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Ceramics International 38 (2012) 6075–6090

CERAMICS INTERNATIONAL

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Review paper

Carbon nanostructures as nerve scaffolds for repairing large gaps in severed nerves

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Received 27 April 2012; received in revised form 12 May 2012; accepted 14 May 2012
Available online 24 May 2012

Abstract

As the field of nerve tissue engineering advances, new biomaterials and structures are required to improve the regeneration of damaged nerves. Carbon nanostructures have been recognized as potential candidates to develop neural prostheses due to their one-dimensional nanostructures and similar nanoscale dimensions to neuritis as well as their unique electrical and mechanical properties when being used as a scaffold. This review addresses the promising application of carbon nanostructures in the repair of injured nerves. As a new viewpoint, the possibility of utilizing carbon nanostructures to repair a long gap in a severed nerve will be discussed as well.

Keywords: B. nanocomposites; D. carbon; E. biomedical applications

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1. Structure of the nervous system

The nervous system can be divided into two main parts: the central nervous system (CNS) (which is composed of the brain and the spinal cord (SC)) and the peripheral nervous system (PNS) (including the somatic and

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0272-8842/$36.00
http://dx.doi.org/10.1016/j.ceramint.2012.05.038

autonomic nerves) [1]. The repair processes of these two systems are different [2–6].

According to the National Spinal Cord Injury Association Resource Center report [7], for instance, approximately 450,000 people live with Spinal Cord Injury (SCI) in the United States. There are about 8000 new SCIs every year; the majority of them (82%) involve males between the ages of 16–30. These injuries result from motor vehicle accidents (44%), violence (24%), falls (22%), sports (8%), or other (2%). Therefore, there is a vital need to find a treatment for nervous system injuries.

2. Repair procedures of the damaged nervous system

Axons serve as important neuronal messengers that transmit electrical signals away from the neuronal cell body. The regeneration of the injured axons in PNS usually takes place through the proliferation of Schwann cells that wrap around nerve fibers forming myelin sheaths, the phagocytosis of myelin by macrophages or monocytes, and the development of Bünger bands by the bundling of Schwann cells and recovering axons in the distal segment (Fig. 1) [5,6,8–10]. In the damaged PNS with a gap of less than 5 mm, the surgical anastomosis of one nerve to another is performed. While for a larger gap, an autologous nerve graft should be implanted to produce a junction between the two severed ends [11–17].

One of the most important approaches of tissue engineering is to provide an alternative to the nerve autografts. At the present time, a long gap in a severed nerve can be treated by implanting a donor nerve from a different location into the injured area. This method has several downsides, which include the loss of the donor nerve function, restricted availability of donor nerve, formation of potentially painful neuromas, size mismatch between the donor nerve and the injured nerve and a lack of vascularization of the donor nerve [18–23]. Hence, there is a crucial need for a bridging-scaffold that can be served as a nerve conduit with similar characteristics to that of donor nerves. Table 1 gives some Food and Drug Administration (FDA) approved nerve guidance conduits (NGC) made up of different materials [24]. In order to complete the healing process of severed nerves, the scaffold should be biodegradable. The degradation rate of the scaffold should match with the growth rate of the nerve fibers so that the nerve fibers connections would have fully restored [25]. On the other hand, in the central nervous system, recovery and regeneration of axons would be more difficult as a result of the absence of Schwann cells [26]. The regeneration of injured SC is even more difficult due to the development of a complex inhibitory environment. After injury, a fluid fills the produced cavity which is surrounded by a dense glial scar. The presence of astrocytes, glycosaminoglycans and other inhibitory molecules prevent neurons and other cells from infiltrating the injured site

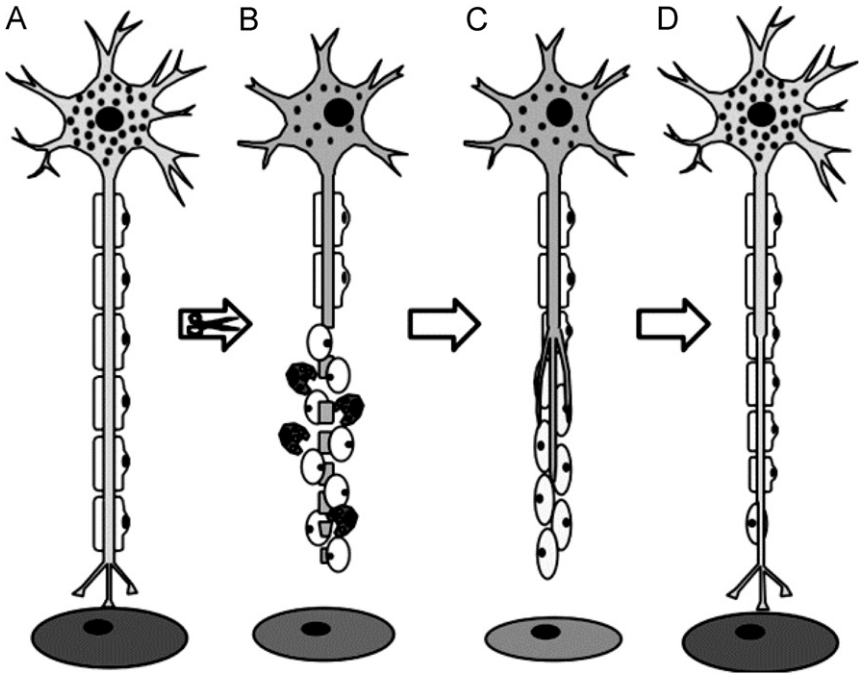

Fig. 1. Schematic of the main events of degeneration and regeneration after peripheral nerve injury. (A) Normal nerve fiber, maintaining synaptic contact with target cells. (B) Transection of the fiber results in distal fragmentation of axon and myelin sheaths. Macrophages and Schwann cells phagocyte degraded materials. Chromatolysis at the neuron soma and dendritic arbor retraction occur. (C) Fine sprouts emerge from the proximal axonal end, and elongate in association with the proliferated Schwann cells in the distal segment, that line up in bands of Büngner. (D) Axonal reconnection with target cells and maturation of the nerve fiber. The regenerated axon remains of smaller caliber and with shorter internodes than normal. The neuron returns to a normal transmitting phenotype. Taget cells may suffer atrophy and phenotypic changes during denervation. Reprinted with the permission from [8].

Table 1
Some FDA approved nerve guidance conduits. Reprinted with the permission from [24].

Product name	Material	Degradation
Neurotube®	Polyglycolic acid (PGA)	3 months
Neuragen	Type I collagen	36–48 months
Neuroflex™	Type I collagen	4–8 months
NeuroMatrix™	Type I collagen	4–8 months
AxoGuard™	Porcine small intestinal	3 months
Nerve connector		
Neurolac	Poly(DL-lactide-ε-caprolactone); PCL	16 months
SaluTunnel™	Polyvinyl Alcohol (PVA)	Non-absorbable
Nerve protector™		

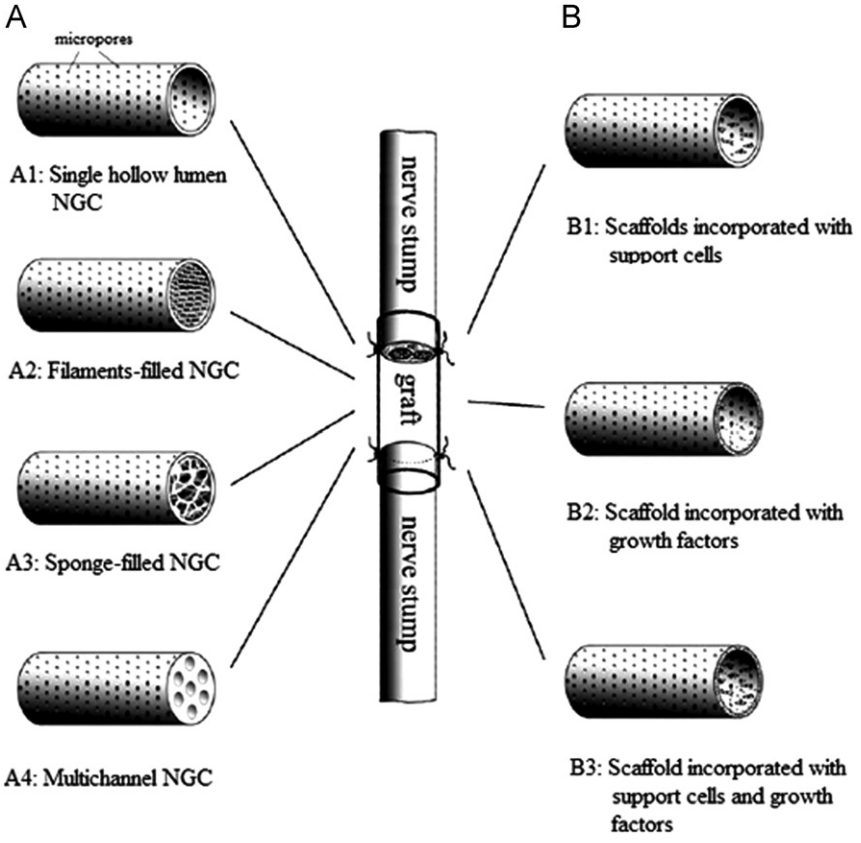

Fig. 2. (A) Schematic diagram showing the common structure of neural scaffolds, and (B) the composition of tissue engineered nerve grafts. Reprinted with the permission from [55].

which in turn lead to the loss of axonal connections [27–34]. Hence, according to the above mentioned reasons, regeneration and recovery of damaged CNS may be much more difficult than PNS.

3. Neural tissue engineering for neuroregeneration

Using an appropriate environment is necessary to bridge the gap between the two severed ends in an injured nerve. To design such an environment, a comprehensive understanding of the microenvironment and mechanism of nerve growth is required. Neural tissue engineering potentially offers new approaches to accelerate the healing rate of damaged nerves by providing biomimetic scaffolds supporting new nervous ingrowth to renovate and sustain the normal functions of the nerves [35–50]. Engineering scaffolds should be designed to facilitate the cell distribution and growth of damaged nerve tissues in three dimensions [51–54]. The structure of proper neural scaffolds and the morphology of some nerve guides approved for clinical use are shown in Figs. 2 and 3, respectively [55–57]. Moreover, pores interconnectivity is another critical parameter which should be considered to ensure cell migration, cell signaling, and mass transportation. Regeneration of damaged nerves with such scaffolds can be compared with those treated through autografts [58,59].

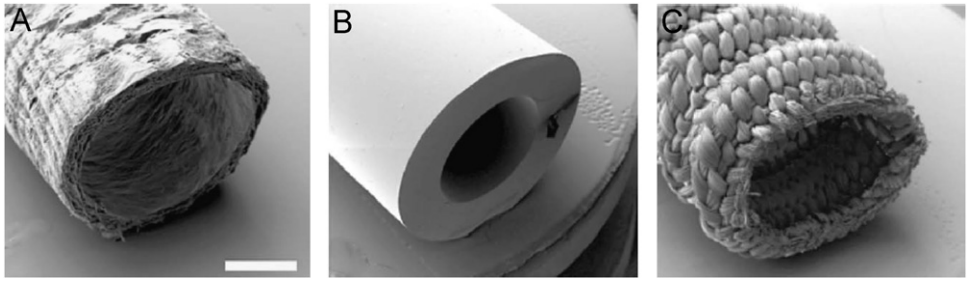

Fig. 3. SEM micrographs of three types of nerve guides approved for clinical use: (A) NeuraGen™ made from collagen, (B) Neurolac made from polylactide/caprolactone, (C) Neurotube made from polyglycolide. Scale bar = 4 mm. Reprinted with the permission from [56,57].

4. Nanotechnology and neuroregeneration

Advances in nanotechnology may result in better treatment of injured nerves. For instance, synthesis of nanofibers and nanotubes with excellent conductivity and biocompatibility provides a medium to stimulate neuron activities. On the other hand, nanomaterials have also been utilized to encapsulate Schwann cells into nanoscaffolds to improve nerve regeneration [60–62]. Nanostructure and surface characteristics of nanoscaffolds enormously enhance the cell adhesion to the surface and consequently result in a better cell viability. Carbon nanostructures provide a large surface area with high surface energy which can easily increase the interaction of nanoscaffolds and cells and improve the performance of implant [63–65].

