Towards the Translation of Electroconductive Organic Materials for Regeneration of Neural Tissues

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Abstract

Carbon-based conductive and electroactive materials (e.g., derivatives of graphene, fullerenes, polypyrrole, polythiophene, polyaniline) have been studied since the 1970s for use in a broad range of applications. These materials have electrical properties comparable to those of commonly used metals, while providing other benefits such as flexibility in processing and modification with biologics (e.g., cells, biomolecules), to yield electroactive materials with biomimetic mechanical and chemical properties. In this review, we focus on the uses of these electroconductive materials in the context of the central and peripheral nervous system, specifically recent studies in the peripheral nerve, spinal cord, brain, eye, and ear. We also highlight *in vivo* studies and clinical trials, as well as a snapshot of emerging classes of electroconductive materials (e.g., biodegradable materials). We believe such specialized electrically conductive biomaterials will clinically impact the field of tissue regeneration in the foreseeable future.

1 Introduction

Many tissues throughout the body respond to electrical stimulation (including bone, muscle, nerve, and skin), and electrical activation is inherent to numerous biological processes (e.g., angiogenesis, cell division, cell signaling, nerve sprouting, prenatal development, wound healing) [1]. The electrophysiological properties of cells and tissues (ionic currents and voltage changes) [2],[3] underpin everything inherent to living organisms from fetal development to an ability to sense the environment [4]. Electrical fields are stimuli known to promote the regeneration of different types of damaged or injured tissues [5]–[8], motivating the development of clinical interventions that utilize electrical stimulation to enhance tissue regeneration, including new materials capable of delivering such stimuli. These electrical signals are fundamental to the function of the nervous system (e.g., peripheral nerves, spinal cord, brain, eye, ear, **Figure 1**), which transmits information about motor and sensory functions throughout the body through axon bundles via a series of electrochemical reactions [9].

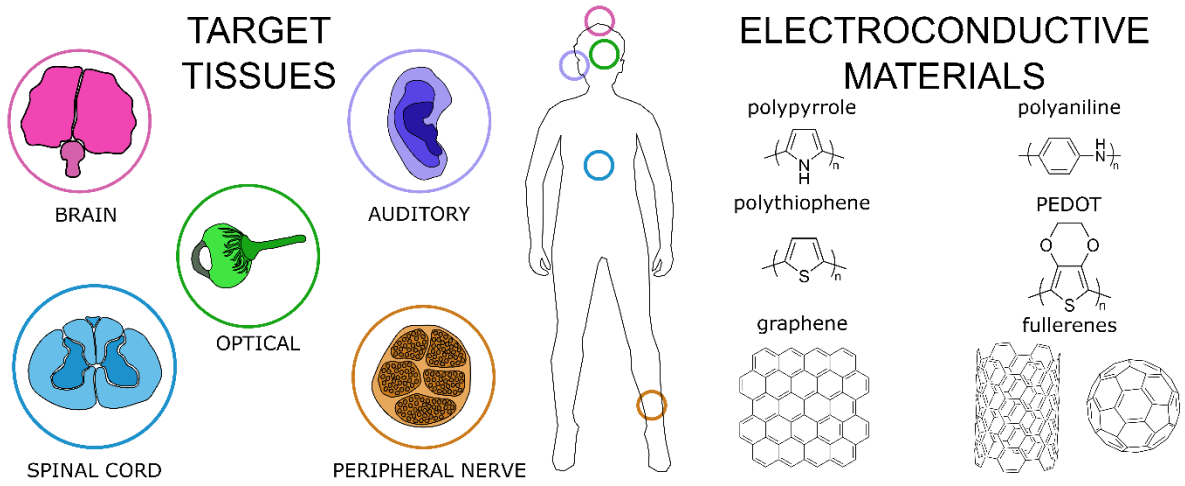

Figure 1: Overview of target tissues of interest and the carbon-based electroconductive materials discussed herein. Chemical structures for polypyrrole, polyaniline, polythiophene, polythiophene derivative PEDOT, graphene, and fullerenes (both a carbon nanotube and buckyball structure) are shown.

Given that the conductivity of nerve tissue is ~0.08-1.3 S/m [10], materials that have a conductivity similar to, or higher than, the conductivity of nerve tissue may transfer electrical signals to neurons [11],[12]. Electroactive materials have a broad range of electrical properties from very low conductivity to high conductivity, and formally include "conductors" that allow for the rapid flow of charge (electrical current) and have conductivities greater than 10^{7} Ω^{-1} m^{-1}, "insulators" that are non-conducting with few or no mobile charges and have conductivities of less than 10^{-10} Ω^{-1} m^{-1}, and "semiconductors" that have electrical conductivities between conductors and insulators (between ca. 10^{-6} Ω^{-1} m^{-1} and ca. 10^{-4} Ω^{-1} m^{-1}). Electroactive materials that have been clinically translated for electrical recording and stimulation are all metals or metal alloys, which are highly conducting, but unfortunately present complications related to mechanical mismatch between the hard material devices and relatively soft neural tissues when implanted for long periods [13]. Additionally, non-biodegradability of typical metals (e.g., gold, platinum, iridium) and metal alloys often cause severe chronic inflammatory tissue reactions, which can be exacerbated following stimulation, or require the secondary surgery for their removal [14]. These drawbacks to metals have motivated the development of flexible electronics and soft conductive materials that overcome current barriers for applications in soft tissue repair and regeneration [15],[16].

Electroconductive conjugated polymers (e.g., derivatives of polypyrrole (ca. 40-200 S/cm), polyaniline (ca. 5 S/cm), polythiophene (ca. 10-100 S/cm) [12]) and carbon-based nanomaterials (derivatives of graphene (ca. 2-9 S/cm) [17], and carbon nanotubes (ca. 400-6600 S/cm) [18],[19]) have significant potential to act as flexible electronic interfaces for the body with tunable bulk and surface properties [20]. Consequently there is a growing body of literature devoted to investigations of the potential application of such carbon-based conductive materials as non-degradable electrodes implanted for long term application for neural tissues, or to aid tissue regeneration efforts by serving as instructive biomaterials to directly and locally

stimulate cells and tissues or deliver drugs in response to electrical stimuli; moreover, if engineered correctly, such materials may be biodegradable or bioerodible and enable regrowth of healthy tissues in their place.

There are prior reviews [12],[17],[20],[21] that describe in detail the synthesis and fabrication techniques that are commonly utilized for conductive materials, and below we briefly highlight a few examples of the challenges and opportunities that exist for carbon-based conductive materials for medical applications, prior to the applications of these conductive materials specifically for neural regeneration.

Conducting polymers have been utilized in groundbreaking investigations to assess their potential to electrically stimulate cells (also paving the way for investigations using other electroactive materials such as derivatives of graphene and nanotubes), and have been successfully implanted as materials constituting components of recording devices in the rat neocortex and hippocampus [22],[23]. Exciting progress since this time has led to the development of sensors capable of mimicking our natural senses [24], facilitating sight (e.g., bionic eyes) [25],[26], hearing (e.g., cochlear implants) [27], smell (e.g., electronic noses) [28]–[33], taste (e.g., electronic tongues) [29],[34],[35], and touch [36],[37] for patients with impaired senses. However, it is important to note that there are challenges related to solubility and processing of some carbon-based conductors to yield biomaterials with biomimetic mechanical or topographical properties, and chemical or biochemical properties that are being addressed by teams of researchers with multidisciplinary research expertise in academic and industrial settings [12]. A comprehensive overview of conjugated polymer synthesis, processing, and applications [38] is outside the scope of this review. Instead we highlight a few examples of matters that influence the potential of these polymers for biomedical applications [12],[39] often employing derivatives of polymers such as polyaniline (PANI), polypyrrole (PPy), and polythiophene (PT) (e.g., poly-3,4-ethylenedioxythiophene, PEDOT) as biosensors

[40], drug delivery devices [41]–[44], electrode coatings [45], and tissue scaffolds for tissue engineering [46]–[51]. The structures of such polymers control their solubility, and concomitantly synthesis (e.g., electrodeposition [52]–[55], enzymatic polymerization [56], photochemical polymerization [40],[56],[57]) and processability (e.g., 3D printing [58],[59]), and influences the chemical/optoelectronic properties of the resulting materials, and moreover whether the polymers are biodegradable [12],[60],[61].

1.1 Polypyrrole (PPy)

One of the most studied inherently conductive polymers (ICP) for tissue engineering applications is polypyrrole because of its high cell biocompatibility, ease of preparation, and high conductivity [58]. PPy is often used as a coating for electrodes because of its ability to elute drugs or biomolecules in a way that can be controlled using electrical stimulation to release the payload [41]–[44]. The pure monomer of PPy (i.e., pyrrole) is water-soluble and colorless [40]. PPy polymerization can be initiated via chemical or electrochemical polymerization by oxidation of an adsorbed pyrrole monomer; oxidation produces radical-cationic pyrrole that reacts with the neutral monomer pyrrole to form a polymeric chain termed polypyrrole [62],[63]. PPy requires additional modification to overcome issues with water solubility and phase separation that make it difficult to use as a standalone biological material [59],[64]. To imbue various characteristics for chemical functionality or bioactivity, various approaches have been taken. These include the use of pyrrole derivatives [65], doping different molecules, and applications of different polymerization conditions [38]. Growth factors, such as neurotrophin-3, have previously been used in conjunction with PPy to increase the ability to interface with neural tissue [66]. One study showed that neurite outgrowth of spiral ganglion neurons was enhanced when neurotrophin-3 was incorporated with PPy, additionally the release of growth factor was increased with electrical stimulation further increasing the number

of neurites per explant [66]. PPy, in combination with electrical stimulation is known to enhance neurite outgrowth *in vitro* [51]. PPy has potential for translation to regenerative tissue engineering applications in the nervous system and has been implemented in research for regeneration of the peripheral nervous system [67], spinal cord [13],[68], brain [69],[70], eye [71], and ear[66]).

1.2 Polythiophene (PT) and Poly(3,4-ethylene dioxythiophene) (PEDOT)

Polythiophene is the polymer formed from the polymerization of monomer thiophene and is a polyheterocycle, similar to polypyrrole, which means it has one or more atoms other than carbon (i.e., sulfur) in at least one of its rings [12]. PEDOT is a commonly used derivative of PT that is formed from the polymerization of thiophene derivative 3,4-ethylenedioxythiophene (EDOT), and has been used for biomedical applications in neural probes and drug delivery [12],[54]. Like polypyrrole, PT generates electrical signals as electrons transfer between polymer chains and can be polymerized using electrochemical polymerization methods [12],[20],[61]. During electropolymerization reactions, extracellular matrix components (e.g., collagen, laminin) can be incorporated within PEDOT to enhance cell adhesion [20]. There are many other derivatives of thiophene, including 3-hexylthiophene that when polymerized yields poly(3-hexylthiophene) commonly known as P3HT [72]. When P3HT was combined with poly(lactide-co-glycolide) into aligned nanofibers, rat Schwann cells grown on the fibers exhibited enhanced proliferation at day 7 of culture [46],[47]. Topological properties as well as functionalization (e.g., ester linkages, anhydride linkages) can alter the bulk properties of PTs, enhancing biodegradability compared to the unaltered polymer form [60]. This makes PT derivates very interesting candidates for the development of fully degradable electroconductive materials.

Interestingly, PEDOT has been polymerized *in vivo* at the site of implanted electrodes

[54],[55], necessitating consideration of monomer toxicity if contemplating use of such methodology; EDOT exposed to primary dissociated mouse cortical cultures (MCC) and a neuroblastoma-derived cell line (SY5Y) yields limited cell viability (i.e., under 60% viable neural cells) at concentrations above 0.1 M EDOT [52]. For concentrations of EDOT less than 0.01 M, cells maintain at least 75% viability out to 72 hours and studies have shown polymerization of EDOT within 10 minutes of electrochemical polymerization, suggesting that the cytotoxic effects of the EDOT can be limited by swift monomer polymerization and are expected to be negligible [52]. PT and PEDOT are not inherently degradable and remain stable in cell culture conditions, and therefore potentially cytotoxic EDOT is not expected to be released and accumulate at the implant site, limiting potential for long term toxicity when used *in vivo* [53].

1.3 Polyaniline (PANI)

Polyaniline is another inherently conducting polymer, which has shown low toxicity and environmental stability [73]. These properties make PANI a promising candidate for bioengineering applications [74], often used in combination with another conducting polymer or carbon-nanomaterial to tune the properties of the resulting materials [40],[73]. Like many conductive polymers discussed in this review, PANI is known to have limited biodegradability, and is often used in conjunction with other biomaterials as composites (e.g., PANI-porous silicon hybrid nanocomposite [75], PANI-poly(ethylene glycol) (PEG) [76], and PANI-polycaprolactone (PCL) [77]) for tissue engineering applications [48],[49]. PANI is known to lose conductivity at pH levels above 4 (i.e., conductivity decreases from 10 S/cm to 0.1 S/cm when the pH increases from below 7 to pH 11), because it reverts back to its neutral state [40]. This has motived the exploration of PANI in combination with another conducting polymer or carbon-nanomaterial with higher conductivity, or pH functional groups (i.e, sulfo, carboxyl, or

hydroxyl groups) to stabilize it at higher pH levels [40],[60]. A review by Zare et al. explores the synthesis, structure, properties, and biocompatibility of PANI and provides an in-depth view on PANI's use for the broader biomedical space [73]. Like the previously described conductive polymers, PANI is synthesized by chemical or electrochemical polymerization via oxidation of its monomer aniline (water soluble at 36 g/L at 20 °C) [40]. There have also been techniques that involve enzyme-catalyzed (e.g., horseradish peroxidase) or photochemically (in conjunction with a metallic ion) initiated polymerization [40],[56],[57]. Unmodified PANI has poor cell adhesion and growth, with some low levels of inflammation (e.g., increase expression levels of the pro-inflammatory cytokines, TNF-α and IL-6 [78]), but modifications can create material formulations that (e.g., PANI-chitosan, PANI-gelatin) show increased biocompatibility *in vitro* and *in vivo* [12],[20]. PANI in combination with poly(ε-caprolactone) and gelatin, in the form of a nanofibrous scaffold, is capable of increasing nerve stem cell proliferation and neurite length following 1 hour of 1.5 V direct current (DC) electrical stimulation [50]. As such, PANI remains a promising candidate for neural tissue engineering applications.

1.4 Fullerenes

Fullerenes are allotropes of carbon that are either spherical (i.e., three-dimensional buckminsterfullerene, commonly known as buckyballs) or tubes (i.e., three-dimensional carbon tubes, commonly known as carbon nanotubes (CNTs), and occasionally referred to as buckytubes) [79],[80]; these materials are of interest to materials scientists and engineers because of their electronic, mechanical, and thermal properties [79],[80]. Carbon nanotubes are classified as single-walled carbon nanotubes (SWCNT), a single sheet of graphite rolled into a tube with a diameter of one nanometer, or multiwalled carbon nanotubes (MWCNT) which

encompass multiple graphene tubes surrounding the core of a SWCNT [81]. MWCNTs are more often used as they have a lower surface area compared to single walled nanotubes which allows for increased dispersal within a polymer matrix [81]; MWCNTs have also been shown to be less toxic [82]. Of note, MWCNTs have been utilized for both sciatic nerve and spinal cord injury studies in combination with a polymer matrix [82],[83].

Fullerenes have been employed for a variety of biomedical applications, including drug delivery [84] and tissue engineering [85]. These structures are of interest to the biomaterials community because they allow for the encapsulation of other molecules, prompting exploration into their usefulness for the delivery of therapeutic agents or other payloads [84]. Additionally, derivatives of fullerenes have been shown to reduce reactive oxygen species levels and inhibit the signaling pathway NF-κB, which is responsible for innate and adaptive immunes responses [85]. Akin to other carbon-based conductors, their solubility can be tuned to facilitate processing into different materials [82],[86],[87]. A review by Anaya-Plaza et al. discusses the fabrication and self-assembly of carbon nanotubes and conjugation with biomolecules to mitigate their issues with low solubility and to enhance their biocompatibility for health concerns [86]. Materials such as carbon nanotubes have a propensity to aggregate, thus, organic solvents (e.g., dimethylformamide (DMF) [82]) are often used to encourage dispersion. This can make processing materials with fullerenes difficult, but there have been protocols designed that use biopolymers (e.g., DNA [87]) to aid in dispersal. The other common carbon allotrope, buckminsterfullerene (C_{60}), is a stable cage-like structure commonly referred to as buckyball molecule that is resistant to the actions of both acids and bases [88]. Although buckyballs are being studied for biological applications (e.g., bactericidal activity, anti-inflammatory properties for inflammatory arthritis) and have been tested for negative effects at the DNA, tissue and organism levels in models such as *Drosophila melanogaster* [88],[89], we have not seen any studies utilizing buckyballs for neural

applications.

1.5 Graphene

Graphene is the two-dimensional allotrope (i.e., structural arrangement) of carbon that can achieve an electron mobility of 20,000 $cm^2 V^{-1} s^{-1}$ [90]–[92] and is mechanically flexible, thus facilitating its inclusion in high performance flexible electronic devices (e.g., field-effect transistors) [93]. A variety of methods can be used to generate graphene and its derivatives, including mechanical exfoliation, chemical exfoliation, liquid phase exfoliation by reduction of graphene oxide (GO), chemical vapor deposition, and others [94]. Graphene has been deposited on flexible substates such as poly(ethylene naphthalate) for use in emerging field-effect transistors (GFETs) research and have been shown to outperform the silicon "gold standard" [93]. Graphene-based materials can be moderately hydrophilic (e.g., graphene oxide) or hydrophobic (e.g., reduced graphene oxide or fluorinated graphene); those with hydrophobic properties can accumulate on cell membrane surfaces causing toxic effects that are much higher in comparison to most of the hydrophilic forms [92],[95]. The use of graphene has shown increased proliferation of human mesenchymal stem cells, often used in bone tissue engineering, and has supported the differentiation of these cells toward osteoblasts, the cells that form new bone [96]. There is significant interest in the potential biomedical applications of graphene derivatives [92], including incorporation into neural applications [97],[98]. Studies *in vitro* have shown that surfaces functionalized with graphene oxide promote neural differentiation [99],[100]. Materials augmented with graphene show great promise and the ability to support neural tissue regeneration *in vivo* needs further exploration.

1.6 Material Characterization

A variety of analytical methods have been employed to characterize properties of electroconductive materials. **Table 1** provides examples of various analytical techniques

commonly applied to the study of such biomaterials. A comprehensive summary of all techniques (including chromatography, mechanics, microscopy, spectrometry, spectroscopy, and *in silico* studies) is beyond the scope of this article, and readers are directed to references on underpinning theory and practice [101]–[105]. Electroconductive materials are often characterized by techniques to analyse reduction and oxidation processes and electron transfer (e.g., using cyclic voltammetry), or to rationally investigate the protonic and electronic contributions towards conduction (e.g., via impedance spectroscopy and dielectric spectroscopy); there are also scanning probe microscopy techniques developed to analyze electrochemical processes (e.g., scanning electrochemical microscopy) [21] that have also been used to study cells and tissues [106],[107]. Such analytical techniques offer insights into electroconductive materials properties and enables their optimization for specific applications.

Table 1: Examples of analytical techniques applied to electroconductive biomaterials.

Analytical Technique	Offers information about:	Reference material.	Fullerene derivatives (e.g., carbon nanotubes)	Graphene derivatives	Conductive Polymers
Nuclear Magnetic Resonance Spectroscopy (NMR) spectroscopy	Chemical environments of spin active nuclei.	[104]	[108]	[108]–[112]	[108],[113],[114]
Electron Paramagnetic Resonance (EPR) or Electron Spin Resonance (ESR) Spectroscopy	The presence and/or type of free radicals and paramagnetic centres.	[104]	[115]	[110],[116]	[117]–[119]
Chemiluminescence Spectroscopy	Light emitted as a result of a chemical reaction.	[120]	[121]	[121]–[123]	[124]
Fluorescence Spectroscopy	Light emission from samples with excited electrons.	[104]	[125]	[111],[123]	[126]
Infrared Spectroscopy	Functional group determined spectral	[104]	[127],[128]	[129]	[130]

	differences for IR transmission, absorbance or reflection.				
Phosphorescence Spectroscopy	Light emitted relatively slowly from a molecule.	[131]	[132]	[123]	[133]
Photoacoustic Spectroscopy	Sound waves emitted by materials that absorb radiation.	[104]	[134]	[135]	[136],[137]
Photothermal Spectroscopy	Heat evolved on absorption of radiation.	[138]	[139]–[142]	[139],[143]	[144]
Pump-Probe Spectroscopy	Photodynamics.	[145]	[146]	[147]	[148],[149]
Raman Spectroscopy	Vibrational/rotational modes of molecules.	[150]	[128],[151]	[151]–[153]	[154]
Terahertz Time-Domain Spectroscopy (THz-TDS)	Material response at THz frequencies.	[104],[155]	[156]	[156]–[159]	[156],[160]–[163]
Ultraviolet-visible (UV-Vis) Spectroscopy	Bond conjugation and connectivity.	[104],[164]	[165],[166]	[111],[167],[168]	[119],[169]
X-ray Photoelectron Spectroscopy (XPS)	Chemical composition and electronic state of the elements.	[170]	[128],[171],[172]	[167],[172],[173]	[62],[174],[175]
Scattering and Diffraction (XRD, SAXS, WAXS)	Crystallinity and microstructure.	[104],[176],[177]	[178]	[178]	[119],[174],[179],[180]
Thermal Characterization (TGA,DSC)	Heat flow within materials.	[181]	[128]	[167]	[182]
Electrical Characterization	Conductivity, reduction/oxidation processes, electron transfer.	[21],[183]	[184]	[185],[186]	[187],[188]
Scanning Electron Microscopy (SEM)	Particle size distributions and elemental compositions when used in combination with energy dispersive X-ray spectroscopy (EDX/EDS)	[189]	[190]	[191]	[174]
Transmission Electron Microscopy (TEM)	Particle size distributions and elemental compositions when used in combination with energy dispersive	[192],[193]	[190]	[191],[194]	[174]

	X-ray spectroscopy (EDX/EDS)				
Scanning Probe Microscopy (Profilometry, SPM, STM, AFM)	Surface characterization electronics, mechanics, spectroscopy, etc.	[195]	[196]	[191],[197],[198]	[119]
Computational Studies	Simulations of material structures.	[199]–[201]	[202],[203]	[204]–[206]	[207]

2 Carbon-Based Conductive Materials for Regeneration of Neural Tissues

Electroconductive materials offer an exciting foundation to develop biomaterials for the repair and regeneration of neural tissues. We discuss herein the use of conductive carbon-based nanomaterials and polymers for the regeneration of neural tissues. Because of the exploratory and early nature of this research, much of the current literature only reports *in vitro* or preliminary *in vivo* biological outcomes (e.g., *in vitro* neurite extension, *in vivo* immune reaction) in response to the material itself, rather than regenerative outcomes when applying an electric stimulus in conjunction with the material *in vivo*. Consequently, we clarify where the use of electrical stimulation is applied in conjunction with the materials of interest. Herein we highlight recent advances towards the translation of electroconductive materials for regeneration of neural tissues (peripheral nerve, spinal cord, brain, optical, and auditory), with a focus, where possible, on recent *in vivo* studies and clinical trials.

