Graphene neuroscience literature

Description

Lin, H. Y., Nurunnabi, M., Chen, W. H., & Huang, C. H.. (2019). Graphene in neuroscience. In Biomedical Applications of Graphene and 2D Nanomaterials

Plain numerical DOI: 10.1016/B978-0-12-815889-0.00016-7
DOI URL
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"Graphene and graphene-derived materials have been widely applied in various biomedical fields. in neuroscience, graphene and its derivatives can be applied as nanocarriers for drug delivery, as compelling biocompatible substrates for tissue engineering, as conductive electrodes for obtaining the stimulation response in studying neural networks, as low photobleaching nanocomposite tags in bioimaging, as enhancers for guiding neural growth and differentiation as regenerative medicine, and so forth. among these applications, the material composition, functionalization, and dimension of graphene are considerably important. in this chapter, we provide a brief review to address the accomplishments and further perspective of graphene and its related materials applied in neuroscience."
Perini, G., Palmieri, V., Ciasca, G., De Spirito, M., & Papi, M.. (2020). Unravelling the potential of graphene quantum dots in biomedicine and neuroscience. International Journal of Molecular Sciences

Plain numerical DOI: 10.3390/ijms21103712
DOI URL
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"Quantum dots (qds) are semiconducting nanoparticles that have been gaining ground in various applications, including the biomedical field, thanks to their unique optical properties. recently, graphene quantum dots (gqds) have earned attention in biomedicine and nanomedicine, thanks to their higher biocompatibility and low cytotoxicity compared to other qds. gqds share the optical properties of qd and have proven ability to cross the blood-brain barrier (bbb). for this reason, gqds are now being employed to deepen our knowledge in neuroscience diagnostics and therapeutics. their size and surface chemistry that ease the loading of chemotherapeutic drugs, makes them ideal drug delivery systems through the bloodstream, across the bbb, up to the brain. gqds-based neuroimaging techniques and theranostic applications, such as photothermal and photodynamic therapy alone or in combination with chemotherapy, have been designed. in this review, optical properties and biocompatibility of gqds will be described. then, the ability of gqds to overtake the bbb and reach the brain will be discussed. at last, applications of gqds in bioimaging, photophysical therapies and drug delivery to the central nervous system will be considered, unraveling their potential in the

neuroscientific field."
Orecchioni, M., Bordoni, V., Fuoco, C., Reina, G., Lin, H., Zoccheddu, M., … Delogu, L. G.. (2020). Toward High-Dimensional Single-Cell Analysis of Graphene Oxide Biological Impact: Tracking on Immune Cells by Single-Cell Mass Cytometry. Small

Plain numerical DOI: 10.1002/smll.202000123
DOI URL
directSciHub download

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"Considering the potential exposure to graphene, the most investigated nanomaterial, the assessment of the impact on human health has become an urgent need. the deep understanding of nanomaterial safety is today possible by high-throughput single-cell technologies. single-cell mass cytometry (cytometry by time-of flight, cytof) shows an unparalleled ability to phenotypically and functionally profile complex cellular systems, in particular related to the immune system, as recently also proved for graphene impact. the next challenge is to track the graphene distribution at the single-cell level. therefore, graphene oxide (go) is functionalized with agins2 nanocrystals (go–in), allowing to trace go immune–cell interactions via the indium (115in) channel. indium is specifically chosen to avoid overlaps with the commercial panels (>30 immune markers). as a proof of concept, the go–in cytof tracking is performed at the single-cell level on blood immune subpopulations, showing the go interaction with monocytes and b cells, therefore guiding future immune studies. the proposed approach can be applied not only to the immune safety assessment of the multitude of graphene physical and chemical parameters, but also for graphene applications in neuroscience. moreover, this approach can be translated to other 2d emerging materials and will likely advance the understanding of their toxicology."
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

Plain numerical DOI: 10.1016/j.biomaterials.2014.05.002
DOI URL
directSciHub download

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"One of the key goals in nerve tissue engineering is to develop new materials which cause less or no neuroinflammation. despite the rapid advances of using graphene as a neural interface material, it still remains unknown whether graphene could provoke neuroinflammation or not, and whether and how the topographical features of graphene influence the neuroinflammation induction. by immunofluorescence, elisa technique, western blot, scanning electron microscope (sem) methods, we investigated the pro- and/or anti-inflammatory responses of microglia in the graphene films (2d-graphene) or graphene foams (3d-graphene) culturing systems. furthermore, the growth situations of the neural stem cells (nscs) in the conditioned culture medium produced in the graphene substrates were evaluated. the results show that: 1) neither 2d nor 3d graphene induced distinct neuroinflammation when compared to the tissue culture polystyrene (tcps) substrates; 2) the topographical structures of the graphene might affect the material/cell interactions, leading to disparate effects on lipopolysaccharide (lps)-induced neuroinflammation; 3) 3d graphene exhibited a remarkable capability of rescuing lps-induced neuroinflammation probably through the restriction of microglia

morphological transformation by the unique topographical features on the surface, showing the ability of anti-inflammation against external insults, while 2d graphene failed to. these results provide insights into the diverse biological effects of the material's topographical structures and open new opportunity for the applications of graphene in neuroscience. © 2014 elsevier ltd."
Kitko, K. E., & Zhang, Q.. (2019). Graphene-based nanomaterials: From production to integration with modern tools in neuroscience. Frontiers in Systems Neuroscience

Plain numerical DOI: 10.3389/fnsys.2019.00026
DOI URL
directSciHub download

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"Graphene, a two-dimensional carbon crystal, has emerged as a promising material for sensing and modulating neuronal activity in vitro and in vivo. in this review, we provide a primer for how manufacturing processes to produce graphene and graphene oxide result in materials properties that may be tailored for a variety of applications. we further discuss how graphene may be composited with other bio-compatible materials of interest to make novel hybrid complexes with desired characteristics for bio-interfacing. we then highlight graphene's ever-widen utility and unique properties that may in the future be multiplexed for cross-modal modulation or interrogation of neuronal network. as the biological effects of graphene are still an area of active investigation, we discuss recent development, with special focus on how surface coatings and surface properties of graphene are relevant to its biological effects. we discuss studies conducted in both non-murine and murine systems, and emphasize the preclinical aspect of graphene's potential without undermining its tangible clinical implementation."
Garcia-Cortadella, R., Schwesig, G., Jeschke, C., Illa, X., Gray, A. L., Savage, S., … Garrido, J. A.. (2021). Graphene active sensor arrays for long-term and wireless mapping of wide frequency band epicortical brain activity. Nature Communications

Plain numerical DOI: 10.1038/s41467-020-20546-w
DOI URL
directSciHub download

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"Graphene active sensors have demonstrated promising capabilities for the detection of electrophysiological signals in the brain. their functional properties, together with their flexibility as well as their expected stability and biocompatibility have raised them as a promising building block for large-scale sensing neural interfaces. however, in order to provide reliable tools for neuroscience and biomedical engineering applications, the maturity of this technology must be thoroughly studied. here, we evaluate the performance of 64-channel graphene sensor arrays in terms of homogeneity, sensitivity and stability using a wireless, quasi-commercial headstage and demonstrate the biocompatibility of epicortical graphene chronic implants. furthermore, to illustrate the potential of the technology to detect cortical signals from infra-slow to high-gamma frequency bands, we perform proof-of-concept long-term wireless recording in a freely behaving rodent. our work demonstrates the maturity of the graphene-based technology, which represents a promising candidate for chronic, wide frequency band neural sensing interfaces."

Cherian, R. S., Sandeman, S., Ray, S., Savina, I. N., Ashtami, J., & Mohanan, P. V.. (2019). Green synthesis of Pluronic stabilized reduced graphene oxide: Chemical and biological characterization. Colloids and Surfaces B: Biointerfaces

Plain numerical DOI: 10.1016/j.colsurfb.2019.03.043
DOI URL
directSciHub download

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“The wonder material graphene has numerous potential applications in nanoelectronics, biomedicine, storage devices, etc. synthesis of graphene is highly challenging due to the toxic chemicals used and its low yield. in the present study, a facile green route for synthesis of reduced graphene oxide (rgo) was carried out using ascorbic acid as reducing agent. rgo was stabilized using pluronic p123 polymer to give pluronic stabilized reduced graphene oxide (rgo-p) and gave superior yield (15 mg graphene oxide yielded ˜13 mg rgo-p). despite the potential neuroscience applications of graphene, the impending toxicological outcome upon interaction with neurons is not well understood. here, differentiated pc-12 neuron-like cells exposed to rgo-p showed a dose-dependent cytotoxicity. membrane disruption and cytoskeletal integrity remained uncompromised after 24 h exposure. oxidative stress in pc-12 was evident due to an increase in ros generation in dose and time-dependent manner. in vivo acute toxicity was assessed in mice administered with 10 mg/kg body weight of rgo-p. there were no evident changes in behaviour, motor function or other morphological changes. in conclusion, rgo-p was successfully synthesized and provided superior yield. even though in vitro toxicity testing showed dose-dependent toxicity, in vivo toxic effect was not apparent.”
Bramini, M., Alberini, G., Colombo, E., Chiacchiaretta, M., DiFrancesco, M. L., Maya-Vetencourt, J. F., … Cesca, F.. (2018). Interfacing graphene-based materials with neural cells. Frontiers in Systems Neuroscience