5. Characteristics of ideal materials for neural tissue engineering application

It is crucially important that a material which is used as a scaffold be cytocompatible, and has great biomechanical and electrical properties [66–68]. It must be biodegradable and exhibit good biocompatibility with extremely low inflammatory, immunogenic, and cytotoxic responses [11,69,70]. A material which does not have a good cytocompatibility, may not contribute to the growth of damaged nerves but would cause severe inflammation or infection [71]. Furthermore, higher electrical conductivity is required for scaffolds used in neural tissue engineering to mimic the electrical properties of nerves and simultaneously stimulate the neuron interaction [72–75]. Table 2 shows some biomaterials which can be used as scaffolds to treat the injured nerves [76–85]. Although autografts provide an appropriate microenvironment for neuroregeneration, there are some disadvantages as well. In most of the times, there is a lack of donor nerves when using autografts. On the other hand, harvesting autograft triggers the loss of healthy nerves and paresthesia or anesthesia at the donor site [86,87]. Allografts are available as much as needed, but they may cause an inflammatory reaction and failure of the nerve graft [88–91]. Other biomaterials such as polymers do not have the proper mechanical properties. They may form glial scar tissue around the implant and decrease a complete healing chance [92–94]. The scaffold should provide sufficient mechanical strength to prevent the scaffold failure during the patient's movements and physically support neural tissue regeneration [95–97]. Simultaneously, the scaffold should have proper elasticity to reduce tensions in the injured spot [98,99]. Moreover, an ideal scaffold should be porous to permit nerve fibers ingrowth and keep the cells alive until the completion of treatment period [100,101].

Table 2
Natural and synthetic nerve grafts.

Materials	References
Polyglycolic acid	[76]
Polylactic acid	[77]
Polyester	[78,79]
Polyglactin	[80]
Fibronectin	[81]
Collagen	[82,83]
Laminin	[84,85]

6. Carbon nanostructures as neural prostheses

Recently, carbon nanostructures are proposed as promising candidates to develop neural scaffolds. There are different types of carbon nanostructures. The three most popular ones are single-walled carbon nanotubes (SWCNT), multi-walled carbon nanotubes (MWCNT), and carbon nanofibers (CNF). Fig. 4 shows various types of carbon nanostructures including one type of CNF [102–106]. It has been reported that neurons and neuronal cell lines can grow and differentiate on CNT substrates [107–115]. Carbon nanostructures have excellent mechanical, electrical, and conduction properties, and have nanostructure similar to neuritis. Hence, they have been utilized to improve neural activities and guide severed ends in a nerve through each other [116–118]. Chemical functionalization can produce various surface charges on MWCNTs which in turn control neural growth [112]. The surface charges of MWCNTs can influence the length of neuritis, branching and the number of growth cones. Hu et al. [112] showed that the positively charged MWCNTs in comparison with negatively charged MWCNTs have a higher number of

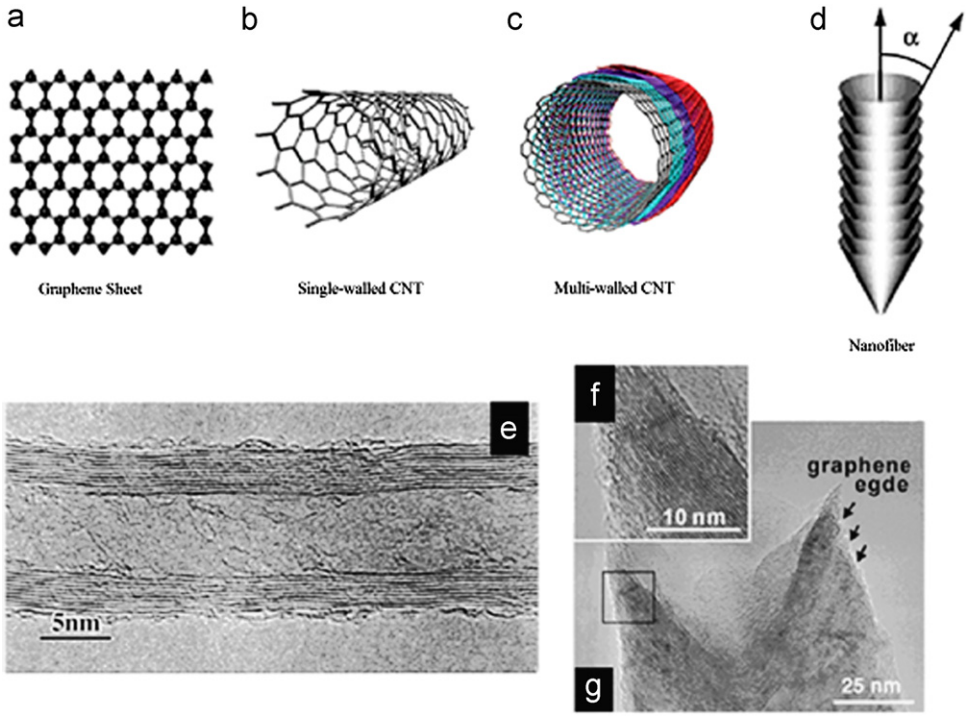

Fig. 4. Schematic representation of (a) a graphene sheet, (b) SWCNT, (c) MWCNT, (d) one type of CNF, and (e) TEM images showing a cross section of a MWCNT (f) and (g) and a CNF. Adapted with permission from [102–106].

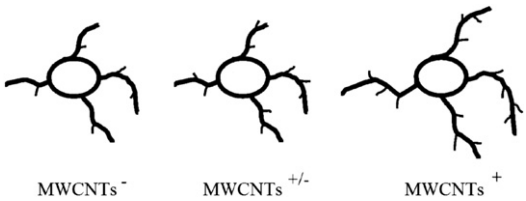

Fig. 5. Drawing summarizing the effects of MWCNT Charges on the neurite outgrowth and branching. Reprinted with the permission from [112].

growth cones and neurite branches (Fig. 5). Mazzatenta et al. [113] developed an integrated SWCNT–neuron system and showed that electrical stimulation delivered via SWCNT can induce neuronal signaling. On the other hand, Lovat et al. [114] showed that the nerves growth on CNTs is accompanied with a significant increase in network activity and purified CNTs can improve neural signal transfer and cell adhesion.

Various carbon nanostructures such as CNTs and CNFs have been synthesized for neural tissue engineering applications [115,119–121]. Firkowska et al. [119] developed free standing nanostructured matrixes by the conventional lithographic technique combined with the layer by layer assembly procedure. They could control the shape, chemical and mechanical stability of the self-assembled monolayers. Gheith et al. [115] showed that free standing structures of modified SWCNTs can guide the outgrowth of neuritis, support cell to cell communications and cell differentiation. Therefore the unique properties of carbon nanostructures including biocompatibility, cell viability, cell growth, cell attachment and differentiation as well as conductivity and excellent mechanical and electrical properties make them a promising candidate for neural tissue engineering applications [122–127].

7. Carbon/polymer composite scaffolds for neuroregeneration

To design a scaffold for treatment of the nervous system injuries, many considerations should be taken into account. The scaffold should decrease the formation of glial scar and provide suitable sites for cell adhesion and proliferation and stimulate the nerves ingrowth to heal the severed ends in a nerve. Furthermore, the scaffold should bridge the gap and recover the function of axons to reconnect the severed ends [128–131]. There are many attempts to prevent the astrocyte functions which result in the formation of glial scar tissue. It is reported that the astrocyte adhesion and proliferation were decreased on CNFs and CNF/polycarbonate urethane composites and consequently reduced the formation of glial scar tissue [132,133]. Vertically aligned CNFs coated with thin conductive polymers are developed to improve mechanical and electrical properties of CNFs and contribute to forming an intimate neural–electrical interface between cells and nanofibers [134]. On the other hand, the stiffness of polymer composites can be increased by adding a small amount of CNTs [135,136]. For instance, Wang et al. [137]

reported that dispersing a small fraction of MWCNTs into chitosan, significantly improve the mechanical strength of the composite. It has been reported that composites with just 2% MWCNTs have the Young's modulus and tensile strength of about two times more than those without MWCNTs [35]. Also it is reported that neural cells aggregate on the CNT islands and extend their neurites to form interconnected neural networks [105,138]. Edwards et al. [139] produced a potential neural scaffold formed by electrospinning poly(lactic-co-glycolic acid) (PLGA) nanofibres onto the knitted MWCNT scaffold (Fig. 6). The prepared scaffolds supported cell growth and promotes a uniform cell distribution in vitro utilizing NR6 mouse fibroblast cells for up to 22 day [139]. These findings show that carbon nanostructures have a high potential to be served as neural tissue implants and provide the necessary structural strength for neural tissue scaffolds.

8. Preparation of carbon nanostructures

Carbon nanostructures are generally prepared via three methods: arc-discharge, laser ablation, and chemical vapor deposition (CVD) [140–145]. CVD is the most widely used commercial method of producing solid materials especially carbon nanotubes. A schematic of a typical reactor is depicted in Fig. 7 [146]. In this process, a metal catalyst reacts with a hydrocarbon feedstock at high temperatures. The features of the obtained CNTs through this procedure depend on the process parameters and the reaction conditions. The presence of metal catalysts in CVD method leads to residual metal particles (Co, Ni, Mo, Fe), which remain either inside the CNTs or outside of CNTs [147]. On the other hand, in most of the times a considerable amount of amorphous carbon can be detected in prepared CNTs [148]. The presence of metal impurities in the CNTs postpones the production of reactive oxygen species (ROS) inside the cells. This in turn may also affect mitochondria and cause mitochondrial injury [149].

9. Toxicity of carbon nanostructures

The toxicity of CNTs is one the controversial issues of utilizing them as therapeutic devices. There is a discussion in the literature regarding the destructive interaction of CNTs with biological tissues [150]. Many publications reported the toxicity of CNTs [151–163], while others reported non-toxic effects in vivo and in vitro [148,164–168]. The cytotoxicity of SWCNTs using human epidermal keratinocytes (HaCaT) was studied by Shvedova et al. [132]. They found that exposure of HaCaT to SWCNTs enhanced oxidative stress and cellular toxicity which can be determined by the formation of free radicals, accumulation of peroxidative

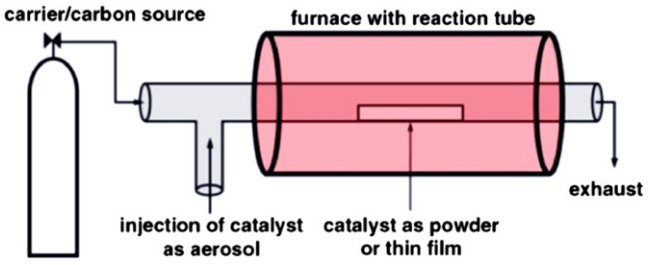

Fig. 7. Schematic design of a thermal CVD system with a tube furnace. Reprinted with the permission from [146].

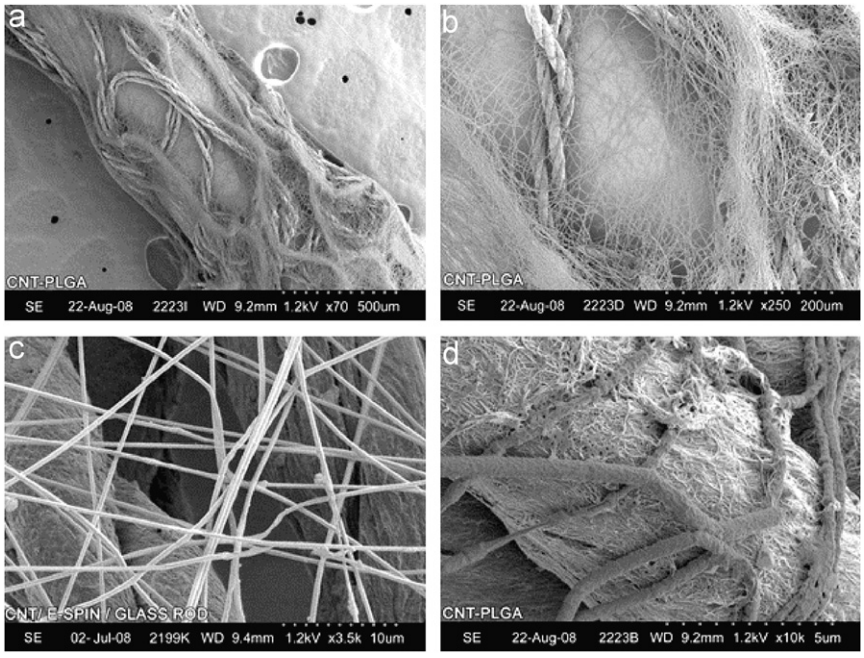

Fig. 6. SEM micrographs of MWCNT/PLGA composite scaffold: (a) low magnification of scaffold, (b) micro-scale and nano-scale pores, (c) micro-scale and nano-scale fibers, and (d) PLGA nanofibres on MWCNT yarn. Reprinted with the permission from [139].

products, and a loss of cell viability. The prepared SWCNTs had a substantial amount of metal impurities which directly affected the oxidative stress and consequently resulted in a decrease in cell viability. Pulskamp et al. [169] investigated the role of metal impurities in CNTs on rat macrophages (NR8383) and human A549 lung cells, and showed that metal impurities cause the formation of reactive oxygen species. Other research also indicated that more purified CNTs similarly showed cellular toxicity as a result of the apoptosis and necrosis of the cells [170–173]. Magrez et al. [172] studied the toxicity of carbon-based nanomaterials (MWCNTs, CNFs, carbon nanoparticles (CNPs)) on lung tumor cell as a function of their aspect ratio and surface chemistry. They found that the toxicity of these materials is dependent on the size of nanomaterials. Also it has been reported that other carbon-based nanomaterials such as carbon black (CB), active carbon, SWCNTs, and carbon graphite appear to be more toxic to human cells than MWCNTs [106,173]. Incubation of SWCNTs with alveolar macrophages (AM) at low doses ($0.38\ mg/cm^2$) seems to decrease the phagocytosis of AM [157]. It can be concluded that CNTs containing amorphous carbon and residual metal catalysts are toxic and cannot be used as therapeutic devices.