2.1 Regeneration of Peripheral Nerve Tissue

Peripheral nerve injuries frequently result in complete motor function loss and muscle paralysis [208],[209]. Among various peripheral nerve injuries, full transections are the most difficult to regenerate because of loss of structural integrity and connection. If a transected peripheral nerve is left untreated, the proximal stump often forms a neuroma, and neurogenic muscle atrophy occurs [210],[211]. Hence, various surgical treatment methods for PNS defects

have been developed. Direct suturing of the damaged nerve ends can be used for very short defect lengths (< a few millimeters), where there is little to no resulting tension on the nerve [212]. On the other hand, for treatment of larger nerve defects, autologous nerve grafts or autografts have been widely employed as the clinical gold standard [213]; however, autografts pose several critical limitations, including donor site morbidity and insufficient functional regeneration [212],[214]. Therefore, artificial nerve guidance conduits have been developed as alternatives for structural and functional recovery of large gap nerve defects [215]. An ideal nerve guidance conduit is proposed to possess several appropriate characteristics that are conducive to regeneration, such as permeability, flexibility, neurotropic activity, and electrical conductivity [67],[216],[217]. Electrically conductive materials have been recognized as potential materials for promoting nerve regeneration, since it is known that electrical stimulation can facilitate cell growth and tissue regeneration [218],[219]. In addition, conductive materials can directly affect behaviors of individual cells (e.g., neurons, Schwann cells) and promote signal communication between cells [220],[221].

Clear roles of electrically conductive materials in promoting peripheral nerve regeneration have not been established; however, several mechanisms have been proposed. For example, electrical stimulation (constant current 10 μA) of PPy substrates enhanced the adsorption of extracellular matrix proteins (e.g., fibronectin) from the culture medium, which encourages cell growth and differentiation [222]. In addition, intracellular Ca^{2+} levels of Schwann cells and neuronal cells have been found to change in response to conductive scaffolds (e.g., aniline pentamer-incorporated polyurethane films, and combined CNT and PPy-incorporated hyaluronic acid hydrogels) [223],[224]. Specifically, Ma and colleagues found that Schwann cells cultured on the conductive poly(glycerol sebacate)-co-aniline pentamer film exhibited substantial decreases in intracellular calcium levels and the expression of the calcium sensing receptor (i.e., a G protein-coupled receptor) [223]. The decreased intracellular Ca^{2+}

level in Schwann cells was demonstrated to subsequently induce myelin gene expression and neurotrophin secretion by Schwann cells, which are essential for functional nerve regeneration. Axon myelination following proliferation and maturation of SCs promotes nerve regeneration [225],[226] (**Figure 2, A**). Cho and colleagues revealed that the expression of voltage-gated Ca^{2+} channel ($Ca_v1.2$) of human induced pluripotent stem cell-derived neural progenitor cells (hiPSC-NPCs) increased when cultured in carbon nanotube (CNT) and PPy-containing hyaluronic acid gels [224]. Overexpression of the $Ca_v1.2$ induced Ca^{2+} influx and increased intracellular Ca^{2+}. Furthermore, upregulated expression of the genes (i.e., neuronal class III β-tubulin (Tuj1) and microtubule-associated protein 2 (MAP2)), related to neurogenesis, was observed (**Figure 2, B**).

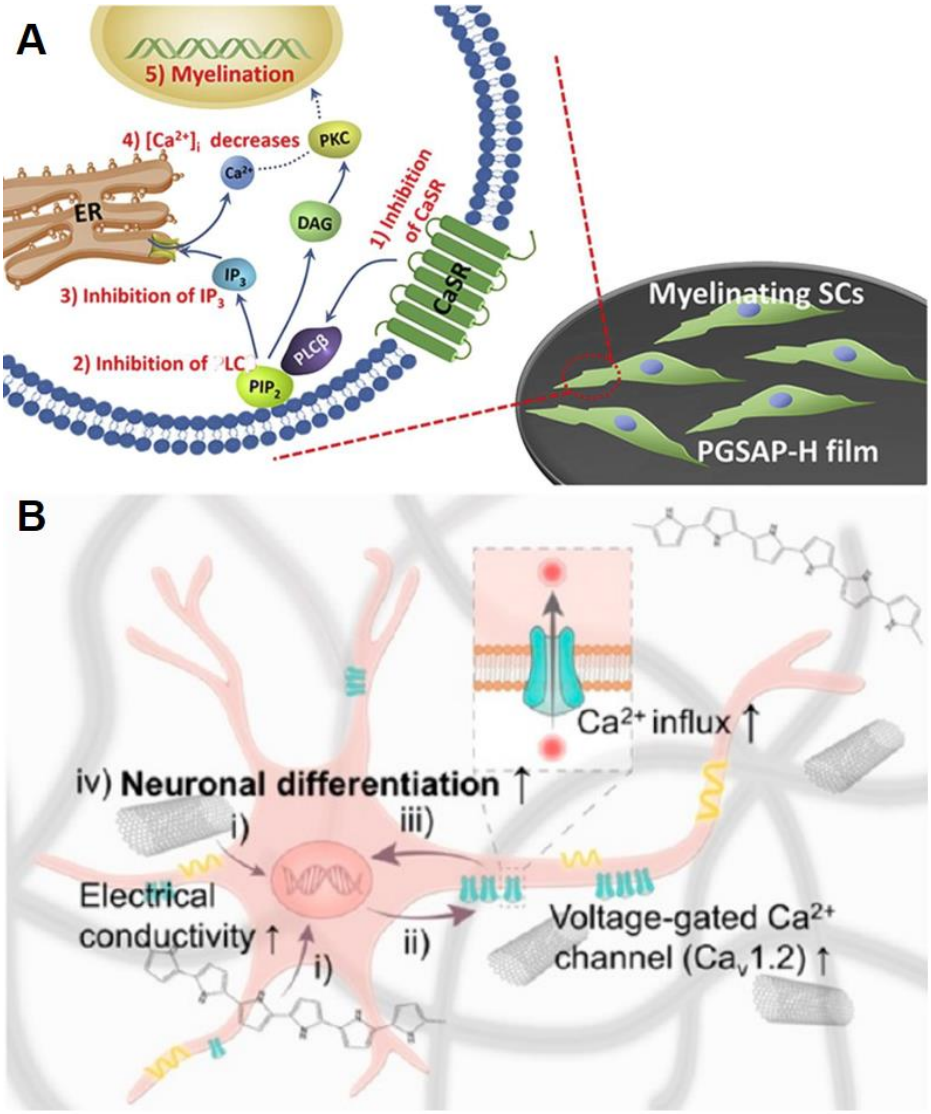

Figure 2. Proposed roles of electrically conductive substrates in modulating intracellular Ca^{2+} levels of Schwann cells and neural progenitor cells. (A) Inhibition of the calcium-sensing receptor-phospholipase C (CaSR-PLC) pathway in cells cultured on a conductive film can decrease the intracellular Ca^{2+} level. Reprinted from [223]**, Copyright (2016), with permission from Elsevier. (B) Upregulation of voltage-gated calcium channel expression of hiPSC-NPCs within conductive hydrogels. Reprinted with permission from** [224]**. Copyright 2017 American Chemical Society.**

In **Table 2**, we list several studies describing the use of conductive nerve guidance

conduits for *in vivo* peripheral nerve regeneration. We compare the ability of various nerve guidance conduits to support functional regeneration of damaged peripheral nerves based on sciatic functional index (SFI), which is a widely employed metric to evaluate the functional recovery of sciatic nerves from geometric footprints of hind paws [227],[228]. A sciatic functional index value of 0 indicates normal sciatic nerve function, whereas a value of -100 reflects complete impairment [229]. Multiple attempts to create conductive nerve guidance conduits have been made using various conductive polymers and electroconductive materials. Xu et al. fabricated conductive nerve guidance conduits consisting of PPy and poly(d, l-lactic acid) (PDLLA) (**Figure 3, A**) [67]. Conductivity of the PPy/PDLLA film was 5.65 mS/cm. This conductive material enhanced nerve regeneration in a rat sciatic nerve defect, displaying performance metrics (SFI value, axon diameter, and myelination) similar to the autologous nerve graft positive control after 6 months (**Figure 3, B**). Wang et al. fabricated reduced graphene oxide (rGO)-coated silk fibrin/poly(l-lactic acid-co-caprolactone) nanofibrous scaffolds [230]. This scaffold, consisting of porous nanofibers, exhibited good permeability and an excellent conductivity of approximately 10 mS/cm. Although research on conductive nerve guidance conduits continues to be performed, conductive materials have some inherent drawbacks, such as mechanical rigidity and brittleness [231],[232]. Matching mechanical moduli of an implanted biomaterial with the mechanics of native nerve tissue is generally critical to reduce inflammation and to enhance neural differentiation [233]. Hence, several efforts have been made to develop soft and conductive hydrogel-based nerve guides. Recently, Park et al. fabricated soft conductive nerve guidance conduits by compounding gelatin methacrylate and rGO in the form of hybrid hydrogels (rGO/GelMA) (**Figure 3, C**) [234]. These hydrogels had a relatively high conductivity (approximately 8.7 mS/cm), excellent permeability, flexibility, and soft mechanical properties (Young's modulus: 57 kPa). In particular, the maintenance of conductive properties was demonstrated during deformation

(e.g., bending and successive compression) (**Figure 3, D**). All analyses values, such as sciatic function index, nerve conduction velocity, and muscle recovery, indicated that the conductive hydrogel-based nerve guidance conduits showed statistically similar values compared to the autograft gold standard after 8 weeks (**Figure 3, E**). Overall, conductive materials are suitable and promising for use as nerve guidance conduits for peripheral nerve regeneration.

Table 2. Conductive nerve guidance conduits. Acronyms of interest include: Polycaprolactone (PCL), Poly (DL-lactide) (PDLLA), oligo(poly(ethylene glycol) fumarate) (OPF), carbon nanotubes (CNT), multi-walled carbon nanotubes (MWCNT), reduced graphene oxide (rGO), polydopamine (PDA), (Poly(L-lactic acid-co-caprolactone)) (PLCL), trifluoroethanol (TFE), polylactic acid (PLA), gelatin-methacrylate (GelMA)

Conduit matrix	Conductive materials	Conductivity	*In vivo*	Outcomes	Reference
PDLLA	PPy	5.65 mS/cm	SD rats, 10 mm defect, 6 months	SFI at 6 months: PPy/PDLLA -24, PDLLA -37	[67]
Zein	PANI	0.016-0.030 S/cm	SD rats, 10 mm defects, 4 months	SFI at 8 weeks: PANI/Zein -50	[235]
OPF	CNT, rGO	5.75 mS/m	-	-	[236]
PCL	PDA coated gold	4.66 mS/cm	SD rats, 15 mm defects, 18 weeks	SFI at 18weeks: PDA-gold/PCL -8, PDA-PCL -11	[237]
Silk fibrin/PLCL	rGO	10 mS/cm	SD rats, 10 mm defects, 12 weeks	SFI at 12 weeks: rGO-coated silk/PLCL -40, silk/PLCL -60	[230]
TFE	rGO	-	SD rats, 2 mm defects, 12 weeks	-	[238]

PLA/Gelatin	MWCNT	0.32 S/cm	SD rats, 10 mm defects, 8 weeks	SFI at 8 weeks: PLA/Gelatin/MWCNT -77, Negative control -89	[83]
GelMA	rGO	8.7 mS/cm	SD rats, 10 mm defects, 8 weeks	SFI at 8 weeks: rGO/GelMA -73, GelMA -91	[234]

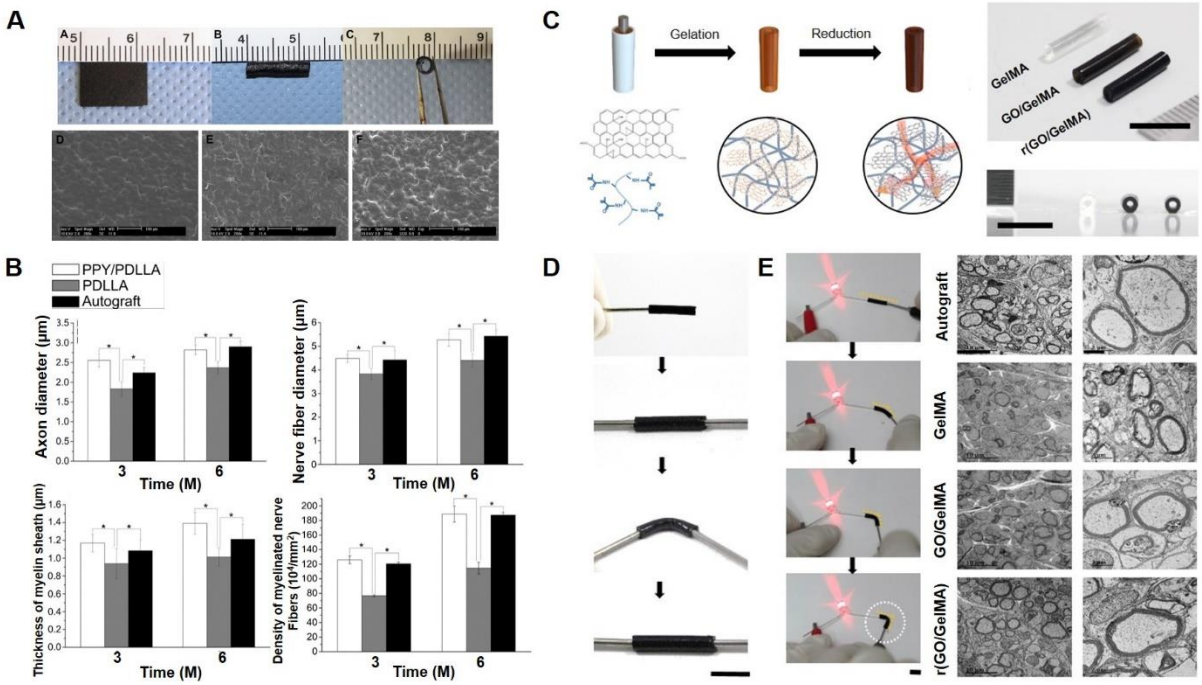

Figure 3. Conductive nerve guidance conduits for peripheral nerve regeneration. (A) Optical and scanning electron microscopy images of the polypyrrole (PPy) and poly(D,L-lactic acid) (PDLLA) film and conduits. (B) Quantification of the histological analysis of the regenerated nerve tissues for various groups (autograft, PDLLA, and PPyPDLLA) 3 and 6 weeks after implantation [67]**. (C) Schematic of reduced graphene oxide (rGO) embedded gelatin hydrogel-based nerve guidance conduits and optical images of the conduits (gelatin-mathacryalte (GelMA), GO/GelMA, and r(GO/GelMA)). (D) Photographs of a r(GO/GelMA) conduit during bending and connection with a cable and a LED bulb. (E) Transmission electron microscopy (TEM) analysis of myelination of the regenerated distal axon. Figure compiled from** [234] **© Wiley 2020 and from** [67] **Copyright (2013), with permission from Elsevier.**

2.2 Regeneration of Spinal Cord Tissue

Spinal cord injury (SCI) results in devastating long-term health complications for patients, and unfortunately there is currently no available treatment for full recovery. Native spinal cord tissue has a high conductivity (1 - 10 S/m), relative to other tissues in the body (e.g., native myocardium 0.16 S/m [239], muscle 0.93 ± 0.26 S/m [240]) [13], as well as soft tissue mechanical properties, making it a difficult tissue for biomaterials development [13],[241]. Recent advances in conductive materials show promise for SCI applications. However, conductive biomaterials applications for spinal cord tissue are in earlier stages of research and *in vivo* validation as compared to the other neural tissues discussed in this review. Techniques such as functional electrical stimulation (FES) are being utilized in a clinical setting to some success for acute SCI. In the injured adult rat central nervous system (CNS), functional electrical stimulation has been shown to promote cell regeneration, with an increase of cells expressing neural progenitor cell marker nestin without expression of glial fibrillary acidic protein associated with astrocytes [242], which could lead to therapies for chronic SCI patients. Stimulation also has been implicated in the enhancement of sensory neuron (i.e., rat femoral nerve) regeneration into cutaneous and muscle branches [243]. Following sciatic nerve injury, immediate electrical stimulation prevented the reduction of sensory afferent nerves in the spinal cord dorsal horn normally associated with this type of injury [244]. Implanted conductive biomaterials for repair of SCI may help with the transmission of signal from proximal nerve fibers and assist in regenerating the damaged spinal tissue to restore function to distal nerves. Current work showcases particle suspension delivery to the injury site (PPy [68]), composites to bridge a spinal cord defect (e.g., **Figure 4** PPy [13], PEDOT-carbon microfiber [245]), nanodrug injection to lesion epicenter (carbon nanotubes [246]), as well as initial *in vitro* testing on spinal cord nerve conduits (e.g., **Figure 5** carbon nanotubes [82]) and organotypic culture on porous cryogels (graphene [247]).

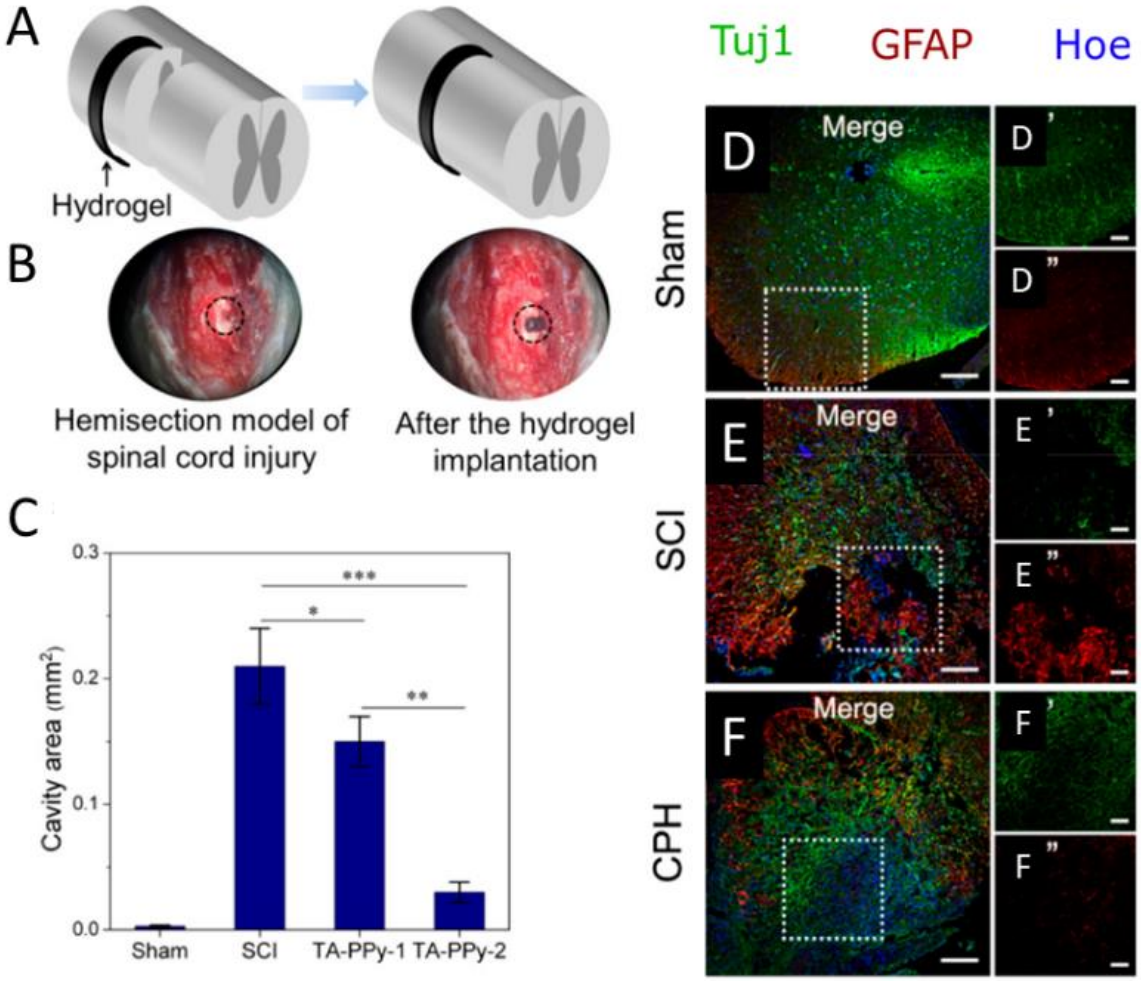

Figure 4: Adapted figure of pyrrole and tannic acid based conducting polymer hydrogel (CPH) implantation promoted new endogenous neurogenesis in a hemisection model of spinal cord injury (SCI). (A) Graphical representation of a "C"-shape, semitubular CPH that was implanted as a bridge to cover the spinal cord hemisection gap. (B) Hemisection spinal cord injury model with and without implantation. (C) Quantification graphs showing the average cystic cavity area of animals with SCI and different hydrogel treatments; *p < 0.05 and **p < 0.01, ***p < 0.001. Immunohistofluorescence images of transverse spinal cord sections obtained from animals in the sham (D), SCI (E), and hydrogel groups (F) at 6 weeks. Boxed regions in D, E, and F are magnified in D′, D″, E′, E″, F′, and F″. Scale bars indicate 200 μm (D–F) and 100 μm (D′–F″). Analysis of the spinal cord protein extracts showing the neuron-specific class III β-tubulin (Tuj1, green) and astrocyte-specific glial fibrillary acidic protein (GFAP, red), and all nuclei were Hoechst (Hoe, blue) stained in the sham, SCI, and conducting hydrogel groups. Figure adapted with permission from [13]**. Copyright 2018 American Chemical Society.**