Plain numerical DOI: 10.3389/fnsys.2018.00012
DOI URL
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“The scientific community has witnessed an exponential increase in the applications of graphene and graphene-based materials in a wide range of fields, from engineering to electronics to biotechnologies and biomedical applications. for what concerns neuroscience, the interest raised by these materials is two-fold. on one side, nanosheets made of graphene or graphene derivatives (graphene oxide, or its reduced form) can be used as carriers for drug delivery. here, an important aspect is to evaluate their toxicity, which strongly depends on flake composition, chemical functionalization and dimensions. on the other side, graphene can be exploited as a substrate for tissue engineering. in this case, conductivity is probably the most relevant amongst the various properties of the different graphene materials, as it may allow to instruct and interrogate neural networks, as well as to drive neural growth and differentiation, which holds a great potential in regenerative medicine. in this review, we try to give a comprehensive view of the accomplishments and new challenges of the field, as well as which in our view are the most exciting directions to take in the immediate future. these include the need to engineer multifunctional nanoparticles (nps) able to cross the blood-brain-barrier to reach neural cells,

and to achieve on-demand delivery of specific drugs. we describe the state-of-the-art in the use of graphene materials to engineer three-dimensional scaffolds to drive neuronal growth and regeneration in vivo, and the possibility of using graphene as a component of hybrid composites/multi-layer organic electronics devices. last but not least, we address the need of an accurate theoretical modeling of the interface between graphene and biological material, by modeling the interaction of graphene with proteins and cell membranes at the nanoscale, and describing the physical mechanism(s) of charge transfer by which the various graphene materials can influence the excitability and physiology of neural cells."
Capasso, A., Rodrigues, J., Moschetta, M., Buonocore, F., Faggio, G., Messina, G., … Lisi, N.. (2021). Interactions between Primary Neurons and Graphene Films with Different Structure and Electrical Conductivity. Advanced Functional Materials

Plain numerical DOI: 10.1002/adfm.202005300
DOI URL
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"Graphene-based materials represent a useful tool for the realization of novel neural interfaces. several studies have demonstrated the biocompatibility of graphene-based supports, but the biological interactions between graphene and neurons still pose open questions. in this work, the influence of graphene films with different characteristics on the growth and maturation of primary cortical neurons is investigated. graphene films are grown by chemical vapor deposition progressively lowering the temperature range from 1070 to 650 °c to change the lattice structure and corresponding electrical conductivity. two graphene-based films with different electrical properties are selected and used as substrate for growing primary cortical neurons: i) highly crystalline and conductive (grown at 1070 °c) and ii) highly disordered and 140-times less conductive (grown at 790 °c). electron and fluorescence microscopy imaging reveal an excellent neuronal viability and the development of a mature, structured, and excitable network onto both substrates, regardless of their microstructure and electrical conductivity. the results underline that high electrical conductivity by itself is not fundamental for graphene-based neuronal interfaces, while other physico–chemical characteristics, including the atomic structure, should be also considered in the design of functional, bio-friendly templates. this finding widens the spectrum of carbon-based materials suitable for neuroscience applications."
Rauti, R., Secomandi, N., Martín, C., Bosi, S., Severino, F. P. U., Scaini, D., … Ballerini, L.. (2020). Tuning Neuronal Circuit Formation in 3D Polymeric Scaffolds by Introducing Graphene at the Bio/Material Interface. Advanced Biosystems

Plain numerical DOI: 10.1002/adbi.201900233
DOI URL
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"2D cultures are useful platforms allowing studies of the fundamental mechanisms governing neuron and synapse functions. yet, such models are limited when exploring changes in network dynamics due to 3d-space topologies. 3d platforms fill this gap and favor investigating topologies closer to the real brain organization. graphene, an atom-thick layer of carbon, possesses remarkable properties and

since its discovery is considered a highly promising material in neuroscience developments. here, elastomeric 3d platforms endowed with graphene cues are exploited to modulate neuronal circuits when interfaced to graphene in 3d topology. ex vivo neuronal networks are successfully reconstructed within 3d scaffolds, with and without graphene, characterized by comparable size and morphology. by confocal microscopy and live imaging, the 3d architecture of synaptic networks is documented to sustain a high rate of bursting in 3d scaffolds, an activity further increased by graphene interfacing. changes are reported in the excitation/inhibition ratio, potentially following 3d-graphene interfacing. a hypothesis is thus proposed, where the combination of synapse formation under 3d architecture and graphene interfaces affects the maturation of gabaergic inhibition. this will tune the balance between hyperpolarizing and depolarizing responses, potentially contributing to network synchronization in the absence of changes in gabaergic phenotype expression."
Thunemann, M., Lu, Y., Liu, X., Klllç, K., Desjardins, M., Vandenberghe, M., … Kuzum, D.. (2018). Deep 2-photon imaging and artifact-free optogenetics through transparent graphene microelectrode arrays. Nature Communications

Plain numerical DOI: 10.1038/s41467-018-04457-5
DOI URL
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"Recent advances in optical technologies such as multi-photon microscopy and optogenetics have revolutionized our ability to record and manipulate neuronal activity. combining optical techniques with electrical recordings is of critical importance to connect the large body of neuroscience knowledge obtained from animal models to human studies mainly relying on electrophysiological recordings of brain-scale activity. however, integration of optical modalities with electrical recordings is challenging due to generation of light-induced artifacts. here we report a transparent graphene microelectrode technology that eliminates light-induced artifacts to enable crosstalk-free integration of 2-photon microscopy, optogenetic stimulation, and cortical recordings in the same in vivo experiment. we achieve fabrication of crack- and residue-free graphene electrode surfaces yielding high optical transmittance for 2-photon imaging down to ~ 1 mm below the cortical surface. transparent graphene microelectrode technology offers a practical pathway to investigate neuronal activity over multiple spatial scales extending from single neurons to large neuronal populations."
Garcia-Cortadella, R., Schäfer, N., Cisneros-Fernandez, J., Ré, L., Illa, X., Schwesig, G., … Guimerà-Brunet, A.. (2020). Switchless multiplexing of graphene active sensor arrays for brain mapping. Nano Letters

Plain numerical DOI: 10.1021/acs.nanolett.0c00467
DOI URL
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"Sensor arrays used to detect electrophysiological signals from the brain are paramount in neuroscience. however, the number of sensors that can be interfaced with macroscopic data acquisition systems currently limits their bandwidth. this bottleneck originates in the fact that, typically, sensors are addressed individually, requiring a connection for each of them. herein, we present the

concept of frequency-division multiplexing (fdm) of neural signals by graphene sensors. we demonstrate the high performance of graphene transistors as mixers to perform amplitude modulation (am) of neural signals in situ, which is used to transmit multiple signals through a shared metal line. this technology eliminates the need for switches, remarkably simplifying the technical complexity of state-of-the-art multiplexed neural probes. besides, the scalability of fdm graphene neural probes has been thoroughly evaluated and their sensitivity demonstrated in vivo. using this technology, we envision a new generation of high-count conformal neural probes for high bandwidth brain machine interfaces."
Liu, X., Lu, Y., Iseri, E., Shi, Y., & Kuzum, D.. (2018). A compact closed-loop optogenetics system based on artifact-free transparent graphene electrodes. Frontiers in Neuroscience

Plain numerical DOI: 10.3389/fnins.2018.00132
DOI URL
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"Electrophysiology is a decades-old technique widely used for monitoring activity of individual neurons and local field potentials. optogenetics has revolutionized neuroscience studies by offering selective and fast control of targeted neurons and neuron populations. the combination of these two techniques is crucial for causal investigation of neural circuits and understanding their functional connectivity. however, electrical artifacts generated by light stimulation interfere with neural recordings and hinder the development of compact closed-loop systems for precise control of neural activity. here, we demonstrate that transparent graphene micro-electrodes fabricated on a clear polyethylene terephthalate film eliminate the light-induced artifact problem and allow development of a compact battery-powered closed-loop optogenetics system. we extensively investigate light-induced artifacts for graphene electrodes in comparison to metal control electrodes. we then design optical stimulation module using micro-led chips coupled to optical fibers to deliver light to intended depth for optogenetic stimulation. for artifact-free integration of graphene micro-electrode recordings with optogenetic stimulation, we design and develop a compact closed-loop system and validate it for different frequencies of interest for neural recordings. this compact closed-loop optogenetics system can be used for various applications involving optogenetic stimulation and electrophysiological recordings."
Lu, Y., Lyu, H., Richardson, A. G., Lucas, T. H., & Kuzum, D.. (2016). Flexible Neural Electrode Array Based-on Porous Graphene for Cortical Microstimulation and Sensing. Scientific Reports

Plain numerical DOI: 10.1038/srep33526
DOI URL
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"Neural sensing and stimulation have been the backbone of neuroscience research, brain-machine interfaces and clinical neuromodulation therapies for decades. to-date, most of the neural stimulation systems have relied on sharp metal microelectrodes with poor electrochemical properties that induce extensive damage to the tissue and significantly degrade the long-term stability of implantable systems. here, we demonstrate a flexible cortical microelectrode array based on porous graphene, which is capable of efficient electrophysiological sensing and stimulation from the brain surface,

without penetrating into the tissue. porous graphene electrodes show superior impedance and charge injection characteristics making them ideal for high efficiency cortical sensing and stimulation. they exhibit no physical delamination or degradation even after 1 million biphasic stimulation cycles, confirming high endurance. in in vivo experiments with rodents, same array is used to sense brain activity patterns with high spatio-temporal resolution and to control leg muscles with high-precision electrical stimulation from the cortical surface. flexible porous graphene array offers a minimally invasive but high efficiency neuromodulation scheme with potential applications in cortical mapping, brain-computer interfaces, treatment of neurological disorders, where high resolution and simultaneous recording and stimulation of neural activity are crucial."
Chen, J., Yu, Q., Fu, W., Chen, X., Zhang, Q., Dong, S., … Zhang, S.. (2020). A highly sensitive amperometric glutamate oxidase microbiosensor based on a reduced graphene oxide/prussian blue nanocube/gold nanoparticle composite film-modified pt electrode. Sensors (Switzerland)

