giglio, E., Sabbatini, L., & Zambonin, P. G. J. (1999). *Biomater. Sci. Polym. Ed*, 10, 845.

[19] Garner, B., Georgevich, A., Hodgson, A. J., Liu, L., & Wallace, G. G. J. (1999). *Biomed. Mater. Res*, 44, 121.

[20] Valentini, R. F., Vargo, T. G., Gardellajr, J. A., & Aebischer, P. (1992). *Biomaterials*, 13, 193.

[21] Kotwal, A., & Schmidt, C. E. (2001). *Biomaterials*, 22, 1055.

[22] Xu, L. B., Chen, W., Mulchandani, A., & Yan, Y. (2005). Reversible Conversion of Conducting Polymer Films from Superhydrophobic to Superhydrophilic. . Angew. Chem. Int. Ed doi:10.1002/anie.200500868 , 44, 6009-6012.

[23] Rajeswari, R., Subramanian, S., Jayarama, R. V., Shayanti, M., & Seeram, R. (2010). Applications of Conducting Polymers and Their Issues in Biomedical Engineering. J. R. Soc. Interface published online 7 July, doi: 10.1098/rsif.2010.0120.focus.

[24] Street, G. B. (1986). Polypyrrole: from Powders to Plastics. In: Skotheim T. A., editor. *Handbook of conducting polymers*, vol. I. New York: Marcel Dekker, 265-291.

[25] Shirakawa, H., Louis, E. J., MacDiarmid, A. G., Chiang, C. K., & Heeger, A. J. (1977). Synthesis of Electrically Conducting Organic Polymers: Halogen Derivatives of Polyacetylene, (CH)x. *J Chem Soc Chem Commun*, 578-580.

[26] Heeger, A. J. (2001). Semiconducting and Metallic Polymers: the Fourth Generation of Polymeric Materials (Nobel Lecture). *Angew Chem Int Ed*, 40, 2591-2611.

[27] Feast, W. J. (1986). Synthesis of Conducting Polymers. In: Skotheim T. A., editor. *Handbook of conducting polymers*, vol. I. New York: Marcel Dekker, 1-43.

[28] Hong, S. Y., & Marnick, D. S. (1992). Understanding the Conformational Stability and Electronic Structures of Modified Polymers Based on Polythiophene. *Macromolecules*, 4652-4657.

[29] Guimard, N. K., Gomez, N., & Schmidt, C. E. (2007). Conducting Polymers in Biomedical Engineering. *Prog. Polym. Sci.*, 32, 876-921.

[30] Green, R. A., Baek, S., Poole-Warren, L. A., & Martens, P. J. (2010). Conducting Polymer-Hydrogels for Medical Electrode Applications. *Sci. Technol. Adv. Mater*, 11 014107 (13pp), doi: 10.1088/1468-6996/11/1/014107.

[31] Kamalesh, S., Tan, P., Wang, J., Lee, T., Kang, E. T., & Wang, C. H. (2000). *J. Biomed. Mater. Res.*, 52, 467.

[32] Wang, H. J., Ji, L. W., Li, D. F., & Wang, J. Y. (2008). *J. Phys. Chem. B*, 112, 2671.

[33] Shreyas, S. R., & Jessica, W. (2009). *Front. Neuroeng.*, 2, 6.

[34] Cogan, S. F. (2008). *Annu. Rev. Biomed. Eng.*, 10, 275.

[35] Li, G. C., & Pickup, P. G. (2000). *PCCP Phys. Chem. Chem. Phys.*, 2, 1255.

[36] Tourillon, G., & Garnier, F. (1983). *J. Electrochem. Soc.*, 130, 2042.

[37] Cui, X., & Martin, D. C. (2003). *Sensors Actuators B*, 89, 92.

[38] Yamato, H., Ohwa, M., & Wernet, W. J. (1995). *Electroanal. Chem.*, 397, 163.

[39] Ghasemi-Mobarakeh, L., Prabhakaran, M. P., Morshed, M., Nasr Esfahani, M. H., Baharvand, H., Kiani, S., & Al-Deyab, S. S. (2011). Ramakrishna S. Application of Conductive Polymers, Scaffolds and Electrical Stimulation for Nerve Tissue Engineering. *J Tissue Eng Regen Med*, 5, 17-35.

