Aykaç et al. Nanoscale Res Lett (2021) 16:65
https://doi.org/10.1186/s11671-021-03519-w

Nanoscale Research Letters

NANO REVIEW

An Overview on Recent Progress of Metal Oxide/Graphene/CNTs-Based Nanobiosensors

Ahmet Aykaç[1,2*], Hazal Gergeroglu[3], Büşra Beşli[2], Emine Özge Akkaş[2], Ahmet Yavaş[4], Saadet Güler[4], Fethullah Güneş[4] and Mustafa Erol[5]

Abstract

Nanobiosensors are convenient, practical, and sensitive analyzers that detect chemical and biological agents and convert the results into meaningful data between a biologically active molecule and a recognition element immobilized on the surface of the signal transducer by a physicochemical detector. Due to their fast, accurate and reliable operating characteristics, nanobiosensors are widely used in clinical and nonclinical applications, bedside testing, medical textile industry, environmental monitoring, food safety, etc. They play an important role in such critical applications. Therefore, the design of the biosensing interface is essential in determining the performance of the nanobiosensor. The unique chemical and physical properties of nanomaterials have paved the way for new and improved sensing devices in biosensors. The growing demand for devices with improved sensing and selectivity capability, short response time, lower limit of detection, and low cost causes novel investigations on nanobiomaterials to be used as biosensor scaffolds. Among all other nanomaterials, studies on developing nanobiosensors based on metal oxide nanostructures, graphene and its derivatives, carbon nanotubes, and the widespread use of these nanomaterials as a hybrid structure have recently attracted attention. Nanohybrid structures created by combining these nanostructures will directly meet the future biosensors' needs with their high electrocatalytic activities. This review addressed the recent developments on these nanomaterials and their derivatives, and their use as biosensor scaffolds. We reviewed these popular nanomaterials by evaluating them with comparative studies, tables, and charts.

Keywords: Nanobiosensors, Metal oxides, Graphene, Carbon nanotubes, Nanohybrids biosensor scaffolds

Introduction

A biosensor is a diagnostic device that converts signals from a biological analyte into a measurable and distinguishable electrical signal for a qualitative and/or a quantitative detection of the analyte that may embroiled with other physicochemical substances [1]. The first known biosensor was developed by Clark et al. [2] for the detection of oxygen, and the first amperometric enzyme electrode developed by Clark and Lyons [3] was an enzyme-based glucose biosensor. Over the years, enzyme-based, tissue-based, deoxyribonucleic acid (DNA)-based, and thermal, optical, electrochemical biosensor types have been developed. Biosensors give more stable and precise results than the traditional methods in some applications like clinical diagnosis, biomedical sector, food production, and analysis [2, 4]. Moreover, with such characteristics as specificity, selectivity, and cost savings with a simple operation, real-time analysis, and continuous use, various types of biosensors were developed rapidly through the second half of the century and have become widely used in related medical, environmental, and forensic fields [5]. Their intensive use in these critical application areas has emerged some anticipated features from a biosensor as high sensitivity, stability, high selectivity, long service life, repeatability, simplicity and cheapness, wide measuring range, and the fast response time [6].

*Correspondence: ahmet.aykac@ikcu.edu.tr
[1] Department of Engineering Sciences, Izmir Katip Çelebi University, 35620 Izmir, Turkey
Full list of author information is available at the end of the article

According to the International Union of Pure and Applied Chemistry (IUPAC), biosensors contain three main components: biological recognition element, transducer component, and electronic system that is often combined with a transducer. As integrated receptor–transducer devices, biosensors are able to provide selective quantitative or semiquantitative analytical information using a biological recognition element [7] (Fig. 1). Within this frame, nucleic acids, enzymes, antibodies, receptors, microorganisms, cells, tissues, and even biomimetic structures may be utilized as bioreceptor for biological detection.

The design of a biosensor is of great importance for a quick and convenient testing under any circumstance or any position that analyte may emerged. Within that design, transducer component materials have also a significant effect on the detection quality. The physical transducers vary significantly with the quantifiable signal source and utilize mostly optical and electrochemical systems [5]. The physicochemical, electronic/optical/electrochemical features of the material used as a physical transducer directly affect biosensors' performance. Additionally, biosensors' efficiency and effectiveness are determined by the matrices, mediators, and stabilizers used for enzyme immobilization. Therefore, the properties of the material from which the physical transducer component is produced play a critical role in obtaining such features as high signal stability and repeatability of biosensors and in their selectivity. Among aforementioned three components of a biosensor, this review mainly focuses on recent development on surface functionalization of transducer components using nanomaterials.