On the other hand, some studies indicate low to very low toxicity levels in various cells [174–179]. Some research reported that SWCNTs are non-toxic biomaterials towards cells, including human lung epitheliallike cells [180], murine and human macrophages [166], and rat cardiac muscle cells [181,182]. Also it is reported that the toxicity of C60 is relatively low [183]. Yokoyama et al. [184] reported that hat-stacked carbon nanofibers (H-CNF) did not show a significant inflammatory response such as necrosis. Ding et al. [170] studied the human skin fibroblast cell populations in contact with MWCNTs and nano-onions (MWCNO). Their finding showed that MWCNOs induce less stress on the cells than MWCNTs. Also they found that certain concentrations can influence the cellular growth and differentiation. Furthermore, they proposed that the regulation and expression of p38/ERK and EGFR from fibroblasts may play a substantial role in cancer therapy, especially derived cancers [170]. On the other hand, there are some research that reported the ability of CNTs to improve neural signal transfer and cell growth, adhesion and proliferation in vitro [114,185–187]. It can be concluded that toxicity of CNTs is dependent on many factors, such as their structure (SWCNT vs. MWCNT), particle size, mobility in the environment, length and aspect ratio, surface area, degree of aggregation, chemical reactivity, extent of oxidation, surface topology, surface functionalization, bond functional group(s), and method of manufacturing (which can leave catalyst residues and produce impurities) [188–190]. Furthermore, the concentration of CNTs in contact with biological cells is another important factor which determines the level of toxicity [189]. Foldvari et al. [106] reported that the toxicity of CNTs has a direct relation with the aspect ratio and a reverse one with the diameter of the nanotube. Generally, it is reported that biocompatibility of carbon nanostructures decreased according to the following order: ND > CB > MWCNT > SWCNT [191].

10. Purification of carbon nanostructures

Prepared CNTs contain lots of impurities including graphite, amorphous carbon, metal catalyst, and smaller fullerenes [192]. Hence a purification step should be applied before utilizing CNTs in therapeutic devices. Generally, the purification methods can be divided into three main parts, including chemical oxidation, physical-based purification, and multi-step purification [193–197]. In Chemical-based purification, besides removing amorphous carbon and metal impurities, a substantial amount of CNTs is lost and the structure of CNTs is destroyed. Physical-based purification maintains the structure of CNTs and can separate them according to their length or conductivity. However, the ability of this method in removing impurities is not as effective as chemical-based method. On the other hand, the CNTs should be dispersed before purification and therefore a pretreatment operation is required. Multi-step purification is a combination of several purification methods simultaneously in one purification process to achieve high purity CNTs [197–200]. For instance, one of the most popular multi-step purification methods is gas phase oxidation followed by acid treatment [201–209]. It should be noticed that not all the purification methods are suitable for treatment of carbon nanostructures to be used as biomedical devices. For example, some researchers reported that the cytotoxicity of MWCNTs was enhanced after acid treatment [171,172].

11. Functionalization of carbon nanostructures

Functionalization is one of the useful methods for surface modifications. The main aim of utilizing this procedure in the treatment of CNTs is to increase their solubility in biological media. Functionalization improves CNTs biocompatibility and consequently decreases their toxicity in comparison with pristine CNTs [210–215]. The molecular structure of some functionalized CNTs is shown in Fig. 8 [216]. Smart et al. [217] reported that chemically functionalized CNTs (f-CNTs) do not exert cytotoxicity. Dumortier et al. [218] found that f-CNTs are nontoxic and maintain the performance of primary immune cells. Sayes et al. [219] showed that the toxicity of SWCNTs decreased with increasing the degree of sidewall functionalization. They have also indicated that sidewall functionalized SWCNTs are significantly less toxic than surfactant stabilized SWCNTs. It is reported that cationic f-CNTs have much lower toxicity in vitro. Kam et al. [220] exhibited that f-SWCNTs are nontoxic at concentration below 0.05 mg/mL. Gao et al. [221] also found a significant improvement in toxicity profile of f-CNTs compared with pristine CNTs. However, it is mentioned that functionalization is not

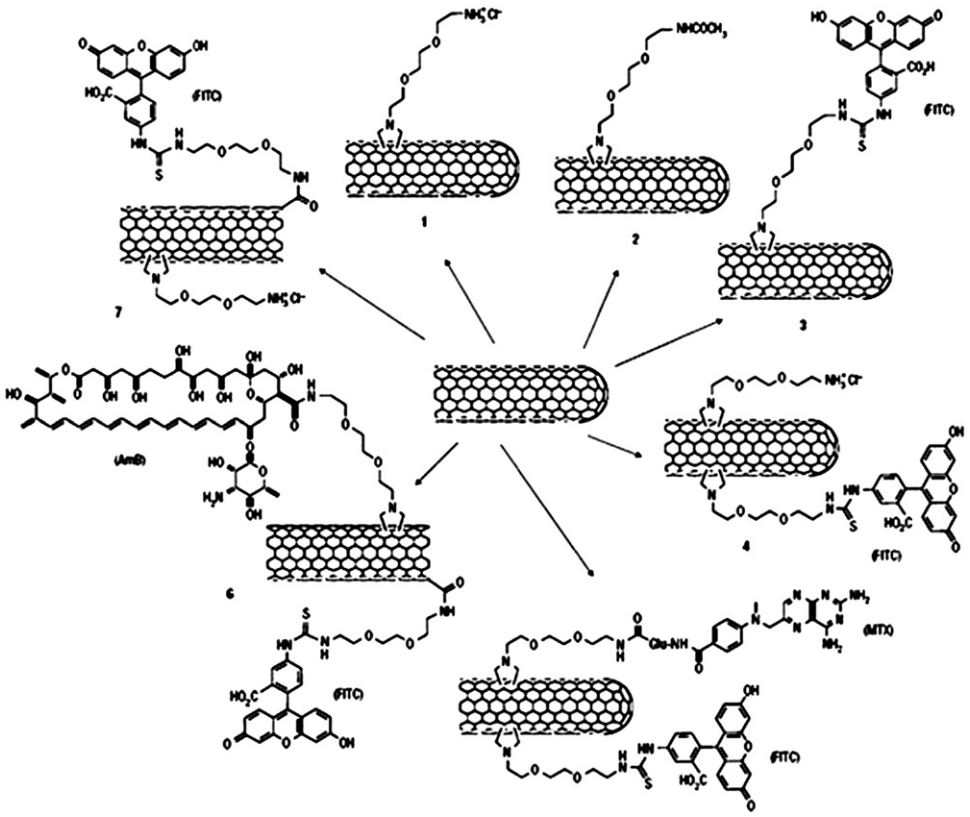

Fig. 8. Molecular structures of CNTs functinalized covalently with different types of small molecules: 1, Ammonium-functionalized CNT; 2, Acetamido-functionalized CNT; 3, CNT functionalized with fluorescein isothiocyanate (FITC); 4, CNT bifunctionalized with ammonium groups and FITC; 5, CNT bifunctionalized with methotrexate (MTX) and FITC; 6, shortened CNT bifunctionalized with amphotericin B (AmB) and FITC; 7, shortened CNT bifunctionalized with ammonium groups and FITC (through an amide linkage). Reprinted with the permission from [216].

essential to attain biocompatibility [222]. Pulskamp et al. [148] indicated that in the absence of metals catalysts and amorphous carbon residues, CNTs are nontoxic toward biological cells. On the other hand, it has been reported that dense amorphous carbon films has minimum toxicity [176]. Therefore, elaborate evaluation is necessary before utilizing carbon nanostructures in biomedical applications.

12. Carbon nanostructures and cell viability

Due to their one-dimensional nanostructures and exceptional electrical and mechanical properties, CNTs could be used as potential scaffolds and improve cell viability and cell growth [223–225]. The issue of cell viability of CNTs is also another controversial aspect of CNTs and further research is needed to comprehend the real reasons for the lack of consistency among most results shown in the literature. Some studies reported that SWCNTs cause a decrease in cell viability through biological membrane ion channel blockers [226,227], distribution of fibronectin, *P*-cadherin, focal adhesion kinase and actin in cells [173], increase cell oxidative stress [158], reduce cell attachment [156], and induce apoptosis [125,182]. On the other hand, Lobo et al. [222] reported very high cell viability of MWCNT films, close to 100% after 96 h of incubation. Zhang et al. [182] indicated that the viability of HeLa cells cultured on different scaffolds decreased in the following order: amylose-wrapped SWCNTs > acid-treated MWCNTs > MWCNTs > acid-treated SWCNTs > SWCNTs. The results of cell viability are shown in Fig. 9 [182]. Some studies have indicated that cell morphology, growth and metabolic activity are related to the diameter and surface charge of CNTs [228–230]. In addition, CNTs are added to other biomaterials to obtain efficient composites, and these CNT composites are proven to be suitable for cell growth [231,232] and increasing enzyme activity [233].

Various studies were performed in order to improve the function of carbon nanostructures. One way is to dissolve or disperse CNTs in water through adding water-soluble functional groups, such as carboxyl, hydroxyl and amino groups [234–236], polyethylene glycol and polyvinyl alcohol [237–244] and so forth [245–250]. Narain et al. [251] reported the functionalization of SWCNTs via bioinspired sugar and phosphocholine polymeric structures through surface-initiated atom transfer radical polymerization and obtained the aqueous dispersion of the f-CNTs. Bardi et al. [110] reported that MWCNTs coated with Pluronic F127 (PF127) surfactant can be injected in the mouse cerebral cortex without causing degeneration of the neurons surrounding the site of injection. Both Dutta et al. [252] and Monteiro-Riviere et al. [253] showed that PF127 has low toxicity in contact with macrophage or keratinocyte

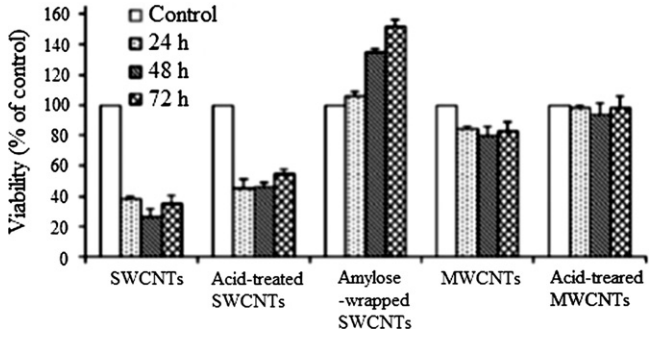

Fig. 9. Viability of HeLa cells cultured on five types of CNT scaffolds measured by WST-1 assay after seeding for 24, 48 and 72 h. HeLa cells cultured on glass slides at the same time intervals were used as controls. Reprinted with the permission from [182].

cell lines. Bardi et al. [110] stated that low concentration (0.01%) of PF127 can induce apoptosis of mouse primary cortical neurons after 24 h. On the other hand, they reported that PF127-coated MWCNTs are nontoxic. Zhang et al. [250] indicated that the phosphoryl choline (PC) group has a zwitterionic structure and therefore is hydrophilic. Consequently, it is reasonable to expect that CNTs coated with this group show hydrophilic properties and be water-soluble. This side-group offered the water solubility as well as cell-compatibility [250]. Brown et al. [254] reported an interesting method to develop CNTs as therapeutic devices. They utilized Pt as a catalyst and grew CNTs on such a biocompatible material. Using biocompatible materials as a CNT growth catalyst can contribute to the development of carbon nanostructures for biomedical purposes. In addition, carbon supported Pt catalyst shows less peroxide generation during electro reduction of oxygen compared with Fe catalyst due to the latter's formation of iron oxide or iron hydroxide phases [255,256]. The main product at a Pt catalyst from the oxygen reduction reaction is water, thus reduces the concern for cellular degeneration due to oxidative stress [254].