[40] Naghavi Alhosseini, S., Moztarzadeh, F., Mozafari, M., Asgari, S., Dodel, M., Samadikuchaksaraei, A., Kargozar, S., & Jalali, N. (2011). Synthesis and Characterization of Electrospun Polyvinyl Alcohol Nanofibrous Scaffolds Modified by Blending with Chitosan for Neural Tissue Engineering. *International Journal of Nanomedicine*, 6, 1-10.

[41] Otero, T. F., & Sansinena, J. M. (1998). Soft and Wet Conducting Polymers for Artificial Muscles. *Adv. Mater.*, 10, 491-494.

[42] Abidian, M. R., Kim, D. H., & Martin, D. C. (1998). Conducting Polymer Nanotubes for Controlled Drug Release. *Adv. Mater.*, 18, 405-409, doi:10.1002/adma.200501726.

[43] Abidian, M. R., Ludwig, K. A., Marzullo, T. C., Martin, D. C., & Kipke, D. R. (2009). Interfacing Conducting Polymer Nanotubes with the Central Nervous System: Chronic Neural Recording Using poly(3,4-ethylenedioxythiophene) Nanotubes. *Adv. Mater.*, 21, 3764-3770, doi:10.1002/adma.200900887.

[44] Schmidt, C.E., Shastri, V. R., Vacanti, J. P., & Langer, R. (1997). Stimulation of Neurite Outgrowth Using an Electrically Conducting Polymer. *Proc. Natl Acad. Sci. USA*, 94, 8948-8953.

[45] Warren, L. F., Walker, J. A., Anderson, D. P., Rhodes, C. G., & Buckley, L. J. (1989). A study of Conducting Polymer Morphology. *J. Electrochem. Soc.*, 136, 2286-2295.

[46] Breads, J. L., & Silbey, R. (1991). Conjugated Polymers. Kluwer Academic: Amsterdam, The Netherlands.

[47] Wong, J. Y., Langer, R., & Ingberi, D. E. (1994). Electrically Conducting Polymers Can Noninvasively Control the Shape and Growth of Mammalian Cells. *Proc Natl Acad Sci USA*, 91, 3201-3204.

[48] Sanchvi, A. B., Miller, K. P. H., Belcher, A. M., et al. (2005). Biomaterials Functionalization Using a Novel Peptide That Selectively Binds to a Conducting Polymer. *Nat Mater*, 4, 496-502.

[49] Huang, L., Hu, J., Lang, L., et al. (2007). Synthesis and Characterization of Electroactive and Biodegradable ABA Block Copolymer of Polylactide and Aniline Pentamer. *Biomaterials*, 28, 1741-1751.

[50] Wong, J. Y., Langer, R., & Ingber, D. E. (1994). Electrically Conducting Polymers Can Noninvasively Control the Shape and Growth of Mammalian Cells. *Proc Natl Acad Sci USA*, 91, 3201-3204.

[51] Moroder, P., Runge, M. B., Wang, H., Ruesink, T., Lu, L., Spinner, R. J., Windebank, A. J., & Yaszemski, M. J. (2011). Material Properties and Electrical Stimulation Regimens of Polycaprolactone Fumarate-Polypyrrole Scaffolds as Potential Conductive Nerve Conduits. *Acta Biomaterialia*, 7, 944-953.

[52] Nalwa, H. S. (1997). Handbook of Organic Conductive Molecules and Polymers. Wiley: New York.

[53] Mattioli-Belmonte, M., Giavaresi, G., Biagini, G., et al. (2003). Tailoring Biomaterial Compatibility: in Vivo Tissue Response Versus in Vitro Cell Behavior. *Int J Artif Organs*, 26, 1077-1085.

[54] Fryczkowski, R., & Kowalczyk, T. (2009). Nanofibres from Polyaniline/Polyhydroxybutyrate Blends. *Synthetic Metals*, 159, 2266-2268.

[55] Crispin, X., Marciniak, S., Osikowicz, W., Zotti, G., van Der Gon, A. W. D., Louwt, F., et al. (2003). *J Polym Sci Pol Phys*, 41, 2561.

[56] Sarac, A. S., Sonmez, G., & Cebeci, F. C. (2003). *J Appl Electrochem*, 33, 295.

[57] Breiby, D. W., Samuelsen, E. J., Groenendaal, L. B., & Struth, B. (2003). *J Polym Sci Pol Phys*, 41, 945.