Plain numerical DOI: 10.3390/s20102924
DOI URL
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"A simple method that relies only on an electrochemical workstation has been investigated to fabricate a highly sensitive glutamate microbiosensor for potential neuroscience applications. in this study, in order to develop the highly sensitive glutamate electrode, a 100 µm platinum wire was modified by the electrochemical deposition of gold nanoparticles, prussian blue nanocubes, and reduced graphene oxide sheets, which increased the electroactive surface area; and the chitosan layer, which provided a suitable environment to bond the glutamate oxidase. the optimization of the fabrication procedure and analytical conditions is described. the modified electrode was characterized using field emission scanning electron microscopy, impedance spectroscopy, and cyclic voltammetry. the results exhibited its excellent sensitivity for glutamate detection (lod = 41.33 nm), adequate linearity (50 nm–40 µm), ascendant reproducibility (rsd = 4.44%), and prolonged stability (more than 30 repetitive potential sweeps, two-week lifespan). because of the important role of glutamate in neurotransmission and brain function, this small-dimension, high-sensitivity glutamate electrode is a promising tool in neuroscience research."
Park, D. W., Ness, J. P., Brodnick, S. K., Esquibel, C., Novello, J., Atry, F., … Ma, Z.. (2018). Electrical Neural Stimulation and Simultaneous in Vivo Monitoring with Transparent Graphene Electrode Arrays Implanted in GCaMP6f Mice. ACS Nano

Plain numerical DOI: 10.1021/acsnano.7b04321
DOI URL
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"Electrical stimulation using implantable electrodes is widely used to treat various neuronal disorders such as parkinson's disease and epilepsy and is a widely used research tool in neuroscience studies. however, to date, devices that help better understand the mechanisms of electrical stimulation in neural tissues have been limited to opaque neural electrodes. imaging spatiotemporal neural responses to electrical stimulation with minimal artifact could allow for various studies that are

impossible with existing opaque electrodes. here, we demonstrate electrical brain stimulation and simultaneous optical monitoring of the underlying neural tissues using carbon-based, fully transparent graphene electrodes implanted in gcamp6f mice. fluorescence imaging of neural activity for varying electrical stimulation parameters was conducted with minimal image artifact through transparent graphene electrodes. in addition, full-field imaging of electrical stimulation verified more efficient neural activation with cathode leading stimulation compared to anode leading stimulation. we have characterized the charge density limitation of capacitive four-layer graphene electrodes as 116.07-174.10 ?c/cm2 based on electrochemical impedance spectroscopy, cyclic voltammetry, failure bench testing, and in vivo testing. this study demonstrates the transparent ability of graphene neural electrodes and provides a method to further increase understanding and potentially improve therapeutic electrical stimulation in the central and peripheral nervous systems."
John, A. A., Subramanian, A. P., Vellayappan, M. V., Balaji, A., Mohandas, H., & Jaganathan, S. K.. (2015). Carbon nanotubes and graphene as emerging candidates in neuroregeneration and neurodrug delivery. International Journal of Nanomedicine

Plain numerical DOI: 10.2147/IJN.S83777
DOI URL
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"Neuroregeneration is the regrowth or repair of nervous tissues, cells, or cell products involved in neurodegeneration and inflammatory diseases of the nervous system like alzheimer's disease and parkinson's disease. nowadays, application of nanotechnology is commonly used in developing nanomedicines to advance pharmacokinetics and drug delivery exclusively for central nervous system pathologies. in addition, nanomedical advances are leading to therapies that disrupt disarranged protein aggregation in the central nervous system, deliver functional neuroprotective growth factors, and change the oxidative stress and excitotoxicity of affected neural tissues to regenerate the damaged neurons. carbon nanotubes and graphene are allotropes of carbon that have been exploited by researchers because of their excellent physical properties and their ability to interface with neurons and neuronal circuits. this review describes the role of carbon nanotubes and graphene in neuroregeneration. in the future, it is hoped that the benefits of nanotechnologies will outweigh their risks, and that the next decade will present huge scope for developing and delivering technologies in the field of neuroscience."
Rauti, R., Musto, M., Bosi, S., Prato, M., & Ballerini, L.. (2019). Properties and behavior of carbon nanomaterials when interfacing neuronal cells: How far have we come?. Carbon

Plain numerical DOI: 10.1016/j.carbon.2018.11.026
DOI URL
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"In the last two decades, an increasing amount of studies have investigated the use of components based on carbon-(nano)materials in the engineering of neural interfaces, to improve the performance of current state of the art devices. carbon is an extremely versatile element, characterized by a variety of allotropes and structures with different properties due to their sp, sp2 or sp3 hybridization. among

the diverse carbon nanomaterials, carbon nanotubes and graphene are naturally excellent electrical conductors, thus representing ideal candidates for interfacing electrical-excitable tissues. in addition, their dimensional range holds the potential to enhance the material interactions with bio-systems. successful interfacing of the nervous system with devices that record or modulate neuronal electrical activity requires their stable electrical coupling with neurons. the efficiency of this coupling can be improved significantly by the use of conductive, ad hoc designed, nanomaterials. here we review different carbon-based nanomaterials currently under investigation in basic and applied neuroscience, and the recent developments in this research field, with a special focus on in vitro studies."
Zheng, Z., Huang, L., Yan, L., Yuan, F., Wang, L., Wang, K., … Liu, Y.. (2019). Polyaniline functionalized graphene nanoelectrodes for the regeneration of PC12 cells via electrical stimulation. International Journal of Molecular Sciences

Plain numerical DOI: 10.3390/ijms20082013
DOI URL
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"The regeneration of neurons is an important goal of neuroscience and clinical medicine. the electrical stimulation of cells is a promising technique to meet this goal. however, its efficiency highly depends on the electrochemical properties of the stimulation electrodes used. this work reports on the preparation and use of a highly electroactive and biocompatible nanoelectrode made from a novel polyaniline functionalized graphene composite. this nanocomposite was prepared using a facile and efficient polymerization-enhanced ball-milling method. it was used to stimulate the growth of pc12 cells under various electrical fields. the enhanced growth of axons and improved wound regeneration of pc12 cells were observed after this treatment, suggesting a promising strategy for neuro traumatology."
Guan, S., Wang, J., & Fang, Y.. (2019). Transparent graphene bioelectronics as a new tool for multimodal neural interfaces. Nano Today

Plain numerical DOI: 10.1016/j.nantod.2019.01.003
DOI URL
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"A central challenge of neuroscience is to monitor the coordinated activity of neural circuits underlying information processing and behavior. combining the advantages of electrical and optical modalities can provide unprecedented access to the spatiotemporal dynamics of neural activity. transparent graphene bioelectronics has emerged as a suitable tool for the seamless integration of electrophysiological recording with optical imaging and optogenetic stimulation, opening up a variety of new opportunities in both neuroscience research and clinical applications."
Lu, Y., Liu, X., & Kuzum, D.. (2018). Graphene-based neurotechnologies for advanced neural interfaces. Current Opinion in Biomedical Engineering

Plain numerical DOI: 10.1016/j.cobme.2018.06.001
DOI URL

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“Understanding how neuron populations transform activities of individual neurons into complex behaviors is one of the biggest challenges of neuroscience research. however, current neural monitoring and controlling technologies provide insufficient spatiotemporal resolution to unravel neural circuit functions. to this end, multifunctional neurotechnologies combining electrical, optical and chemical sensing and stimulation modalities have been proposed to overcome resolution limits. research in multifunctional probes has fueled the demand for new materials to build minimally invasive chronic interfaces to the brain. graphene has recently emerged as a neural interface material offering several outstanding properties, such as optical transparency, flexibility, high conductivity, functionalization and biocompatibility. the unique combination of these properties in a single material system makes graphene an attractive choice for multi-modal probing of neural activity. in this review, we discuss recent advances in graphene-based neurotechnologies, highlight different approaches and consider emerging directions inspired by unique characteristics of graphene.”
Fischer, R. A., Zhang, Y., Risner, M. L., Li, D., Xu, Y., & Sappington, R. M.. (2018). Impact of Graphene on the Efficacy of Neuron Culture Substrates. Advanced Healthcare Materials

Plain numerical DOI: 10.1002/adhm.201701290
DOI URL
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“How graphene influences the behavior of living cells or tissues remains a critical issue for its application in biomedical studies, despite the general acceptance that graphene is biocompatible. while direct contact between cells and graphene is not a requirement for all biomedical applications, it is often mandatory for biosensing. therefore, it is important to clarify whether graphene impedes the ability of cells to interact with biological elements in their environment. here, a systematic study is reported to determine whether applying graphene on top of matrix substrates masks interactions between these substrates and retinal ganglion cells (rgcs). six different platforms are tested for primary rgc cultures with three platforms comprised of matrix substrates compatible with these neurons, and another three having a layer of graphene placed on top of the matrix substrates. the results demonstrate that graphene does not impede interactions between rgcs and underlying substrate matrix, such that their positive or negative effects on neuron viability and vitality are retained. however, direct contact between rgcs and graphene reduces the number, but increases basal activity, of functional cation channels. the data indicate that, when proper baselines are established, graphene is a promising biosensing material for in vitro applications in neuroscience.”
Wang, R., Shi, M., Brewer, B., Yang, L., Zhang, Y., Webb, D. J., … Xu, Y. Q.. (2018). Ultrasensitive Graphene Optoelectronic Probes for Recording Electrical Activities of Individual Synapses. Nano Letters