A complete recovery of nerve functions can be obtained through proper guiding and conducting axon regeneration between the two severed ends. This goal can be achieved through the use of knowingly engineered artificial nerve guidance channels (NGCs). Artificial NGCs have been produced using a variety of natural and synthetic materials [257]. For instance, it is reported that chitosan tubes can be used as a biocompatible and biodegradable NGC for peripheral nervous injury. The chitosan gel sponge could provide a suitable scaffold for cell adhesion, including Schwann cell and macrophages [258].

13. Conclusions and future outlook

In the topic of nervous system injury, cell viability and cell growth are extremely important. Design and fabrication of new biomaterials which affect cell viability and cell growth can open a new horizon for neuroregeneration. Carbon nanostructures are well suited as biomaterials and may play a critical role in nervous system regeneration. Since most of the preparation procedures of carbon nanostructures reported to date rely heavily on metal catalysts, a chemical functionalization is necessary to mitigate the cytotoxicity risk. A promising new approach to regenerate the injured nerve is to produce carbon nanostructured scaffolds to bridge the gap in a severed nerve. Due to the fact that carbon nanostructures influence the cell viability and cell growth, they may be used as biomimetic scaffolds to guide axon regeneration and improve neural activities. Furthermore, the use of carbon nanostructures in combination with other biomaterials such as biodegradable polymers may be essential to achieve the goals of nerve tissue engineering.

References

[1] H. Cohen, Neuroscience for Rehabilitation, second ed., Lippincott Williams and Wilkins, Philadelphia, PA, New York, 1993.
[2] Y.C. Huang, Y.Y. Huang, Biomaterials and strategies for nerve regeneration, Artificial Organs 30 (2006) 514–522.
[3] N. Zhang, H. Yan, X. Wen, Tissue-engineering approaches for axonal guidance, Brain Research Reviews 49 (2005) 48–64.
[4] M. Bahr, F. Bonhoeffer, Perspectives on axonal regeneration in the mammalian CNS, Trends Neuroscience 17 (1994) 473–479.
[5] D. Belen, A. Aciduman, U. Er, History of peripheral nerve repair: may the procedure have been practiced in Hippocratic School?, Surgery Neurology 72 (2009) 190–193
[6] J.K. Terzis, K.J. Smith, Repair of severed peripheral nerves: Comparison of the de Medinaceli and standard microsuture methods, Experimental Neurology 96 (1987) 672–680.
[7] 〈http://www.sci-info-pages.com/factsheets.html〉 (accessed January 2012).
[8] X. Navarro, M. Vivo, A. Valero-Cabre, Neural plasticity after peripheral nerve injury and regeneration, Progress in Neurobiology 82 (2007) 163–201.
[9] L. Zhang, T.J. Webster, Nanotechnology and nanomaterials: promises for improved tissue regeneration, Nano Today 4 (2009) 66–80.
[10] L. Zhang, B. Ercan, T.J. Webster, Carbon nanotubes and nanofibers for tissue engineering applications, in: C. Liu (Ed.), The Area of 'Carbon', Research Signpost, Trivandrum, 2009.
[11] C. Cunha, S. Panseri, S. Antonini, Emerging nanotechnology approaches in tissue engineering for peripheral nerve regeneration, Nanomedicine: Nanotechnology 7 (2011) 50–59.
[12] P. Wang, Z. Zhou, Q. Dong, Small gap anastomosis to repair peripheral nerve rupture using a nerve regeneration chamber constructed by scissoring and sleeve jointing autologous epineurium, Neural Regeneration Research 6 (2011) 623–628.
[13] A. Valero-Cabré, K. Tsironis, E. Skouras, G. Perego, X. Navarro, W.F. Neiss, Superior muscle reinnervation after autologous nerve graft or poly-L-lactide-epsilon-caprolactone (PLC) tube implantation in comparison to silicone tube repair, Journal of Neuroscience Research 63 (2001) 214–223.
[14] J.G. Spector, P. Lee, Axonal regeneration in severed peripheral facial nerve of the rabbit: relation of the number of axonal regenerates to behavioral and evoked muscle activity, Annals of Otology, Rhinology and Laryngology 107 (1998) 141–148.
[15] L. Wan, L. Xuequn, Electrical stimulation effects on PNS injury and repair are mediated by accelerating intracellular trafficking?, International Review of Neurobiology 87 (2009) 141–172
[16] E. Raibon, Y. Sauvé, D.A. Carter, F. Gaillard, Microglial changes accompanying the promotion of retinal ganglion cell axonal regeneration into peripheral nerve grafts, Journal of Neurocytology 31 (2002) 57–71.

[17] A.P. Lal, T. Joseph, S.M. Chandi, B. Pant, Facial neurorrhaphy with autologous sural nerve graft using the CO_2-laser in a primate model, Neurosurgery 32 (1993) 1011–1014.
[18] S.M. Willerth, S.E. Sakiyama-Elbert, Approaches to neural tissue engineering using scaffolds for drug delivery, Advanced Drug Delivery Reviews 59 (2007) 325–388.
[19] M. Dadsetan, A.M. Knight, L. Lu, A.J. Windebank, M.J. Yaszemski, Stimulation of neurite outgrowth using positively charged hydrogels, Biomaterials 30 (2009) 3874–3881.
[20] C.M. Valmikinathan, V.J. Mukhatyar, A. Jain, L. Karumbaiah, M. Dasari, R.V. Bellamkonda, Photocrosslinkable chitosan based hydrogels for neural tissue engineering, Soft Matterials 8 (2012) 1964–1976.
[21] S. Serel, B. Kaya, Y. Sara, R. Onur, A.O. Heper, Is it possible to prefabricate a vascularized peripheral nerve graft?, Annals of Plastic Surgery 64 (2010) 323–326
[22] F. Stang, G. Keilhoff, H. Fansa, Biocompatibility of different nerve tubes, Materials 2 (2009) 1480–1507.
[23] I. Kardas, W. Marcol, A. Niekraszewicz, M. Kucharska, D. Ciechańska, D. Wawro, et al., Utilization of biodegradable polymers for peripheral nerve reconstruction, Progress in the Chemistry of Applications of Chitin and its Derivatives 15 (2010) 159–168.
[24] S. Kehoe, X.F. Zhang, D. Boyd, FDA approved guidance conduits and wraps for peripheral nerve injury: a review of materials and efficacy, Injury 43 (2011) 553–572.
[25] W. Yu, W. Zhao, C. Zhu, X. Zhang, D. Ye, W. Zhang, Y. Zhou, X. Jiang, Z. Zhang, Sciatic nerve regeneration in rats by a promising electrospun collagen/poly(ε-caprolactone) nerve conduit with tailored degradation rate, BMC Neuroscience 12 (2011) 68.
[26] H.H. Nash, R.C. Borke, J.J. Anders, Ensheathing cells and methylprednisolone promote axonal regeneration and functional recovery in the lesioned adult rat spinal cord, Journal of Neuroscience 22 (2002) 7111–7120.
[27] A. Mingorance, X. Fontana, M. Solé, F. Burgaya, J.M. Ureña, F.Y. Teng, et al., Regulation of Nogo and Nogo receptor during the development of the entorhino-hippocampal pathway and after adult hippocampal lesions, Molecular and Cellular Neuroscience 26 (2004) 34–49.
[28] C.A. Willson, M. Irizarry-Ramírez, H.E. Gaskins, L. Cruz-Orengo, J.D. Figueroa, S.R. Whittemore, et al., Upregulation of EphA receptor expression in the injured adult rat spinal cord, Cell Transplantation 11 (2002) 229–239.
[29] A. El Maarouf, A.K. Petridis, U. Rutishauser, Use of polysialic acid in repair of the central nervous system, Proceedings of the National academy of Sciences of the United States of America 103 (2006) 16989–16994.
[30] M.H. Tuszynski, R. Grill, L.L. Jones, H.M. McKay, A. Blesch, Spontaneous and augmented growth of axons in the primate spinal cord: effects of local injury and nerve growth factor-secreting cell grafts, Journal of Comparative Neurology 449 (2002) 88–101.
[31] J.K. Alexander, B. Fuss, R.J. Colello, Electric field-induced astrocyte alignment directs neurite outgrowth, Neuron Glia Biology 2 (2006) 93–103.
[32] Y. Li, D. Li, G. Raisman, Interaction of olfactory ensheathing cells with astrocytes may be the key to repair of tract injuries in the spinal cord: the 'pathway hypothesis', Journal of Neurology 34 (2005) 343–351.
[33] Y. Chiba, S. Kuroda, K. Maruichi, T. Osanai, M. Hokari, S. Yano, et al., Transplanted bone marrow stromal cells promote axonal regeneration and improve motor function in a rat spinal cord injury model, Neurosurgery 64 (2009) 991–999.
[34] E.N. Kozlova, Strategies to repair lost sensory connections to the spinal cord, Molecular Biology 42 (2008) 729–737.
[35] B.S. Harrison, A. Atala, Carbon nanotube applications for tissue engineering, Biomaterials 28 (2007) 344–353.
[36] D.K. Cullen, J.A. Wolf, D.H. Smith, B.J. Pfister, Neural tissue engineering for neuroregeneration and biohybridized interface microsystems in vivo (Part 2), Critical Reviews in Biomedical Engineering 39 (2011) 241–259.
[37] K.D. Barron, The microglial cell. A historical review, Journal of Neurological Sciences 134 (1995) 57–68.
[38] S.T. Carmichael, Cellular and molecular mechanisms of neural repair after stroke: making waves, Annals of Neurology 59 (2006) 735–742.
[39] N. Sinis, H.E. Schaller, C. Schulte-Eversum, B. Schlosshauer, M. Doser, K. Dietz, et al., Tissue engineering of peripheral nerves, International Review of Neurobiology 87 (2009) 227–249.
[40] Z. Zhang, C. Ren, C. Zhang, F. Liu, L. Li, Bridging sciatic nerve gap using tissue-engineered nerves constructed with neural tissue-committed stem cells derived from bone marrow, Neural Regeneration Research 4 (2009) 344–349.
[41] A. Subramanian, U.M. Krishnan, S. Sethuraman, Development of biomaterial scaffold for nerve tissue engineering: biomaterial mediated neural regeneration, Journal of Biomedical Science 16 (2009) 108.
[42] W. Potter, R.E. Kalil, W.J. Kao, Biomimetic material systems for neural progenitor cell-based therapy, Frontiers in Bioscience 13 (2008) 806–821.
[43] M. Jurga, M.B. Dainiak, A. Sarnowska, A. Jablonska, A. Tripathi, F.M. Plieva, et al., The performance of laminin-containing cryogel scaffolds in neural tissue regeneration, Biomaterials 32 (2011) 3423–3434.
[44] J.L. Gilmore, X. Yi, L. Quan, A.V. Kabanov, Novel nanomaterials for clinical neuroscience, Journal of NeuroImmune Pharmacology 3 (2008) 83–94.
[45] J.Y. Chang, J.H. Lin, C.H. Yao, J.H. Chen, T.Y. Lai, Y.S. Chen, In vivo evaluation of a biodegradable EDC/NHS-cross-linked gelatin peripheral nerve guide conduit material, Micromolecular Bioscience 7 (2007) 500–507.
[46] B. Chaudhry, H. Ashton, A. Muhamed, M. Yost, S. Bull, D. Frankel, Nanoscale viscoelastic properties of an aligned collagen scaffold, Journal of Materials Science Materials in Medicine 20 (2009) 257–263.
[47] J.D. Flax, S. Aurora, C. Yang, C. Simonin, A.M. Wills, L.L. Billinghurst, et al., Engraftable human neural stem cells respond to developmental cues, replace neurons, and express foreign genes, Nature Biotechnology 16 (1998) 1033–1039.
[48] F. Yang, R. Murugan, S. Wang, S. Ramakrishna, Electrospinning of nano/micro scale poly(L-lactic acid) aligned fibers and their potential in neural tissue engineering, Biomaterials 26 (2005) 2603–2610.
[49] S.K. Kang, D.H. Lee, Y.C. Bae, H.K. Kim, S.Y. Baik, J.S. Jung, Improvement of neurological deficits by intracerebral transplantation of human adipose tissue-derived stromal cells after cerebral ischemia in rats, Experimental Neurology 183 (2003) 355–366.
[50] J.E. Babensee, L.V. McIntire, A.G. Mikos, Growth factor delivery for tissue engineering, Pharmaceutical Research 17 (2000) 497–504.
[51] X. Liu, P.X. Ma, Polymeric scaffolds for bone tissue engineering, Annals of Biomedical Engineering 32 (2004) 477–486.
[52] F. Yang, R. Murugan, S. Ramakrishna, X. Wang, Y.X. Ma, S. Wang, Fabrication of nano-structured porous PLLA scaffold intended for nerve tissue engineering, Biomaterials 25 (2004) 1891–1900.
[53] J.R. Jacobs, Perturbed glial scaffold formation precede axon tract malformation in drosophila mutants, Journal of Neurobiology 24 (1993) 611–626.
[54] H. Shin, S. Jo, A.G. Mikos, Biomimetic materials for tissue engineering, Biomaterial 24 (2003) 4353–4364.
[55] X. Gu, F. Ding, Y. Yang, J. Liu, Construction of tissue engineered nerve grafts and their application in peripheral nerve regeneration, Progress in Neurobiology 93 (2011) 204–230.
[56] R. Deumens, A. Bozkurt, M.F. Meek, M.A.E. Marcus, E.A.J. Joosten, J. Weis, G.A. Brook, Repairing injured peripheral nerves: bridging the gap, Progress in Neurobiology 92 (2010) 245–276.
[57] B. Schlosshauer, L. Dreesmann, H.E. Schaller, N. Sinis, Synthetic nerve guide implants in humans: a comprehensive survey, Neurosurgery 59 (2006) 740–748.
[58] C.L. Vleggeert-Lankamp, J. Wolfs, A.P. Pego, R. van den Berg, H. Feirabend, E. Lakke, Pores in synthetic nerve conduits are