[58] Jonsson, S. K. M., Birgersson, J., Crispin, X., Grezynsky, G., Osikowicz, W., van der Gon, A. W. D., et al. (2003). *Synthetic Met*, 139, 1.

[59] Ocampo, C., Oliver, R., Armelin, E., Alema´n, C., & Estrany, F. (2006). *J Polym Res*, 13, 193.

[60] Liesa, F., Ocampo, C., Alema´n, C., Armelin, E., Oliver, R., & Estrany, F. (2006). *J Appl Polym Sci*, 102, 1592.

[61] Marsella, M. J., & Reid, R. (1999). *J. Macromolecules*, 32, 5982.

[62] Otero, T. F., & Cortes, M. T. (2003). *Adv Mater*, 15, 279.

[63] Yu, H. H., Xu, B., & Swager, T. M. (2003). *J Am Chem Soc*, 125, 1142.

[64] Casanovas, J., Zanuy, D., & Alema´n, C. (2006). *Angew Chem Int Edit*, 45, 1103.

[65] Kros, A., Van Hovell, S. W. F. M., Sommerdijk, N. A. J. M., & Nolte, R. J. M. (2001). *Adv Mater*, 13, 1555.

[66] Bolin, M. H., Svennersten, K., Wang, X., Chronakis, I. S., Richter-Dahlfors, A., Jager, E. W. H., & Berggren, M. (2009). Nano-Fiber Scaffold Electrodes Based on PEDOT for Cell Stimulation. *Sensors and Actuators B*, 142, 451-456.

[67] Valentini, R. F., Vargo, T. G., Gardella, J. A., et al. (1992). Electrically Charged Polymeric Substrates Enhance Nerve Fibre Outgrowth in Vivo. *Biomaterials*, 13, 183-190.

[68] Weber, N., Lee, Y. S., Shanmugasundaram, S., Jaffe, M., & Arinzeh, T. L. (2010). Characterization and in Vitro Cytocompatibility of Piezoelectric Electrospun Scaffolds. *Acta Biomaterialia*, 6, 3550-3556.

[69] Heeger, A. J. (2002). Semiconducting and Metallic Polymers: the Fourth Generation of Polymeric Materials. *Synth Met*, 125, 23-42.

[70] Foulds, N. C., & Lowe, C. R. (1986). Enzyme Entrapment in Electrically Conducting Polymers. *J Chem Soc Faraday Trans*, 82, 1259-1264.

[71] Umana, M., & Waller, J. (1986). Protein Modified Electrodes: the Glucose/Oxidase/Polypyrrole System. *Anal Chem*, 58, 2979-2983.

[72] Venugopal, J., Molamma, P., Choon, A. T., Deepika, G., Giri Dev, V. R., & Ramakrishna, S. (2009). Continuous Nanostructures for the Controlled Release of Drugs. *Curr. Pharm. Des.*, 15, 1799-1808.

[73] Adeloju, S. B., & Wallace, G. G. (1996). Conducting Polymers and the Bioanalytical Sciences: New Tools for Biomolecular Communication. *A review. Analyst*, 121, 699-703.

[74] Harwood, G. W. J., & Pouton, C. W. (1996). Amperometric Enzyme Biosensors for the Analysis of Drug and Metabolites. *Adv. Drug. Deliv. Rev.*, 18, 163-191, doi: 10.1016/0169-409X(95)00093-M.

[75] Stassen, I., Sloboda, T., & Hambitzer, G. (1995). Membrane with Controllable Permeability for Drugs. *Synth. Met.*, 71, 2243-2244, doi:10.1016/0379-6779(94)03241-W.

[76] Pernaut, J. M., & Reynolds, J. R. (2000). Use of Conducting Electroactive Polymers for Drug Delivery and Sensing of Bioactive Molecules. A Redox Chemistry Approach. *J. Phys. Chem. B*, 104, 4080-4090, doi:10.1021/jp994274o).

[77] Hodgson, A. J., John, M. J., Campbell, T., Georgevich, A., Woodhouse, S., & Aoki, T. (1996). Integration of Biocomponents with Synthetic Structures: Use of Conducting Polymer Polyelectrolyte Composites. *Proc. SPIE. Int. Soc. Opt. Eng.*, 2716, 164-176, doi: 10.1117/12.232137.