Plain numerical DOI: 10.1021/acs.nanolett.8b02298
DOI URL

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“The complex neuronal circuitry connected by submicron synapses in our brain calls for technologies that can map neural networks with ultrahigh spatiotemporal resolution to decipher the underlying mechanisms for multiple aspects of neuroscience. here we show that, through combining graphene transistor arrays with scanning photocurrent microscopy, we can detect the electrical activities of individual synapses of primary hippocampal neurons. through measuring the local conductance change of graphene optoelectronic probes directly underneath neuronal processes, we are able to estimate millivolt extracellular potential variations of individual synapses during depolarization. the ultrafast nature of graphene photocurrent response allows for decoding of activity patterns of individual synapses with a sub-millisecond temporal resolution. this new neurotechnology provides promising potentials for recording of electrophysiological outcomes of individual synapses in neural networks.”
Bourrier, A., Shkorbatova, P., Bonizzato, M., Rey, E., Barraud, Q., Courtine, G., … Delacour, C.. (2019). Monolayer Graphene Coating of Intracortical Probes for Long-Lasting Neural Activity Monitoring. Advanced Healthcare Materials

Plain numerical DOI: 10.1002/adhm.201801331
DOI URL
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“The invasiveness of intracortical interfaces currently used today is responsible for the formation of an intense immunoresponse and inflammatory reaction from neural cells and tissues. this leads to a high concentration of reactive glial cells around the implant site, creating a physical barrier between the neurons and the recording channels. such a rejection of foreign analog interfaces causes neural signals to fade from recordings which become flooded by background noise after a few weeks. despite their invasiveness, those devices are required to track single neuron activity and decode fine sensory or motor commands. in particular, such quantitative and long-lasting recordings of individual neurons are crucial during a long time period (several months) to restore essential functions of the cortex, disrupted after injuries, stroke, or neurodegenerative diseases. to overcome this limitation, graphene and related materials have attracted numerous interests, as they gather in the same material many suitable properties for interfacing living matter, such as an exceptionally high neural affinity, diffusion barrier, and high physical robustness. in this work, the neural affinity of a graphene monolayer with numerous materials commonly used in neuroprostheses is compared, and its impact on the performance and durability of intracortical probes is investigated. for that purpose, an innovative coating method to wrap 3d intracortical probes with a continuous monolayer graphene is developed. experimental evidence demonstrate the positive impact of graphene on the bioacceptance of conventional intracortical probes, in terms of detection efficiency and tissues responses, allowing real-time samplings of motor neuron activity during 5 weeks. since continuous graphene coatings can easily be implemented on a wide range of 3d surfaces, this study further motivates the use of graphene and related materials as it could significantly contribute to reduce the current rejection of neural probes currently used in many research areas, from fundamental neurosciences to medicine and

neuroprostheses."
Moschetta, M., Lee, J. Y., Rodrigues, J., Podestà, A., Varvicchio, O., Son, J., … Capasso, A.. (2021). Hydrogenated Graphene Improves Neuronal Network Maturation and Excitatory Transmission. Advanced Biology

Plain numerical DOI: 10.1002/adbi.202000177
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"Graphene is regarded as a viable bio-interface for neuroscience due to its biocompatibility and electrical conductivity, which would contribute to efficient neuronal network signaling. here, monolayer graphene grown via chemical vapor deposition is treated with remote hydrogen plasma to demonstrate that hydrogenated graphene (hgr) fosters improved cell-to-cell communication with respect to pristine graphene in primary cortical neurons. when transferred to polyethylene terephthalate, hgr exhibits higher wettability than graphene (water contact angle of 83.7° vs 40.7°), while preserving electrical conductivity (?3 k? ?-1). a rich and mature network is observed to develop onto hgr. the intrinsic excitability and firing properties of neurons plated onto hgr appears unaltered, while the basic passive and active membrane properties are fully preserved. the formation of excitatory synaptic connections increases in hgr with respect to pristine graphene, leading to a doubled miniature excitatory postsynaptic current frequency. this study supports the use of hydrogenation for tailoring graphene into an improved neuronal interface, indicating that wettability, more than electrical conductivity, is the key parameter to be controlled. the use of hgr can bring about a deeper understanding of neuronal behavior on artificial bio-interfaces and provide new insight for graphene-based biomedical applications."
Liu, X., Lu, Y., & Kuzum, D.. (2018). High-Density Porous Graphene Arrays Enable Detection and Analysis of Propagating Cortical Waves and Spirals. Scientific Reports

Plain numerical DOI: 10.1038/s41598-018-35613-y
DOI URL
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"Cortical propagating waves have recently attracted significant attention by the neuroscience community. these travelling waves have been suggested to coordinate different brain areas and play roles in assisting neural plasticity and learning. however, it is extremely challenging to record them with very fine spatial scales over large areas to investigate their effect on neural dynamics or network connectivity changes. in this work, we employ high-density porous graphene microelectrode arrays fabricated using laser pyrolysis on flexible substrates to study the functional network connectivity during cortical propagating waves. the low-impedance porous graphene arrays are used to record cortical potentials during theta oscillations and drug-induced seizures in vivo. spatiotemporal analysis on the neural recordings reveal that theta oscillations and epileptiform activities have distinct characteristics in terms of both synchronization and resulting propagating wave patterns. to investigate the network connectivity during the propagating waves, we perform network analysis. the results show that the propagating waves are consistent with the functional connectivity changes in the neural

circuits, suggesting that the underlying network states are reflected by the cortical potential propagation patterns."
Ye, S., Yang, P., Cheng, K., Zhou, T., Wang, Y., Hou, Z., … Ren, L.. (2016). Drp1-Dependent Mitochondrial Fission Mediates Toxicity of Positively Charged Graphene in Microglia. ACS Biomaterials Science and Engineering

Plain numerical DOI: 10.1021/acsbiomaterials.5b00465
DOI URL
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"The unique physicochemical properties of graphene and its derivatives enable their application in the diagnostics and therapy of central nervous system (cns) diseases. however, the potential impacts of surface properties of functionalized graphene on microglia remain poorly understood. herein, we used graphene oxides (go), polyethylene glycol (peg)- and polyethylenimine (pei)-functionalized go, which possess different surface charges, to investigate their effects on microglia by focusing on mitochondrial dynamics. the positively charged go-pei was found to promote mitochondrial fission as observed in bv-2 cells with mitochondria labeled by dsred2-mito, indicating that alterations in mitochondrial dynamics depend on the surface properties of graphene. concurrent to mitochondrial fragmentation, treatment with positively charged go-pei induced an increase in mitochondrial recruitment of dynamin-related protein (drp1). additionally, go-pei treatment also led to apoptotic and autophagic cell death. however, drp1 silencing by small interfering rna (sirna) could effectively attenuate go-pei-induced apoptotic and autophagic cell death, indicating that mitochondrial fragmentation occurs upstream of go-pei-mediated toxicity in microglia. overall, our study indicated that positively charged go-pei might cause deleterious influence on the central immune homeostasis by drp1-dependent mitochondrial fragmentation, and provide the strategies for the rational design of graphene-based materials in neuroscience."
Balch, H. B., McGuire, A. F., Horng, J., Tsai, H. Z., Qi, K. K., Duh, Y. S., … Wang, F.. (2021). Graphene Electric Field Sensor Enables Single Shot Label-Free Imaging of Bioelectric Potentials. Nano Letters

Plain numerical DOI: 10.1021/acs.nanolett.1c00543
DOI URL
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"The measurement of electrical activity across systems of excitable cells underlies current progress in neuroscience, cardiac pharmacology, and neurotechnology. however, bioelectricity spans orders of magnitude in intensity, space, and time, posing substantial technological challenges. the development of methods permitting network-scale recordings with high spatial resolution remains key to studies of electrogenic cells, emergent networks, and bioelectric computation. here, we demonstrate single-shot and label-free imaging of extracellular potentials with high resolution across a wide field-of-view. the critically coupled waveguide-amplified graphene electric field (cage) sensor leverages the field-sensitive optical transitions in graphene to convert electric potentials into the optical regime. as a proof-of-concept, we use the cage sensor to detect native electrical activity from cardiac action potentials with tens-of-microns resolution, simultaneously map the propagation of these potentials at tissue-scale,

and monitor their modification by pharmacological agents. this platform is robust, scalable, and compatible with existing microscopy techniques for multimodal correlative imaging."
Shokoueinejad, M., Park, D. W., Jung, Y. H., Brodnick, S. K., Novello, J., Dingle, A., … Williams, J.. (2019). Progress in the field of micro-electrocorticography. Micromachines

Plain numerical DOI: 10.3390/mi10010062
DOI URL
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"Since the 1940s electrocorticography (ecog) devices and, more recently, in the last decade, micro-electrocorticography (?ecog) cortical electrode arrays were used for a wide set of experimental and clinical applications, such as epilepsy localization and brain-computer interface (bci) technologies. miniaturized implantable ?ecog devices have the advantage of providing greater-density neural signal acquisition and stimulation capabilities in a minimally invasive fashion. an increased spatial resolution of the ?ecog array will be useful for greater specificity diagnosis and treatment of neuronal diseases and the advancement of basic neuroscience and bci research. in this review, recent achievements of ecog and ?ecog are discussed. the electrode configurations and varying material choices used to design ?ecog arrays are discussed, including advantages and disadvantages of ?ecog technology compared to electroencephalography (eeg), ecog, and intracortical electrode arrays. electrode materials that are the primary focus include platinum, iridium oxide, poly(3,4-ethylenedioxythiophene) (pedot), indium tin oxide (ito), and graphene. we discuss the biological immune response to ?ecog devices compared to other electrode array types, the role of ?ecog in clinical pathology, and brain-computer interface technology. the information presented in this review will be helpful to understand the current status, organize available knowledge, and guide future clinical and research applications of ?ecog technologies."
Monaco, A. M., & Giugliano, M.. (2014). Carbon-based smart nanomaterials in biomedicine and neuroengineering. Beilstein Journal of Nanotechnology