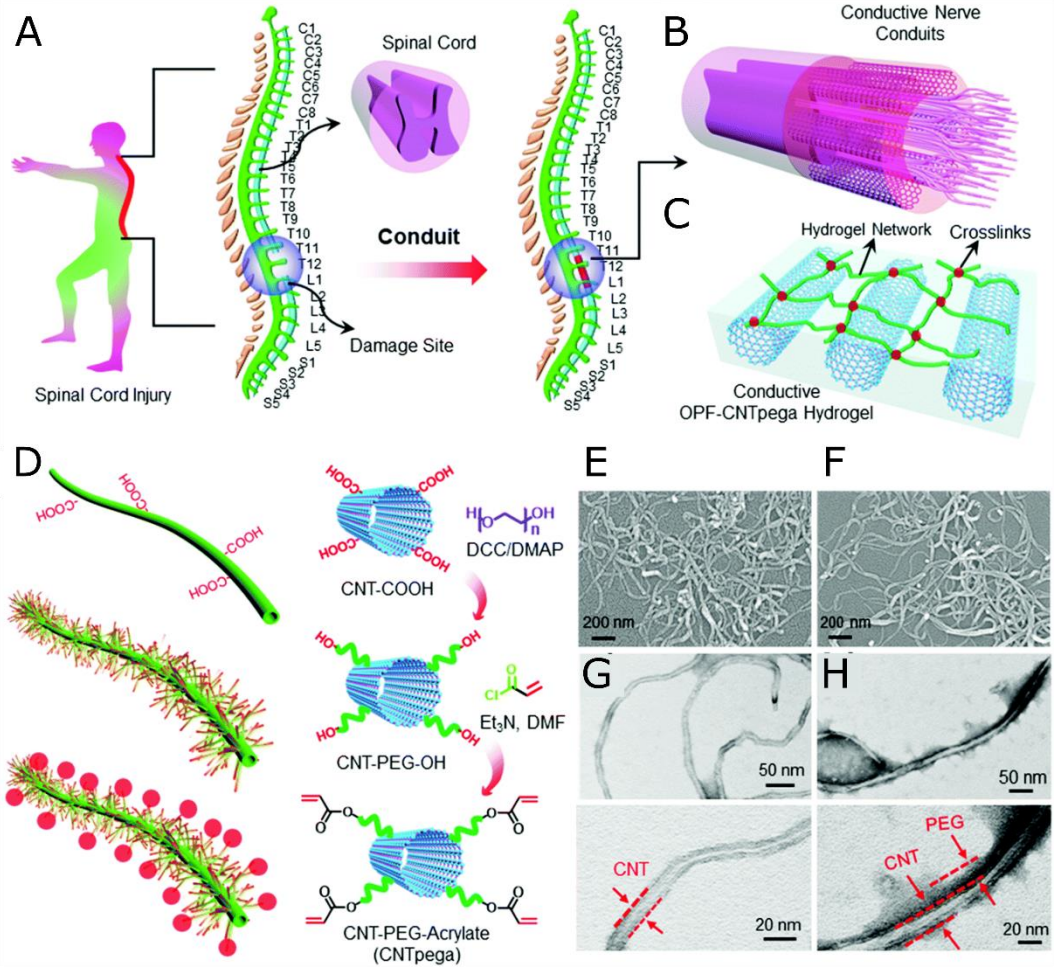

Figure 5: (A) Schematic demonstration of the spinal cord in the human body. (B) Conductive nerve conduits for spinal cord injury treatment. (C) Structure of the conductive oligo(poly(ethylene glycol) fumarate)-carbon-nanotube-poly(ethylene glycol)-acrylate (OPF-CNTpega) hydrogel. (D) Synthesis route to crosslinkable CNTs grafted with hydrophilic poly(ethylene glycol) (PEG) chains. Scanning electron microscopy images of (E) CNT-COOH tubes and (F) CNTpega tubes. TEM images of (G) CNT-COOH tubes and (H) CNTpega tubes with schematic demonstration. Figure © The Royal Society of Chemistry and the Centre National de la Recherche Scientifique 2018 [82]**.**

Following induced SCI in *in vivo* studies, long-term behavioral outcomes are often assessed utilizing the Basso, Beattie, Bresnahan (BBB) Locomotor Rating Scale [248]. This 21-point scale was developed to improve the sensitivity and reliability of locomotor assessment observed during recovery from spinal cord contusion in rats. The test offers robust locomotor criteria, such that examiners with varied experience can apply the scale consistently and obtain similar scores [248],[249]. When assessing the outcomes for some of the conductive materials

in vivo, the BBB score is used to showcase the functional changes resulting from biomaterial implantation (**Table 3**). In adult female Long Evans rats, moderate contusion spinal cord injury was performed and allowed to progress naturally for 48 hours before application of PPy-iodine particle suspension to the injury site, which was then assessed out to 8 weeks [68]. When assessed for BBB score, the animals in the vehicle only control group (i.e., lacking PPy-iodine particle suspension) received a score of 4.25±1.30 at week 8 and showed limited movement in three joints of the hind legs, whereas the rats that received the PPy-iodine particles received a score of 12.5±1.85 at week 8 and showed coordinated movement between forelegs and hind legs [68]. In adult male mice with a 2 mm hemisection spinal cord injury, implantation of a PPy-based hydrogel (**Figure 4**) showed a similar jump in BBB score for the conductive material group at 6 weeks following injury, around a score of 14 for the injury with conductive material treatment and around a score of 7 for the injury without treatment [13]. Injection of carbon nanotube and synthetic polymer Nafion, showed an increase in neurofilament positive fibers into the lesion in transection spinal cord injury, as well as increase motor coordination with the rotarod test, in which the animal balances on a rotating rod [246]. Since BBB scoring was not used in the rest of the studies, it is difficult to compare the results with other animal trials. In adult Wistar rats, 2-3 mm transections of the spinal cord were performed and PEDOT-carbon microfibers (MF) rolled in alginate sheaths were inserted into the injury site [245]. Transected spinal cords with PEDOT-MF showed significate decrease in tissue gap, and an increase of tissues growth into the lesion site [245]. *In vitro* studies in this area have looked at both collagen-graphene porous hydrogels, which show an increase in adult rat spinal cord cell viability [247], and carbon nanotube conduits, which increase proliferation of PC12 cells in culture. These materials have yet to be used in conjunction with electrical stimulation or make it into clinical trials for spinal cord injury applications, but the current *in vivo* results show potential for future translation.

Table 3: Conductive materials for spinal cord regeneration

Matrix	Conductive materials	Stimulation	Conductivity	*In vivo*	Outcomes	Reference
0.9% sodium chloride solution	polypyrrole-iodine (PPy-I)	-	-	Adult female Long Evans rats (220–240 g), contusion SCI	BBB at 8 weeks: SCI-PPy-I 12.5±1.85, SCI-vehicle 4.25±1.30	[68], 2017
tannic acid (TA)	PPy	-	0.05–0.18 S/cm	Adult male C57BL/6N mice (6–8 weeks old) Hemisection SCI	BBB at 6 weeks: Hydrogel 14±2, SCI 6±2	[13], 2018
oligo(poly(ethylene glycol) fumarate) (OPF)	Carbon Nanotubes (CNT) functionalized with poly(ethylene glycol) (PEG)	-	OPF-CNTpega-1 ($4.59 \pm 3.58 \times 10^{-4}$ S m^{-1}) OPF-CNTpega-5 of ($8.16 \pm 5.66 \times 10^{-4}$ S m^{-1}) OPF-CNTpega-10 $2.04 \pm 1.22 \times 10^{-3}$ S m^{-1}	*In vitro* PC12	As compared to OPF control, OPF-CNTpega increased cell proliferation, focal adhesion density and size	[82], 2018
Collagen cryogel	Graphene	-	0.1% w/v graphene 2.91 mS/cm, 0.5% w/v graphene 3.93 mS/cm	Organotypic Culture Adult male rat (250–300 g) spinal cord cultured on cryogels	Increased cell proliferation on 0.5% w/v graphene collagen cryogels as compare to EDC/NHS crosslinked control collagen cryogels	[247], 2020
Nafion® perfluorinated resin solution (20 wt. %)	multi-walled carbon nanotubes (MWCNTs)	-	-	Adult male Sprague-Dawley rats (200–250 g, 1.8 months old) Transection SCI	CNT/Nafion nanocomposite decreased lesion volume, increased neurofilament-positive fibers and corticospinal tract fibers in the lesion	[246], 2015
Alginate	Poly(3, 4-ethylenedioxythiophene)-coated carbon microfibers (PEDOT-	-	-	Adult male Wistar rats (300–390 g, 14–20 weeks old) Transection SCI	MFs modified with PLL/heparin/bFGF/fibronectin produced little or absent inflammation and fibrosis. Inflammation,	[245], 2016

MFs)	scarring, and neural damage were prominent around non-functionalized or PLL-functionalized MFs

2.3 Regeneration of Brain Tissue

One of the most well established areas of research on electroconductive materials for neural applications is the development of electrodes for brain-machine/human-computer interfaces and deep brain stimulation that present a variety of exciting opportunities for long term medical and veterinary interventions [250]. Significant attention has been directed towards the development of technologies containing carbon-based electronic component for long term applications (including electrode coatings [45] and/or biosensors [251]) and there is growing interest in short term applications such as theranostics (for conditions such as brain cancers and neurodegenerative conditions [252]) or tissue scaffolds to maintain and regenerate brain tissue employing electrical stimuli as summarized below. However, it is important to note that by comparison with research on neural electrodes, research on electronics for brain tissue engineering is relatively nascent in part because it is only recently that it was understood that CNS tissue is capable of regeneration [253]–[257], and we will summarize progress towards this goal. A consequence of its relatively nascent status is that in contrast to peripheral nerve tissue or spinal cord tissue, there are as yet no well-defined general metrics of success for brain tissue regeneration, however, the literature indicates progress in developing instructive biomaterials in combination with neuronal cell lines or primary cells that employ topographical cues or electrical stimuli to influence cell differentiation or increase neurite formation/outgrowth to enhance regenerative outcomes.

Composites of PEDOT and gelatin were observed to support bovine brain capillary endothelial cell adhesion and growth which may be important for successful vascularization of

brain tissue scaffolds [258]. Collazos-Castro et al. demonstrated that electrical stimulation of PEDOT-coated carbon microfibers can trigger the release of basic fibroblast growth factor (bFGF) from the fibers **(Figure 6, A)** [259]. Additionally, these aligned microfibers encourage the alignment of the cells growing on the fibers (**Figure 6, B**). In combination with the capability of bFGF release, these characteristics promote the differentiation of glial progenitor cells into astrocytes denoted by staining with glial fibrillary acidic protein (GFAP) (**Figure 6, C, D**) [259]. This work showcases that stimulation, in combination with an electroconductive biomaterial, chemical cue (i.e., growth factor), and physical cue (i.e., microfiber) can have a marked effect toward the differentiation of cells *in vitro* which yields promising results for future *in vivo* studies.

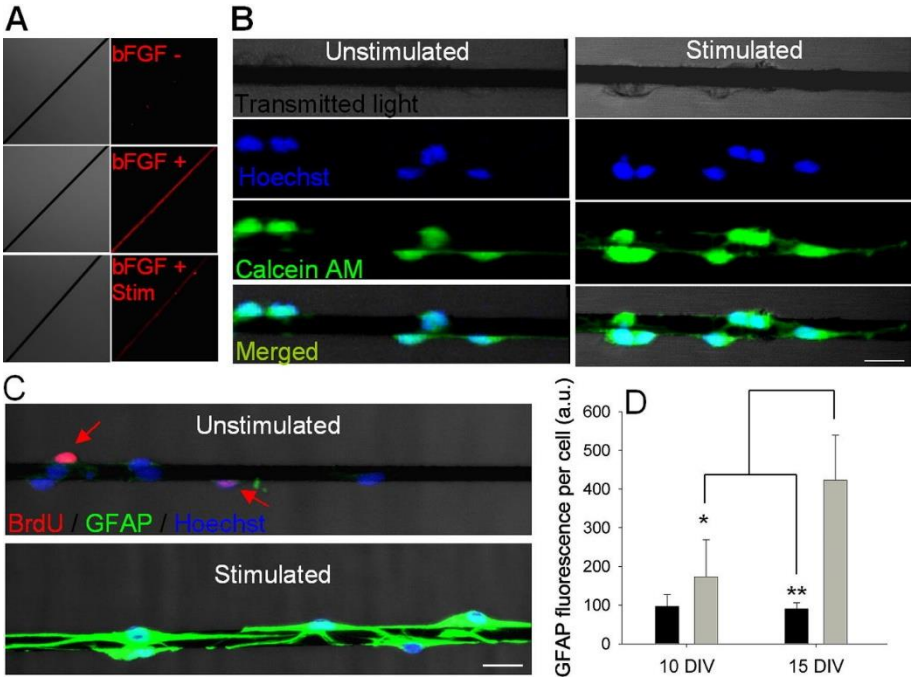

Figure 6: Biological effects of cathodic electrostimulation applied through microfibers functionalized with PLL/Heparin/bFGF/Fibronectin. (A) Electrostimulation partially released bFGF from the microfiber surface, as detected by fluorescence confocal microscopy of microfibers without bFGF (bFGF−), with bFGF but no stimulation (bFGF+), and with bFGF and stimulation (bFGF+ Stim), processed for bFGF immunochemistry. (B) Cells on electro-stimulated microfibers preserved their viability, as indicated by Calcein AM fluorescence at 10 days *in vitro* (DIV). Notice that the stimulated cells showed more complex cytoplasmic processes. (C) Electrical stimulation reduced cell proliferation (BrdU staining, red), and increased astrocyte differentiation

(GFAP staining, green). (D) Quantification of GFAP fluorescence per cell in unstimulated (black columns) and electrically stimulated (gray columns) cells. **p < 0.01; *p < 0.05. Scale bars: B, 15 μm; C, 20 μm. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.) Reprinted from Acta Biomaterialia, 35/15, Jorge E. Collazos-Castro, Concepción García-Rama, Alexandra Alves-Sampaio, Glial progenitor cell migration promotes CNS axon growth on functionalized electroconducting microfibers, 42-56, Copyright (2016), with permission from Elsevier. [259]

An interesting study reported that neuroinflammatory responses of microglia on 2D- or 3D-graphene-based materials was similar to that of the microglia on tissue culture polystyrene, with lipopolysaccharide-induced neuroinflammation on 3D foam substrates lower than neuroinflammation on 2D film substrates [260]. An interesting complementary study showed that the medium produced by microglia grown on the 3D-graphene foams could promote neurosphere formation and facilitate neural stem cell migration from neurospheres [261]. Reduced graphene oxide (rGO) coated fibers acted as topographical guidance cues for the alignment of cells (astrocytes and neuroblasts) grown thereon when implanted into the striatum or subventricular zone of adult rats; interestingly, the activation levels of microglia and astrocytes were lower on reduced graphene oxide coated scaffolds as compared to non-functionalized polycaprolactone, and the reduced graphene oxide coated scaffolds exhibited no glial scarring at the scaffold-tissue interface after 7 weeks *in vivo* which is important as it is indicative of improved integration with native tissue and diminished glial scar-related barriers (e.g., mechanical barriers) to neuronal regrowth [262],[263]. Injectable hydrogels composed of acetylcholine-functionalized graphene oxide and poly(acrylic acid) were supportive of the growth of primary cortical neurons and reactive astrocytes in the hippocampal dentate gyrus region of injured mouse brains [264]. Interestingly, studies showed that primary neurons cultured in 3D scaffolds composed of parylene and graphene extended their axons through the pores [265]. Additionally, synaptic networks formed by primary neurons cultured in 3D

scaffolds composed of polydimethylsiloxane (PDMS) or PDMS/graphene sustained a high rate of bursting, which is implicated in synchronous neuronal firing, that was increased by the presence of graphene [266].

Conductive biomaterials can influence cell differentiation towards more specialised roles supporting tissue maturation and tissue repair. Conductive materials (e.g., PANI films [267], or composites composed of single-walled carbon nanotubes, nanocellulose fibers and alginate [268]) were shown to support the differentiation of the neuroblastoma cell line (SH-SY5Y cells) into more neural phenotypes. Electrical stimulation of brain-derived neurotrophic factor (BDNF) hypersecreting mesenchymal stem cells on graphene-based materials was shown to encourage their transdifferentiation to both neuronal and Schwann cell-like phenotypes at low voltages (25-50 mV at 50 Hz) or exclusively Schwann cell-like phenotypes at higher voltages (100 mV at 50 Hz) [269]. Mats of electrospun polycaprolactone that were coated with GO were used to promote the differentiation of neuronal stem cells (NSCs) into mature oligodendrocytes [270]. Nanofibrous scaffolds composed of pyrolyzed composites of polyacrylonitrile and multiwalled carbon nanotubes were shown to enhance the differentiation of mouse neural stem/progenitor cells [271]. Electrical stimulation (5 mV, 0.5 mA, 25 ms intermittent stimulation) of neural stem cells on bundles of single walled carbon nanotubes promoted their differentiation into mature neurons [272], likewise, electrical stimulation (100 mV, 1h/day) of NSCs on PLGA/GO membranes promoted NSC proliferation, neuronal differentiation, and neurite elongation [273].

Conductive biomaterials can enhance neuronal repair using neurite outgrowth as a biomarker for axonal formation/extension/navigation. Electrical stimulation (20 mV/mm, 100 Hz, 5 min) of NB-39-Nu human neuroblastoma cells on carbon nanotube-PEDOT-based films enhanced the number and length of neurites which may be important for cell connectivity and tissue maturation [274]. Films composed of polyethylene terephthalate (PET) and graphene

were used to create a transient non-contact electric field (as low as 4.5 mV/mm for 32 min), which resulted in new and strengthened existing cell-to-cell couplings between SH-SY5Y cells [275]. The electrical stimulation (charge-balanced biphasic electrical stimulation at 250 Hz, 20-60 mV, 8h/day, 5 days) of PC12 cells using PEDOT functionalized with biomimetic features (phosphoryl choline to mimic cell membranes, and cell adhesive peptides (e.g., Ile-Lys-Val-Ala-Val (IKVAV) from laminin) enhanced neurite outgrowth and length [276]. Electrical stimulation (100 mV, 1h) of PC12 cells cultured on heparin-doped PPy was shown to enhance the number and length of neurites from the PC12 cells [69], as was electrical stimulation (100 mV/mm, 20 Hz, 2h/day) of PC12 cells cultured on carbon nanotube loaded polycaprolactone derivatives [277]. Neurite outgrowth from embryonic hippocampal neurons on mats of multiwalled carbon nanotubes could be enhanced by coating the nanotubes with 4-hydroxynonenal [221]. Electrical stimulation (0.25 mA/cm^2 using a biphasic waveform of 100 μs pulses, 8h/day, 3 days) of primary pre-frontal cortical neurons, isolated from murine gene knockout models for schizophrenia, on PPy substrates was observed to enhance neurite outgrowth, which is potentially interesting for treating schizophrenia and other neurodevelopmental diseases [70]. Electrical stimulation (1 Hz, 10 μA, 30 min/day, 3 days) of induced pluripotent stem cell (iPSC) derived neural progenitor cell (NPC) lines (collected from patients with Rett syndrome) using 3D graphene scaffolds showed increased cell maturation and improvements in cell morphology of the cells after electrical stimulation, which is potentially interesting for treating patients with Rett syndrome.[278] Although the majority of work aimed at brain tissue regeneration remains in the *in vitro* stages of study, the literature highlighted indicates the growing potential to utilize instructive electroconductive materials in combination with biological cues or electrical stimuli to enhance regenerative outcomes in CNS tissues.

2.4 Optical Applications

Although not as extensively studied as the brain, the last decade of development and clinical approval of bionic eye implant prostheses represents a significant step forward in the ability to aid patients with sight impairment [279]–[285]. Attention has been directed towards the development of technologies containing organic electronic components, including arrays of photodetectors [286]–[290], biosensors [291]–[293], devices to deliver ions (e.g., drugs) [294]–[296], and smart contact lenses [297]–[300]. Concomitantly there is growing interest in maintaining and regenerating nerves in damaged optical tissue via various methods [301]–[305], particularly because transcorneal electrical stimulation (TES) has been shown to enhance the survival of retinal ganglion cells (RGCs) [306], to prolong the survival of photoreceptors [307], and to result in retinal neovascular changes [308],[309]. Furthermore, organic electronic materials have shown some promise for ocular nerve regeneration; for example, electrical stimulation of retinal progenitor cells (RPCs) using PPy coated electrodes was observed to direct their differentiation towards neural fates [310]. Moreover, electrical stimulation of retinal ganglion cells on aligned nanofibers containing PPy and graphene was shown to enhance cell viability and neurite outgrowth (**Figure 7**) [71]. Although progress has been made with respect to relevant cell populations for optical applications, it is still at a very nascent stage and depending on the location the conductive biomaterials are employed their optical properties may be important (i.e., not impacting retinal function) which we believe will be a focus of future studies.

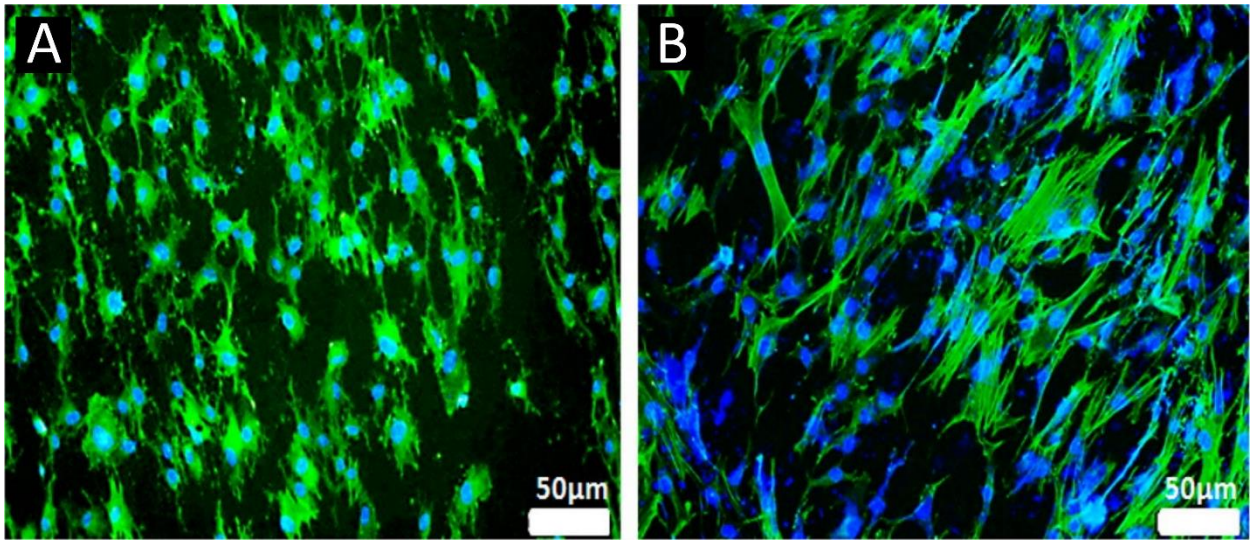

Figure 7: Confocal micrographs of aged retinal ganglion cells on the 6% (w/w) polypyrrole functionalized graphene hybrids with the presence of biocompatible poly(lactic-co-glycolic acid) (PPy-G/PLGA) nanofibers (A) without electrical stimulation and (B) after electrical stimulation. All cells were cultured for 10 days. Electrical stimulation step potential was pulsed between −700 and +700 mV/cm, and was performed 1 hour every day for 3 days. Image reprinted with permission from [71]**. Copyright (2016) American Chemical Society.**

2.5 Auditory Applications

Cochlear implants dramatically aid patients with hearing impairment [311]–[314]. However, to provide further improvement to current devices, there is growing interest in maintaining and regenerating nerves in damaged ears using a variety of approaches, with those techniques involving electricity, summarized briefly here [315]–[320]. Electrical stimulation is of great interest in auditory applications because of the prevailing idea that neuronal survival is dependent on both the presence of hair cells, the sensory receptor cell in the ear, as well as on electrical stimulation [315]. Electrical stimulation of spiral ganglion cells (SGCs), neural cell bodies that innervate hair cells, has been shown to enhance their survival, and the combination of electrical stimulation (chronic stimulation via a cochlear implant electrode) and delivery of glial cell line-derived neurotrophic factor (GDNF) significantly improved the preservation of SGC density *in vivo* in guinea pigs [321]. Electrical stimulation has also been used to deliver drugs (e.g., neurotropin-3 [NT-3] [66],[322],[323] alone or combined with

brain-derived neurotrophic factor (BDNF) [324]) from PPy-coated electrodes. Neural explants in rats demonstrate efficacy of the drugs released from the modified electrodes *in vitro*, similarly, this efficacy is seen in the release of BDNF from PEDOT-coated electrodes in guinea pigs [325]. Despite the potential for using electric fields in a tissue engineering and regenerative medicine approach for auditory tissues, forays in this direction include: bundles of carbon nanotubes that may act as artificial hairs [326], the incorporation of carbon nanotubes in tissue scaffolds [327],[328] for ear cartilage [329], and 3D printed ear cartilage scaffolds with an embedded metal inductive coil antenna inside it (**Figure 8**) enabling readout of inductively-coupled signals from cochlea-shaped electrodes (notably, so that left and right printed ears can hear in stereo) [330].