[78] Wadhwa, R., Lagenaur, C. F., & Cui, X. T. (2006). Electrochemically Controlled Release of Dexamethasone from Conducting Polymer Polypyrrole Coated Electrode. *J. Control. Rel.*, 110, 531-541, doi: 10.1016/j.jconrel.2005.10.027.

[79] Li, Y., Neoh, K. G., Cen, L., & Kang, E. T. (2005a). Controlled Release of Heparin from Polypyrrole-Poly(Vinyl Alcohol) Assembly by Electrical Stimulation. *J. Biomed. Mater. Res. A*, 73A, 171-181, doi:10.1002/jbm.a.30286.

[80] Abidian, M. R., Kim, D. H., & Martin, D. C. (2006). Conducting-Polymer Nanotubes for Controlled Drug Release. *Adv. Mater.*, 18, 405-409.

[81] Otero, T. F., & Cortes, M. T. (2003). A Sensing Muscle. *Sens. Actuat. B*, 96, 152-156, doi: 10.1016/S0925-4005(03)00518-5.

[82] Smela, E. (2003). Conjugated Polymer Actuators for Biomedical Applications. *Adv. Mater.*, 15, 481-494, doi: 10.1002/ adma.200390113.

[83] Otero, T. F., & Cortés, M. T. (2003). A Sensing Muscle. *Sensors and Actuators B*, 96, 152-156.

[84] Bartlett, P. N., & Whitaker, R. G. (1988). Modified Electrode Surface in Amperometric Biosensors. *Med. Biol. Eng. Comput.*, 28, 10-17, doi:10.1007/BF02442675.

[85] George, P. M., LaVan, D. A., Burdick, J. A., Chen, C. Y., Liang, E., & Langer, R. (2006). Electrically Controlled Drug Delivery from Biotindoped Conductive Polypyrrole. *Adv Mater*, 18, 577-581.

[86] Li, Y., Neoh, K. G., & Kang, E. T. (2005). Controlled Release of Heparin from Polypyrrole-Poly(Vinyl Alcohol) Assembly by Electrical Stimulation. *J Biomed Mater Res A*, 73A, 171-181.

[87] Chronakis, I. S., Grapenson, S., & Jakob, A. (2006). Conductive Polypyrrole Nanofibers via Electrospinning: Electrical and Morphological Properties. *Polymer*, 47, 1597-1603.

[88] Zhang, Q., Yan, Y., Li, S., et al. (2010). The Synthesis and Characterization of a Novel Biodegradable and Electroactive Polyphosphazene for Nerve Regeneration. *Mater Sci Eng C*, 30, 160-166.

[89] Bettinger, C. J., Bruggeman, J. P., Misra, A., et al. (2009). Biocompatibility of Biodegradable Semiconducting Melanin Films for Nerve Tissue Engineering. *Biomaterials*, 30, 3050-3057.

[90] Li, M., Guo, Y., Wei, Y., MacDiarmid, A. G., & Lelkes, P. I. (2006). Electrospinning Polyaniline-Contained Gelatin Nanofibers for Tissue Engineering Applications. *Biomaterials*, 27, 2705-2715.

[91] Buijtenhuijs, P., Buttafoco, L., Poot, A. A., Daamen, W. F., van Kuppevelt, T. H., Dijkstra, P. J., et al. (2004). Tissue Engineering of Blood Vessels: Characterization of Smooth-Muscle Cells for Culturing on Collagen-and-Elastinbased Scaffolds. *Biotechnol Appl Biochem*, 39, (Pt 2) 141-149.

[92] Lu, Q., Ganesan, K., Simionescu, D. T., & Vyavahare, N. R. (2004). Novel Porous Aortic Elastin and Collagen Scaffolds for Tissue Engineering. *Biomaterials*, 25(22), 5227-5237.

[93] Tan, K. H., Chua, C. K., Leong, K. F., Naing, M. W., & Cheah, C. M. (2005). Fabrication and Characterization of Three-Dimensional Poly(ether-ether-ketone)-Hydroxyapatite Biocomposite Scaffolds Using Laser Sintering. *Proc Inst Mech Eng [H]*, 219(3), 183-194.

[94] Di Martino, A., Sittinger, M., & Risbud, M. V. (2005). Chitosan: a Versatile Biopolymer for Orthopaedic Tissue-Engineering. *Biomaterials*, [Epub ahead of print].