Plain numerical DOI: 10.3762/bjnano.5.196
DOI URL
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"The search for advanced biomimetic materials that are capable of offering a scaffold for biological tissues during regeneration or of electrically connecting artificial devices with cellular structures to restore damaged brain functions is at the forefront of interdisciplinary research in materials science. bioactive nanoparticles for drug delivery, substrates for nerve regeneration and active guidance, as well as supramolecular architectures mimicking the extracellular environment to reduce inflammatory responses in brain implants, are within reach thanks to the advancements in nanotechnology. in particular, carbon-based nanostructured materials, such as graphene, carbon nanotubes (cnts) and nanodiamonds (nds), have demonstrated to be highly promising materials for designing and fabricating nanoelectrodes and substrates for cell growth, by virtue of their peerless optical, electrical, thermal, and mechanical properties. in this review we discuss the state-of-the-art in the applications of

nanomaterials in biological and biomedical fields, with a particular emphasis on neuroengineering."
Zhao, S., Liu, X., Xu, Z., Ren, H., Deng, B., Tang, M., … Duan, X.. (2016). Graphene Encapsulated Copper Microwires as Highly MRI Compatible Neural Electrodes. Nano Letters

Plain numerical DOI: 10.1021/acs.nanolett.6b03829
DOI URL
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"Magnetic resonance imaging (mri) compatible neural electrodes are important for combining high-resolution electrophysiological measurements with more global mri mapping of brain activity, which is critical for fundamental neuroscience studies, as well as clinical evaluation and monitoring. copper is a favorable material to use in mri because it has magnetic susceptibility close to water and tissues. however, the cytotoxicity of copper precludes its direct implantation for neural recording. here, we overcome this limitation by developing a graphene encapsulated copper (g-cu) microelectrode. the toxicity of copper is largely eliminated, as evidenced by the in vitro cell tests and in vivo histology studies. local field potentials and single-unit spikes were recorded from rodent brains with the g-cu microelectrodes. notably, the g-cu microelectrodes show no image artifacts in a 7.0 t mri scanner, indicating minimal magnetic field distortion in their vicinity. this high mri compatibility of our g-cu probes would open up new opportunities for fundamental brain activity studies and clinical applications requiring continuous mri and electrophysiological recordings."
Li, G., Yang, J., Yang, W., Wang, F., Wang, Y., Wang, W., & Liu, L.. (2018). Label-free multidimensional information acquisition from optogenetically engineered cells using a graphene transistor. Nanoscale

Plain numerical DOI: 10.1039/c7nr07264c
DOI URL
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"The optogenetic technique, which allows the manipulation of cellular activity patterns in space and time by light, has transformed the field of neuroscience. however, acquiring multidimensional optogenetic information remains challenging despite the fact that several cellular information detection methods have been proposed. herein, we present a new method to acquire label-free multidimensional information from optogenetically engineered cells using a graphene transistor. using a graphene film to form a strong densely packed layer with cells, the cellular action potentials were characterized as light-activated transistor conductance signals, which quantified the multidimensional optogenetic information. based on this approach, some important cellular optogenetic information, including electrophysiological state, cell concentration, expression levels of opsin and response to variable light intensity, were also precisely detected. furthermore, the graphene transistor was also used to distinguish cells expressing different channelrhodopsin-2 variants. our study offers a general detection method of multidimensional optogenetic information for extending the applications of the optogenetic technique and provides a novel sensor for the development of future biological prosthetic devices."
Liu, S., Zhao, Y., Hao, W., Zhang, X. D., & Ming, D.. (2020). Micro- and nanotechnology for neural electrode-tissue interfaces

. Biosensors and Bioelectronics

Plain numerical DOI: 10.1016/j.bios.2020.112645
DOI URL
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“Implantable neural electrodes can record and regulate neural activities with high spatial resolution of single-neuron and high time resolution of sub-millisecond, which are the most extensive window in neuroscience research. however, the mechanical mismatch between conventional stiff electrodes and soft neural tissue can lead to inflammatory responses and degradation of signals in chronic recordings. although remarkable breakthroughs have been made in sensing and regulation of neural signals, the long-term stability and chronic inflammatory response of the neural electrode-tissue interfaces still needs further development. in this review, we focus on the latest developments for the optimization of neural electrode-tissue interfaces, including electrode materials (graphene fiber-based and cnt fiber-based), electrode structures (flexible electrodes), nano-coatings and hydrogel-based neural interfaces. the parameters of impedance, charge injection limit, signal-to-noise ratio and neuron lost zone are used to evaluate the electrochemical performance of the devices, the recording performance of biosignals and the stability of the neural interfaces, respectively. these optimization methods can effectively improve the long-term stability and the chronic inflammatory response of neural interfaces during the recording and modulation of biosignals.”
Wu, T., Li, Y., Liang, X., Liu, X., & Tang, M.. (2021). Identification of potential circRNA-miRNA-mRNA regulatory networks in response to graphene quantum dots in microglia by microarray analysis. Ecotoxicology and Environmental Safety

Plain numerical DOI: 10.1016/j.ecoenv.2020.111672
DOI URL
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“Along with the increasing application of graphene quantum dots (gqds) in the fields of biomedicine and neuroscience, it is important to assess the probably adverse effects of gqds in the central nervous system (cns) but their underlying toxic mechanisms is still unclear. in this study, we evaluate the molecular mechanisms associated with circular rnas (circrnas) of nitrogen-doped gqds (n-gqds) and amino-functionalized gqds (a-gqds) damaging the cell viability and cellular structure in microglia by an integrative analysis of rna microarray. the differentially expressed circrna (decircrnas)-mirna-differentially expressed mrna (demrnas) regulatory networks were conducted in bv2 microglial cells treated with 25 µg/ml n-gqds, 100 µg/ml n-gqds and 100 µg/ml a-gqds. based on that, the protein-coding genes in each cerna network were collected to do bio-functional analysis to evaluate signaling pathways that were indirectly mediated by circrnas. some pathways that could play indispensable roles in the neurotoxicity of n-gqds or both two kinds of gqds were found. low-dosed n-gqds exposure mainly induced inflammatory action in microglia, while high-dosed n-gqds and a-gqds exposure both affect olfactory transduction and gabaergic synapse. meanwhile, several classical signaling pathways, including mtor, erbb and mapk, could make diverse contributions to the neurotoxicity of both two kinds of gqds. these circrnas could be toxic biomarkers or protective targets in neurotoxicity of gqds. more

importantly, they emphasized the necessity of comprehensive analysis of latent molecular mechanisms through epigenetics approaches in biosafety assessment of graphene-based nanomaterials."
Guo, C. X., Ng, S. R., Khoo, S. Y., Zheng, X., Chen, P., & Li, C. M.. (2012). RGD-peptide functionalized graphene biomimetic live-cell sensor for real-time detection of nitric oxide molecules. ACS Nano

Plain numerical DOI: 10.1021/nn301974u
DOI URL
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"It is always challenging to construct a smart functional nanostructure with specific physicochemical properties to real time detect biointeresting molecules released from live-cells. we report here a new approach to build a free-standing biomimetic sensor by covalently bonding rgd-peptide on the surface of pyrenebutyric acid functionalized graphene film. the resulted graphene biofilm sensor comprises a well-packed layered nanostructure, in which the rgd-peptide component provides desired biomimetic properties for superior human cell attachment and growth on the film surface to allow real-time detection of nitric oxide, an important signal yet short-life molecule released from the attached human endothelial cells under drug stimulations. the film sensor exhibits good flexibility and stability by retaining its original response after 45 bending/relaxing cycles and high reproducibility from its almost unchanged current responses after 15 repeated measurements, while possessing high sensitivity, good selectivity against interferences often existing in biological systems, and demonstrating real time quantitative detection capability toward nitric oxide molecule released from living cells. this study not only demonstrates a facial approach to fabricate a smart nanostructured graphene-based functional biofilm, but also provides a powerful and reliable platform to the real-time study of biointeresting molecules released from living cells, thus rendering potential broad applications in neuroscience, screening drug therapy effect, and live-cell assays. © 2012 american chemical society."
Liu, & Speranza. (2019). Functionalization of Carbon Nanomaterials for Biomedical Applications. C — Journal of Carbon Research