beneficial to regeneration, Journal of Biomedial Materials Research Part A 80 (2007) 965–982.
[59] C.L. Vleggeert-Lankamp, J. Wolfs, A.P. Pego, R. van den Berg, H. Feirabend, E. Lakke, Effect of nerve graft porosity on the refractory period of regenerating nerve fibers, Journal of Neurosurgery 109 (2008) 294–305.
[60] N. Ashammakhi, A. Ndreu, L. Nikkola, I. Wimpenny, Y. Yang, Advancing tissue engineering by using electrospun nanofibers, Regenerative Medicine 3 (2008) 547–574.
[61] W. Wang, S. Itoh, A. Matsuda, T. Aizawa, M. Demura, S. Ichinose, et al., Enhanced nerve regeneration through a bilayered chitosan tube: the effect of introduction of glycine spacer into the CYIGSK sequence, Journal of Biomedial Materials Research Part A 85 (2008) 919–928.
[62] Y. Sakai, Y. Matsuyama, K. Takahashi, T. Sato, T. Hattori, S. Nakashima, et al., New artificial nerve conduits made with photocrosslinked hyaluronic acid for peripheral nerve regeneration, Bio-Medical Materials and Engineering 17 (2007) 191–197.
[63] V.L. Chavez, L. Song, S. Barau, X. Li, D.Y. Zhao, K. Rege, B.D. Vogt, Impact of nanopore morphology on osteoblast viability on mesoporous polymer and carbon surfaces, Acta Biomaterialia 6 (2010) 3035–3043.
[64] T. Stieglitz, Considerations on surface and structural biocompatibility as prerequisite for long-term stability of neural prostheses, Journal of Nanoscience and Nanotechnology 4 (2004) 496–503.
[65] H.S. Koh, T. Yong, C.K. Chan, S. Ramakrishna, Enhancement of neurite outgrowth using nano-structured scaffolds coupled with laminin, Biomaterials 29 (2008) 3574–3582.
[66] D. Khang, J.L. McKenzie, T.J. Webster, Carbon nanofibers:polycarbonate urethane composites as a neural biomaterial, Bioengineering Conference 17 (2004) 241–242.
[67] L. Ghasemi-Mobarakeh, M.P. Prabhakaran, M. Morshed, M.H. Nasr-Esfahani, H. Baharvand, S. Kiani, et al., Application of conductive polymers, scaffolds and electrical stimulation for nerve tissue engineering, Journal of Tissue Engineering and Regenerative Medicine 5 (2011) 17–35.
[68] J.A. Stella, A.D. Amore, W.R. Wagner, M.S. Sacks, On the biomechanical function of scaffolds for engineering load-bearing soft tissues, Acta Biomaterialia 6 (2010) 2365–2381.
[69] C.R. Lamar, W. Gardner, A. Brazda, R.A. Kesterson, Surface strategies for control of neuronal cell adhesion: a review, Surface Science 65 (2010) 145–173.
[70] S. Möllers, I. Heschel, L.H. Damink, F. Schügner, R. Deumens, B. Müller, et al., Cytocompatibility of a novel, longitudinally microstructured collagen scaffold intended for nerve tissue repair, Tissue Engineering Part A 15 (2009) 461–472.
[71] P.H. Long, Medical devices in orthopedic applications, Toxicologic Pathology 36 (2008) 85–91.
[72] U.M. Krishnan, S. Sethuraman, Development of biomaterial scaffold for nerve tissue engineering: biomaterial mediated neural regeneration, Journal of Biomedical Science 16 (2009) 108.
[73] N. Gomez, J.Y. Lee, J.D. Nickels, C.E. Schmidt, Micropatterned polypyrrole: a combination of electrical and topographical characteristics for the stimulation of cells, Advanced Functional Materials 17 (2007) 1645–1653.
[74] M.B. Runge, M. Dadsetan, J. Baltrusaitis, A.M. Knight, T. Ruesink, E.A. Lazcano, et al., The development of electrically conductive polycaprolactone fumarate-polypyrrole composite materials for nerve regeneration, Biomaterials 31 (2010) 5916–5926.
[75] J.Y. Lee, C.A. Bashur, C.A. Milroy, L. Forciniti, A.S. Goldstein, C.E. Schmidt, Nerve growth factor-immobilized electrically conducting fibrous scaffolds for potential use in neural engineering applications, NanoBioscience 11 (2012) 15–21.
[76] T. Waitayawinyu, D.M. Parisi, B. Miller, S. Luria, H.J. Morton, S.H. Chin, T.E. Trumble, A comparison of polyglycolic acid versus type 1 collagen bioabsorbable nerve conduits in a rat model: an alternative to autografting, Journal of Hand Surgery 32 (2007) 1521–1529.
[77] S.H. Hsu, S.H. Chan, C.M. Chiang, C. Chen, C.F. Jiang, Peripheral nerve regeneration using a microporous polylactic acid asymmetric conduit in a rabbit long-gap sciatic nerve transection model, Biomaterials 32 (2011) 3764–3775.
[78] D. Yucel, G.T. Kose, V. Hasirci, Polyester based nerve guidance conduit design, Biomaterials 31 (2010) 1596–1603.
[79] E.W. Henry, T.H. Chiu, E. Nyilas, T.M. Brushart, P. Dikkes, R.L. Sidman, Nerve regeneration through biodegradable polyester tubes, Experimental Neurology 90 (1985) 652–676.
[80] H. Molander, O. Engkvist, J. Hägglund, Y. Olsson, E. TorebjöPkt, Nerve repair using a polyglactin tube and nerve graft: an experimental study in the rabbit, Biomaterials 4 (1983) 276–280.
[81] I.H. Whitworth, R.A. Brown, C.J. Doré, P. Anand, C.J. Green, G. Terenghi, Nerve growth factor enhances nerve regeneration through fibronectin grafts, Journal of Hand Surgery 21 (1996) 514–522.
[82] S. Yoshii, M. Oka, M. Shima, A. Taniguchi, M. Akagi, 30 mm regeneration of rat sciatic nerve along collagen filaments, Brain Research 949 (2002) 202–208.
[83] F. Stang, H. Fansa, G. Wolf, M. Reppin, G. Keilhoff, Structural parameters of collagen nerve grafts influence peripheral nerve regeneration, Biomaterials 26 (2005) 3083–3091.
[84] L. Luckenbill-Edds, Laminin and the mechanism of neuronal outgrowth, Brain Research Reviews 23 (1997) 1–27.
[85] D.J. Trigg, K.M. O'Grady, T. Bhattacharyya, M. Reinke, D.M. Toriumi, Peripheral nerve regeneration: comparison of laminin and acidic fibroblast growth factor, American Journal of Otolaryngology 19 (1998) 29–32.
[86] J.K. Terzis, D.D. Sun, P.K. Thanos, Historical and basic science review: past, present, and future of nerve repair, Journal of Reconstructive Microsurgery 13 (1997) 215–225.
[87] H.S. Neto, M.C. Somazz, M.J. Marques, R.M. Teodori, Axonal regeneration through muscle autografts submitted to local anaesthetic pretreatment, British Journal of Plastic Surgery 51 (1998) 555–560.
[88] R. Levinthal, W.J. Brown, R.W. Rand, Fascicular nerve allograft evaluation, Part 1: comparison with autografts by light microscopy, Journal of Neurosurgery 48 (1978) 423–427.
[89] H. Fansa, G. Keilhoff, G. Wolf, W. Schneider, Tissue engineering of peripheral nerves: a comparison of venous and acellular muscle grafts with cultured Schwann cells, Plastic and Reconstructive Surgery 107 (2001) 485–494.
[90] H. Fansa, G. Keilhoff, Comparison of different biogenic matrices seeded with cultured Schwann cells for bridging peripheral nerve defects, Neurology Research 26 (2004) 167–173.
[91] S.C. Haase, J.M. Rovak, R.G. Dennis, W.M. Kuzon, P.S. Cederna, Recovery of muscle contractile function following nerve gap repair with chemically acellularized peripheral nerve grafts, Journal of Reconstructive Microsurgery 19 (2003) 241–248.
[92] P. Lesný, J. De Croos, M. Prádný, J. Vacík, J. Michálek, S. Woerly, E. Syková, Polymer hydrogels usable for nervous tissue repair, Journal of Chemical Neuroanatomy 23 (2002) 243–247.
[93] S.Y. Chew, R. Mi, A. Hoke, K.W. Leong, Aligned protein-polymer composite fibers enhance nerve regeneration: a potential tissue-engineering platform, Advanced Functional Materials 17 (2007) 1288–1296.
[94] M. Oudega, S.E. Gautier, P. Chapon, M. Fragoso, M.L. Bates, J.M. Parel, et al., Axonal regeneration into Schwann cell grafts within resorbable poly(alpha-hydroxyacid) guidance channels in the adult rat spinal cord, Biomaterials 22 (2001) 1125–1136.
[95] M. Radisic, H. Park, S. Gerecht, R. Langer, G. Vunjak-Novakovic, Biomimetic approach to cardiac tissue engineering, Philosophical Transactions of the Royal Society of London, Series B 362 (2007) 1357–1368.
[96] M.S. Widmer, P.K. Gupta, L. Lu, R.K. Meszlenyi, G.R. Evans, K. Brandt, et al., Manufacture of porous biodegradable polymer conduits by an extrusion process for guided tissue regeneration, Biomaterials 19 (1998) 1945–1955.