[95] Kim, K., Yu, M., Zong, X., Chiu, J., Fang, D., Seo, Y. S., et al. (2003). Control of Degradation Rate and Hydrophilicity in Electrospun Non-Woven Poly(D,L-lactide) Nanofiber Scaffolds for Biomedical Applications. *Biomaterials*, 24, 4977-4985.

[96] Zong, X., Bien, H., Chung, C. Y., Yin, L., Fang, D., Hsiao, B. S., et al. (2005). Electrospun Fine-Textured Scaffolds for Heart Tissue Constructs. *Biomaterials*, 26(26), 5330-5338.

[97] Metzke, M., O'Connor, N., Maiti, S., Nelson, E., & Guan, Z. (2005). Saccharidepeptide Hybrid Copolymers as Biomaterials. *Angew Chem Int Ed Engl*, 44(40), 6529-6533.

[98] Boland, E. D., Matthews, J. A., Pawlowski, K. J., Simpson, D. G., Wnek, G. E., & Bowlin, G. L. (2004). Electrospinning Collagen and Elastin: Preliminary Vascular Tissue Engineering. *Front Biosci*, 9, 1422-1432.

[99] Li, M., Mondrinos, M. J., Gandhi, M. R., Ko, F. K., Weiss, A. S., & Lelkes, P. I. (2005). Electrospun Protein Fibers as Matrices for Tissue Engineering. *Biomaterials*, 26(30), 5999-6008.

[100] Rho, K. S., Jeong, L., Lee, G., Seo, B. M., Park, Y. J., Hong, S. D., et al. (2005). Electrospinning of Collagen Nanofibers: Effects on the Behavior of Normal Human Keratinocytes and Early Stage Wound Healing. *Biomaterials*, [Epub ahead of print].

[101] Riboldi, S. A., Sampaolesi, M., Neuenschwander, P., Cossu, G., & Mantero, S. (2005). Electrospun Degradable Polyesterurethane Membranes: Potential Scaffolds for Skeletal Muscle Tissue Engineering. *Biomaterials*, 26(22), 4606-4615.

[102] Ma, Z., Kotaki, M., Inai, R., & Ramakrishna, S. (2005). Potential of Nanofiber Matrix as Tissue-Engineering Scaffolds. *Tissue Eng*, 11(1-2), 101-109.

[103] Yang, F., Murugan, R., Wang, S., & Ramakrishna, S. (2005). Electrospinning of Nano/Micro Scale Poly(L-lactic acid) Aligned Fibers and Their Potential in Neural Tissue Engineering. *Biomaterials*, 26(15), 2603-2610.

[104] Khil, M. S., Bhattarai, S. R., Kim, H. Y., Kim, S. Z., & Lee, K. H. (2005). Novel Fabricated Matrix via Electrospinning for Tissue Engineering. *J Biomed Mater Res B Appl Biomater*, 72(1), 117-124.

[105] Khil, M. S., Cha, D. I., Kim, H. Y., Kim, I. S., & Bhattarai, N. (2003). Electrospun Nanofibrous Polyurethane Membrane as Wound Dressing. *J Biomed Mater Res B Appl Biomater*, 67(2), 675-679.

[106] Zeng, J., Yang, L., Liang, Q., Zhang, X., Guan, H., Xu, X., et al. (2005). Influence of the Drug Compatibility with Polymer Solution on the Release Kinetics of Electrospun Fiber Formulation. *J Control Release*, 105(1-2), 43-51.

[107] Buttafoco, L., Kolkman, N. G., Poot, A. A., Dijkstra, P. J., Vermes, I., & Feijen, J. (2005). Electrospinning Collagen and Elastin for Tissue Engineering Small Diameter Blood Vessels. *J Control Release*, 101(1-3), 322-324.

[108] MacDiarmid, A. G. (2001). Nobel lecture: Synthetic Metals: a Novel Role for Organic Polymers. *Rev Mod Phys*, 73, 701-712.

[109] Pedrotty, D. M., Koh, J., Davis, B. H., Taylor, D. A., Wolf, P., & Niklason, L. E. (2005). Engineering Skeletal Myoblasts: Roles of Three-Dimensional Culture and Electrical Stimulation. *Am J Physiol Heart Circ Physiol*, 288(4), H1620-1626.