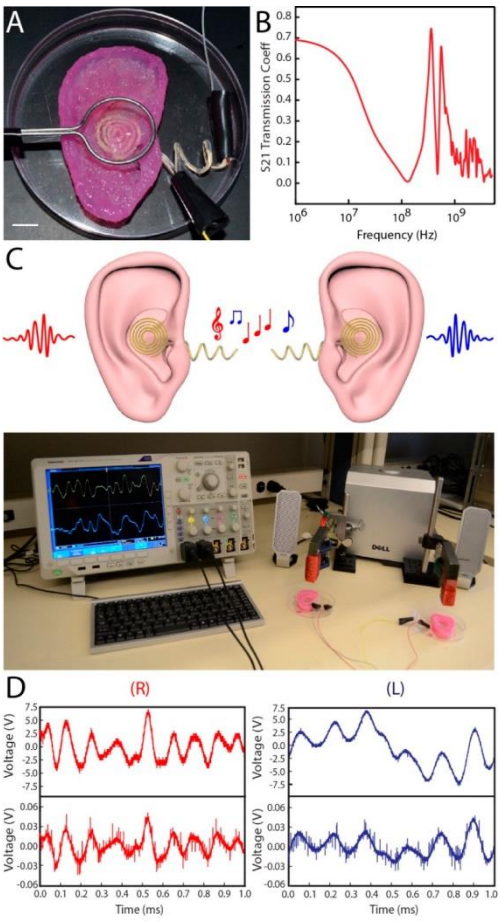

Figure 8: Electrical characterization of the bionic ear. (A) Image of the experimental setup used to characterize the bionic ear. The ear is exposed to a signal from a

transmitting loop antenna. The output signal is collected via connections to two electrodes on the cochlea. Scale bar is 1 cm. (B) Response of the bionic ear to radio frequencies in terms of S21, the forward power transmission coefficient. (C) (top) Schematic representation of the radio signal reception of two complementary (left and right) bionic ears. (bottom) Photograph of complementary bionic ears listening to stereophonic audio music (Supporting Information Movie 2). (D) Transmitted (top) and received (bottom) audio signals of the right (R) and left (L) bionic ears. Image reprinted with permission from [330]**. Copyright (2013) American Chemical Society.**

3 Emerging materials

Recently, several electrically conductive organic materials have been discovered and explored for potential biomedical applications. In addition to conductive polymers and electroconductive carbon-based nanomaterials, which are discussed in this review, there are natural compounds (e.g., melanin), and inorganic conductors including metals (e.g., gold nanomaterials) and 2D materials (e.g., molybdenum disulfide (MoS_2) and black phosphorous) that can be used for tissue engineering, which we introduce with a view to highlighting their potential for the future.

Degradable biomaterial scaffolds are desirable for regenerative tissue engineering applications as they allow for full regrowth of the native tissue into the injury site previously occupied by the biomaterial, minimizing possible complications with chronic implants [331]. However, most conducting polymers and carbon-based electroconductive materials are not degraded *in vivo* impeding their use in the development of *in vivo* devices. Hence, with an attempt to develop biodegradable conductive materials, a method of biodegradable modification of conductive monomers or conjugates using a degradable linker between monomers has been studied [332],[333]. These methods can lead to complete biodegradation of conducting polymers. For example, hydrolytic ester links were introduced between aniline pentamer units, which were found to be degraded at pH 7.4 [334]. In addition, Lei et al. synthesized a novel conductive biodegradable polymer using diketopyrrolopyrrole (DPP) to

develop field effect transistors, which can be fully degradable degraded under weak acidic conditions [335]. The authors conjugated DPP monomer with an imine bond (-C=N-) for degradation, and found that the substrate was eventually hydrolyzed under weak acid conditions (pH 4.6) (**Figure 9, A**); and the organic electronic device fabricated with this degradable conducting polymer was completely decomposed in 30 days in a pH 4.6 buffer solution (**Figure 9, B**). These hydrolyzable conductive materials remain stable in neutral pH and only degrade at low pH, implying that *in vivo* degradation would be limited to tissues with local acidity (e.g., stomach); it is also possible that these materials could degrade upon exposure to hydrolytic enzymes such as esterases *in vivo*. Another group synthesized this DPP polymer and found that the conductivities of undoped DPP film and p-doped DPP film were 10^{-6} S/cm for undoped type and 30-70 S/cm, respectively [336].

Biologically derived conductive materials, versus conventional fabricated conductive materials, may address the issue associated with poor biodegradability because of their ability to degrade under some biologically relevant conditions (**Figure 9, B**). Among biologically derived materials, melanins (e.g., eumelanin or pheomelanin) are synthesized via oxidation of tyrosine and its derivatives *in vivo* and exhibits both electroactivity and biodegradability [337], with conductivity ranging from 10^{-8} S/m to 10^{-3} S/m, depending on the synthetic methodology [11]. For practical *in vivo* applications, it is necessary to ensure the conductivity of the melanin-based material meets the requirements of the specific application (potentially tuning the monomer composition) or preparation of composites for use as conductive biomaterials for tissue regeneration applications.

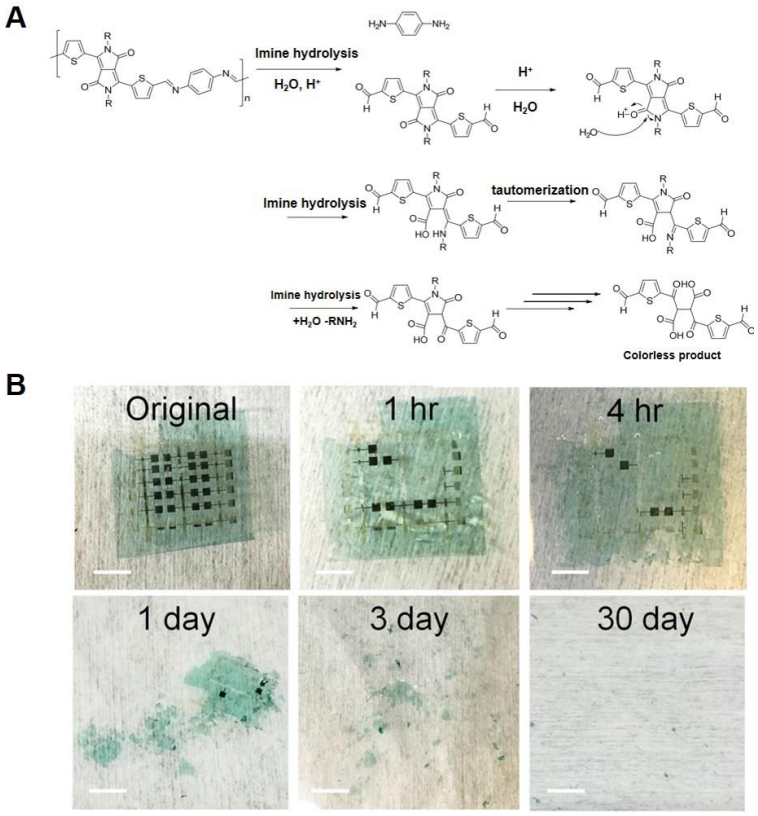

Figure 9. Degradable conducting polymer synthesized with diketopyrrolopyrrole (DPP) via imine chemistry. A) Proposed degradation chemistry via hydrolysis under acidic condition. B) Disintegration of organic electronic device with synthesized fully decomposable polymer at pH 4.6. Reproduced from [335]**, copyright (2017) National Academy of Sciences.**

4 Conclusion

The development of carbon-based conductive and electroactive materials (e.g., derivatives of polypyrrole, polythiophene, polyaniline, graphene, fullerenes) has made great progress for biomedical applications in the nervous system (i.e., peripheral nerve, spinal cord, brain, eye, ear) in the last 20 years. Herein we review the use of carbon-based conductive and electroactive biomaterials for tissue engineering and regenerative medicine applications within the central/peripheral nervous system, highlighting *in vivo* studies as a useful benchmark for

progress towards clinical trials prior to the eventual translation of them from the lab to the clinic [12],[20].

We believe electroconductive materials can be used to fabricate clinically relevant tissue scaffolds mimicking endogenous tissue electrical properties as well as providing bioactive cues to aid in regeneration and potentially harnessing their ability to control the release of various payloads. We foresee significant opportunities for non-degradable flexible carbon-based electronics for long term applications (e.g., neural electrodes) where their flexibility minimizes adverse inflammatory reactions resulting from mismatch between the mechanical properties of the implanted materials and the nervous tissue; and that biodegradable or bioerodible electronics may be particularly useful for applications including drug delivery, tissue engineering and regenerative medicine within the nervous system where their inherently transient nature is appealing (however, recognize the significant challenge in designing biocompatible and cytocompatible materials). Still, new conductive materials (either organic or inorganic), offering new or enhanced performances, have been actively synthesized and explored as biomaterials.

Materials that are considered inorganic were not discussed further in this review; however, we would like to draw attention to the recently developed inorganic 2D nanomaterial MXenes as a promising alternative to carbon-based nanomaterials (e.g., graphene oxide) because they can provide several beneficial characteristics for fabrication of electrically conductive biomaterials [338]–[340]. MXene exhibits high conductivity (e.g., pure MXene film (Ti3C2Tx) 2.4×10^5 S/m), low toxicity, and biodegradability, and, especially, good water solubility as MXene has a hydrophilic functional group [341]–[344]. Hence, MXenes are expected to offer new opportunities particularly when used in combination with electroactive materials discussed herein to create novel biomaterials for neural regeneration clinical applications.

As we demonstrated in this review, carbon-based conductive and electroactive materials have been utilized for *in vivo* nerve tissue studies and electrical stimulation of neural cells has been performed *in vitro*. However, the electrical stimulation for regeneration of nerve tissues *in vivo* utilizing the conductive biomaterials discussed in this review has not been explored. As the field further develops, future studies should address the application of electrical stimulation in combination with electroconductive materials as alterations to stimulation parameters could benefit neural regeneration. To the best of our knowledge there are as yet no clinical trials using such materials for neuroregeneration, although there are a couple that utilize some of the materials mentioned for other purposes. One clinical trial used fullerene-C60 (i.e., buckyballs) as a cosmetic ingredient with antioxidant ability, that was applied to the face for 8 weeks as part of an anti-wrinkle formulation and showed no severe side effects in the 23 person randomized control trial [345]. Another clinical trial utilizes graphene incorporated into latex condoms to study performance and safety [346]. The lack of clinical trials using electroconductive materials leaves considerable room to explore *in vivo* and clinical studies related to optical neurons and conductive materials. Even though there was only the application of the fullerene material on the skin near the eye for the anti-wrinkle study, and the graphene material that would come in contact with skin and mucus membranes, the indication of electroconductive materials moving into the non-invasive clinical space is promising.

Organic electroconductive materials (e.g., derivatives of polypyrrole, polythiophene, polyaniline, graphene, fullerenes) have made great progress for nervous system applications in the brain, eye, ear, spinal cord, and peripheral nerve as they offer great opportunities to efficiently mediate electrical signals with such system and lead to unique responses (e.g., functional regeneration). Herein we highlight *in vivo* studies in addition to the limited clinical trials available utilizing these electroconductive materials [12],[20], and briefly examined

emerging electroconductive materials, including biodegradable conductive substances that are promising materials for future studies.

We believe electroconductive materials have been extensively studied to fabricate clinically relevant tissue scaffolds, displaying good biocompatibility and biofunctionality, in a various manner, such as by mimicking endogenous tissue electrical properties, providing bioactive cues to aid in regeneration, controlling biodegradation *in vivo*, and potentially harnessing their ability to control the release of various payloads release. Altogether, such specialized electrically conductive biomaterials will clinically impact on the field of tissue regeneration.

5 References

[1] Hosoyama, K., Ahumada, M., Goel, K., Ruel, M., Suuronen, E. J., & Alarcon, E. I. (2019). Electroconductive materials as biomimetic platforms for tissue regeneration. Biotechnology Advances, *37*(3), 444–458. PMID:30797094

[2] Bretschneider, F., & de Weille, J. R. (2006). *Introduction to Electrophysiological Methods and Instrumentation*. Elsevier.

[3] Bretschneider, F., & De Weille, J. R. (2018). *Introduction to electrophysiological methods and instrumentation*. Academic Press.

[4] Smith, R. S., & Walsh, C. A. (2020). Ion Channel Functions in Early Brain Development. Trends in Neurosciences, *43*(2), 103–114. PMCID:PMC7092371

[5] Gordon, T. (2016). Electrical Stimulation to Enhance Axon Regeneration After Peripheral Nerve Injuries in Animal Models and Humans. Neurotherapeutics : The Journal of the American Society for Experimental NeuroTherapeutics, *13*(2), 295–310. PMCID:PMC4824030

[6] Thakral, G., LaFontaine, J., Najafi, B., Talal, T. K., Kim, P., & Lavery, L. A. (2013). Electrical stimulation to accelerate wound healing. Diabetic Foot & Ankle, *4*(1), 22081. PMCID:PMC3776323

[7] Leppik, L., Zhihua, H., Mobini, S., Thottakkattumana Parameswaran, V., Eischen-Loges, M., Slavici, A., Helbing, J., Pindur, L., Oliveira, K. M. C., Bhavsar, M. B., Hudak, L., Henrich, D., & Barker, J. H. (2018). Combining electrical stimulation and tissue engineering to treat large bone defects in a rat model. Scientific Reports, *8*(1), 6307. PMCID:PMC5910383

[8] Enoka, R. M., Amiridis, I. G., & Duchateau, J. (2020). Electrical Stimulation of Muscle: Electrophysiology and Rehabilitation. Physiology, *35*(1), 40–56. doi: 10.1152/physiol.00015.2019

[9] Stevens, B., Porta, S., Haak, L. L., Gallo, V., & Fields, R. D. (2002). Adenosine: A Neuron-Glial Transmitter Promoting Myelination in the CNS in Response to Action Potentials. Neuron, *36*(5), 855–868. doi: 10.1016/S0896-6273(02)01067-X

[10] Zarrintaj, P., Manouchehri, S., Ahmadi, Z., Saeb, M. R., Urbanska, A. M., Kaplan, D. L., & Mozafari, M. (2018). Agarose-based biomaterials for tissue engineering. Carbohydrate Polymers, *187*, 66–84. doi: 10.1016/j.carbpol.2018.01.060

[11] Saberi, A., Jabbari, F., Zarrintaj, P., Saeb, M. R., & Mozafari, M. (2019). Electrically Conductive Materials: Opportunities and Challenges in Tissue Engineering. Biomolecules, *9*(9), 448. PMCID:PMC6770812

[12] Guimard, N. K., Gomez, N., & Schmidt, C. E. (2007). Conducting polymers in biomedical engineering. Progress in Polymer Science, *32*(8–9), 876–921. doi: 10.1016/j.progpolymsci.2007.05.012

[13] Zhou, L., Fan, L., Yi, X., Zhou, Z., Liu, C., Fu, R., Dai, C., Wang, Z., Chen, X., Yu, P., Chen, D., Tan, G., Wang, Q., & Ning, C. (2018). Soft Conducting Polymer Hydrogels Cross-Linked and Doped by Tannic Acid for Spinal Cord Injury Repair. ACS Nano, *12*(11), 10957–10967. PMID:30285411

[14] Woeppel, K., Yang, Q., & Cui, X. T. (2017). Recent Advances in Neural Electrode-Tissue Interfaces. Current

Opinion in Biomedical Engineering, *4*, 21–31. PMCID:PMC5798641
[15] Wang, D., Zhang, Y., Lu, X., Ma, Z., Xie, C., & Zheng, Z. (2018). Chemical formation of soft metal electrodes for flexible and wearable electronics. Chemical Society Reviews, *47*(12), 4611–4641. PMID:29722373
[16] Biran, R., Martin, D. C., & Tresco, P. A. (2005). Neuronal cell loss accompanies the brain tissue response to chronically implanted silicon microelectrode arrays. Experimental Neurology, *195*(1), 115–126. PMID:16045910
[17] Wang, W., Hou, Y., Martinez, D., Kurniawan, D., Chiang, W.-H., & Bartolo, P. (2020). Carbon Nanomaterials for Electro-Active Structures: A Review. Polymers, *12*(12), 2946. doi: 10.3390/polym12122946
[18] Bekyarova, E., Itkis, M. E., Cabrera, N., Zhao, B., Yu, A., Gao, J., & Haddon, R. C. (2005). Electronic properties of single-walled carbon nanotube networks. Journal of the American Chemical Society, *127*(16), 5990–5995. PMID:15839699
[19] Li, E. Y., & Marzari, N. (2011). Improving the electrical conductivity of carbon nanotube networks: a first-principles study. ACS Nano, *5*(12), 9726–9736. PMID:22059779
[20] Hardy, J. G., Lee, J. Y., & Schmidt, C. E. (2013). Biomimetic conducting polymer-based tissue scaffolds. Current Opinion in Biotechnology, *24*(5), 847–854. PMID:23578463
[21] Bard, A. J., & Faulkner, L. R. (2001). *Electrochemical methods fundamentals and applications*. John Wiley & Sons.
[22] Williams, R. L., & Doherty, P. J. (1994). A preliminary assessment of poly(pyrrole) in nerve guide studies. Journal of Materials Science: Materials in Medicine, *5*(6–7), 429–433. doi: 10.1007/BF00058978
[23] Khodagholy, D., Gelinas, J. N., Thesen, T., Doyle, W., Devinsky, O., Malliaras, G. G., & Buzsáki, G. (2015). NeuroGrid: recording action potentials from the surface of the brain. Nature Neuroscience, *18*(2), 310–315. PMCID:PMC4308485
[24] Jung, Y. H., Park, B., Kim, J. U., & Kim, T. (2019). Bioinspired Electronics for Artificial Sensory Systems. Advanced Materials, *31*(34), 1803637. PMID:30345558
[25] Nowik, K., Langwińska-Wośko, E., Skopiński, P., Nowik, K. E., & Szaflik, J. P. (2020). Bionic eye review - An update. Journal of Clinical Neuroscience : Official Journal of the Neurosurgical Society of Australasia, *78*, 8–19. PMID:32571603
[26] Ong, J. M., & da Cruz, L. (2012). The bionic eye: a review. Clinical & Experimental Ophthalmology, *40*(1), 6–17. PMID:21575116
[27] Pattisapu, P., Lindquist, N. R., Appelbaum, E. N., Silva, R. C., Vrabec, J. T., & Sweeney, A. D. (2020). A Systematic Review of Cochlear Implant Outcomes in Prelingually-deafened, Late-implanted Patients. Otology & Neurotology : Official Publication of the American Otological Society, American Neurotology Society [and] European Academy of Otology and Neurotology, *41*(4), 444–451. PMID:32176122
[28] Orzechowska, S., Mazurek, A., Świsłocka, R., & Lewandowski, W. (2019). Electronic Nose: Recent Developments in Gas Sensing and Molecular Mechanisms of Graphene Detection and Other Materials. Materials (Basel, Switzerland), *13*(1). PMCID:PMC6981730
[29] Moon, D., Cha, Y. K., Kim, S.-O., Cho, S., Ko, H. J., & Park, T. H. (2020). FET-based nanobiosensors for the detection of smell and taste. Science China. Life Sciences, *63*(8), 1159–1167. PMID:31974862
[30] Wang, Y., Liu, A., Han, Y., & Li, T. (2020). Sensors based on conductive polymers and their composites: a review. Polymer International, *69*(1), 7–17.
[31] Jeong, S.-Y., Kim, J.-S., & Lee, J.-H. (2020). Rational Design of Semiconductor-Based Chemiresistors and their Libraries for Next-Generation Artificial Olfaction. Advanced Materials (Deerfield Beach, Fla.), *32*(51), e2002075. PMID:32930431
[32] Hurot, C., Scaramozzino, N., Buhot, A., & Hou, Y. (2020). Bio-Inspired Strategies for Improving the Selectivity and Sensitivity of Artificial Noses: A Review. Sensors (Basel, Switzerland), *20*(6). PMCID:PMC7146165
[33] Freund, M. S., & Lewis, N. S. (1995). A chemically diverse conducting polymer-based "electronic nose". Proceedings of the National Academy of Sciences of the United States of America, *92*(7), 2652–2656. PMCID:PMC42276
[34] Podrażka, M., Bączyńska, E., Kundys, M., Jeleń, P. S., & Witkowska Nery, E. (2017). Electronic Tongue-A Tool for All Tastes? Biosensors, *8*(1). PMCID:PMC5872051
[35] Tahara, Y., & Toko, K. (2013). Electronic Tongues–A Review. IEEE Sensors Journal, *13*(8), 3001–3011. doi: 10.1109/JSEN.2013.2263125
[36] Tiwana, M. I., Redmond, S. J., & Lovell, N. H. (2012). A review of tactile sensing technologies with applications in biomedical engineering. Sensors and Actuators A: Physical, *179*, 17–31. doi: https://doi.org/10.1016/j.sna.2012.02.051
[37] Chi, C., Sun, X., Xue, N., Li, T., & Liu, C. (2018). Recent Progress in Technologies for Tactile Sensors. Sensors (Basel, Switzerland), *18*(4). PMCID:PMC5948515
[38] K, N., & Rout, C. S. (2021). Conducting polymers: a comprehensive review on recent advances in synthesis,