[97] A.P. Pêgo, A.A. Poot, D.W. Grijpma, J. Feijen, Biodegradable elastomeric scaffolds for soft tissue engineering, Journal of Controlled Release 87 (2003) 69–79.
[98] Z. She, C. Jin, Z. Huang, B. Zhang, Q. Feng, Y. Xu, Silk fibroin/chitosan scaffold: preparation, characterization, and culture with HepG2 cell, Journal of Materials Science Materials in Medicine 19 (2008) 3545–3553.
[99] M. Rafat, F. Li, P. Fagerholm, N.S. Lagali, M.A. Watsky, R. Munger, et al., PEG-stabilized carbodiimide crosslinked collagen-chitosan hydrogels for corneal tissue engineering, Biomaterials 29 (2008) 3960–3972.
[100] H. Yoshimoto, Y.M. Shin, H. Terai, J.P. Vacanti, A biodegradable nanofiber scaffold by electrospinning and its potential for bone tissue engineering, Biomaterials 24 (2003) 2077–2082.
[101] X. Zong, K. Kim, D. Fang, S. Ran, B. Hsiao, B. Chu, Structure and process relationship of electrospun bioabsorbable nanofiber membranes, Polymer 43 (2002) 4403–4412.
[102] E.T. Thostenson, Z. Ren, T.W. Chou, Advances in the science and technology of carbon nanotubes and their composites: a review, Composites Science and Technology 61 (2001) 1899–1912.
[103] A. Yokoyama, Y. Sato, Y. Nodasaka, S. Yamamoto, T. Kawasaki, M. Shindoh, T. Kohgo, T. Akasaka, M. Uo, F. Watari, K. Tohji, Biological behavior of hat-stacked carbon nanofibers in the subcutaneous tissue in rats, Nano Letters 5 (2005) 157–161.
[104] K.L. Klein, A.V. Melechko, T.E. McKnight, S.T. Retterer, P.D. Rack, J.D. Fowlkes, D.C. Joy, M.L. Simpson, Surface characterization and functionalization of carbon nanofibers, Journal of Applied Physics 103 (2008) 061301–061326.
[105] P.A. Tran, L. Zhang, T.J. Webster, Carbon nanofibers and carbon nanotubes in regenerative medicine, Advanced Drug Delivery Reviews 61 (2009) 1097–1114.
[106] M. Foldvari, M. Bagonluri, Carbon nanotubes as functional excipients for nanomedicines: II. Drug delivery and biocompatibility issues, Nanomedicine: Nanotechnology 4 (2008) 183–200.
[107] P. Galvan-Garcia, E.W. Keefer, F. Yang, M. Zhang, S. Fang, A.A. Zakhidov, R.H. Baughman, M.I. Romero, Robust cell migration and neuronal growth on pristine carbon nanotube sheets and yarns, Journal of Biomaterials Science Polymer Edition 18 (2007) 1245–1261.
[108] E. Jan, N.A. Kotov, Successful differentiation of mouse neural stem cells on layer-by-layer assembled single-walled carbon nanotube composite, Nano Letters 7 (2007) 1123–1128.
[109] M.P. Mattson, R.C. Haddon, A.M. Rao, Molecular functionalization of carbon nanotubes and use as substrates for neuronal growth, Journal of Molecular Neuroscience 14 (2000) 175–182.
[110] G. Bardi, P. Tognini, G. Ciofani, V. Raffa, M. Costa, T. Pizzorusso, Pluronic-coated carbon nanotubes do not induce degeneration of cortical neurons in vivo and in vitro, Nanomedicine: Nanotechnology 5 (2009) 96–104.
[111] K.D. Sattler, handbook of Nanophysics: Nanomedicine and Nanorobotics, CRC Press Taylor &Francis Group, Boca Raton, London, New York, 2011.
[112] H. Hu, Y. Ni, V. Montana, R.C. Haddon, V. Parpura, Chemically functionalized carbon nanotubes as substrates for neuronal growth, Nano Letters 4 (2004) 507–511.
[113] A. Mazzatenta, M. Giugliano, S. Campidelli, L. Gambazzi, L. Businaro, H. Markram, M. Prato, L. Ballerini, Interfacing neurons with carbon nanotubes: electrical signal transfer and synaptic stimulation in cultured brain circuits, Journal of Neuroscience 27 (2007) 6931–6936.
[114] V. Lovat, D. Pantarotto, L. Lagostena, B. Cacciari, M. Grandolfo, M. Righi, G. Spalluto, M. Prato, L. Ballerini, Carbon nanotube substrates boost neuronal electrical signaling, Nano Letters 5 (2005) 1107–1110.
[115] M.K. Gheith, V.A. Sinani, J.P. Wicksted, R.L. Matts, N.A. Kotov, Single-walled carbon nanotube polyelectrolyte multilayers and freestanding films as a biocompatible platform for neuroprosthetic implants, Advanced Materials 17 (2005) 2663–2670.
[116] W.H. Suh, K.S. Suslick, G.D. Stucky, Y.H. Suh, Nanotechnology, nanotoxicology, and neuroscience, Progress in Neurobiology 87 (2009) 133–170.
[117] E. Jan, N.A. Kotov, Successful differentiation of mouse neural stem cells on layer-by-layer assembled single-walled carbon nanotube composite, Nano Letters 7 (2007) 1123–1128.
[118] W.M. Tsang, A.L. Stone, D. Otten, Z.N. Aldworth, T.L. Daniel, J.G. Hildebrand, et al., Insect-machine interface: a carbon nanotube-enhanced flexible neural probe, Journal of Neuroscience Methods 204 (2012) 335–365.
[119] I. Firkowska, M. Olek, N. Pazos-Peréz, J. Rojas-Chapana, M. Giersig, Highly ordered MWNT-based matrixes: topography at the nanoscale conceived for tissue engineering, Langmuir 22 (2006) 5427–5434.
[120] A. Bianco, C. Del Gaudio, S. Baiguera, I. Armentano, C. Bertarelli, M. Dottori, et al., Microstructure and cytocompatibility of electrospun nanocomposites based on poly(epsilon-caprolactone) and carbon nanostructures, International Journal of Artificial Organs 33 (2010) 271–282.
[121] N.A. Kotov, J.O. Winter, I.P. Clements, E. Jan, B.P. Timko, S. Campidelli, et al., Nanomaterials for Neural Interfaces, Advanced Materials 21 (2009) 3970–4004.
[122] N.B. Chauhan, H.M. Figlewicz, T. Khan, Carbon filaments direct the growth of postlesional plastic axons after spinal cord injury, International Journal of Developmental Neuroscience 17 (1999) 255–264.
[123] K.L. Elias, R.L. Price, T.J. Webster, Enhanced functions of osteoblasts on nanometer diameter carbon fibers, Biomaterials 23 (2002) 3279–3287.
[124] T. Khan, M. Dauzvardis, S. Sayers, Carbon filament implants promote axonal growth across the transected rat spinal cord, Brain Research 541 (1991) 139–145.
[125] V. Pesakova, Z. Klezl, K. Balik, M. Adam, Biomechanical and biological properties of the implant material carbon-carbon composite covered with pyrolytic carbon, Journal of Materials Science Materials in Medicine 11 (2000) 793–798.
[126] G. Cellot, E. Cilia, S. Cipollone, V. Rancic, A. Sucapane, S. Giordani, L. Gambazzi, H. Markram, M. Grandolfo, D. Scaini, F. Gelain, L. Casalis, M. Prato, M. Giugliano, L. Ballerini, Carbon nanotubes might improve neuronal performance by favouring electrical shortcuts, Nature Nanotechnology 4 (2009) 126–133.
[127] G. Hummer, J.C. Rasaiah, J.P. Noworyta, Water conduction through the hydrophobic channel of a carbon nanotube, Nature 414 (2001) 188–190.
[128] G. Chen, Y.R. Hu, H. Wan, L. Xia, J.H. Li, F. Yang, et al., Functional recovery following traumatic spinal cord injury mediated by a unique polymer scaffold seeded with neural stem cells and Schwann cells, Chinese Medical Journal 123 (2010) 2424–2431.
[129] M.I. Rehermann, N. Marichal, R.E. Russo, O. Trujillo-Cenóz, Neural reconnection in the transected spinal cord of the freshwater turtle trachemys dorbignyi, Journal of Comparative Neurology 515 (2009) 197–214.
[130] S.M.Z. Hossain, S.M.E. Babar, S.M.G. Azam, S.N. Sarma, G.D. Haki, Spinal cord injury treatment using a noble Biocompatible bridge, Molecular & Cellular Toxicology 3 (2007) 151–158.
[131] A.G. Dervan, B.L. Roberts, Reaction of spinal cord central canal cells to cord transection and their contribution to cord regeneration, Journal of Comparative Neurology 458 (2003) 293–306.
[132] L. Yang, L. Zhang, T.J. Webster, Nanobiomaterials: state of the art and future trends, Advanced Engineering Materials 13 (2011) 197–217.
[133] J.L. McKenzie, M.C. Waid, R. Shi, T.J. Webster, Decreased function of astrocytes on carbon nanofibers materials, Biomaterials 25 (2004) 1309–1317.
[134] T.D.B. Nguyen-Vu, H. Chen, A.M. Cassell, R.J. Andrews, M. Meyyappan, J. Li, Vertically aligned carbon nanofiber

architecture as a multifunctional 3-D neural electrical interface, IEEE Transactions on Biomedical Engineering 54 (2007) 1121–1128.
[135] L. Belyanskaya, P. Manser, P. Spohn, A. Bruinink, P. Wick, The reliability and limits of the MTT reduction assay for carbon nanotubes–cell interaction, Carbon 45 (2007) 2643–2648.
[136] H. Miyagawa, M. Misra, A.K. Mohanty, Mechanical properties of carbon nanotubes and their polymer nanocomposites: a review, Journal of Nanoscience and Nanotechnology 5 (2005) 1593–1615.
[137] S.F. Wang, L. Shen, W.D. Zhang, Y.J. Tong, Preparation and mechanical properties of chitosan/carbon nanotubes composites, Biomacromolecules 6 (2005) 3067–3072.
[138] T. Gabay, E. Jakobs, E. Ben-Jacob, Y. Hanein, Engineered self-organization of neural networks using carbon nanotube clusters, Physica A: Statistical Mechanics and its Applications 350 (2005) 611–621.
[139] S.L. Edwards, J.S. Church, J.A. Werkmeister, J.A.M. Ramshaw, Tubular micro-scale multiwalled carbon nanotube-based scaffolds for tissue engineering, Biomaterials 30 (2009) 1725–1731.
[140] C. Journet, W.K. Maser, P. Bernier, A. Loiseau, M. Lamy de la Chappelle, S. Lefrant, P. Deniard, R. Lee, J.E. Fischer, Large-scale production of single-walled carbon nanotubes by the electric-arc technique, Nature 388 (1997) 756–758.
[141] A. Thess, Roland Lee, H. Pavel Nikolaev, P. Dai, J. Petit, C. Robert, Y. Xu, S. Hee Lee, A.G. Gon Kim, D.T. Rinzler, G.E. Colbert, D. Scuseria, J.E. Tománek, R.E. Fischer, Smalley, crystalline ropes of metallic carbon nanotubes, Science 273 (1996) 483–487.
[142] A.M. Cassell, J.A. Raymakers, J. Kong, H. Dai, Large scale CVD synthesis of single-walled carbon nanotubes, Journal of Physical Chemistry B 103 (1999) 6484–6492.
[143] E.T. Thostenson, Z.F. Ren, T.W. Chou, Advances in the science and technology of carbon nanotubes and their composites: a review, Composites Science and Technology 61 (2001) 1899–1912.
[144] T.W. Ebbeseb, P.M. Ajayan, Large-scale synthesis of carbon nanotubes, Nature 358 (1992) 220–222.
[145] T. Sugai, H. Yoshida, T. Shimada, T. Okazaki, H. Shinohara, New synthesis of high-quality double-walled carbon nanotubes by high-temperature pulsed arc discharge, Nano Letters 3 (2003) 769–773.
[146] K. Koziol, B.O. Boskovic, N. Yahya, Synthesis of Carbon Nanostructures by CVD Method, Carbon and Oxide Nanostructures Synthesis, Characterisation and Application, Yahya, N. 2011, VIII, 450, ISBN:978-3-642-14672-5.
[147] N. Sinha, J.T.W. Yeow, Carbon nanotubes for biomedical applications, IEEE Transactions on Nanobioscience 4 (2005) 180–195.
[148] K. Pulskamp, J.M. Wörle-Knirsch, K. Kern, H.F. Krug, Human lung epithelial cells show biphasic oxidative burst after single-walled carbon nanotube contact, Carbon 45 (2007) 2241–2249.
[149] T.C. Long, N. Saleh, R.D. Tilton, G.V. Lowry, B. Veronesi, Non-photoactivated titanium dioxide nanoparticles produce reactive oxygen species in immortalized mouse microglia (BV2), Environmental Science and Technology 40 (2006) 4346.
[150] L. Lacerda, A. Bianco, M. Prato, K. Kostarelos, Carbon nanotubes as nanomedicines: from toxicology to pharmacology, Advanced Drug Delivery Reviews 58 (2006) 1460–1470.
[151] D.B. Warheit, B.R. Laurence, K.L. Reed, D.H. Roach, G.A.M. Reynolds, T.R. Webb, Comparative pulmonary toxicity assessment of single-wall carbon nanotubes in rats, Toxicological Sciences 77 (2004) 117–125.
[152] S. Koyama, M. Endo, Y.A. Kim, T. Hayashi, T. Yanagisawa, K. Osaka, H. Koyama, N. Kuroiwa, Progress and perspectives in the carbon nanotube world, Carbon 44 (2006) 1079–1092.
[153] J. Muller, F. Huaux, D. Lison, Respiratory toxicity of carbon nanotubes: how worried should we be?, Carbon 44 (2006) 1048–1056
[154] C.W. Lam, J.T. James, R. McCluskey, R.L. Hunter, Pulmonary toxicity of single wall carbon nanotubes in mice 7 and 90 day after intratracheal instillation, Toxicological Sciences 77 (2004) 126–134.
[155] M. Bottini, A. Magrini, N. Bottini, A. Bergamaschi, Nanotubes and fullerenes: an overview of the possible environmental and biological impact of bio-nanotechnologies, Medical Lav. 94 (2003) 497–505.
[156] D. Cui, F.R. Tian, C.S. Ozkan, M. Wang, H.J. Gao, Effect of single wall carbon nanotubes on human HEK293 cells, Toxicology Letters 155 (2005) 73–85.
[157] G. Jia, H. Wang, L. Yan, X. Wang, R. Pei, T. Yan, Y. Zhao, X. Guo, Cytotoxicity of carbon nanomaterials: single-wall nanotube, multi-wall nanotube, and fullerene, Environmental Science and Technology 39 (2005) 1378–1383.
[158] S.K. Manna, S. Sarkar, J. Barr, K. Wise, E.V. Barrera, O. Jejelowo, A.C. Rice-Ficht, G.T. Ramesh, Single-walled carbon nanotube induces oxidative stress and activates nuclear transcription factor-κB in human keratinocytes, Nano Letters 5 (2005) 1676–1684.
[159] N.A. Monteiro-Riviere, R.J. Nemanichb, A.O. Inmana, Y.Y. Wangb, J.E. Riviere, Multi-walled carbon nanotube interactions with human epidermal keratinocytes, Toxicology Letters 155 (2005) 377–384.
[160] J. Muller, F. Huaux, N. Moreau, P. Misson, J.F. Heilier, M. Delos, M. Arras, A. Fonseca, J.B. Nagy, D. Lison, Respiratory toxicity of multi-wall carbon nanotubes, Toxicology and Applied Pharmacology 207 (2005) 221–231.
[161] L.E. Murr, K.M. Garza, K.F. Soto, A. Carrasco, T.G. Powell, D.A. Ramirez, P.A. Guerrero, D.A. Lopez, J. Venzor, Cytotoxicity assessment of some carbon nanotubes and related carbon nanoparticle aggregates and the implications for anthropogenic carbon nanotube aggregates in the environment, International Journal of Environment Research and Public Health 2 (2005) 31–42.
[162] A.A. Shvedova, V. Castranova, E. Kisin, D. Schwegler-Berry, A. Murray, V. Gandelsman, A. Maynard, P. Baron, Exposure to carbon nanotube material: assessment of nanotube cytotoxicity using human keratinocyte cells, Journal of Toxicology & Environmental Health Part A: Current Issues 66 (2003) 1909–1926.
[163] A.A. Shvedova, E.R. Kisin, R. Mercer, A.R. Murray, V.J. Johnson, A.I. Potapovich, et al., Unusual inflammatory and fibrogenic pulmonary responses to single-walled carbon nanotubes in mice, American Journal of Physiology—Lung Cellular and Molecular Physiology 289 (2005) 698–708.
[164] J. Chlopek, B. Czajkowska, B. Szaraniec, E. Frackowiak, K. Szostak, F. Béguin, In vitro studies of carbon nanotubes biocompatibility, Carbon 44 (2006) 1106–1111.
[165] S. Fiorito, A. Serafino, F. Andreola, A. Togna, G. Togna, Toxicity and biocompatibility of carbon nanoparticies, Journal of Nanoscience and Nanotechnology 6 (2006) 591–599.
[166] S. Fiorito, A. Serafino, F. Andreola, P. Bernier, Effects of fullerenes and single-wall carbon nanotubes on murine and human macrophages, Carbon 44 (2006) 1100–1105.
[167] E. Flahaut, M.C. Durrieu, M. Remy-Zholgadri, R. Bareille, Ch. Baquey, Investigation of the cytotoxicity of CCVD carbon nanotubes towards human umbilical vein endothelial cells, Carbon 44 (2006) 1093–1099.
[168] E. Flahaut, M.C. Durrieu, M. Remy-Zolghadri, R. Bareille, C. Baquey, Study of the cytotoxicity of CCVD carbon nanotubes, Journal of Materials Science 41 (2006) 2411–2416.
[169] K. Pulskamp, S. Diabate, H.F. Krug, Carbon nanotubes show no sign of acute toxicity but induce intracellular reactive oxygen species in dependence on contaminants, Toxicology Letters 168 (2007) 58–74.
[170] L. Ding, J. Stilwell, T. Zhang, O. Elboudwarej, H. Jiang, J.P. Selegue, P.A. Kooke, J.W. Gray, F.F. Chen, Molecular, molecular characterization of the cytotoxic mechanism of multiwall carbon nanotubes and nano-onions on human skin fibroblast, Nano Letters 5 (2005) 2448–2464.
[171] M. Bottini, S. Bruckner, K. Nika, N. Bottini, S. Bellucci, A. Magrini, A. Bergamaschi, T. Mustelin, Multi-walled carbon nanotubes induce T lymphocyte apoptosis, Toxicology Letters 160 (2006) 121–126.
[172] A. Magrez, S. Kasas, V. Salicio, N. Pasquier, J.W. Seo, M. Celio, S. Catsicas, B. Schwaller, L. Forro, Cellular toxicity of carbon-based nanomaterials, Nano Letters 6 (2006) 1121–1125.