[110] Azioune, A., Slimane, A. B., Hamou, L. A., Pleuvy, A., Chehimi, M. M., Perruchot, C., et al. (2004). Synthesis and Characterization of Active Esterfunctionalized Polypyrrole-Silica Nanoparticles: Application to the Covalent Attachment of Proteins. *Langmuir*, 20(8), 3350-3356.

[111] Arslan, A., Kiralp, S., Toppare, L., & Yagci, Y. (2005). Immobilization of Tyrosinase in Polysiloxane/Polypyrrole Copolymer Matrices. *Int J Biol Macromol*, 35(3-4), 163-167.

[112] Kim, D. H., Abidian, M., & Martin, D. C. (2004). Conducting Polymers Grown in Hydrogel Scaffolds Coated on Neural Prosthetic Devices. *J Biomed Mater Res A*, 71(4), 577-585.

[113] Kotwal, A., & Schmidt, C. E. (2001). Electrical Stimulation Alters Protein Adsorption and Nerve Cell Interactions with Electrically Conducting Biomaterials. *Biomaterials*, 22(10), 1055-1064.

[114] Sanghvi, A. B., Miller, K. P., Belcher, A. M., & Schmidt, C. E. (2005). Biomaterials Functionalization Using a Novel Peptide That Selectively Binds to a Conducting Polymer. *Nat Mater*, 4(6), 496-502.

[115] Lakard, S., Herlem, G., Valles-Villareal, N., Michel, G., Propper, A., Gharbi, T., et al. (2005). Culture of Neural Cells on Polymers Coated Surfaces for Biosensor Applications. *Biosens Bioelectron*, 20(10), 1946-1954.

[116] George, P. M., Lyckman, A. W., La Van , D. A., Hegde, A., Leung, Y., Avasare, R., et al. (2005). Fabrication and Biocompatibility of Polypyrrole Implants Suitable for Neural Prosthetics. *Biomaterials*, 26(17), 3511-3519.

[117] Wan, Y., Wu, H., & Wen, D. (2004). Porous-Conductive Chitosan Scaffolds for Tissue Engineering. 1. Preparation and Characterization. *Macromol Biosci*, 4(9), 882-890.

[118] Jiang, X., Marois, Y., Traore, A., Tessier, D., Dao, L. H., Guidoin, R., et al. (2002). Tissue Reaction to Polypyrrole-Coated Polyester Fabrics: an in Vivo Study in Rats. *Tissue Eng*, 8(4), 635-647.

[119] Bidez, P. R., Li, S., MacDiarmid, A. G., Venancio, E. C., Wei, Y., & Lelkes, P. I. (2006). Polyaniline, an Electroactive Polymer with Potential Applications in Tissue Engineering. *J Biomater Sci Polym*, 17(1-2), 199-212.

[120] Kamalesh, S., Tan, P., Wang, J., Lee, T., Kang, E. T., & Wang, C. H. (2000). Biocompatibility of Electroactive Polymers in Tissues. *J Biomed Mat Res*, 52(3), 467-478.

[121] Ahmad, N., & MacDiarmid, A. G. (1996). Inhibition of Corrosion of Steels with the Exploitation of Conducting Polymers. *Synth Met*, 78, 103-110.

[122] Yang, Y., Westerweele, E., Zhang, C., Smith, P., & Heeger, A. J. (1995). Enhanced Performance of Polymer Light-Emitting Diodes Using High-Surface Area Polyaniline Network Electrodes. *J Appl Phys*, 77, 694-698.

[123] MacDiarmid, A. G., Yang, L. S., Huang, W. S., & Humphrey, B. D. (1987). Polyaniline: Electrochemistry and Application to Rechargeable Batteries. *Synth Met*, 18, 393-398.

[124] Karyakin, A. A., Bobrova, O. A., Lukachova, L. V., & Karyakina, E. E. (1996). Potentiometric Biosensors Based on Polyaniline Semiconductor Films. *Sensors Actuators, B: Chem.*, B33(1-3), 34-38.

[125] Wei, Y., Lelkes, P. I., MacDiarmid, A. G., Guterman, E., Cheng, S., Palouian, K., et al. (2004). Electroactive Polymers and Nanostructured Materials for Neural Tissue Engineering. In: Qi-Feng Z., Cheng S. Z. D., editors. *Contemporary Topics in Advanced Polymer Science and Technology*, Beijing, China: Peking University Press, 430-436.

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