Plain numerical DOI: 10.3390/c5040072
DOI URL
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"Over the past decade, carbon nanostructures (cnss) have been widely used in a variety of biomedical applications. examples are the use of cnss for drug and protein delivery or in tools to locally dispense nucleic acids to fight tumor affections. cnss were successfully utilized in diagnostics and in noninvasive and highly sensitive imaging devices thanks to their optical properties in the near infrared region. however, biomedical applications require a complete biocompatibility to avoid adverse reactions of the immune system and cnss potentials for biodegradability. water is one of the main constituents of the living matter. unfortunately, one of the disadvantages of cnss is their poor solubility. surface functionalization of cnss is commonly utilized as an efficient solution to both tune the surface wettability of cnss and impart biocompatible properties. grafting functional groups onto the cnss surface consists in bonding the desired chemical species on the carbon nanoparticles via wet or dry processes leading

to the formation of a stable interaction. this latter may be of different nature as the van der waals, the electrostatic or the covalent, the ?-? interaction, the hydrogen bond etc. depending on the process and on the functional molecule at play. grafting is utilized for multiple purposes including bonding mimetic agents such as polyethylene glycol, drug/protein adsorption, attaching nanostructures to increase the cnss opacity to selected wavelengths or provide magnetic properties. this makes the cnss a very versatile tool for a broad selection of applications as medicinal biochips, new high-performance platforms for magnetic resonance (mr), photothermal therapy, molecular imaging, tissue engineering, and neuroscience. the scope of this work is to highlight up-to-date using of the functionalized carbon materials such as graphene, carbon fibers, carbon nanotubes, fullerene and nanodiamonds in biomedical applications."
Crowe, M., Lai, Y., Wang, Y., Lu, J., Zhao, M., Tian, Z., … Diao, J.. (2017). A Proteoliposome Method for Assessing Nanotoxicity on Synaptic Fusion and Membrane Integrity. Small Methods

Plain numerical DOI: 10.1002/smtd.201700207
DOI URL
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"Nanoparticles have received significant research interest for potential biomedical applications. before nanomaterials are administered to patients, their biocompatibility should be thoroughly evaluated through in vitro experiments and other preclinical procedures. many studies have sought to assess the toxicity of nanomaterials on synaptic transmission for neuroscience applications. however, it may be hard to perform such experiments because of the difficulty associated with delivering synthesized nanomaterials across cell membranes. here, an in vitro method is demonstrated that mimics neuronal exocytosis, which features protein-reconstituted liposomes for nanotoxicity testing; the effects of graphene oxide and pristine graphene on fusogenic activity and membrane integrity are examined. these results demonstrate the potential of this system as a novel in vitro platform for assessing the biocompatibility of nanomaterials, drug molecules, and other substances."
Liu, Y., & Duan, X.. (2020). Carbon-based nanomaterials for neural electrode technology. Wuli Huaxue Xuebao/ Acta Physico – Chimica Sinica

Plain numerical DOI: 10.3866/PKU.WHXB202007066
DOI URL
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"As a powerful tool for monitoring and modulating neural activities, implantable neural electrodes constitute the basis for a wide range of applications, including fundamental studies of brain circuits and functions, treatment of various neurological diseases, and realization of brain-machine interfaces. however, conventional neural electrodes have the issue of mechanical mismatch with soft neural tissues, which can result in tissue inflammation and gliosis, thus causing degradation of function over chronic implantation. furthermore, implantable neural electrodes, especially depth electrodes, can only carry out limited data sampling within predefined anatomical regions, making it challenging to perform large-area brain mapping. with excellent electrical, mechanical, and chemical properties, carbonbased nanomaterials, including graphene and carbon nanotubes (cnts), have been used as materials of

implantable neural electrodes in recent years. electrodes made from graphene and cnt fibers exhibit low electrochemical impedance, benefiting from the porous microstructure of the fibers. this enables a much smaller size of neural electrode. together with the low young's modulus of the fibers, this small size results in very soft electrodes. soft neural electrodes made from graphene and cnt fibers show a much-reduced inflammatory response and enable stable chronic in vivo action potential recording for 4-5 months. combining different modalities of neural interfacing, including electrophysiological measurement, optical imaging/stimulation, and magnetic resonance imaging (mri), could leverage the spatial and temporal resolution advantages of different techniques, thus providing new insights into how neural circuits process information. transparent neural electrode arrays made from graphene or cnts enable simultaneous calcium imaging through the transparent electrodes, from which concurrent electrical recording is taken, thus providing complementary cellular information in addition to high-temporal-resolution electrical recording. transparent neural electrodes from carbon-based nanomaterials can record well-defined neuronal response signals with negligible light-induced artifacts from cortical surfaces under optogenetic stimulation. graphene and cnt-based materials were used to fabricate mri-compatible neural electrodes with negligible artifacts under high field mri. simultaneous deep brain stimulation (dbs) and functional magnetic resonance imaging (fmri) with graph…"
Bramini, M., Rocchi, A., Benfenati, F., & Cesca, F.. (2019). Neuronal Cultures and Nanomaterials. In Advances in Neurobiology

Plain numerical DOI: 10.1007/978-3-030-11135-9_3
DOI URL
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"In recent years, the scientific community has witnessed an exponential increase in the use of nanomaterials for biomedical applications. in particular, the interest of graphene and graphene-based materials has rapidly risen in the neuroscience field due to the properties of this material, such as high conductivity, transparency and flexibility. as for any new material that aims to play a role in the biomedical area, a fundamental aspect is the evaluation of its toxicity, which strongly depends on material composition, chemical functionalization and dimensions. furthermore, a wide variety of three-dimensional scaffolds have also started to be exploited as a substrate for tissue engineering. in this application, the topography is probably the most relevant amongst the various properties of the different materials, as it may allow to instruct and interrogate neural networks, as well as to drive neural growth and differentiation. this chapter discusses the in vitro approaches, ranging from microscopy analysis to physiology measurements, to investigate the interaction of graphene with the central nervous system. moreover, the in vitro use of three-dimensional scaffolds is described and commented."
Govindhan, M., Liu, Z., & Chen, A.. (2016). Design and electrochemical study of platinum-based nanomaterials for sensitive detection of nitric oxide in biomedical applications. Nanomaterials

Plain numerical DOI: 10.3390/nano6110211
DOI URL
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“The extensive physiological and regulatory roles of nitric oxide (no) have spurred the development of no sensors, which are of critical importance in neuroscience and various medical applications. the development of electrochemical no sensors is of significant importance, and has garnered a tremendous amount of attention due to their high sensitivity and selectivity, rapid response, low cost, miniaturization, and the possibility of real-time monitoring. nanostructured platinum (pt)-based materials have attracted considerable interest regarding their use in the design of electrochemical sensors for the detection of no, due to their unique properties and the potential for new and innovative applications. this review focuses primarily on advances and insights into the utilization of nanostructured pt-based electrode materials, such as nanoporous pt, pt and ptau nanoparticles, ptau nanoparticle/reduced graphene oxide (rgo), and ptw nanoparticle/rgo-ionic liquid (il) nanocomposites, for the detection of no. the design, fabrication, characterization, and integration of electrochemical no sensing performance, selectivity, and durability are addressed. the attractive electrochemical properties of pt-based nanomaterials have great potential for increasing the competitiveness of these new sensors and open up new opportunities in the creation of novel no-sensing technologies for biological and medical applications.”
Kostarelos, K., Vincent, M., Hebert, C., & Garrido, J. A.. (2017). Graphene in the Design and Engineering of Next-Generation Neural Interfaces. Advanced Materials

Plain numerical DOI: 10.1002/adma.201700909
DOI URL
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“Neural interfaces are becoming a powerful toolkit for clinical interventions requiring stimulation and/or recording of the electrical activity of the nervous system. active implantable devices offer a promising approach for the treatment of various diseases affecting the central or peripheral nervous systems by electrically stimulating different neuronal structures. all currently used neural interface devices are designed to perform a single function: either record activity or electrically stimulate tissue. because of their electrical and electrochemical performance and their suitability for integration into flexible devices, graphene-based materials constitute a versatile platform that could help address many of the current challenges in neural interface design. here, how graphene and other 2d materials possess an array of properties that can enable enhanced functional capabilities for neural interfaces is illustrated. it is emphasized that the technological challenges are similar for all alternative types of materials used in the engineering of neural interface devices, each offering a unique set of advantages and limitations. graphene and 2d materials can indeed play a commanding role in the efforts toward wider clinical adoption of bioelectronics and electroceuticals.”
Pampaloni, N. P., Giugliano, M., Scaini, D., Ballerini, L., & Rauti, R.. (2019). Advances in nano neuroscience: From nanomaterials to nanotools. Frontiers in Neuroscience

Plain numerical DOI: 10.3389/fnins.2018.00953
DOI URL
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“During the last decades, neuroscientists have increasingly exploited a variety of artificial, de-novo synthesized materials with controlled nano-sized features. for instance, a renewed interest in the development of prostheses or neural interfaces was driven by the availability of novel nanomaterials that enabled the fabrication of implantable bioelectronics interfaces with reduced side effects and increased integration with the target biological tissue. the peculiar physical-chemical properties of nanomaterials have also contributed to the engineering of novel imaging devices toward sophisticated experimental settings, to smart fabricated scaffolds and microelectrodes, or other tools ultimately aimed at a better understanding of neural tissue functions. in this review, we focus on nanomaterials and specifically on carbon-based nanomaterials, such as carbon nanotubes (cnts) and graphene. while these materials raise potential safety concerns, they represent a tremendous technological opportunity for the restoration of neuronal functions. we then describe nanotools such as nanowires and nano-modified mea for high-performance electrophysiological recording and stimulation of neuronal electrical activity. we finally focus on the fabrication of three-dimensional synthetic nanostructures, used as substrates to interface biological cells and tissues in vitro and in vivo.”
Liu, X., Ren, C., Lu, Y., Hattori, R., Shi, Y., Zhao, R., … Kuzum, D.. (2019). Decoding ECoG High Gamma Power from Cellular Calcium Response using Transparent Graphene Microelectrodes. In International IEEE/EMBS Conference on Neural Engineering, NER