[173] F. Tian, D. Cui, H. Schwarz, G.G. Estrada, H. Kobayashi, Cytotoxicity of single-wall carbon nanotubes on human fibroblasts, Toxicology in Vitro 20 (2006) 1202–1212.
[174] N.W.S. Kam, T.C. Jessop, P.A. Wender, H. Dai, Nanotube molecular transporters: internalization of carbon nanotube–protein conjugates into mammalian cells, Journal of the American Chemical Society 126 (2004) 6850–6851.
[175] M. de Nicola, S. Bellucci, E. Traversa, G. DeBellis, F. Micciulla, L. Ghibelli, Effect of different carbon nanotubes on cell viability and proliferation, Journal of Physics: Condensed Matter 19 (2007) 395013.
[176] S. Kang, M. Pinault, L.D. Pfefferle, M. Elimelech, Single-walled carbon nanotubes exhibit strong antimicrobial activity, Langmuir 23 (2007) 8670–8673.
[177] H.N. Yehia, R.K. Draper, C. Mikoryak, E.K. Walker, P. Bajaj, I.H. Musselman, M.C. Daigrepont, G.R. Dieckmann, P. Pantano, Single-walled carbon nanotube interactions with HeLa cells, Journal of Nanbiotechnology 5 (2007) 8–24.
[178] M. Davoren, E. Herzog, A. Casey, B. Cottineau, G. Chambers, H.J. Byrne, F.M. Lyng, In vitro toxicity evaluation of single walled carbon nanotubes on human A549 lung cells, Toxicology in Vitro 21 (2007) 438–448.
[179] A.E. Porter, Direct imaging of single-walled carbon nanotubes in cells, Nature Nanotechnology 2 (2007) 713–717.
[180] J.M. Worle-Knirsch, K. Pulskamp, H.F. Krug, Oops They Did It, Again! carbon nanotubes Hoax scientists in viability assays, Nano Letters 6 (2006) 1261–1268.
[181] S. Garibaldi, C. Brunelli, V. Bavastrello, G. Ghigliotti, C. Nicolini, Carbon nanotube biocompatibility with cardiac muscle cells, Nanotechnology 17 (2006) 391–397.
[182] X. Zhang, X. Wang, Q. Lu, C. Fu, Influence of carbon nanotube scaffolds on human cervical carcinoma HeLa cell viability and focal adhesion kinase expression, Carbon 46 (2008) 453–460.
[183] J.E. Roberts, A.R. Wielgus, W.K. Boyes, U. Andley, C.F. Chignell, Phototoxicity and cytotoxicity of fullerol in human lens epithelial cells, Toxicology and Applied Pharmacology 228 (2008) 49–58.
[184] A. Yokoyama, Y. Sato, Y. Nodasaka, S. Yamamoto, T. Kawasaki, M. Shindoh, T. Kohgo, T. Akasaka, M. Uo, F. Watari, K. Tohji, Biological behavior of hat-stacked carbon nanofibers in the subcutaneous tissue in rats, Nano Letters 5 (2005) 157–161.
[185] R.A. MacDonald, B.F. Laurenzi, G. Viswanathan, P.M. Ajayan, J.P. Stegemann, Collagen-carbon nanotube composite materials as scaffolds in tissue engineering, Journal of Biomedial Materials Research 74 (2005) 489–496.
[186] M.A. Correa-Duarte, N. Wagner, J. Rojas-Chapana, C. Morsczeck, M. Thie, M. Giersig, Fabrication and biocompatibility of carbon nanotube-based 3D networks as scaffolds for cell seeding and growth, Nano Letters 4 (2004) 2233–2236.
[187] P.R. Supronowicz, P.M. Ajayan, K.R. Ullmann, B.P. Arulanandam, D.W. Metzger, R. Bizios, Novel current-conducting composite substrates for exposing osteoblasts to alternating current stimulation, Journal of Biomedial Materials Research 59 (2002) 499–506.
[188] A. Helland, P. Wick, A. Koehler, K. Schmid, C. Som, Reviewing the environmental and human health knowledge base of carbon nanotubes, Environmental Health Perspectives 115 (2007) 1125–1131.
[189] C.P. Firme, P.R. Bandaru, Toxicity issues in the application of carbon nanotubes to biological systems, Nanomedicine: Nanotechnology 6 (2010) 245–256.
[190] A. Nimmagadda, K. Thurston, M.U. Nollert, P.S. McFetridge, Chemical modification of SWNT alters in vitro cell-SWNT interactions, Journal of Biomedial Materials Research 76 (2006) 614–625.
[191] A.M. Schrand, L.M. Dai, J.J. Schlager, S.M. Hussain, E. Osawa, Differential biocompatibility of carbon nanotubes and nanodiamonds, Diamond and Related Materials 16 (2007) 2118–2123.
[192] A.E. Agboola, R.W. Pike, T.A. Hertwig, H.H. Lou, Conceptual design of carbon nanotube processes, Clean Technologies and Environmental Policy 9 (2007) 289–311.
[193] K.L. Strong, D.P. Anderson, K. Lafdi, J.N. Kuhn, Purification process for single-wall carbon nanotubes, Carbon 41 (2003) 1477–1488.
[194] D. Chattopadhyay, I. Galeska, F. Papadimitrakopoulos, Complete elimination of metal catalyst from single wall carbon nanotubes, Carbon 40 (2002) 985–988.
[195] R. Andrews, D. Jacques, D. Qian, E.C. Dickey, Purification and structural annealing of multiwalled carbon nanotubes at graphitization temperatures, Carbon 39 (2001) 1681–1687.
[196] A.C. Dillon, T. Gennett, K.M. Jones, J.L. Alleman, P.A. Parilla, M.J. Heben, A simple and complete purification of single-walled carbon nanotube materials, Advanced Materials 11 (1999) 1354–1358.
[197] P.X. Hou, C. Liu, H.M. Cheng, Purification of carbon nanotubes, Carbon 46 (2008) 2003–2025.
[198] N. Zhao, C. He, G. Li, Z. Jiang, Y. Li, Study on purification and tip-opening of CNTs fabricated by CVD, Materials Research Bulletin 41 (2006) 2204–2209.
[199] A.F. Ismail, P.S. Goh, J.C. Tee, S.S. Mohd, M.Abd Aziz, A review of purification techniques for carbon nanotubes, Nano 3 (2008) 127–143.
[200] A.E. Agboola, R.W. Pike, T.A. Hertwig, H.H. Lou, Conceptual design of carbon nanotube processes, Clean Technologies and Environment 9 (2007) 289–311.
[201] D.W. Yan, J. Zhong, C.R. Wang, Z.Y. Wu, Near-edge X-ray absorption fine structure spectroscopy assisted purification of single-walled carbon nanotubes, Spectrochimica Acta Part B: Atomic Spectroscopy 62 (2007) 711–716.
[202] X.H. Chen, C.S. Chen, Q. Chen, F.Q. Cheng, G. Zhang, Z.Z. Chen, Non-destructive purification of multi walled carbon nanotubes produced by catalyzed CVD, Materials Letters 57 (2002) 734–738.
[203] M.T. Martinez, M.A. Callejas, A.M. Benito, M. Cochet, T. Seeqer, A. Anson, Modifications of single-wall carbon nanotubes upon oxidative purification treatments, Nanotechnology 14 (2003) 691–695.
[204] B. Zheng, Y. Li, J. Liu, CVD synthesis and purification of single-walled carbon nanotubes on aerogel supported catalyst, Applied Physics A 74 (2002) 345–348.
[205] S. Delpeux, K. Szostak, E. Frackowiak, F. Beguin, An efficient two-step process for producing opened multi-walled carbon nanotubes-sofhighpurity, Chemical Physics Letters 404 (2005) 374–378.
[206] J.M. Moon, K.H. An, Y.H. Lee, Y.S. Park, D.J. Bae, G.S. Park, High-yield purification process of single walled carbon nanotubes, Journal of Physical Chemistry B 105 (2001) 5677–5681.
[207] H.J. Li, L. Feng, L.H. Guan, Z.J. Shi, Z.N. Gu, Synthesis and purification of single-walled carbon nanotubes in the cottonlike soot, Solid State Communications 132 (2004) 219–224.
[208] R.B. Mathur, S. Seth, C. Lal, R. Rao, B.P. Singh, T.L. Dhami, A.M. Rao, Co-synthesis, purification and characterization of single- and multi-walled carbon nanotubes using the electric arc method, Carbon 45 (2007) 132–140.
[209] P. Ramesh, T. Okazaki, T. Sugai, J. Kimura, N. Kishi, K. Sato, Purification and characterization of double-wall carbon nanotubes synthesized by catalytic chemical vapor deposition on mesoporous silica, Chemical Physics Letters 418 (2006) 408–412.
[210] L.W. Zhang, L. Zeng, A.R. Barron, N.A. Monteiro-Riviere, Biological interactions of functionalized single-wall carbon nanotubes in human epidermal keratinocytes, International Journal of Toxicology 26 (2007) 103–113.
[211] N. Saito, Y. Usui, K. Aoki, N. Narita, M. Shimizu, K. Hara, et al., Carbon nanotubes: biomaterial applications, Chemical Society Reviews 38 (2009) 1897–1903.
[212] N.A. Kumar, H.S. Ganapathy, J.S. Kim, Y.S. Jeong, Y.T. Jeong, Preparation of poly 2-hydroxyethyl methaerylate functionalized carbon nanotubes as novel biomaterial nanocomposites, European Polymer Journal 44 (2008) 579–586.
[213] M. Kawaguchi, T. Fukushima, T. Hayakawa, N. Nakashima, Y. Inoue, S. Takeda, et al., Preparation of carbon nanotube-alginate