properties and applications. RSC Advances, *11*(10), 5659–5697. doi: 10.1039/D0RA07800J
[39] Meyer, J. C. (2014). Transmission electron microscopy (TEM) of graphene. In *Graphene* (pp. 101–123). Elsevier. doi: 10.1533/9780857099334.2.101
[40] Luong, J. H. T., Narayan, T., Solanki, S., & Malhotra, B. D. (2020). Recent Advances of Conducting Polymers and Their Composites for Electrochemical Biosensing Applications. Journal of Functional Biomaterials, *11*(4), 71. PMCID:PMC7712382
[41] Wadhwa, R., Lagenaur, C. F., & Cui, X. T. (2006). Electrochemically controlled release of dexamethasone from conducting polymer polypyrrole coated electrode. Journal of Controlled Release : Official Journal of the Controlled Release Society, *110*(3), 531–541. PMID:16360955
[42] Wallace, G. G., & Kane-Maguire, L. A. P. (2002). Manipulating and monitoring biomolecular interactions with conducting electroactive polymers. Advanced Materials, *14*(13-14), 953–960.
[43] Richardson, R. T., Wise, A. K., Thompson, B. C., Flynn, B. O., Atkinson, P. J., Fretwell, N. J., Fallon, J. B., Wallace, G. G., Shepherd, R. K., Clark, G. M., & O'Leary, S. J. (2009). Polypyrrole-coated electrodes for the delivery of charge and neurotrophins to cochlear neurons. Biomaterials, *30*(13), 2614–2624. PMCID:PMC3563695
[44] Cheah, E., Wu, Z., Thakur, S. S., O'Carroll, S. J., & Svirskis, D. (2021). Externally triggered release of growth factors - A tissue regeneration approach. Journal of Controlled Release : Official Journal of the Controlled Release Society, *332*, 74–95. PMID:33600882
[45] Aregueta-Robles, U. A., Woolley, A. J., Poole-Warren, L. A., Lovell, N. H., & Green, R. A. (2014). Organic electrode coatings for next-generation neural interfaces. Frontiers in Neuroengineering, *7*, 15. PMCID:PMC4034607
[46] Subramanian, A., Krishnan, U. M., & Sethuraman, S. (2019). Correction to: Axially aligned electrically conducting biodegradable nanofibers for neural regeneration. Journal of Materials Science. Materials in Medicine, *30*(5), 56. PMID:31087155
[47] Subramanian, A., Krishnan, U. M., & Sethuraman, S. (2012). Axially aligned electrically conducting biodegradable nanofibers for neural regeneration. Journal of Materials Science: Materials in Medicine, *23*(7), 1797–1809. PMID:22544170
[48] Visakh, P. M., Della Pina, C., & Falletta, E. (2017). *Polyaniline blends, composites, and nanocomposites*. Elsevier.
[49] Zare, E. N., & Lakouraj, M. M. (2014). Biodegradable polyaniline/dextrin conductive nanocomposites: synthesis, characterization, and study of antioxidant activity and sorption of heavy metal ions. Iranian Polymer Journal, *23*(4), 257–266. doi: 10.1007/s13726-014-0221-3
[50] Ghasemi-Mobarakeh, L., Prabhakaran, M. P., Morshed, M., Nasr-Esfahani, M. H., & Ramakrishna, S. (2009). Electrical Stimulation of Nerve Cells Using Conductive Nanofibrous Scaffolds for Nerve Tissue Engineering. Tissue Engineering Part A, *15*(11), 3605–3619. doi: 10.1089/ten.tea.2008.0689
[51] Schmidt, C. E., Shastri, V. R., Vacanti, J. P., & Langer, R. (1997). Stimulation of neurite outgrowth using an electrically conducting polymer. Proceedings of the National Academy of Sciences of the United States of America, *94*(17), 8948–8953. PMCID:PMC22977
[52] Richardson-Burns, S. M., Hendricks, J. L., Foster, B., Povlich, L. K., Kim, D.-H., & Martin, D. C. (2007). Polymerization of the conducting polymer poly(3,4-ethylenedioxythiophene) (PEDOT) around living neural cells. Biomaterials, *28*(8), 1539–1552. PMCID:PMC1941689
[53] Miriani, R. M., Abidian, M. R., & Kipke, D. R. (2008). Cytotoxic analysis of the conducting polymer PEDOT using myocytes. Annual International Conference of the IEEE Engineering in Medicine and Biology Society. IEEE Engineering in Medicine and Biology Society. Annual International Conference, *2008*, 1841–1844. PMID:19163041
[54] Wilks, S. J., Woolley, A. J., Ouyang, L., Martin, D. C., & Otto, K. J. (2011). In vivo polymerization of poly(3,4-ethylenedioxythiophene) (PEDOT) in rodent cerebral cortex. Annual International Conference of the IEEE Engineering in Medicine and Biology Society. IEEE Engineering in Medicine and Biology Society. Annual International Conference, *2011*, 5412–5415. PMID:22255561
[55] Ouyang, L., Shaw, C. L., Kuo, C., Griffin, A. L., & Martin, D. C. (2014). In vivo polymerization of poly(3,4-ethylenedioxythiophene) in the living rat hippocampus does not cause a significant loss of performance in a delayed alternation task. Journal of Neural Engineering, *11*(2), 026005. doi: 10.1088/1741-2560/11/2/026005
[56] Nagarajan, R., Tripathy, S., Kumar, J., Bruno, F. F., & Samuelson, L. (2000). An Enzymatically Synthesized Conducting Molecular Complex of Polyaniline and Poly(vinylphosphonic acid). Macromolecules, *33*(26), 9542–9547. doi: 10.1021/ma000954+
[57] de Barros, R. A., de Azevedo, W. M., & de Aguiar, F. M. (2003). Photo-induced polymerization of polyaniline. Materials Characterization, *50*(2–3), 131–134. doi: 10.1016/S1044-5803(03)00080-9
[58] Ma, C., Jiang, L., Wang, Y., Gang, F., Xu, N., Li, T., Liu, Z., Chi, Y., Wang, X., Zhao, L., Feng, Q., & Sun,

X. (2019). 3D Printing of Conductive Tissue Engineering Scaffolds Containing Polypyrrole Nanoparticles with Different Morphologies and Concentrations. Materials (Basel, Switzerland), *12*(15). PMCID:PMC6696326

[59] Jiang, L., Wang, Y., Liu, Z., Ma, C., Yan, H., Xu, N., Gang, F., Wang, X., Zhao, L., & Sun, X. (2019). Three-Dimensional Printing and Injectable Conductive Hydrogels for Tissue Engineering Application. Tissue Engineering. Part B, Reviews, *25*(5), 398–411. PMID:31115274

[60] Mawad, D., Stewart, E., Officer, D. L., Romeo, T., Wagner, P., Wagner, K., & Wallace, G. G. (2012). A Single Component Conducting Polymer Hydrogel as a Scaffold for Tissue Engineering. Advanced Functional Materials, *22*(13), 2692–2699. doi: 10.1002/adfm.201102373

[61] Rivers, T. J., Hudson, T. W., & Schmidt, C. E. (2002). Synthesis of a Novel, Biodegradable Electrically Conducting Polymer for Biomedical Applications. Advanced Functional Materials, *12*(1), 33. doi: 10.1002/1616-3028(20020101)12:1<33::AID-ADFM33>3.0.CO;2-E

[62] Atanasoska, L., Naoi, K., & Smyrl, W. H. (1992). XPS studies on conducting polymers: polypyrrole films doped with perchlorate and polymeric anions. Chemistry of Materials, *4*(5), 988–994. doi: 10.1021/cm00023a012

[63] Razavi, M. (2017). *Biomaterials for Tissue Engineering* (Vol. 4). Bentham Science Publishers.

[64] Ma, C., Jiang, L., Wang, Y., Gang, F., Xu, N., Li, T., Liu, Z., Chi, Y., Wang, X., Zhao, L., Feng, Q., & Sun, X. (2019). 3D Printing of Conductive Tissue Engineering Scaffolds Containing Polypyrrole Nanoparticles with Different Morphologies and Concentrations. Materials (Basel, Switzerland), *12*(15). PMID:31390733

[65] Tikhomirov, A. S., Litvinova, V. A., Andreeva, D. V, Tsvetkov, V. B., Dezhenkova, L. G., Volodina, Y. L., Kaluzhny, D. N., Treshalin, I. D., Schols, D., Ramonova, A. A., Moisenovich, M. M., Shtil, A. A., & Shchekotikhin, A. E. (2020). Amides of pyrrole- and thiophene-fused anthraquinone derivatives: A role of the heterocyclic core in antitumor properties. European Journal of Medicinal Chemistry, *199*, 112294. PMID:32428792

[66] Richardson, R. T., Thompson, B., Moulton, S., Newbold, C., Lum, M. G., Cameron, A., Wallace, G., Kapsa, R., Clark, G., & O'Leary, S. (2007). The effect of polypyrrole with incorporated neurotrophin-3 on the promotion of neurite outgrowth from auditory neurons. Biomaterials, *28*(3), 513–523. doi: 10.1016/j.biomaterials.2006.09.008

[67] Xu, H., Holzwarth, J. M., Yan, Y., Xu, P., Zheng, H., Yin, Y., Li, S., & Ma, P. X. (2014). Conductive PPY/PDLLA conduit for peripheral nerve regeneration. Biomaterials, *35*(1), 225–235. doi: 10.1016/j.biomaterials.2013.10.002

[68] Mondragon-Lozano, R., Ríos, C., Roldan-Valadez, E., Cruz, G. J., Olayo, M. G., Olayo, R., Salgado-Ceballos, H., Morales, J., Mendez-Armenta, M., Alvarez-Mejia, L., Fabela, O., Morales-Guadarrama, A., Sánchez-Torres, S., & Diaz-Ruiz, A. (2017). Delayed injection of polypyrrole doped with iodine particle suspension after spinal cord injury in rats improves functional recovery and decreased tissue damage evaluated by 3.0 Tesla in vivo magnetic resonance imaging. The Spine Journal : Official Journal of the North American Spine Society, *17*(4), 562–573. PMID:26911415

[69] Park, K.-H., Jo, E. A., & Na, K. (2007). Heparin/polypyrrole (PPy) composite on gold-coated matrix for the neurite outgrowth of PC12 cells by electrical stimulation. Biotechnology and Bioprocess Engineering, *12*(5), 463–469. doi: 10.1007/BF02931341

[70] Zhang, Q., Esrafilzadeh, D., Crook, J. M., Kapsa, R., Stewart, E. M., Tomaskovic-Crook, E., Wallace, G. G., & Huang, X.-F. (2017). Electrical Stimulation Using Conductive Polymer Polypyrrole Counters Reduced Neurite Outgrowth of Primary Prefrontal Cortical Neurons from NRG1-KO and DISC1-LI Mice. Scientific Reports, *7*(1), 42525. PMCID:PMC5309772

[71] Yan, L., Zhao, B., Liu, X., Li, X., Zeng, C., Shi, H., Xu, X., Lin, T., Dai, L., & Liu, Y. (2016). Aligned Nanofibers from Polypyrrole/Graphene as Electrodes for Regeneration of Optic Nerve via Electrical Stimulation. ACS Applied Materials & Interfaces, *8*(11), 6834–6840. doi: 10.1021/acsami.5b12843

[72] Balint, R., Cassidy, N. J., & Cartmell, S. H. (2014). Conductive polymers: towards a smart biomaterial for tissue engineering. Acta Biomaterialia, *10*(6), 2341–2353. PMID:24556448

[73] Zare, E. N., Makvandi, P., Ashtari, B., Rossi, F., Motahari, A., & Perale, G. (2020). Progress in Conductive Polyaniline-Based Nanocomposites for Biomedical Applications: A Review. Journal of Medicinal Chemistry, *63*(1), 1–22. PMID:31502840

[74] Garrudo, F. F. F., Chapman, C. A., Hoffman, P. R., Udangawa, R. W., Silva, J. C., Mikael, P. E., Rodrigues, C. A. V., Cabral, J. M. S., Morgado, J. M. F., Ferreira, F. C., & Linhardt, R. J. (2019). Polyaniline-polycaprolactone blended nanofibers for neural cell culture. European Polymer Journal, *117*, 28–37. doi: 10.1016/j.eurpolymj.2019.04.048

[75] Xia, B., Wang, B., Shi, J., Zhang, Y., Zhang, Q., Chen, Z., & Li, J. (2017). Photothermal and biodegradable polyaniline/porous silicon hybrid nanocomposites as drug carriers for combined chemo-photothermal therapy of cancer. Acta Biomaterialia, *51*, 197–208. PMID:28069501

[76] Luo, Y.-L., Nan, Y.-F., Xu, F., Chen, Y.-S., & Zhao, P. (2010). Degradation behavior and biocompatibility of PEG/PANI-derived polyurethane co-polymers. Journal of Biomaterials Science. Polymer Edition, *21*(8–9), 1143–1172. PMID:20507713

[77] Sarvari, R., Akbari-Alanjaraghi, M., Massoumi, B., Beygi-Khosrowshahi, Y., & Agbolaghi, S. (2017). Conductive and biodegradable scaffolds based on a five-arm and functionalized star-like polyaniline–polycaprolactone copolymer with a <scp>d</scp> -glucose core. New Journal of Chemistry, *41*(14), 6371–6384. doi: 10.1039/C7NJ01063J

[78] Prabhakar, P. K., Raj, S., Anuradha, P. R., Sawant, S. N., & Doble, M. (2011). Biocompatibility studies on polyaniline and polyaniline-silver nanoparticle coated polyurethane composite. Colloids and Surfaces. B, Biointerfaces, *86*(1), 146–153. PMID:21501952

[79] Anaya-Plaza, E., Shaukat, A., Lehtonen, I., & Kostiainen, M. A. (2021). Biomolecule-Directed Carbon Nanotube Self-Assembly. Advanced Healthcare Materials, *10*(1), e2001162. PMID:33124183

[80] Beg, S., Rizwan, M., Sheikh, A. M., Hasnain, M. S., Anwer, K., & Kohli, K. (2011). Advancement in carbon nanotubes: basics, biomedical applications and toxicity. The Journal of Pharmacy and Pharmacology, *63*(2), 141–163. PMID:21235578

[81] Mohd Nurazzi, N., Asyraf, M. R. M., Khalina, A., Abdullah, N., Sabaruddin, F. A., Kamarudin, S. H., Ahmad, S., Mahat, A. M., Lee, C. L., Aisyah, H. A., Norrrahim, M. N. F., Ilyas, R. A., Harussani, M. M., Ishak, M. R., & Sapuan, S. M. (2021). Fabrication, Functionalization, and Application of Carbon Nanotube-Reinforced Polymer Composite: An Overview. Polymers, *13*(7). PMCID:PMC8037012

[82] Liu, X., Kim, J. C., Miller, A. L., Waletzki, B. E., & Lu, L. (2018). Electrically conductive nanocomposite hydrogels embedded with functionalized carbon nanotubes for spinal cord injury. New Journal of Chemistry, *42*(21), 17671–17681. doi: 10.1039/C8NJ03038C

[83] Salehi, M., Naseri-Nosar, M., Ebrahimi-Barough, S., Nourani, M., Khojasteh, A., Hamidieh, A.-A., Amani, A., Farzamfar, S., & Ai, J. (2018). Sciatic nerve regeneration by transplantation of Schwann cells via erythropoietin controlled-releasing polylactic acid/multiwalled carbon nanotubes/gelatin nanofibrils neural guidance conduit. Journal of Biomedical Materials Research. Part B, Applied Biomaterials, *106*(4), 1463–1476. doi: 10.1002/jbm.b.33952

[84] Lyon, D. Y., Adams, L. K., Falkner, J. C., & Alvarezt, P. J. J. (2006). Antibacterial activity of fullerene water suspensions: effects of preparation method and particle size. Environmental Science & Technology, *40*(14), 4360–4366. PMID:16903271

[85] Dellinger, A. L., Cunin, P., Lee, D., Kung, A. L., Brooks, D. B., Zhou, Z., Nigrovic, P. A., & Kepley, C. L. (2015). Inhibition of Inflammatory Arthritis Using Fullerene Nanomaterials. PLOS ONE, *10*(4), e0126290. doi: 10.1371/journal.pone.0126290

[86] Anaya-Plaza, E., Shaukat, A., Lehtonen, I., & Kostiainen, M. A. (2021). Biomolecule-Directed Carbon Nanotube Self-Assembly. Advanced Healthcare Materials, *10*(1), e2001162. PMID:33124183

[87] Yang, D., Yang, S. J., Del Bonis-O'Donnell, J. T., Pinals, R. L., & Landry, M. P. (2020). Mitigation of Carbon Nanotube Neurosensor Induced Transcriptomic and Morphological Changes in Mouse Microglia with Surface Passivation. ACS Nano, *14*(10), 13794–13805. doi: 10.1021/acsnano.0c06154

[88] Yasinskyi, Y., O, P., O, M., V, R., Prylutskyy, Y., Tauscher, E., Ritter, U., & Kozeretska, I. (2019). Reconciling the controversial data on the effects of C(60) fullerene at the organismal and molecular levels using as a model Drosophila melanogaster. Toxicology Letters, *310*, 92–98. PMID:30999038

[89] Baranwal, A., Srivastava, A., Kumar, P., Bajpai, V. K., Maurya, P. K., & Chandra, P. (2018). Prospects of Nanostructure Materials and Their Composites as Antimicrobial Agents. Frontiers in Microbiology, *9*, 422. PMCID:PMC5855923

[90] Katsnelson, M. I. (2007). Graphene: carbon in two dimensions. Materials Today, *10*(1–2), 20–27. doi: 10.1016/S1369-7021(06)71788-6

[91] Liang, Y., Liang, X., Zhang, Z., Li, W., Huo, X., & Peng, L. (2015). High mobility flexible graphene field-effect transistors and ambipolar radio-frequency circuits. Nanoscale, *7*(25), 10954–10962. PMID:26061485

[92] Mohan, V. B., Lau, K., Hui, D., & Bhattacharyya, D. (2018). Graphene-based materials and their composites: A review on production, applications and product limitations. Composites Part B: Engineering, *142*, 200–220. doi: 10.1016/j.compositesb.2018.01.013

[93] Liang, Y., Liang, X., Zhang, Z., Li, W., Huo, X., & Peng, L. (2015). High mobility flexible graphene field-effect transistors and ambipolar radio-frequency circuits. Nanoscale, *7*(25), 10954–10962. PMID:26061485

[94] Novoselov, K. S., Fal'ko, V. I., Colombo, L., Gellert, P. R., Schwab, M. G., & Kim, K. (2012). A roadmap for graphene. Nature, *490*(7419), 192–200. PMID:23060189

[95] Zeng, X., Peng, Y., Yu, M., Lang, H., Cao, X., & Zou, K. (2018). Dynamic Sliding Enhancement on the Friction and Adhesion of Graphene, Graphene Oxide, and Fluorinated Graphene. ACS Applied Materials

& Interfaces, *10*(9), 8214–8224. PMID:29443495
[96] Nayak, T. R., Andersen, H., Makam, V. S., Khaw, C., Bae, S., Xu, X., Ee, P.-L. R., Ahn, J.-H., Hong, B. H., Pastorin, G., & Özyilmaz, B. (2011). Graphene for controlled and accelerated osteogenic differentiation of human mesenchymal stem cells. ACS Nano, *5*(6), 4670–4678. PMID:21528849
[97] Li, N., Zhang, X., Song, Q., Su, R., Zhang, Q., Kong, T., Liu, L., Jin, G., Tang, M., & Cheng, G. (2011). The promotion of neurite sprouting and outgrowth of mouse hippocampal cells in culture by graphene substrates. Biomaterials, *32*(35), 9374–9382. PMID:21903256
[98] Wang, Y., Lee, W. C., Manga, K. K., Ang, P. K., Lu, J., Liu, Y. P., Lim, C. T., & Loh, K. P. (2012). Fluorinated graphene for promoting neuro-induction of stem cells. Advanced Materials (Deerfield Beach, Fla.), *24*(31), 4285–4290. PMID:22689093
[99] Yang, D., Li, T., Xu, M., Gao, F., Yang, J., Yang, Z., & Le, W. (2014). Graphene oxide promotes the differentiation of mouse embryonic stem cells to dopamine neurons. Nanomedicine (London, England), *9*(16), 2445–2455. PMID:24564300
[100] Polo, Y., Luzuriaga, J., Iturri, J., Irastorza, I., Toca-Herrera, J. L., Ibarretxe, G., Unda, F., Sarasua, J.-R., Pineda, J. R., & Larrañaga, A. (2021). Nanostructured scaffolds based on bioresorbable polymers and graphene oxide induce the aligned migration and accelerate the neuronal differentiation of neural stem cells. Nanomedicine : Nanotechnology, Biology, and Medicine, *31*, 102314. PMID:33059092
[101] Lindner, J., Meckenstock, R., & Farle, M. (2012). *Characterization of Materials 2nd edn, ed EN Kaufmann*. New York: Wiley.
[102] Bhagyaraj, S. M., Oluwafemi, O. S., Kalarikkal, N., & Thomas, S. (2018). *Characterization of Nanomaterials*. Elsevier. doi: 10.1016/C2016-0-01721-7
[103] Bandyopadhyay, A., & Bose, S. (2013). *Characterization of biomaterials*. Newnes.
[104] Lindon, J. C., Tranter, G. E., & Koppenaal, D. (2016). *Encyclopedia of spectroscopy and spectrometry*. Academic Press.
[105] Cahn, R. W. (2004). *Concise encyclopedia of materials characterization* (2nd ed.). Elsevier.
[106] Lin, T.-E., Rapino, S., Girault, H. H., & Lesch, A. (2018). Electrochemical imaging of cells and tissues. Chemical Science, *9*(20), 4546–4554. PMCID:PMC5969511
[107] Huang, L., Li, Z., Lou, Y., Cao, F., Zhang, D., & Li, X. (2018). Recent Advances in Scanning Electrochemical Microscopy for Biological Applications. Materials (Basel, Switzerland), *11*(8). PMCID:PMC6119995
[108] Straasø, L. A., Saleem, Q., & Hansen, M. R. (2016). *Chapter Six - A Toolbox of Solid-State NMR Experiments for the Characterization of Soft Organic Nanomaterials* (G. A. B. T.-A. R. on N. M. R. S. Webb (Ed.); Vol. 88, pp. 307–383). Academic Press. doi: https://doi.org/10.1016/bs.arnmr.2015.12.001
[109] de Souza, F. A. L., Ambrozio, A. R., Souza, E. S., Cipriano, D. F., Scopel, W. L., & Freitas, J. C. C. (2016). NMR spectral parameters in graphene, graphite, and related materials: Ab Initio calculations and experimental results. The Journal of Physical Chemistry C, *120*(48), 27707–27716.
[110] Goze-Bac, C., Latil, S., Lauginie, P., Jourdain, V., Conard, J., Duclaux, L., Rubio, A., & Bernier, P. (2002). Magnetic interactions in carbon nanostructures. Carbon, *40*(10), 1825–1842. doi: 10.1016/S0008-6223(02)00061-1
[111] Galande, C., Gao, W., Mathkar, A., Dattelbaum, A. M., Narayanan, T. N., Mohite, A. D., & Ajayan, P. M. (2014). Science and engineering of graphene oxide. Particle & Particle Systems Characterization, *31*(6), 619–638.
[112] Mazur, A. S., Vovk, M. A., & Tolstoy, P. M. (2020). Solid-state 13C NMR of carbon nanostructures (milled graphite, graphene, carbon nanotubes, nanodiamonds, fullerenes) in 2000–2019: a mini-review. Fullerenes, Nanotubes and Carbon Nanostructures, *28*(3), 202–213. doi: 10.1080/1536383X.2019.1686622
[113] Seifrid, M., Reddy, G. N. M., Chmelka, B. F., & Bazan, G. C. (2020). Insight into the structures and dynamics of organic semiconductors through solid-state NMR spectroscopy. Nature Reviews Materials, 1–21.
[114] Zujovic, Z., Kilmartin, P. A., & Travas-Sejdic, J. (2020). The Applications of Solid-State NMR to Conducting Polymers. The Special Case on Polyaniline. Molecules (Basel, Switzerland), *25*(3). PMCID:PMC7037364
[115] De Martino, A., Egger, R., Murphy-Armando, F., & Hallberg, K. (2004). Spin–orbit coupling and electron spin resonance for interacting electrons in carbon nanotubes. Journal of Physics: Condensed Matter, *16*(17), S1437.
[116] Rhodes, C. J. (2015). The Role of ESR Spectroscopy in Advancing Catalytic Science: Some Recent Developments. Progress in Reaction Kinetics and Mechanism, *40*(3), 201–248. doi: 10.3184/146867815X14297237081532
[117] Li, Y., Li, L., Wu, Y., & Li, Y. (2017). A Review on the Origin of Synthetic Metal Radical: Singlet Open-Shell Radical Ground State? The Journal of Physical Chemistry C, *121*(15), 8579–8588. doi:

10.1021/acs.jpcc.6b12936
[118] Krinichnyi, V. I. (2000). 2-mm Waveband electron paramagnetic resonance spectroscopy of conducting polymers. Synthetic Metals, *108*(3), 173–222. doi: https://doi.org/10.1016/S0379-6779(99)00262-3
[119] Bujak, P., Kulszewicz-Bajer, I., Zagorska, M., Maurel, V., Wielgus, I., & Pron, A. (2013). Polymers for electronics and spintronics. Chemical Society Reviews, *42*(23), 8895–8999. PMID:24030727
[120] da Silva, L. P. (2019). *A comprehensive guide to chemiluminescence*. Nova Science Publishers.
[121] Su, Y., Xie, Y., Hou, X., & Lv, Y. (2014). Recent Advances in Analytical Applications of Nanomaterials in Liquid-Phase Chemiluminescence. Applied Spectroscopy Reviews, *49*(3), 201–232. doi: 10.1080/05704928.2013.819514
[122] Chen, H., Gao, Q., Li, J., & Lin, J.-M. (2016). Graphene materials-based chemiluminescence for sensing. Journal of Photochemistry and Photobiology C: Photochemistry Reviews, *27*, 54–71. doi: https://doi.org/10.1016/j.jphotochemrev.2016.04.003
[123] Siraj, N., El-Zahab, B., Hamdan, S., Karam, T. E., Haber, L. H., Li, M., Fakayode, S. O., Das, S., Valle, B., Strongin, R. M., Patonay, G., Sintim, H. O., Baker, G. A., Powe, A., Lowry, M., Karolin, J. O., Geddes, C. D., & Warner, I. M. (2016). Fluorescence, Phosphorescence, and Chemiluminescence. Analytical Chemistry, *88*(1), 170–202. PMID:26575092
[124] Janakiraman, U., Dini, D., Preusser, A., Holmes, A. B., Martin, R. E., & Doblhofer, K. (2001). Electrochemiluminescence of conjugated polymer. Synthetic Metals, *121*(1), 1685–1686. doi: https://doi.org/10.1016/S0379-6779(00)01122-X
[125] Li, C., & Shi, G. (2014). Carbon nanotube-based fluorescence sensors. Journal of Photochemistry and Photobiology C: Photochemistry Reviews, *19*, 20–34. doi: https://doi.org/10.1016/j.jphotochemrev.2013.10.005
[126] Alvarez, A., Costa-Fernández, J. M., Pereiro, R., Sanz-Medel, A., & Salinas-Castillo, A. (2011). Fluorescent conjugated polymers for chemical and biochemical sensing. TrAC Trends in Analytical Chemistry, *30*(9), 1513–1525. doi: https://doi.org/10.1016/j.trac.2011.04.017
[127] Dendisová, M., Jeništová, A., Parchaňská-Kokaislová, A., Matějka, P., Prokopec, V., & Švecová, M. (2018). The use of infrared spectroscopic techniques to characterize nanomaterials and nanostructures: A review. Analytica Chimica Acta, *1031*, 1–14. PMID:30119727
[128] Wepasnick, K. A., Smith, B. A., Bitter, J. L., & Howard Fairbrother, D. (2010). Chemical and structural characterization of carbon nanotube surfaces. Analytical and Bioanalytical Chemistry, *396*(3), 1003–1014. PMID:20052581
[129] Guerrero-Pérez, M. O., & Patience, G. S. (2020). Experimental methods in chemical engineering: Fourier transform infrared spectroscopy—FTIR. The Canadian Journal of Chemical Engineering, *98*(1), 25–33. doi: https://doi.org/10.1002/cjce.23664
[130] Furukawa, Y. (2001). Vibrational Spectroscopy of Conducting Polymers: Fundamentals and Applications. In *Handbook of Vibrational Spectroscopy*. doi: https://doi.org/10.1002/9780470027325.s6107.pub2
[131] Schulman, S. G. (1977). *Fluorescence and Phosphorescence Spectroscopy*. Elsevier. doi: 10.1016/C2013-0-02750-8
[132] Habenicht, B. F., & Prezhdo, O. V. (2012). Ab initio time-domain study of the triplet state in a semiconducting carbon nanotube: intersystem crossing, phosphorescence time, and line width. Journal of the American Chemical Society, *134*(38), 15648–15651. PMID:22967091
[133] Banerjee, D., & Kar, A. K. (2021). Photophysics behind luminescence phenomenon in conducting conjugate polymer blends for application as an emissive layer in PLEDs. Journal of Applied Physics, *129*(1), 13102. doi: 10.1063/5.0029037
[134] De la Zerda, A., Zavaleta, C., Keren, S., Vaithilingam, S., Bodapati, S., Liu, Z., Levi, J., Smith, B. R., Ma, T.-J., Oralkan, O., Cheng, Z., Chen, X., Dai, H., Khuri-Yakub, B. T., & Gambhir, S. S. (2008). Carbon nanotubes as photoacoustic molecular imaging agents in living mice. In *Nature nanotechnology* (Vol. 3, Issue 9, pp. 557–562). PMCID:PMC2562547
[135] Lalwani, G., Cai, X., Nie, L., Wang, L. V, & Sitharaman, B. (2013). Graphene-based contrast agents for photoacoustic and thermoacoustic tomography. Photoacoustics, *1*(3–4), 62–67. PMCID:PMC3904379
[136] Yee, L. M., Mahmud, H. N. M. E., Kassim, A., & Yunus, W. M. M. (2007). Polypyrrole-polyethylene glycol conducting polymer composite films: Preparation and characterization. Synthetic Metals, *157*(8), 386–389. doi: https://doi.org/10.1016/j.synthmet.2007.04.011
[137] Riseman, S. M., Yaniger, S. I., Eyring, E. M., Macinnes, D., Macdiarmid, A. G., & Heeger, A. J. (1981). Infrared Photoacoustic Spectroscopy of Conducting Polymers. I. Undoped and n-Doped Polyacetylene. Applied Spectroscopy, *35*(6), 557–559.
[138] Sell, J. A. (1989). *Photothermal Investigations of Solids and Fluids*. Elsevier. doi: 10.1016/B978-0-12-636345-6.X5001-4
[139] Havener, R. W., Tsen, A. W., Choi, H. C., & Park, J. (2011). Laser-based imaging of individual carbon

nanostructures. NPG Asia Materials, *3*(10), 91–99. doi: 10.1038/asiamat.2011.145
[140] Sobhani, Z., Behnam, M. A., Emami, F., Dehghanian, A., & Jamhiri, I. (2017). Photothermal therapy of melanoma tumor using multiwalled carbon nanotubes. International Journal of Nanomedicine, *12*, 4509–4517. PMCID:PMC5484561
[141] Adhikari, S., Spaeth, P., Kar, A., Baaske, M. D., Khatua, S., & Orrit, M. (2020). Photothermal Microscopy: Imaging the Optical Absorption of Single Nanoparticles and Single Molecules. ACS Nano, *14*(12), 16414–16445. PMCID:PMC7760091
[142] Berciaud, S., Cognet, L., Poulin, P., Weisman, R. B., & Lounis, B. (2007). Absorption Spectroscopy of Individual Single-Walled Carbon Nanotubes. Nano Letters, *7*(5), 1203–1207. doi: 10.1021/nl062933k
[143] Li, Z., Lei, H., Kan, A., Xie, H., & Yu, W. (2021). Photothermal applications based on graphene and its derivatives: A state-of-the-art review. Energy, *216*, 119262. doi: https://doi.org/10.1016/j.energy.2020.119262
[144] Wang, Y., Zhang, H., Wang, Z., & Feng, L. (2020). Photothermal Conjugated Polymers and Their Biological Applications in Imaging and Therapy. ACS Applied Polymer Materials, *2*(10), 4222–4240. doi: 10.1021/acsapm.0c00672
[145] Parson, W. W. (2007). *Modern Optical Spectroscopy*. Springer Berlin Heidelberg. doi: 10.1007/978-3-540-37542-5
[146] Dong, P.-T., & Cheng, J.-X. (2017). Pump–probe microscopy: theory, instrumentation, and applications. Spectroscopy, *32*(4), 2–11.
[147] Ahmed, S., Jiang, X., Zhang, F., & Zhang, H. (2020). Pump–probe micro-spectroscopy and 2D materials. Journal of Physics D: Applied Physics, *53*(47), 473001. doi: 10.1088/1361-6463/ab77dc
[148] Sheng, C.-X., Tong, M., & Vardeny, Z. V. (2010). Nonlinear optical spectroscopy of excited states in disubstituted polyacetylene. Physical Review B, *81*(20), 205103. doi: 10.1103/PhysRevB.81.205103
[149] Melnikov, A., Ivanov, V., & Chekalin, S. (2010). Femtosecond pump-broadband probe study of primary doped polyaniline – The evidence of neutral primary photoexcitations. Chemical Physics Letters, *488*(1–3), 38–43. doi: 10.1016/j.cplett.2010.01.067
[150] Ferraro, J. R., Nakamoto, K., & Brown, C. W. (2003). *Introductory Raman Spectroscopy*. Elsevier. doi: 10.1016/B978-0-12-254105-6.X5000-8
[151] Dresselhaus, M. S., Jorio, A., Hofmann, M., Dresselhaus, G., & Saito, R. (2010). Perspectives on Carbon Nanotubes and Graphene Raman Spectroscopy. Nano Letters, *10*(3), 751–758. PMID:20085345
[152] Nazari, M., & Holtz, M. W. (2018). Near-ultraviolet Raman and micro-Raman analysis of electronic materials. Applied Physics Reviews, *5*(4), 041303. doi: 10.1063/1.5054660
[153] Jabłońska, A., Jaworska, A., Kasztelan, M., Berbeć, S., & Pałys, B. (2019). Graphene and Graphene Oxide Applications for SERS Sensing and Imaging. Current Medicinal Chemistry, *26*(38), 6878–6895. doi: 10.2174/0929867325666181004152247
[154] Furukawa, Y. (2007). Vibrational Spectroscopy of Conducting Polymers: Fundamentals and Applications. In N. J. Everall (Ed.), *Handbook of Vibrational Spectroscopy*. John Wiley & Sons, Ltd. doi: 10.1002/9780470027325.s6107.pub2
[155] Coutaz, J.-L., Garet, F., & Wallace, V. P. (2018). *Principles of Terahertz Time-Domain Spectroscopy*. Jenny Stanford Publishing. doi: 10.1201/b22478
[156] Kužel, P., & Němec, H. (2020). Terahertz Spectroscopy of Nanomaterials: a Close Look at Charge-Carrier Transport. Advanced Optical Materials, *8*(3), 1900623. doi: 10.1002/adom.201900623
[157] Koroliov, A., Chen, G., Goodfellow, K. M., Vamivakas, A. N., Staniszewski, Z., Sobolewski, P., Fray, M. El, Łaszcz, A., Czerwinski, A., Richter, C. P., & Sobolewski, R. (2019). Terahertz Time-Domain Spectroscopy of Graphene Nanoflakes Embedded in Polymer Matrix. Applied Sciences, *9*(3), 391. doi: 10.3390/app9030391
[158] Lu, J., & Liu, H. (2018). A critical review on the carrier dynamics in 2D layered materials investigated using THz spectroscopy. Optics Communications, *406*, 24–35. doi: 10.1016/j.optcom.2017.06.069
[159] In, C., & Choi, H. (2018). Terahertz Investigation of Dirac Materials: Graphene and Topological Insulators. Journal of the Korean Physical Society, *72*(12), 1484–1490. doi: 10.3938/jkps.72.1484
[160] Dutin, F., Degert, J., Tondusson, M., & Freysz, E. (2019). Time-resolved THz spectroscopy of conducting polymers. 2019 44th International Conference on Infrared, Millimeter, and Terahertz Waves (IRMMW-THz), 1–1. doi: 10.1109/IRMMW-THz.2019.8874403
[161] Jeon, T.-I., Grischkowsky, D., Mukherjee, A. K., & Menon, R. (2000). Electrical characterization of conducting polypyrrole by THz time-domain spectroscopy. Applied Physics Letters, *77*(16), 2452–2454. doi: 10.1063/1.1319188
[162] Nguema, E., Vigneras, V., Miane, J. L., & Mounaix, P. (2008). Dielectric properties of conducting polyaniline films by THz time-domain spectroscopy. European Polymer Journal, *44*(1), 124–129. doi: 10.1016/j.eurpolymj.2007.10.020

[163] Andrianov, A. V., Aleshin, A. N., Khripunov, A. K., & Trukhin, V. N. (2015). Terahertz properties of bacterial cellulose films and its composite with conducting polymer PEDOT/PSS. Synthetic Metals, *205*, 201–205. doi: 10.1016/j.synthmet.2015.04.016
[164] McClelland, A., & Mankin, M. (2018). *Optical measurements for scientists and engineers: a practical guide*. Cambridge University Press.
[165] Pfohl, M., Tune, D. D., Graf, A., Zaumseil, J., Krupke, R., & Flavel, B. S. (2017). Fitting Single-Walled Carbon Nanotube Optical Spectra. ACS Omega, *2*(3), 1163–1171. PMCID:PMC5377271
[166] Njuguna, J., Vanli, O. A., & Liang, R. (2015). A Review of Spectral Methods for Dispersion Characterization of Carbon Nanotubes in Aqueous Suspensions. Journal of Spectroscopy, *2015*, 1–11. doi: 10.1155/2015/463156
[167] Goodwin, D. G. J., Adeleye, A. S., Sung, L., Ho, K. T., Burgess, R. M., & Petersen, E. J. (2018). Detection and Quantification of Graphene-Family Nanomaterials in the Environment. Environmental Science & Technology, *52*(8), 4491–4513. PMCID:PMC5940015
[168] Lai, Q., Zhu, S., Luo, X., Zou, M., & Huang, S. (2012). Ultraviolet-visible spectroscopy of graphene oxides. AIP Advances, *2*(3), 032146. doi: 10.1063/1.4747817
[169] Barford, W., & Marcus, M. (2017). Perspective: Optical spectroscopy in π -conjugated polymers and how it can be used to determine multiscale polymer structures. The Journal of Chemical Physics, *146*(13), 130902. doi: 10.1063/1.4979495
[170] Suga, S., & Sekiyama, A. (2014). *Photoelectron Spectroscopy* (Vol. 176). Springer Berlin Heidelberg. doi: 10.1007/978-3-642-37530-9
[171] Okpalugo, T. I. T., Papakonstantinou, P., Murphy, H., McLaughlin, J., & Brown, N. M. D. (2005). High resolution XPS characterization of chemical functionalised MWCNTs and SWCNTs. Carbon, *43*(1), 153–161. doi: 10.1016/j.carbon.2004.08.033
[172] Chen, X., Wang, X., & Fang, D. (2020). A review on C1s XPS-spectra for some kinds of carbon materials. Fullerenes, Nanotubes and Carbon Nanostructures, *28*(12), 1048–1058. doi: 10.1080/1536383X.2020.1794851
[173] Vesel, A., Zaplotnik, R., Primc, G., & Mozetič, M. (2020). A Review of Strategies for the Synthesis of N-Doped Graphene-Like Materials. Nanomaterials (Basel, Switzerland), *10*(11). PMCID:PMC7698902
[174] Ates, M., & Sarac, A. S. (2009). Conducting polymer coated carbon surfaces and biosensor applications. Progress in Organic Coatings, *66*(4), 337–358. doi: 10.1016/j.porgcoat.2009.08.014
[175] Sabbatini, L., Malitesta, C., De Giglio, E., Losito, I., Torsi, L., & Zambonin, P. G. (1999). Electrosynthesised thin polymer films: the role of XPS in the design of application oriented innovative materials. Journal of Electron Spectroscopy and Related Phenomena, *100*(1–3), 35–53. doi: 10.1016/S0368-2048(99)00039-0
[176] Fauber, T. L. (2020). *Radiographic Imaging and Exposure* (6th ed.).
[177] Staron, P., Schreyer, A., Clemens, H., & Mayer, S. (Eds.). (2017). *Neutrons and Synchrotron Radiation in Engineering Materials Science*. Wiley-VCH Verlag GmbH & Co. KGaA. doi: 10.1002/9783527684489
[178] Li, T., Senesi, A. J., & Lee, B. (2016). Small Angle X-ray Scattering for Nanoparticle Research. Chemical Reviews, *116*(18), 11128–11180. PMID:27054962
[179] Bagchi, D., & Menon, R. (2006). Conformational modification of conducting polymer chains by solvents: Small-angle X-ray scattering study. Chemical Physics Letters, *425*(1–3), 114–117. doi: 10.1016/j.cplett.2006.05.014
[180] Choudhury, P. K., Bagchi, D., Sangeeth, C. S. S., & Menon, R. (2011). Modified conformation and physical properties in conducting polymers due to varying conjugation and solvent interactions. J. Mater. Chem., *21*(5), 1607–1614. doi: 10.1039/C0JM02304C
[181] Jannot, Y., & Degiovanni, A. (2018). *Thermal properties measurement of materials*. Wiley Online Library.
[182] Dominguez-Alfaro, A., Alegret, N., Arnaiz, B., González-Domínguez, J. M., Martin-Pacheco, A., Cossío, U., Porcarelli, L., Bosi, S., Vázquez, E., Mecerreyes, D., & Prato, M. (2020). Tailored Methodology Based on Vapor Phase Polymerization to Manufacture PEDOT/CNT Scaffolds for Tissue Engineering. ACS Biomaterials Science & Engineering, *6*(2), 1269–1278. doi: 10.1021/acsbiomaterials.9b01316
[183] Barsoukov, E., & Macdonald, J. R. (Eds.). (2018). *Impedance Spectroscopy*. John Wiley & Sons, Inc. doi: 10.1002/9781119381860
[184] Min, C., Shen, X., Shi, Z., Chen, L., & Xu, Z. (2010). The Electrical Properties and Conducting Mechanisms of Carbon Nanotube/Polymer Nanocomposites: A Review. Polymer-Plastics Technology and Engineering, *49*(12), 1172–1181. doi: 10.1080/03602559.2010.496405
[185] Cooper, D. R., D'Anjou, B., Ghattamaneni, N., Harack, B., Hilke, M., Horth, A., Majlis, N., Massicotte, M., Vandsburger, L., Whiteway, E., & Yu, V. (2012). Experimental Review of Graphene. ISRN Condensed Matter Physics, *2012*, 1–56. doi: 10.5402/2012/501686
[186] Alemour, B., Yaacob, M. H., Lim, H. N., & Hassan, M. R. (2018). Review of Electrical Properties of Graphene Conductive Composites. International Journal of Nanoelectronics & Materials, *11*(4).

[187] Gueye, M. N., Carella, A., Faure-Vincent, J., Demadrille, R., & Simonato, J.-P. (2020). Progress in understanding structure and transport properties of PEDOT-based materials: A critical review. Progress in Materials Science, *108*, 100616. doi: 10.1016/j.pmatsci.2019.100616
[188] Le, T.-H., Kim, Y., & Yoon, H. (2017). Electrical and Electrochemical Properties of Conducting Polymers. Polymers, *9*(4). PMCID:PMC6432010
[189] Hoppert, M. (2005). Electron Microscopy. In *Microscopic Techniques in Biotechnology* (pp. 147–286). Wiley-VCH Verlag GmbH & Co. KGaA. doi: 10.1002/3527602615.ch2
[190] Wang, Z. L., & Hui, C. (2003). *Electron Microscopy of Nanotubes* (Z. L. Wang & C. Hui (Eds.)). Springer US. doi: 10.1007/978-1-4615-0315-6
[191] Kim, J., Kim, F., & Huang, J. (2010). Seeing graphene-based sheets. Materials Today, *13*(3), 28–38. doi: 10.1016/S1369-7021(10)70031-6
[192] Williams, D. B., & Carter, C. B. (2009). *Transmission Electron Microscopy*. Springer US. doi: 10.1007/978-0-387-76501-3
[193] Hayat, M. A. (1986). *Basic Techniques for Transmission Electron Microscopy*. Elsevier. doi: 10.1016/B978-0-12-333926-3.X5001-5
[194] Meyer, J. C. (2014). Transmission electron microscopy (TEM) of graphene. In *Graphene* (pp. 101–123). Elsevier. doi: 10.1533/9780857099334.2.101
[195] Klapetek, P. (2018). *Quantitative Data Processing in Scanning Probe Microscopy* (2nd ed.). Elsevier. doi: 10.1016/C2016-0-04404-2
[196] Umemura, K., & Sato, S. (2018). Scanning Techniques for Nanobioconjugates of Carbon Nanotubes. Scanning, *2018*, 1–19. PMCID:PMC6020491
[197] Basov, D. N., Fogler, M. M., Lanzara, A., Wang, F., & Zhang, Y. (2014). Colloquium : Graphene spectroscopy. Reviews of Modern Physics, *86*(3), 959–994. doi: 10.1103/RevModPhys.86.959
[198] Musumeci, C. (2017). Advanced Scanning Probe Microscopy of Graphene and Other 2D Materials. Crystals, *7*(7), 216. doi: 10.3390/cryst7070216
[199] Abu-Jamous, B., Fa, R., & Nandi, A. K. (2015). Introduction to Bioinformatics. In *Integrative Cluster Analysis in Bioinformatics* (pp. 1–8). John Wiley & Sons, Ltd. doi: 10.1002/9781118906545.ch1
[200] Altman, R. B., & Dugan, J. M. (2003). Defining Bioinformatics and Structural Bioinformatics. In *Structural Bioinformatics* (pp. 1–14). doi: https://doi.org/10.1002/0471721204.ch1
[201] Varnek, A., & Baskin, I. I. (2011). Chemoinformatics as a Theoretical Chemistry Discipline. Molecular Informatics, *30*(1), 20–32. PMID:27467875
[202] Yeung, C. S., Tian, W. Q., Liu, L. V., & Wang, Y. A. (2009). Chemistry of Single-Walled Carbon Nanotubes. Journal of Computational and Theoretical Nanoscience, *6*(6), 1213–1235. doi: 10.1166/jctn.2009.1171
[203] Tandon, H., Shalini, Ranjan, P., Suhag, V., & Chakraborty, T. (2019). A Review of a Computational Study of Carbon Nanotubes. In *Carbon Nanotubes and Nanoparticles* (pp. 25–38). Apple Academic Press. doi: 10.1201/9780429463877-2
[204] Momeni, K., Ji, Y., Wang, Y., Paul, S., Neshani, S., Yilmaz, D. E., Shin, Y. K., Zhang, D., Jiang, J.-W., Park, H. S., Sinnott, S., van Duin, A., Crespi, V., & Chen, L.-Q. (2020). Multiscale computational understanding and growth of 2D materials: a review. Npj Computational Materials, *6*(1), 22. doi: 10.1038/s41524-020-0280-2
[205] Polini, M., Tomadin, A., Asgari, R., & MacDonald, A. H. (2008). Density functional theory of graphene sheets. Physical Review B, *78*(11), 115426. doi: 10.1103/PhysRevB.78.115426
[206] Boukhvalov, D. W. (2013). DFT modeling of the covalent functionalization of graphene: from ideal to realistic models. RSC Advances, *3*(20), 7150. doi: 10.1039/c3ra23372c
[207] Salzner, U. (2014). Electronic structure of conducting organic polymers: insights from time-dependent density functional theory. WIREs Computational Molecular Science, *4*(6), 601–622. doi: https://doi.org/10.1002/wcms.1194
[208] Bell, J. H. A., & Haycock, J. W. (2012). Next generation nerve guides: materials, fabrication, growth factors, and cell delivery. Tissue Engineering. Part B, Reviews, *18*(2), 116–128. doi: 10.1089/ten.TEB.2011.0498
[209] Kovačič, U., Sketelj, J., & Bajrović, F. F. (2009). Chapter 26 Age-Related Differences in the Reinnervation after Peripheral Nerve Injury. In *International Review of Neurobiology* (Vol. 87, pp. 465–482). Academic Press.
[210] Sunderland, S. (1951). A classification of peripheral nerve injuries producing loss of function. Brain: A Journal of Neurology, *74*(4), 491–516. doi: 10.1093/brain/74.4.491
[211] Arslantunali, D., Dursun, T., Yucel, D., Hasirci, N., & Hasirci, V. (2014). Peripheral nerve conduits: technology update. Medical Devices (Auckland, N.Z.), *7*, 405–424. doi: 10.2147/MDER.S59124
[212] Ray, W. Z., & Mackinnon, S. E. (2010). Management of nerve gaps: Autografts, allografts, nerve transfers, and end-to-side neurorrhaphy. Experimental Neurology, *223*(1), 77–85. doi: 10.1016/j.expneurol.2009.03.031