Plain numerical DOI: 10.1109/NER.2019.8717147
DOI URL
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“The ecog has been widely used in human brain research, while 2-photon microscopy has been broadly applied to basic neuroscience studies using animal models. bridging the gap between the 2-photon microscopy and the ecog is critical for transferring the vast amount of neuroscience knowledge obtained from animal models to human brain studies. here we develop an lstm recurrent neural network model to decode the ecog high gamma power from the cellular calcium activities obtained by multimodal ecog recordings and 2-photon calcium imaging enabled by transparent graphene microelectrode arrays. in both awake and anesthetized states, our model can successfully decode the stimulus-induced ecog high gamma power increases and its spontaneous fluctuations in the absence of stimulus.”
Lee, J. H., Shin, Y. C., Jin, O. S., Han, D. W., Kang, S. H., Hong, S. W., & Kim, J. M.. (2012). Enhanced neurite outgrowth of PC-12 cells on graphene-monolayer-coated substrates as biomimetic cues. Journal of the Korean Physical Society

Plain numerical DOI: 10.3938/jkps.61.1696
DOI URL
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“Neurons are electrically excitable cells that transmit and process information in the nervous system.

recently, the differentiation of human neural stem cells to neurons has been shown to be enhanced on graphene substrates, and differentiated neurons have been shown to be able to still carry electrical signals when stimulated by graphene electrodes. graphene films grown by using chemical vapor deposition were transferred onto glass coverslips by using the scooping method and were then coated with fetal bovine serum for a neuronal cell culture. the graphene substrates as biomimetic cues have been shown to enhance the neurite outgrowth of pc-12 cells. our findings suggest that graphene has a unique surface property that can promote neuronal cells, which should open tremendous opportunities in neuroscience, neural engineering and regenerative medicine. © 2012 the korean physical society."
Gutruf, P., Good, C. H., & Rogers, J. A.. (2018). Perspective: Implantable optical systems for neuroscience research in behaving animal models—Current approaches and future directions.
APL Photonics

Plain numerical DOI: 10.1063/1.5040256
DOI URL
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"Perspective: biomedical sensing and imaging with optical fibers-innovation through convergence of science disciplines apl photonics 3, 100902 (2018); doi.org/10.1063/1.5040861 invited article: enhanced four-wave mixing in waveguides integrated with graphene oxide apl photonics 3, 120803 (2018); doi.org/10.1063/1.5045509 single crystal diamond micro-disk resonators by focused ion beam milling apl photonics 3, 126101 (2018); doi."
Geracitano, L. A., Fagan, S. B., & Monserrat, J. M.. (2021). Analysis of global and Latin-American trends in nanotoxicology with a focus on carbon nanomaterials: a scientometric approach.
Journal of Chemical Technology and Biotechnology

Plain numerical DOI: 10.1002/jctb.6729
DOI URL
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"BACKGROUND: the scientific trends and developments in the field of nanotoxicology were analyzed through a scientometric approach. this study aimed to describe and unravel the main topics on nanomaterials concerning their potential toxicity. it was generated four databases: two for global nanotoxicological papers (ds1 and ds2) and two with a latin-american focus (la1 and la2). ds2 and la2 databases were constructed with studies dealing with the toxic effects of carbon nanomaterials. scientometric analyses were performed using citespace software. the following items were evaluated: frequencies, burst, centrality for co-citations of web of science categories, keywords, references, authors, and countries. results: global analysis resulted in a total of 29 798 papers for ds1 and 3835 for ds2. latin-american papers resulted in 1397 articles for la1 and 148 for la2. scientometric analyses indicated a specialization of the topics covered over time, ranging from general categories (such as chemistry) to more specialized ones (such as genetics or neurosciences). nano-silver prevailed in the nanotoxicological studies and graphene dominated in the field of carbon nanomaterials. in the last 5 years, a prominent growth has been observed in the number of studies that focus on the potential impact of nanomaterials on the environment. conclusion: the research efforts in nanotoxicology have

been mainly concentrated on assays that use nano-silver; meanwhile, in carbon nanomaterials, the focus has been concentrated on toxicological tests with graphene. overall, we stress the importance of nanotoxicology as a strategy to obtain scientific information that can aid in the environmental sustainability of nanotechnologies."
Abbasi, R.. (2018). Interpretable Machine Learning with Applications in Neuroscience. UC Berkeley Electronic Theses and Dissertations

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"This thesis is divided into two parts. in part i, we examine the properties of thin sheets of carbon and boron nitride. we begin with an introduction to the theory of elastic sheets, where the stretching and bending modes are considered in detail. the coupling between stretching and bending modes is thought to play a crucial role in the thermodynamic stability of atomically-thin 2d sheets such as graphene."
Wang, L., Jiang, T., Song, Y., Shi, W., & Cai, X.. (2014). Dopamine detection using a patch-clamp system on a planar microeletrode array electrodeposited by polypyrrole/graphene nanocomposites. Science China Technological Sciences

Plain numerical DOI: 10.1007/s11431-014-5465-9
DOI URL
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"To achieve a dopamine (da) response with high sensitivity and high signal-to-noise ratio (s/n) with a patch-clamp system, polypyrrole/graphene (ppy/gr) nanocomposites were steadily electrodeposited by an electrochemical method on a planar microelectrode array (pmea) fabricated by a standard micromachining process. the electrodeposition process was carried out by chronopotentimetry measurement scanning from 0.1 to 0.8 c/cm2 at the current of 2 ma; 0.5 c/cm2 was found to be optimal. the pmea modified by ppy/gr at the 0.5 c/cm2 exhibits remarkable properties; for instance, the standard deviation (sd) decreases from 8.4614×10 -11 to 5.62×10-11 a, reduced by 33.52%, and the sensitivity increases from 2566.88 to 76114.65 ?ammcm-2, 29.65 times higher than the bare pt (platinum). a good linear relationship between the current and da concentration in the range of 0.30 to 61.71 ?m was obtained, with a correlation coefficient of 0.997. the sensor is meaningful for neuroscience research and the treatment of neurological diseases. © 2014 science china press and springer-verlag berlin heidelberg."
Golparvar, A. J., & Yapici, M. K.. (2018). Graphene-coated wearable textiles for EOG-based human-computer interaction. In 2018 IEEE 15th International Conference on Wearable and Implantable Body Sensor Networks, BSN 2018

Plain numerical DOI: 10.1109/BSN.2018.8329690
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"Electrooculography (eog) is a well-known approach to analyze eye movement features. applications of eog can be found in various areas including medical diagnosis, neurosciences, control systems, sensors and interfaces for human-computer interaction (hci). however, standard gel-based electrodes limit wearability and portability which hinder the development of long-term eog monitoring applications. to overcome these limitations, we have employed graphene-coated fabric electrodes as suitable alternatives for the currently used silver/silver chloride (ag/agcl) ‘wet’ electrodes. proof of the concept is provided by side by side comparison of conventional electrodes and fabric electrodes in automatic blink detection with sequential multi-step thresholding algorithm. additionally, the eog biopotentials are converted into real-time digital signals which could be used as clock signals to facilitate the development of hci applications.”

Govindhan, M., & Chen, A.. (2016). Enhanced electrochemical sensing of nitric oxide using a nanocomposite consisting of platinum-tungsten nanoparticles, reduced graphene oxide and an ionic liquid. Microchimica Acta

Plain numerical DOI: 10.1007/s00604-016-1936-y
DOI URL
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“We describe a high-performance nitric oxide (no) sensor by using a nanocomposite consisting of platinum-tungsten alloy nanoparticles, sheets of reduced graphene oxide and an ionic liquid (ptw/rgo-il) that was deposited onto the surface of a glassy carbon (gc) electrode. the modified gc electrode exhibits excellent electrocatalytic activity toward the oxidation of no with a strong peak at 0.78 v vs. ag/agcl due to the synergistic effects of bimetallic ptw nanoparticles, reduced graphene oxide nanosheets and an ionic liquid. the sensor possesses a detection limit as low as 0.13 nm, high sensitivity (3.01 ?a ?m?1 cm2), and good selectivity over electroactive interferents that may exist in biological systems. the sensor was tested to selectively distinguish no in actual human serum and urine samples, confirming potential practical applications. in our perception, the approach described here may be extended to the fabrication of various kind of composites made from metal nanostructures, graphene and ionic liquids for medical and environmental analysis. [figure not available: see fulltext.]”

Monaco, A. M., & Giugliano, M.. (2015). Correction to Carbon-based smart nanomaterials in biomedicine and neuroengineering [Beilstein J. Nanotechnol. 5, (2014) 1849-1863] doi:10.3762/bjnano.5.196. Beilstein Journal of Nanotechnology

Plain numerical DOI: 10.3762/bjnano.6.51
DOI URL
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Vázquez-Guardado, A., Yang, Y., Bandodkar, A. J., & Rogers, J. A.. (2021). Author Correction: Recent advances in neurotechnologies with broad potential for neuroscience research (Nature Neuroscience, (2020), 23, 12, (1522-1536), 10.1038/s41593-020-00739-8). Nature Neuroscience