nanocomposite gel for tissue engineering, Dental Materials Journal 25 (2006) 719–725.
[214] O. Vittorio, V. Raffa, A. Cuschieri, Influence of purity and surface oxidation on cytotoxicity of multiwalled carbon nanotubes with human neuroblastoma cells, Nanomedicine: Nanotechnology 5 (2009) 424–431.
[215] E. Heister, C. Lamprecht, V. Neves, C. Tîlmaciu, L. Datas, E. Flahaut, et al., Higher dispersion efficacy of functionalized carbon nanotubes in chemical and biological environments, ACS Nano 4 (2010) 2615–2626.
[216] K. Kostarelos, L. Lacerda, G. Pastorin, W. Wu, S. Wieckowski, J. Luangsivilay, S. Godefroy, D. Pantarotto, J.P. Briand, S. Muller, M. Prato, A. Bianco, Cellular uptake of functionalized carbon nanotubes is independent of functional group and cell type, Nature Nanotechnology 2 (2007) 108–113.
[217] S. Smart, A. Cassady, G. Lu, D. Martin, the biocompatibility of carbon nanotubes, Carbon 44 (2006) 1034–1047.
[218] H. Dumortier, S. Lacotte, G. Pastorin, R. Marega, W. Wu, D. Bonifazi, J. Briand, M. Prato, S. Muller, A. Bianco, Functionalized carbon nanotubes are non-cytotoxic and preserve the functionality of primary immune cells, Nano Letters 6 (2006) 1522–1528.
[219] C.M. Sayes, F. Liang, J.L. Hudson, J. Mendez, W. Guo, J.M. Beach, V.C. Moore, C.D. Doyle, J.L. West, W.E. Billups, K.D. Ausman, V.L. Colvin, Functionalization density dependence of single walled carbon nanotubes cytotoxicity in vitro, Toxicology Letters 161 (2006) 135–142.
[220] N.W. Kam, Z. Liu, H. Dai, Carbon nanotubes as intracellular transporters for proteins and DNA: an investigation of the uptake mechanism and pathway, Angewandte Chemie International Edition English 45 (2006) 577–581.
[221] C. Gao, W. Li, H. Moromonto, Y. Nagaoka, T. Maekawa, Magnetic carbon magnetic carbon nanotubes: synthesis by electrostatic self-assembly approach and application in biomanipulations, Journal of Physical Chemistry B 110 (2006) 7213–7220.
[222] A.O. Lobo, E.F. Antunes, A.H.A. Machado, C. Pacheco-Soares, V.J. Trava-Airoldi, E.J. Corat, An evaluation of cell proliferation and adhesion on vertically-aligned multi-walled carbon nanotube films, Materials Science and Engineering C 28 (2008) 264–269.
[223] H. Koga, T. Fujigaya, N. Nakashima, K. Nakazawa, Morphological and functional behaviors of rat hepatocytes cultured on single-walled carbon nanotubes, Journal of Materials Science Materials in Medicine 22 (2011) 2071–2078.
[224] J. Cheng, K.A. Fernando, L.M. Veca, Y.P. Sun, A.I. Lamond, Y.W. Lam, et al., Reversible accumulation of PEGylated single-walled carbon nanotubes in the mammalian nucleus, ASC Nano 2 (2008) 2085–2094.
[225] I. Firkowska, E. Godehardt, M. Giersig, Interaction between human osteoblast cells and inorganic two-dimensional scaffolds based on multiwalled carbon nanotubes: a quantitative AFM study, Advanced Functional Materials 18 (2008) 3765–3771.
[226] S.E. Rodil, R. Olivares, H. Arzate, In vitro cytotoxicity of amorphous carbon films, Bio-Medical Materials and Engineering 15 (2005) 101–112.
[227] K.H. Park, M. Chhowalla, Z. Iqbal, F. Sesti, Single-walled carbon nanotubes are a new class of ion channel blockers, Journal of Biological Chemistry 278 (2003) 50212–50216.
[228] L.P. Zanello, Hui Hu, R.C. Bin Zhao, Haddon, bone cell proliferation on carbon nanotubes, Nano Letters 6 (2006) 562–567.
[229] S. Mwenifumbo, M.S. Shaffer, M.M. Stevens, Exploring cellular behaviour with multi-walled carbon nanotube constructs, Journal of Materials Chemistry 17 (2007) 1894–1902.
[230] E.J. Park, J. Roh, S.N. Kim, M.S. Kang, B.S. Lee, Y. Kim, et al., Biological toxicity and inflammatory response of semi-single-walled carbon nanotubes, PLoS One 6 (2011) e25892.
[231] K. Balani, R. Anderson, T. Laha, M. Andara, J. Tercero, E. Crumpler, A. Agarwa, Plasma sprayed carbon nanotube reinforced hydroxyapatite coatings and their interaction with human osteoblasts in vitro, Biomaterials 28 (2007) 618–624.
[232] T.J. Webster, M.C. Waid, J.L. McKenzie, R.L. Price, J.U. Ejiofor, Nano-biotechnology: carbon nanofibres as improved neural and orthopaedic implants, Nanotechnology 15 (2004) 48–54.
[233] K. Rege, N.R. Raravikar, D.Y. Kim, L.S. Schadler, P.M. Ajayan, J.S. Dordick, Enzyme–polymer–single walled carbon nanotube composites as biocatalytic films, Nano Letters 3 (2003) 829–832.
[234] A. Arrais, E. Boccaleri, E. Diana, Efficient direct watersolubilisation of singlewalled carbon nanotube derivatives, Fullerence, Nanotubes, and Carbon Nanostructures 12 (2004) 789–809.
[235] K. Imasaka, J. Suehiro, Y. Kanatake, Y. Kato, M. Hara, Preparation of water-soluble carbon nanotubes using a pulsed streamer discharge in water, Nanotechnology 17 (2006) 3421–3427.
[236] L. Lacerda, G. Pastorin, W. Wu, M. Prato, A. Bianco, K. Kostarelo, Luminescence of functionalized carbon nanotubes as a tool to monitor bundle formation and dissociation in water: the effect of plasmid-DNA complexation, Advanced Functional Materials 16 (2006) 1839–1846.
[237] N. Nakayama-Ratchford, S. Bangsaruntip, X. Sun, K. Welsher, H. Dai, Noncovalent functionalization of carbon nanotubes by fluorescein–polyethylene glycol: supramolecular conjugates with pH-dependent absorbance and fluorescence, Journal of the American Chemical Society 129 (2007) 2448–2449.
[238] J. Chattopadhyay, F. Cortez, S. Chakraborty, N. Slater, W. Billups, Synthesis of water-soluble PEGylated single-walled carbon nanotubes, Chemistry of Materials 18 (2006) 5864–5868.
[239] B. Zhao, H. Hu, A. Yu, D. Perea, R.C. Haddon, Synthesis and characterization of water soluble single-walled carbon nanotube graft copolymers, Journal of the American Chemical Society 127 (2005) 8197–8203.
[240] B. Zhao, H. Hu, R.C. Haddon, Synthesis of a water-soluble single-walled carbon nanotube-poly(m-aminobenzene sulfonic acid) graft copolymer, Advanced Functional Materials 14 (2004) 71–76.
[241] M.C. Paiva, B. Zhou, K. Fernando, Y. Lin, J. Kennedy, Y. Sun, Mechanical and morphological characterization of polymer carbon nanocomposites from functionalized carbon nanotubes, Carbon 42 (2004) 2849–2854.
[242] Y. Lin, B. Zhou, K.A.S. Fernando, P. Liu, L.F. Allard, Y.P. Sun, Polymeric carbon nanocomposites from carbon nanotubes functionalized with matrix polymer, Macromolecules 36 (2003) 7199–7204.
[243] K.F. Fu, W. Huang, Y. Lin, D. Zhang, T.W. Hanks, A.M. Rao, Y.P. Sun, Functionalization of carbon nanotubes with bovine serum albumin in homogeneous aqueous solution, Journal of Nanoscience and Nanotechnology 2 (2002) 457–461.
[244] Y.P. Sun, W. Huang, Y. Lin, Y. Kefu, A. Kitaygorodskiy, L.A. Riddle, Y. Yu, D.L. Caroll, Soluble dendron-functionalized carbon nanotubes: preparation, characterization, and properties, Chemistry of Materials 13 (2001) 2864–2869.
[245] J.B. Kim, T. Premkumar, K. Lee, K.E. Geckeler, A facile approach to single-wall carbon nanotube/poly(allylamine) nanocomposites, Macromolecular Rapid Communications 28 (2007) 276–280.
[246] M. Alvaro, P. Atienzar, P. de La Cruz, J.L. Delgado, H. Garcia, F. Langa, Sidewall functionalization of single-walled carbon nanotubes with nitrile imines. Electron transfer from the substituent to the carbon nanotube, Journal of Physical Chemistry B 108 (2004) 12691–12697.
[247] W.J. Huang, S. Taylor, K.F. Fu, Y. Lin, D.H. Zhang, T.W. Hanks, A.M. Rao, Y.P. Sun, Attaching proteins to carbon nanotubes via diimide-activated amidation, Nano Letters 2 (2002) 311–314.
[248] Y. Lin, A.M. Rao, B. Sadanadan, E.A. Kenik, Y.P. Sun, Functionalizing multiple-walled carbon nanotubes with aminopolymers, Journal of Physical Chemistry B 106 (2002) 1294–1298.
[249] J.E. Riggs, D.B. Walker, D.L. Carroll, Y.P. Sun, Optical limiting properties of suspended and solubilized carbon nanotubes, Journal of Physical Chemistry B 104 (2000) 7071–7076.
[250] T. Zhang, M. Xub, L. Hec, K. Xid, M. Gue, Z. Jiang, Synthesis, characterization and cytotoxicity of phosphoryl choline-grafted water-soluble carbon nanotubes, Carbon 46 (2008) 1782–1791.

[251] R. Narain, A. Housni, L. Lane, Modification of carboxyl-functionalized single-walled carbon nanotubes with biocompatible, water-soluble phosphorylcholine and sugar-based polymers: bioinspired nanorods, Journal of Polymer Science Part A: Polymer Chemistry 44 (2006) 6558–6568.

[252] D. Dutta, S.K. Sundaram, J.G. Teeguarden, B.J. Riley, L.S. Fifield, J.M. Jacobs, S.R. Addleman, G.A. Kaysen, B.M. Moudgil, T.J. Weber, Adsorbed proteins influence the biological activity and molecular targeting of nanomaterials, Toxicological Sciences 100 (2007) 303–315.

[253] N.A. Monteiro-Riviere, A.O. Inman, Y.Y. Wang, R.J. Nemanich, Surfactant effects on carbon nanotube interactions with human keratinocytes, Nanomedicine 1 (2005) 293–299.

[254] B. Brown, C.B. Parker, B.R. Stoner, J.T. Glass, Growth of vertically aligned bamboo-like carbon nanotubes from ammonia/methane precursors using a platinum catalyst, Carbon 49 (2011) 266–274.

[255] M. Inaba, M. Ando, A. Hatanaka, A. Nomoto, K. Matsuzawa, A. Tasaka, T. Kinumoto, Y. Iriyama, Z. Ogumi, Controlled growth and shape formation of platinum nanoparticles and their electrochemical properties, Electrochimica Acta 52 (2006) 1632–1638.

[256] C. Médard, M. Lefèvre, J.P. Dodelet, F. Jaouen, G. Lindbergh, Oxygen reduction by Fe-based catalysts in PEM fuel cell conditions: activity and selectivity of the catalysts obtained with two Fe precursors and various carbon supports, Electrochimica Acta 51 (2006) 3202–3213.

[257] V. Chiono, C. Tonda-Turo, G. Ciardelli, Artificial scaffolds for peripheral nerve reconstruction, International Review of Neurobiology 87 (2009) 173–198.

[258] Z. Zhang, S. Wang, X. Tian, Z. Zhao, J. Zhang, D. Lv, A new effective scaffold to facilitate peripheral nerve regeneration: chitosan tube coated with maggot homogenate product, Medical Hypotheses 74 (2010) 12–14.