[213] Gao, Y., Wang, Y.-L., Kong, D., Qu, B., Su, X.-J., Li, H., & Pi, H.-Y. (2015). Nerve autografts and tissue-engineered materials for the repair of peripheral nerve injuries: a 5-year bibliometric analysis. Neural Regeneration Research, *10*(6), 1003–1008. doi: 10.4103/1673-5374.158369
[214] Hallgren, A., Björkman, A., Chemnitz, A., & Dahlin, L. B. (2013). Subjective outcome related to donor site morbidity after sural nerve graft harvesting: a survey in 41 patients. BMC Surgery, *13*(1), 39. doi: 10.1186/1471-2482-13-39
[215] Sarker, M. D., Naghieh, S., Sharma, N. K., & Chen, X. (2018). 3D biofabrication of vascular networks for tissue regeneration: A report on recent advances. Journal of Pharmaceutical Analysis, *8*(5), 277–296. doi: 10.1016/j.jpha.2018.08.005
[216] Chang, C.-J., & Hsu, S. (2006). The effect of high outflow permeability in asymmetric poly(dl-lactic acid-co-glycolic acid) conduits for peripheral nerve regeneration. Biomaterials, *27*(7), 1035–1042. doi: 10.1016/j.biomaterials.2005.07.003
[217] Xie, J., MacEwan, M. R., Liu, W., Jesuraj, N., Li, X., Hunter, D., & Xia, Y. (2014). Nerve Guidance Conduits Based on Double-Layered Scaffolds of Electrospun Nanofibers for Repairing the Peripheral Nervous System. ACS Applied Materials & Interfaces, *6*(12), 9472–9480. doi: 10.1021/am5018557
[218] Bhang, S. H., Jeong, S. I., Lee, T.-J., Jun, I., Lee, Y. Bin, Kim, B.-S., & Shin, H. (2012). Electroactive electrospun polyaniline/poly[(L-lactide)-co-(ε-caprolactone)] fibers for control of neural cell function. Macromolecular Bioscience, *12*(3), 402–411. PMCID:PMC2268907
[219] Yang, H. S., Lee, B., Tsui, J. H., Macadangdang, J., Jang, S.-Y., Im, S. G., & Kim, D.-H. (2016). Electroconductive nanopatterned substrates for enhanced myogenic differentiation and maturation. Advanced Healthcare Materials, *5*(1), 137–145. doi: 10.1002/adhm.201500003
[220] Hu, H., Ni, Y., Montana, V., Haddon, R. C., & Parpura, V. (2004). Chemically Functionalized Carbon Nanotubes as Substrates for Neuronal Growth. Nano Letters, *4*(3), 507–511. PMCID:PMC3050644
[221] Mattson, M. P., Haddon, R. C., & Rao, A. M. (2000). Molecular Functionalization of Carbon Nanotubes and Use as Substrates for Neuronal Growth. Journal of Molecular Neuroscience, *14*(3), 175–182. doi: 10.1385/JMN:14:3:175
[222] Kotwal, A., & Schmidt, C. E. (2001). Electrical stimulation alters protein adsorption and nerve cell interactions with electrically conducting biomaterials. Biomaterials, *22*(10), 1055–1064. PMID:11352099
[223] Wu, Y., Wang, L., Guo, B., Shao, Y., & Ma, P. X. (2016). Electroactive biodegradable polyurethane significantly enhanced Schwann cells myelin gene expression and neurotrophin secretion for peripheral nerve tissue engineering. Biomaterials, *87*, 18–31. doi: 10.1016/j.biomaterials.2016.02.010
[224] Shin, J., Choi, E. J., Cho, J. H., Cho, A.-N., Jin, Y., Yang, K., Song, C., & Cho, S.-W. (2017). Three-Dimensional Electroconductive Hyaluronic Acid Hydrogels Incorporated with Carbon Nanotubes and Polypyrrole by Catechol-Mediated Dispersion Enhance Neurogenesis of Human Neural Stem Cells. Biomacromolecules, *18*(10), 3060–3072. doi: 10.1021/acs.biomac.7b00568
[225] Jessen, K. R., & Mirsky, R. (2019). The Success and Failure of the Schwann Cell Response to Nerve Injury. Frontiers in Cellular Neuroscience, *13*. doi: 10.3389/fncel.2019.00033
[226] Jessen, K. R., Mirsky, R., & Lloyd, A. C. (2015). Schwann Cells: Development and Role in Nerve Repair. Cold Spring Harbor Perspectives in Biology, *7*(7). doi: 10.1101/cshperspect.a020487
[227] Amniattalab, A., & Mohammadi, R. (2017). Functional, Histopathological and Immunohistichemical Assessments of Cyclosporine A on Sciatic Nerve Regeneration Using Allografts: A Rat Sciatic Nerve Model. Bulletin of Emergency and Trauma, *5*(3), 152–159. PMCID:PMC5547201
[228] Kanaya, F., Firrell, J. C., & Breidenbach, W. C. (1996). Sciatic function index, nerve conduction tests, muscle contraction, and axon morphometry as indicators of regeneration. Plastic and Reconstructive Surgery, *98*(7), 1264–71, discussion 1272-4. PMID:8942915
[229] Wang, T., Ito, A., Aoyama, T., Nakahara, R., Nakahata, A., Ji, X., Zhang, J., Kawai, H., & Kuroki, H. (2018). Functional evaluation outcomes correlate with histomorphometric changes in the rat sciatic nerve crush injury model: A comparison between sciatic functional index and kinematic analysis. PloS One, *13*(12), e0208985. PMCID:PMC6291147
[230] Wang, J., Cheng, Y., Chen, L., Zhu, T., Ye, K., Jia, C., Wang, H., Zhu, M., Fan, C., & Mo, X. (2019). In vitro and in vivo studies of electroactive reduced graphene oxide-modified nanofiber scaffolds for peripheral nerve regeneration. Acta Biomaterialia, *84*, 98–113. doi: 10.1016/j.actbio.2018.11.032
[231] Shi, Y., Pan, L., Liu, B., Wang, Y., Cui, Y., Bao, Z., & Yu, G. (2014). Nanostructured conductive polypyrrole hydrogels as high-performance, flexible supercapacitor electrodes. J. Mater. Chem. A, *2*(17), 6086–6091. doi: 10.1039/C4TA00484A
[232] Dai, T., Qing, X., Lu, Y., & Xia, Y. (2009). Conducting hydrogels with enhanced mechanical strength. Polymer, *50*(22), 5236–5241. doi: 10.1016/j.polymer.2009.09.025
[233] Zhu, Y., Li, X., Janairo, R. R. R., Kwong, G., Tsou, A. D., Chu, J. S., Wang, A., Yu, J., Wang, D., & Li, S. (2019). Matrix stiffness modulates the differentiation of neural crest stem cells in vivo. Journal of Cellular

Physiology, *234*(5), 7569–7578. doi: 10.1002/jcp.27518
[234] Park, J., Jeon, J., Kim, B., Lee, M. S., Park, S., Lim, J., Yi, J., Lee, H., Yang, H. S., & Lee, J. Y. (2020). Electrically Conductive Hydrogel Nerve Guidance Conduits for Peripheral Nerve Regeneration. Advanced Functional Materials, *30*(39), 2003759. doi: 10.1002/adfm.202003759
[235] Wang, G., Wu, W., Yang, H., Zhang, P., & Wang, J.-Y. (2020). Intact polyaniline coating as a conductive guidance is beneficial to repairing sciatic nerve injury. Journal of Biomedical Materials Research Part B: Applied Biomaterials, *108*(1), 128–142. doi: 10.1002/jbm.b.34372
[236] Liu, X., Miller, A. L., Park, S., Waletzki, B. E., Zhou, Z., Terzic, A., & Lu, L. (2017). Functionalized Carbon Nanotube and Graphene Oxide Embedded Electrically Conductive Hydrogel Synergistically Stimulates Nerve Cell Differentiation. ACS Applied Materials & Interfaces, *9*(17), 14677–14690. doi: 10.1021/acsami.7b02072
[237] Qian, Y., Song, J., Zheng, W., Zhao, X., Ouyang, Y., Yuan, W., & Fan, C. (2018). 3D Manufacture of Gold Nanocomposite Channels Facilitates Neural Differentiation and Regeneration. Advanced Functional Materials, *28*(14), 1707077. doi: 10.1002/adfm.201707077
[238] Fang, X., Deng, J., Zhang, W., Guo, H., Yu, F., Rao, F., Li, Q., Zhang, P., Bai, S., & Jiang, B. (2020). Conductive conduit small gap tubulization for peripheral nerve repair. RSC Advances, *10*(28), 16769–16775. doi: 10.1039/D0RA02143A
[239] Kalishwaralal, K., Jeyabharathi, S., Sundar, K., Selvamani, S., Prasanna, M., & Muthukumaran, A. (2018). A novel biocompatible chitosan-Selenium nanoparticles (SeNPs) film with electrical conductivity for cardiac tissue engineering application. Materials Science & Engineering. C, Materials for Biological Applications, *92*, 151–160. PMID:30184738
[240] Balidemaj, E., de Boer, P., van Lier, A. L. H. M. W., Remis, R. F., Stalpers, L. J. A., Westerveld, G. H., Nederveen, A. J., van den Berg, C. A. T., & Crezee, J. (2016). In vivo electric conductivity of cervical cancer patients based on B_1^+ maps at 3T MRI. Physics in Medicine and Biology, *61*(4), 1596–607. PMID:26836010
[241] Holsheimer, J. (1998). Computer modelling of spinal cord stimulation and its contribution to therapeutic efficacy. Spinal Cord, *36*(8), 531–540. PMID:9713921
[242] Becker, D., Gary, D. S., Rosenzweig, E. S., Grill, W. M., & McDonald, J. W. (2010). Functional electrical stimulation helps replenish progenitor cells in the injured spinal cord of adult rats. Experimental Neurology, *222*(2), 211–218. PMCID:PMC2834811
[243] Geremia, N. M., Gordon, T., Brushart, T. M., Al-Majed, A. A., & Verge, V. M. K. (2007). Electrical stimulation promotes sensory neuron regeneration and growth-associated gene expression. Experimental Neurology, *205*(2), 347–359. PMID:17428474
[244] Vivó, M., Puigdemasa, A., Casals, L., Asensio, E., Udina, E., & Navarro, X. (2008). Immediate electrical stimulation enhances regeneration and reinnervation and modulates spinal plastic changes after sciatic nerve injury and repair. Experimental Neurology, *211*(1), 180–193. PMID:18316076
[245] Alves-Sampaio, A., García-Rama, C., & Collazos-Castro, J. E. (2016). Biofunctionalized PEDOT-coated microfibers for the treatment of spinal cord injury. Biomaterials, *89*, 98–113. PMID:26963900
[246] Imani, S., Zagari, Z., Rezaei Zarchi, S., Jorjani, M., & Nasri, S. (2016). Functional Recovery of Carbon Nanotube/Nafion Nanocomposite in Rat Model of Spinal Cord Injury. Artificial Cells, Nanomedicine, and Biotechnology, *44*(1), 144–149. PMID:25861814
[247] Agarwal, G., Kumar, N., & Srivastava, A. (2021). Highly elastic, electroconductive, immunomodulatory graphene crosslinked collagen cryogel for spinal cord regeneration. Materials Science and Engineering: C, *118*, 111518. doi: https://doi.org/10.1016/j.msec.2020.111518
[248] Basso, D. M., Beattie, M. S., & Bresnahan, J. C. (1995). A sensitive and reliable locomotor rating scale for open field testing in rats. Journal of Neurotrauma, *12*(1), 1–21. PMID:7783230
[249] Beattie, M. S. (2004). Inflammation and apoptosis: linked therapeutic targets in spinal cord injury. Trends in Molecular Medicine, *10*(12), 580–583. PMID:15567326
[250] Hong, G., & Lieber, C. M. (2019). Novel electrode technologies for neural recordings. Nature Reviews. Neuroscience, *20*(6), 330–345. PMCID:PMC6531316
[251] Hopkins, J., Fidanovski, K., Lauto, A., & Mawad, D. (2019). All-Organic Semiconductors for Electrochemical Biosensors: An Overview of Recent Progress in Material Design. Frontiers in Bioengineering and Biotechnology, *7*, 237. PMCID:PMC6773807
[252] Qian, C.-G., Chen, Y.-L., Feng, P.-J., Xiao, X.-Z., Dong, M., Yu, J.-C., Hu, Q.-Y., Shen, Q.-D., & Gu, Z. (2017). Conjugated polymer nanomaterials for theranostics. Acta Pharmacologica Sinica, *38*(6), 764–781. PMCID:PMC5520193
[253] Moskow, J., Ferrigno, B., Mistry, N., Jaiswal, D., Bulsara, K., Rudraiah, S., & Kumbar, S. G. (2019). Review: Bioengineering approach for the repair and regeneration of peripheral nerve. Bioactive Materials, *4*(1), 107–113. PMCID:PMC6351356
[254] Krucoff, M. O., Miller, J. P., Saxena, T., Bellamkonda, R., Rahimpour, S., Harward, S. C., Lad, S. P., &

Turner, D. A. (2019). Toward Functional Restoration of the Central Nervous System: A Review of Translational Neuroscience Principles. Neurosurgery, *84*(1), 30–40. PMCID:PMC6292792

[255] Fawcett, J. W. (2020). The Struggle to Make CNS Axons Regenerate: Why Has It Been so Difficult? Neurochemical Research, *45*(1), 144–158. PMCID:PMC6942574

[256] Nagappan, P. G., Chen, H., & Wang, D.-Y. (2020). Neuroregeneration and plasticity: a review of the physiological mechanisms for achieving functional recovery postinjury. Military Medical Research, *7*(1), 30. PMCID:PMC7288425

[257] Tam, R. Y., Fuehrmann, T., Mitrousis, N., & Shoichet, M. S. (2014). Regenerative therapies for central nervous system diseases: a biomaterials approach. Neuropsychopharmacology : Official Publication of the American College of Neuropsychopharmacology, *39*(1), 169–188. PMCID:PMC3857664

[258] Bongo, M., Winther-Jensen, O., Himmelberger, S., Strakosas, X., Ramuz, M., Hama, A., Stavrinidou, E., Malliaras, G. G., Salleo, A., Winther-Jensen, B., & Owens, R. M. (2013). PEDOT:gelatin composites mediate brain endothelial cell adhesion. Journal of Materials Chemistry B, *1*(31), 3860. doi: 10.1039/c3tb20374c

[259] Collazos-Castro, J. E., García-Rama, C., & Alves-Sampaio, A. (2016). Glial progenitor cell migration promotes CNS axon growth on functionalized electroconducting microfibers. Acta Biomaterialia, *35*, 42–56. PMID:26884276

[260] Song, Q., Jiang, Z., Li, N., Liu, P., Liu, L., Tang, M., & Cheng, G. (2014). Anti-inflammatory effects of three-dimensional graphene foams cultured with microglial cells. Biomaterials, *35*(25), 6930–6940. doi: 10.1016/j.biomaterials.2014.05.002

[261] Jiang, Z., Song, Q., Tang, M., Yang, L., Cheng, Y., Zhang, M., Xu, D., & Cheng, G. (2016). Enhanced Migration of Neural Stem Cells by Microglia Grown on a Three-Dimensional Graphene Scaffold. ACS Applied Materials & Interfaces, *8*(38), 25069–25077. doi: 10.1021/acsami.6b06780

[262] Zhou, K., Motamed, S., Thouas, G. A., Bernard, C. C., Li, D., Parkington, H. C., Coleman, H. A., Finkelstein, D. I., & Forsythe, J. S. (2016). Graphene Functionalized Scaffolds Reduce the Inflammatory Response and Supports Endogenous Neuroblast Migration when Implanted in the Adult Brain. PLOS ONE, *11*(3), e0151589. PMCID:PMC4792446

[263] Fitch, M. T., & Silver, J. (2008). CNS injury, glial scars, and inflammation: Inhibitory extracellular matrices and regeneration failure. Experimental Neurology, *209*(2), 294–301. PMCID:PMC2268907

[264] Pradhan, K., Das, G., Khan, J., Gupta, V., Barman, S., Adak, A., & Ghosh, S. (2019). Neuro-Regenerative Choline-Functionalized Injectable Graphene Oxide Hydrogel Repairs Focal Brain Injury. ACS Chemical Neuroscience, *10*(3), 1535–1543. doi: 10.1021/acschemneuro.8b00514

[265] Sakai, K., Teshima, T. F., Nakashima, H., & Ueno, Y. (2019). Graphene-based neuron encapsulation with controlled axonal outgrowth. Nanoscale, *11*(28), 13249–13259. doi: 10.1039/C9NR04165F

[266] Rauti, R., Secomandi, N., Martín, C., Bosi, S., Severino, F. P. U., Scaini, D., Prato, M., Vázquez, E., & Ballerini, L. (2020). Tuning Neuronal Circuit Formation in 3D Polymeric Scaffolds by Introducing Graphene at the Bio/Material Interface. Advanced Biosystems, *4*(4), 1900233. doi: 10.1002/adbi.201900233

[267] Juarez-Hernandez, L. J., Cornella, N., Pasquardini, L., Battistoni, S., Vidalino, L., Vanzetti, L., Caponi, S., Serra, M. D., Iannotta, S., Pederzolli, C., Macchi, P., & Musio, C. (2016). Bio-hybrid interfaces to study neuromorphic functionalities: New multidisciplinary evidences of cell viability on poly(anyline) (PANI), a semiconductor polymer with memristive properties. Biophysical Chemistry, *208*, 40–47. doi: 10.1016/j.bpc.2015.07.008

[268] Bordoni, M., Karabulut, E., Kuzmenko, V., Fantini, V., Pansarasa, O., Cereda, C., & Gatenholm, P. (2020). 3D Printed Conductive Nanocellulose Scaffolds for the Differentiation of Human Neuroblastoma Cells. Cells, *9*(3), 682. PMCID:PMC7140699

[269] Uz, M., Hondred, J. A., Donta, M., Jung, J., Kozik, E., Green, J., Sandquist, E. J., Sakaguchi, D. S., Claussen, J. C., & Mallapragada, S. (2020). Determination of Electrical Stimuli Parameters To Transdifferentiate Genetically Engineered Mesenchymal Stem Cells into Neuronal or Glial Lineages. Regenerative Engineering and Translational Medicine, *6*(1), 18–28. doi: 10.1007/s40883-019-00126-1

[270] Shah, S., Yin, P. T., Uehara, T. M., Chueng, S.-T. D., Yang, L., & Lee, K.-B. (2014). Guiding Stem Cell Differentiation into Oligodendrocytes Using Graphene-Nanofiber Hybrid Scaffolds. Advanced Materials, *26*(22), 3673–3680. PMCID:PMC4048813

[271] Perebikovsky, A., Hwu, A. T., Yale, A. R., Ghazinejad, M., & Madou, M. (2020). Nanofibrous Carbon Multifunctional Smart Scaffolds for Simultaneous Cell Differentiation and Dopamine Detection. ACS Biomaterials Science & Engineering, *6*(1), 225–234. doi: 10.1021/acsbiomaterials.9b01156

[272] Huang, Y.-J., Wu, H.-C., Tai, N.-H., & Wang, T.-W. (2012). Carbon Nanotube Rope with Electrical Stimulation Promotes the Differentiation and Maturity of Neural Stem Cells. Small, *8*(18), 2869–2877. doi: 10.1002/smll.201200715