Plain numerical DOI: 10.1038/s41593-021-00813-9
DOI URL
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“In the version of this article initially published, errors occurred in the text and fig. 2 legend. in the paragraph beginning ‘advances in materials science are essential attempts…’ the platinum–silicone composites should have been described as ‘300 µm electrode diameter, 35 nm thickness, 1.4 ocm2 impedance, 57 µc/cm2 cics.’ in the paragraph beginning ‘microand nanofabrication techniques …’ the array of 360 recording sites for fast addressing should have been described as having sampling rates of ~277 hz. in the paragraph beginning ‘another area of progress …’ single- or few-layer sheets of graphene should have been described as having impedances of 1.6 ocm2 and 91 ocm2, respectively, while structures defined by colloidal sphere lithography and traditional photolithography should have been described as having impedances of 1.63 ocm2 and 0.14 oµm2, respectively. in the paragraph beginning ‘incorporating lenses and imaging …’ the phrase ‘at high sampling rates (16 hz) and fine resolution (~15 µm)’ should have cited ref. 74. in the fig. 2 legend, panel f should read ‘flexible array of 360 gold electrodes (300 × 300 µm2, spaced by 500 µm) supported by a backplane of active matrix electronics on a thin (25 µm) polyimide substrate for micro-electrocorticography (10 × 9 mm2) from the auditory cortex at a density of 400 electrodes cm–2.’ the references for panels g and h were swapped; they should read ‘g, ref. 34, springer nature; h, ref. 29, aaas.’ the errors have been corrected in the pdf and html versions of this article.”
Nasri, B., Wu, T., Alharbi, A., Gupta, M., Ranjitkumar, R., Sebastian, S., … Shahrjerdi, D.. (2017). Heterogeneous integrated CMOS-graphene sensor array for dopamine detection. In Digest of Technical Papers – IEEE International Solid-State Circuits Conference

Plain numerical DOI: 10.1109/ISSCC.2017.7870364
DOI URL
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“Understanding dopamine (da) signaling in the brain is essential for advancing our knowledge of pathological disorders such as drug addiction, parkinson’s disease, and schizophrenia. currently, fast-scan cyclic voltammetry (fscv) with carbon microfiber (cmf) electrodes is the method of choice in neuroscience labs for monitoring the concentration of phasic (transient) da release. this method offers sub-second temporal resolution and high specificity because the signal of interest occurs at a known potential. however, existing cmf electrodes are bulky, limiting the spatial resolution to single-site measurements. further, they are produced through manual processes (e.g. cutting cmfs under optical microscope), thus introducing significant device variability [1]. lastly, when long probes (3-to-5cm) are used to monitor da release in deep brain structures of large animals, environmental noise severely diminishes the detection limit [1]. to address these problems, we combine advances in nanofabrication with silicon chip manufacturing to create a heterogeneous integrated cmos-graphene sensor for accurate measurement of da with high spatiotemporal resolution (fig. 15.7.1).”
Tasnim, N.. (2018). An Integrated Study Towards Curing Neurodegenerative Disorders Using Materials Science and Stem Cell-based Tissue Engineering Approaches. ProQuest Dissertations and Theses

Show/hide publication abstract

“Neurodegenerative diseases affect around one billion people globally that are characterized by

irreversible degeneration of brain tissues. these diseases cause serious effects on patients degrading their brain functions and causing enormous physical and mental health issues. parkinson’s disease (pd) is one of the most common neurodegenerative disorder affecting millions of people worldwide which results from loss of dopaminergic (da) neurons in the mid-brain. unfortunately, no medical treatment is effective to date for these significant brain disorders, except some symptomatic therapies only focusing on improving the quality of patient’s life. two current approaches hold great promise in targeting pd as well as other neurodegenerative diseases, by surgically implanting electrodes for deep brain stimulation (dbs) and transplanting healthy neuronal cells at the site of tissue loss, due to disease in the brain. however, cells for transplantation need to be delivered via a scaffold. nerve regeneration in a scaffold of appropriate biomaterial is of great importance while being implanted inside the animal body for further clinical applications. in this dissertation, both approaches for treating pd were incorporated by in vitro studies using surface-engineering and tissue-engineering techniques. for the first approach, graphene oxide (go) coatings on commercially available 316l stainless steel (ss) surfaces was done to reduce the neurotoxicity of ss and modified surfaces showed hydrophilicity, biocompatibility, cell proliferation, and decreased reactive oxygen species (ros) expression with shsy-5y neuroblastoma cell lines. transplantation of stem cells in vivo is another approach for reducing the progression of pd by reversing the loss of affected da neurons. so, our second approach included differentiation of mesenchymal stem cells into da neurons using sonic hedgehog, fibroblast growth factor, basic fibroblast growth factor and brain-derived neurotrophic factor, while they were cultured within collagen coated three-dimensional (3d) graphene foams. 3d multilayer graphene scaffold could mimic the actual brain tissue environment and more closely exhibit morphologies, functions and other necessary characteristics compared to 2d culture on tissue culture plastic. the graphene-based scaffolds were not cytotoxic as cells seemed to retain viability and proliferated substantially during in vitro culture. these results suggest the utility of graphene-based mater…”
Rastogi, S. K., & Cohen-Karni, T.. (2019). Nanoelectronics for neuroscience. In Encyclopedia of Biomedical Engineering

Plain numerical DOI: 10.1016/B978-0-12-801238-3.99893-3
DOI URL
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“Characterizing the electrical activity between neuronal cells is crucial in understanding the complex processes in the brain, both in healthy and diseased tissue. neural interface technology that enables recording of the neuronal electrical activity as well as stimulation of the neurons has attracted great attention for both experimental and clinical applications. in this article, we discuss the fundamentals of the bioelectrical signals recording, and the advancements in the field of nano-bioelectronics, that is, the different kinds of materials and designs used to improve the cellular-device interface to enable recording and stimulation of the neuronal cells. furthermore, we discuss the development of synthetic biomaterials that enable fusion of electronics and bioactive scaffolds which are essential to regenerative engineering. we also discuss the technical and scientific challenges associated with these technologies, and the future prospects and opportunities.”
Salazar, P., Martín, M., Ford, R., O’Neill, R. D., & González-Mora, J. L.. (2018). Neurotransmitter microsensors for neuroscience. In Encyclopedia of Interfacial Chemistry: Surface Science and Electrochemistry

Plain numerical DOI: 10.1016/B978-0-12-409547-2.13917-4

DOI URL
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“Brain communication is mediated by exocytosis release of neurotransmitters into the synaptic cleft. over the last four decades researchers have explored diverse electrochemical techniques for sensing different oxidizable catecholamines such as dopamine, serotonin, and norepinephrine and their metabolites in individual cells, culture cells, and in in vivo applications. nowadays, carbon fiber microelectrodes are still the gold standard in neurochemical and neurophysiological studies although new materials, such as carbon nanotubes, polymers, graphene, and nanoparticles, have been introduced to improve their sensitivity, selectivity, and long-term stability. this article reviews the main issues involved in the design and application of such electrochemical microsensors for in vivo monitoring of key electroactive neurotransmitters.”

CHAPTER 4. Nanosensing the Brain. (2013)

Plain numerical DOI: 10.1039/9781849735414-00130
DOI URL
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“This chapter provides an overview of the features and application of emerging nanomaterials and miniaturized electronic circuits for in vitro neuroscience research. innovative detection methods and sensors based on nanomaterials offer unprecedented spatial and temporal resolution to elucidate patterns of neuronal firings less invasively and with better signal-to-noise ratio. the chapter begins with a brief discussion of nanoparticles and quantum dots{,} and their application in sensor technology. incorporation of one-dimensional nanostructures in cell cultures can be used to induce superior and directed neuronal adhesion and growth. possibilities for the use of nanowires as probes{,} nanoelectrodes{,} optical enhancers and electrical detectors are explored and the use of the amazing two-dimensional nanostructure graphene in the field of neuroscience is examined{,} including some of the challenges with incorporating graphene in sensing field effect transistors for detection of neural cells activity. example applications of nanotechnologies in neuroscience{,} ranging from sensing of structural deformation of cells to stimulation of neuroregeneration{,} are described. the chapter concludes with a perspective on the challenges and developments anticipated with the application of nanotechnologies in neuroscience.”

Liu, X., Lu, Y., & Kuzum, D.. (2018). Investigation of Propagating Cortical Waves and Spirals Recorded by High Density Porous Graphene Arrays. In Proceedings of the Annual International Conference of the IEEE Engineering in Medicine and Biology Society, EMBS

Plain numerical DOI: 10.1109/EMBC.2018.8512428
DOI URL
directSciHub download

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“Propagating waves along the cortical surface have recently attracted significant attention by the neuroscience community. however, whether these propagating waves imply network connectivity changes for the neural circuits is not known. in this work, we employ a high density porous graphene microelectrode array and perform in vivo experiments with rodents to investigate network connectivity during cortical propagating waves. the spatial-temporal analysis of the cortical recordings reveals various types of propagating waves across the recording area. network analysis results show that these propagating waves are consistent with the functional connectivity changes in the neural circuits, suggesting that the underlying network states are reflected by the cortical potential propagation patterns.”
Du, L., Hu, L., & Wu, C.. (2016). Micro/nano neuronal network cell biosensors. In Micro/Nano Cell and Molecular Sensors

Plain numerical DOI: 10.1007/978-981-10-1658-5_6
DOI URL
directSciHub download

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“Neuronal network cell biosensors were developed by coupling the neuronal network with multisite detection devices. in this chapter, we will mainly focus on three major issues, including the patterned growth of neuronal networks, principles of various detection devices, and the application of neuronal network-based biosensors in the field of neuroscience and biomedicine. in the culture of neuronal networks, several neuronal patterning techniques will be discussed in detail, such as photolithography, micro-contact printing, microfluidics, etc. the transfection methods were employed in the bioengineering of neuronal networks in order to modify the function of neuronal network. in the field of neuronal network-based biosensor, there are two kinds of multisite detection devices: microelectrode array (mea) and field-effect transistor (fet). the basic working principle of fet and its advantages will be presented. based on this knowledge, two other emerging fetsutilized nanomaterials (graphene fet and nanowire fet) will also be introduced. at the end, some examples of neuronal network-based biosensors will be presented by discussing their application in the neuroscience research and drug detection.”