[273] Fu, C., Pan, S., Ma, Y., Kong, W., Qi, Z., & Yang, X. (2019). Effect of electrical stimulation combined with

graphene-oxide-based membranes on neural stem cell proliferation and differentiation. Artificial Cells, Nanomedicine, and Biotechnology, *47*(1), 1867–1876. doi: 10.1080/21691401.2019.1613422
[274] Depan, D., & Misra, R. D. K. (2014). The development, characterization, and cellular response of a novel electroactive nanostructured composite for electrical stimulation of neural cells. Biomater. Sci., *2*(12), 1727–1739. doi: 10.1039/C4BM00168K
[275] Heo, C., Yoo, J., Lee, S., Jo, A., Jung, S., Yoo, H., Lee, Y. H., & Suh, M. (2011). The control of neural cell-to-cell interactions through non-contact electrical field stimulation using graphene electrodes. Biomaterials, *32*(1), 19–27. doi: 10.1016/j.biomaterials.2010.08.095
[276] Zhu, B., Luo, S.-C., Zhao, H., Lin, H.-A., Sekine, J., Nakao, A., Chen, C., Yamashita, Y., & Yu, H. (2014). Large enhancement in neurite outgrowth on a cell membrane-mimicking conducting polymer. Nature Communications, *5*(1), 4523. PMID:25060339
[277] Zhou, Z., Liu, X., Wu, W., Park, S., Miller II, A. L., Terzic, A., & Lu, L. (2018). Effective nerve cell modulation by electrical stimulation of carbon nanotube embedded conductive polymeric scaffolds. Biomaterials Science, *6*(9), 2375–2385. doi: 10.1039/C8BM00553B
[278] Nguyen, A. T., Mattiassi, S., Loeblein, M., Chin, E., Ma, D., Coquet, P., Viasnoff, V., Teo, E. H. T., Goh, E. L., & Yim, E. K. F. (2018). Human Rett-derived neuronal progenitor cells in 3D graphene scaffold as an in vitro platform to study the effect of electrical stimulation on neuronal differentiation. Biomedical Materials, *13*(3), 034111. doi: 10.1088/1748-605X/aaaf2b
[279] Doorish, J. F. (2006). Artificial epi-Retinal Prosthesis (AeRP). Journal of Modern Optics, *53*(9), 1245–1266. doi: 10.1080/09500340600618629
[280] Goetz, G. A., & Palanker, D. V. (2016). Electronic approaches to restoration of sight. Reports on Progress in Physics. Physical Society (Great Britain), *79*(9), 96701. PMCID:PMC5031080
[281] Özmert, E., & Arslan, U. (2019). Retinal Prostheses and Artificial Vision. Turkish Journal of Ophthalmology, *49*(4), 213–219. PMCID:PMC6761377
[282] Shim, S., Eom, K., Jeong, J., & Kim, S. J. (2020). Retinal Prosthetic Approaches to Enhance Visual Perception for Blind Patients. Micromachines, *11*(5). PMCID:PMC7281011
[283] Zeng, Q., Zhao, S., Yang, H., Zhang, Y., & Wu, T. (2019). Micro/Nano Technologies for High-Density Retinal Implant. Micromachines, *10*(6). PMCID:PMC6630275
[284] Barriga-Rivera, A., Bareket, L., Goding, J., Aregueta-Robles, U. A., & Suaning, G. J. (2017). Visual Prosthesis: Interfacing Stimulating Electrodes with Retinal Neurons to Restore Vision. Frontiers in Neuroscience, *11*, 620. PMCID:PMC5694472
[285] Yang, J.-W., Yu, Z.-Y., Cheng, S.-J., Chung, J. H. Y., Liu, X., Wu, C.-Y., Lin, S.-F., & Chen, G.-Y. (2020). Graphene Oxide-Based Nanomaterials: An Insight into Retinal Prosthesis. International Journal of Molecular Sciences, *21*(8). PMCID:PMC7216005
[286] Han, M., Srivastava, S. B., Yildiz, E., Melikov, R., Surme, S., Dogru-Yuksel, I. B., Kavakli, I. H., Sahin, A., & Nizamoglu, S. (2020). Organic Photovoltaic Pseudocapacitors for Neurostimulation. ACS Applied Materials & Interfaces, *12*(38), 42997–43008. PMCID:PMC7582621
[287] Park, B., Yang, H., Ha, T. H., Park, H. S., Oh, S. J., Ryu, Y.-S., Cho, Y., Kim, H.-S., Oh, J., Lee, D. K., Kim, C., Lee, T., Seo, M., Choi, J., Jhon, Y. M., Woo, D. H., Lee, S., Kim, S. H., Lee, H.-J., … Kim, J. H. (2018). Artificial Rod and Cone Photoreceptors with Human-Like Spectral Sensitivities. Advanced Materials, *30*(27), 1706764. doi: 10.1002/adma.201706764
[288] Yu, Z.-H., Chen, W.-J., Liu, X., Xia, Q.-Y., Yang, Y.-N., Dong, M., Liu, J.-H., Guan, H.-J., Sun, C., Feng, F.-D., & Shen, Q.-D. (2020). Folate-Modified Photoelectric Responsive Polymer Microarray as Bionic Artificial Retina to Restore Visual Function. ACS Applied Materials & Interfaces, *12*(25), 28759–28767. doi: 10.1021/acsami.0c04058
[289] Doorish, J. F. (2006). A wireless photovoltaic Mini epi-Retinal Prosthesis (MeRP) 1: concept and design. Journal of Modern Optics, *53*(9), 1267–1285. doi: 10.1080/09500340600618637
[290] Lee, E. K., Baruah, R. K., Leem, J. W., Park, W., Kim, B. H., Urbas, A., Ku, Z., Kim, Y. L., Alam, M. A., & Lee, C. H. (2020). Fractal Web Design of a Hemispherical Photodetector Array with Organic-Dye-Sensitized Graphene Hybrid Composites. Advanced Materials, *32*(46), 2004456. doi: 10.1002/adma.202004456
[291] Khan, M. S., Misra, S. K., Schwartz-Duval, A. S., Daza, E., Ostadhossein, F., Bowman, M., Jain, A., Taylor, G., McDonagh, D., Labriola, L. T., & Pan, D. (2017). Real-Time Monitoring of Post-Surgical and Post-Traumatic Eye Injuries Using Multilayered Electrical Biosensor Chip. ACS Applied Materials & Interfaces, *9*(10), 8609–8622. doi: 10.1021/acsami.7b01675
[292] Kim, M., Iezzi, R., Shim, B. S., & Martin, D. C. (2019). Impedimetric Biosensors for Detecting Vascular Endothelial Growth Factor (VEGF) Based on Poly(3,4-ethylene dioxythiophene) (PEDOT)/Gold Nanoparticle (Au NP) Composites. Frontiers in Chemistry, *7*. PMCID:PMC6477177
[293] Zhang, W., Dong, G., Feng, H., Shan, S., Huang, L., Yuan, F., Bao, B., Yan, L., Xia, Z., Lawson, T., Chen,

J., Qu, J., & Liu, Y. (2020). Wearable Corneal Biosensors Fabricated from PEDOT Functionalized Sulfur-Doped Graphene for Use in the Early Detection of Myopia. Advanced Materials Technologies, *5*(12), 2000682. doi: 10.1002/admt.202000682

[294] Zhang, Y., Chen, Y., Yu, X., Qi, Y., Chen, Y., Liu, Y., Hu, Y., & Li, Z. (2016). A flexible device for ocular iontophoretic drug delivery. Biomicrofluidics, *10*(1), 011911. PMCID:PMC4769262

[295] Zhang, Y., Chen, Y., Qi, Y., Huang, D., Yang, M., Yu, X., Hu, Y., & Li, Z. (2016). An ocular iontophoretic device using PEDOT electrode for local drug delivery. Sensors and Actuators B: Chemical, *237*, 1007–1014. doi: 10.1016/j.snb.2016.01.057

[296] Ramtin, A., Seyfoddin, A., Coutinho, F. P., Waterhouse, G. I. N., Rupenthal, I. D., & Svirskis, D. (2016). Cytotoxicity considerations and electrically tunable release of dexamethasone from polypyrrole for the treatment of back-of-the-eye conditions. Drug Delivery and Translational Research, *6*(6), 793–799. doi: 10.1007/s13346-016-0284-0

[297] Liu, Z., Wang, G., Pei, W., Wei, C., Wu, X., Dou, Z., Li, Y., Wang, Y., & Chen, H. (2020). Application of graphene nanowalls in an intraocular pressure sensor. Journal of Materials Chemistry B, *8*(38), 8794–8802. doi: 10.1039/D0TB01687J

[298] Choi, K., & Park, H. G. (2017). Smart Reinvention of the Contact Lens with Graphene. ACS Nano, *11*(6), 5223–5226. doi: 10.1021/acsnano.7b03180

[299] Lee, S., Jo, I., Kang, S., Jang, B., Moon, J., Park, J. B., Lee, S., Rho, S., Kim, Y., & Hong, B. H. (2017). Smart Contact Lenses with Graphene Coating for Electromagnetic Interference Shielding and Dehydration Protection. ACS Nano, *11*(6), 5318–5324. doi: 10.1021/acsnano.7b00370

[300] Takamatsu, T., Sijie, Y., Shujie, F., Xiaohan, L., & Miyake, T. (2020). Multifunctional High-Power Sources for Smart Contact Lenses. Advanced Functional Materials, *30*(29), 1906225. doi: 10.1002/adfm.201906225

[301] Kleinlogel, S., Vogl, C., Jeschke, M., Neef, J., & Moser, T. (2020). Emerging approaches for restoration of hearing and vision. Physiological Reviews, physrev.00035.2019. doi: 10.1152/physrev.00035.2019

[302] TR, S., & M, A. (2017). Drug Treatment of Corneal Neuropathies: Mini Review. Journal of Clinical & Experimental Ophthalmology, *08*(04). doi: 10.4172/2155-9570.1000667

[303] Rahmani, S., Bogdanowicz, L., Thomas, J., & Hetling, J. R. (2013). Chronic delivery of low-level exogenous current preserves retinal function in pigmented P23H rat. Vision Research, *76*, 105–113. doi: 10.1016/j.visres.2012.10.016

[304] Liu, Y., & Lee, R. (2016). Neuro-rejuvenation for neuronal function. Neural Regeneration Research, *11*(10), 1560. PMCID:PMC5116826

[305] Sehic, A., Guo, S., Cho, K.-S., Corraya, R. M., Chen, D. F., & Utheim, T. P. (2016). Electrical Stimulation as a Means for Improving Vision. The American Journal of Pathology, *186*(11), 2783–2797. PMCID:PMC5225285

[306] Henrich-Noack, P., Voigt, N., Prilloff, S., Fedorov, A., & Sabel, B. A. (2013). Transcorneal electrical stimulation alters morphology and survival of retinal ganglion cells after optic nerve damage. Neuroscience Letters, *543*, 1–6. doi: 10.1016/j.neulet.2013.03.013

[307] Morimoto, T., Kanda, H., Kondo, M., Terasaki, H., Nishida, K., & Fujikado, T. (2012). Transcorneal Electrical Stimulation Promotes Survival of Photoreceptors and Improves Retinal Function in Rhodopsin P347L Transgenic Rabbits. Investigative Opthalmology & Visual Science, *53*(7), 4254. doi: 10.1167/iovs.11-9067

[308] Freitag, S., Hunold, A., Klemm, M., Klee, S., Link, D., Nagel, E., & Haueisen, J. (2019). Pulsed Electrical Stimulation of the Human Eye Enhances Retinal Vessel Reaction to Flickering Light. Frontiers in Human Neuroscience, *13*. PMCID:PMC6817672

[309] Zhou, C., Zheng, H., Li, Q., & Sun, P. C. (2018). In vivo measurement of retinal neurovascular changes with transcorneal electrical stimulation using optical coherence tomography. In Q. Luo, X. Li, Y. Tang, & Y. Gu (Eds.), *Optics in Health Care and Biomedical Optics VIII* (p. 30). SPIE. doi: 10.1117/12.2500996

[310] Saigal, R., Cimetta, E., Tandon, N., Zhou, J., Langer, R., Young, M., Vunjak-Novakovic, G., & Redenti, S. (2013). Electrical stimulation via a biocompatible conductive polymer directs retinal progenitor cell differentiation. Annual International Conference of the IEEE Engineering in Medicine and Biology Society. IEEE Engineering in Medicine and Biology Society. Annual International Conference, *2013*, 1627–31. PMCID:PMC4480863

[311] Forli, F., Arslan, E., Bellelli, S., Burdo, S., Mancini, P., Martini, A., Miccoli, M., Quaranta, N., & Berrettini, S. (2011). Systematic review of the literature on the clinical effectiveness of the cochlear implant procedure in paediatric patients. Acta Otorhinolaryngologica Italica : Organo Ufficiale Della Societa Italiana Di Otorinolaringologia e Chirurgia Cervico-Facciale, *31*(5), 281–298. PMCID:PMC3262414

[312] Gaylor, J. M., Raman, G., Chung, M., Lee, J., Rao, M., Lau, J., & Poe, D. S. (2013). Cochlear implantation in adults: a systematic review and meta-analysis. JAMA Otolaryngology-- Head & Neck Surgery, *139*(3), 265–272. PMID:23429927

[313] Boisvert, I., Reis, M., Au, A., Cowan, R., & Dowell, R. C. (2020). Cochlear implantation outcomes in adults: A scoping review. PloS One, *15*(5), e0232421. PMCID:PMC7199932
[314] Merzenich, M. M., Byers, C. L., White, M., & Vivion, M. C. (1980). Cochlear implant prostheses: strategies and progress. Annals of Biomedical Engineering, *8*(4–6), 361–368. PMID:7027838
[315] Holley, M. C. (2002). Application of new biological approaches to stimulate sensory repair and protection. British Medical Bulletin, *63*(1), 157–69. PMID:12324391
[316] Kanzaki, S., Toyoda, M., Umezawa, A., & Ogawa, K. (2020). Application of Mesenchymal Stem Cell Therapy and Inner Ear Regeneration for Hearing Loss: A Review. International Journal of Molecular Sciences, *21*(16), 5764. PMCID:PMC7460950
[317] Pinyon, J. L., von Jonquieres, G., Crawford, E. N., Duxbury, M., Al Abed, A., Lovell, N. H., Klugmann, M., Wise, A. K., Fallon, J. B., Shepherd, R. K., Birman, C. S., Lai, W., McAlpine, D., McMahon, C., Carter, P. M., Enke, Y. L., Patrick, J. F., Schilder, A. G. M., Marie, C., … Housley, G. D. (2019). Neurotrophin gene augmentation by electrotransfer to improve cochlear implant hearing outcomes. Hearing Research, *380*, 137–149. doi: 10.1016/j.heares.2019.06.002
[318] Wise, A. K., & Gillespie, L. N. (2012). Drug delivery to the inner ear. Journal of Neural Engineering, *9*(6), 065002. PMCID:PMC4222974
[319] Ma, Y., Wise, A. K., Shepherd, R. K., & Richardson, R. T. (2019). New molecular therapies for the treatment of hearing loss. Pharmacology & Therapeutics, *200*, 190–209. PMCID:PMC6626560
[320] Shibata, S. B., Budenz, C. L., Bowling, S. A., Pfingst, B. E., & Raphael, Y. (2011). Nerve maintenance and regeneration in the damaged cochlea. Hearing Research, *281*(1–2), 56–64. PMCID:PMC3196294
[321] Kanzaki, S., Stöver, T., Kawamoto, K., Prieskorn, D. M., Altschuler, R. A., Miller, J. M., & Raphael, Y. (2002). Glial cell line-derived neurotrophic factor and chronic electrical stimulation prevent VIII cranial nerve degeneration following denervation. The Journal of Comparative Neurology, *454*(3), 350–360. PMID:12442325
[322] Thompson, B. C., Moulton, S. E., Ding, J., Richardson, R., Cameron, A., O'Leary, S., Wallace, G. G., & Clark, G. M. (2006). Optimising the incorporation and release of a neurotrophic factor using conducting polypyrrole. Journal of Controlled Release, *116*(3), 285–294. doi: 10.1016/j.jconrel.2006.09.004
[323] Thompson, B. C., Richardson, R. T., Moulton, S. E., Evans, A. J., O'Leary, S., Clark, G. M., & Wallace, G. G. (2010). Conducting polymers, dual neurotrophins and pulsed electrical stimulation — Dramatic effects on neurite outgrowth. Journal of Controlled Release, *141*(2), 161–167. doi: 10.1016/j.jconrel.2009.09.016
[324] Thompson, B. C., Richardson, R. T., Moulton, S. E., Evans, A. J., O'Leary, S., Clark, G. M., & Wallace, G. G. (2010). Conducting polymers, dual neurotrophins and pulsed electrical stimulation--dramatic effects on neurite outgrowth. Journal of Controlled Release : Official Journal of the Controlled Release Society, *141*(2), 161–167. PMID:19788902
[325] Chikar, J. A., Hendricks, J. L., Richardson-Burns, S. M., Raphael, Y., Pfingst, B. E., & Martin, D. C. (2012). The use of a dual PEDOT and RGD-functionalized alginate hydrogel coating to provide sustained drug delivery and improved cochlear implant function. Biomaterials, *33*(7), 1982–1990. PMCID:PMC3261353
[326] Yilmazoglu, O., Yadav, S., Cicek, D., & Schneider, J. J. (2016). A nano-microstructured artificial-hair-cell-type sensor based on topologically graded 3D carbon nanotube bundles. Nanotechnology, *27*(36), 365502. PMID:27481641
[327] Mohammadie, Z. M., Parivar, K., Shahri, N. M., Fereidoni, M., & Hayati-Roodbari, N. (2018). Decellularized Bovine Articular Cartilage Matrix Reinforced by Carboxylated-SWCNT for Tissue Engineering Application. Brazilian Archives of Biology and Technology, *60*. doi: 10.1590/1678-4324-2017160083
[328] Ageeva, S. A., Bobrinetskii, I. I., Nevolin, V. K., Podgaetskii, V. M., Selishchev, S. V., Simunin, M. M., Konov, V. I., & Savranskii, V. V. (2009). Nanotube-based three-dimensional albumin composite obtained using continuous laser radiation. Semiconductors, *43*(13), 1714–1718. doi: 10.1134/S1063782609130211
[329] Tangerino Filho, E. P., Fachi, J. L., Vasconcelos, I. C., Dos Santos, G. M. T., Mendonça, F. A. S., de Aro, A. A., Pimentel, E. R., & Esquisatto, M. A. M. (2016). Effects of microcurrent therapy on excisional elastic cartilage defects in young rats. Tissue & Cell, *48*(3), 224–234. PMID:27138327
[330] Mannoor, M. S., Jiang, Z., James, T., Kong, Y. L., Malatesta, K. A., Soboyejo, W. O., Verma, N., Gracias, D. H., & McAlpine, M. C. (2013). 3D Printed Bionic Ears. Nano Letters, *13*(6), 2634–2639. PMCID:PMC3925752
[331] McBane, J. E., Sharifpoor, S., Cai, K., Labow, R. S., & Santerre, J. P. (2011). Biodegradation and in vivo biocompatibility of a degradable, polar/hydrophobic/ionic polyurethane for tissue engineering applications. Biomaterials, *32*(26), 6034–6044. doi: 10.1016/j.biomaterials.2011.04.048
[332] Liu, M., Liu, M., She, L., Zha, Z., Pan, J., Li, S., Li, T., He, Y., Cai, Z., Wang, J., Zheng, Y., Qiu, X., & Zhong, D. (2017). Graphene-like nanoribbons periodically embedded with four- and eight-membered rings. Nature Communications, *8*, 14924. PMID:28361958

[333] Xie, M., Wang, L., Guo, B., Wang, Z., Chen, Y. E., & Ma, P. X. (2015). Ductile electroactive biodegradable hyperbranched polylactide copolymers enhancing myoblast differentiation. Biomaterials, *71*, 158–167. PMID:26335860

[334] Huang, L., Hu, J., Lang, L., Wang, X., Zhang, P., Jing, X., Wang, X., Chen, X., Lelkes, P. I., Macdiarmid, A. G., & Wei, Y. (2007). Synthesis and characterization of electroactive and biodegradable ABA block copolymer of polylactide and aniline pentamer. Biomaterials, *28*(10), 1741–1751. PMID:17218007

[335] Lei, T., Guan, M., Liu, J., Lin, H.-C., Pfattner, R., Shaw, L., McGuire, A. F., Huang, T.-C., Shao, L., Cheng, K.-T., Tok, J. B.-H., & Bao, Z. (2017). Biocompatible and totally disintegrable semiconducting polymer for ultrathin and ultralightweight transient electronics. Proceedings of the National Academy of Sciences, *114*(20), 5107–5112. doi: 10.1073/pnas.1701478114

[336] Karpov, Y., Erdmann, T., Raguzin, I., Al-Hussein, M., Binner, M., Lappan, U., Stamm, M., Gerasimov, K. L., Beryozkina, T., Bakulev, V., Anokhin, D. V., Ivanov, D. A., Günther, F., Gemming, S., Seifert, G., Voit, B., Di Pietro, R., & Kiriy, A. (2016). High Conductivity in Molecularly p-Doped Diketopyrrolopyrrole-Based Polymer: The Impact of a High Dopant Strength and Good Structural Order. Advanced Materials, *28*(28), 6003–6010. doi: 10.1002/adma.201506295

[337] Goncalves, R. de C. R., & Pombeiro-Sponchiado, S. R. (2005). Antioxidant Activity of the Melanin Pigment Extracted from Aspergillus nidulans. Biological and Pharmaceutical Bulletin, *28*(6), 1129–1131. doi: 10.1248/bpb.28.1129

[338] Zhang, H. (2015). Ultrathin Two-Dimensional Nanomaterials. ACS Nano, *9*(10), 9451–9469. doi: 10.1021/acsnano.5b05040

[339] Gogotsi, Y., & Anasori, B. (2019). The Rise of MXenes. ACS Nano, *13*(8), 8491–8494. doi: 10.1021/acsnano.9b06394

[340] Soleymaniha, M., Shahbazi, M.-A., Rafieerad, A. R., Maleki, A., & Amiri, A. (2019). Promoting Role of MXene Nanosheets in Biomedical Sciences: Therapeutic and Biosensing Innovations. Advanced Healthcare Materials, *8*(1), e1801137. PMID:30362268

[341] Naguib, M., Kurtoglu, M., Presser, V., Lu, J., Niu, J., Heon, M., Hultman, L., Gogotsi, Y., & Barsoum, M. W. (2011). Two-Dimensional Nanocrystals Produced by Exfoliation of Ti3AlC2. Advanced Materials, *23*(37), 4248–4253. doi: 10.1002/adma.201102306

[342] Lin, H., Gao, S., Dai, C., Chen, Y., & Shi, J. (2017). A Two-Dimensional Biodegradable Niobium Carbide (MXene) for Photothermal Tumor Eradication in NIR-I and NIR-II Biowindows. Journal of the American Chemical Society, *139*(45), 16235–16247. doi: 10.1021/jacs.7b07818

[343] Jastrzębska, A. M., Szuplewska, A., Wojciechowski, T., Chudy, M., Ziemkowska, W., Chlubny, L., Rozmysłowska, A., & Olszyna, A. (2017). In vitro studies on cytotoxicity of delaminated Ti3C2 MXene. Journal of Hazardous Materials, *339*, 1–8. doi: 10.1016/j.jhazmat.2017.06.004

[344] Ling, Z., Ren, C. E., Zhao, M.-Q., Yang, J., Giammarco, J. M., Qiu, J., Barsoum, M. W., & Gogotsi, Y. (2014). Flexible and conductive MXene films and nanocomposites with high capacitance. Proceedings of the National Academy of Sciences of the United States of America, *111*(47), 16676–16681. PMCID:PMC4250111

[345] Kato, S., Taira, H., Aoshima, H., Saitoh, Y., & Miwa, N. (2010). Clinical evaluation of fullerene-C60 dissolved in squalane for anti-wrinkle cosmetics. Journal of Nanoscience and Nanotechnology, *10*(10), 6769–6774. PMID:21137794

[346] *A study to compare the sexual pleasure, performance, acceptability and safety of graphene incorporated natural rubber latex condoms and natural rubber latex condoms*. (2018). Cochrane Central Register of Controlled Trials (CENTRAL).