Transducers can be classified mainly into four classes: electrochemical, bioluminescent, piezoelectric, calorimetric, and optical. The surface of transducer can be modified by using many different functional materials so as to improve the sensor performance. Controlling the structure, morphology, and properties of these materials can also help in the same manner. Among these materials, nanosized materials, referred as nanomaterials, have a great potential to be crucial for the development of novel, adaptive, and highly sensitive biosensors for a broader application area with their unique size-dependent properties such as large surface area, improved electrical conductivity, and high chemical reactivity. Considering these extra-ordinary properties, nanomaterials have been one of the preferred candidates to meet the desired requirements for the construction of highly sensitive biosensors [6].

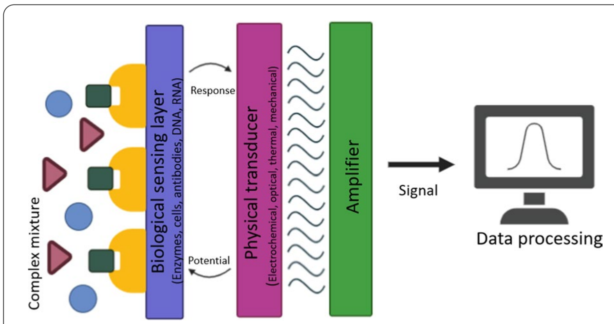

Fig. 1 Schematic representation of biosensors

To be considered as a nanomaterial, at least in one dimension the size of a nanomaterial should be in between 1 and 100 nm [8]. Due to their highly minute size, in nanomaterials most of the atoms exist close to the surface or present on the surface. These nanoparticles (NPs), duly gaining remarkable features as enhanced physicochemical properties, higher surface area, shortened distance of electrons, bring out a significant difference compared to that of their bulk-sized counterparts. Thus, boosted performances would be maintained in the optical, thermal, electrical, and magnetic properties of those nanoscale materials to be highly effective for use as a biosensor component. Moreover, nanosized materials having higher surface area provide a suitable space for the immobilization of a sufficient number of bioreceptors on the surface of electrodes. Therefore, researchers have recently shown a great interest in the production, characterization, and use of nanomaterials for biosensor applications [9, 10].

Among all nanomaterials, MONs, graphene and its derivatives, and CNTs have stood out for their unique features [11, 12]. MONs exhibit significant catalytic properties due to their impressive morphological diversity, nontoxicity, and biocompatibility. It should also be noted that MONs provide a suitable structure for the immobilization of biomolecules.

Their crystal lattice allowing modification of the cell parameters and electrochemical properties due to quantum confinement effect, and the controllability of the bandgap by altering their surface properties affecting conductivity and chemical reactivity made them highly potential to be used as biosensing elements and differentiate MONs from their bulk counterparts [12, 13]. Moreover, to improve these properties further by forming a composite structure, MONs have recently been extensively combined with carbon nanomaterials such as graphene and CNTs to form a nanohybrid structure. Doing so improves the electrochemical reactivity for detection and diagnostic to meet the future requirements such as sensitivity and selectivity of a biosensor [14].

The hybridization of these carbon nanomaterials with MONs provides the production of advanced biosensors with one or more functions equipped with superior optical, magnetic, and electrical properties [14–16]. Graphene and its derivatives can be easily integrated with other nanomaterials to create nanohybrid materials to obtain desired electrochemical activity [13, 17, 18]. For instance, in many applications, graphene is regarded as a useful tool to promote electron transfer to proteins' redox response [19]. However, graphene's physical stability in the biological environment and its toxicity assessment to cells is still controversial [20–22]. On the other hand, CNTs, unlike graphene, have variant optical features due to their changing chirality making them advantageous compared to graphene in optical biosensing applications [23]. CNTs, having outstanding electrochemical ability, are readily chemically modifiable, and have high surface area to volume ratio like graphene [24]. In terms of surface properties, when exposed to an ambient, although graphene is exposed with its all volume due to its monolayer two-dimensional nature, this exposure is limited in the case of one-dimensional (1D) CNTs [25]. Additionally, it has been reported many times in previous studies that graphene has higher selectivity against interferences due to its excellent biomolecular sensing and signal-to-noise ratio properties compared to that of CNTs. It is mainly due to the metal-free graphitic edges of graphene with a high surface area. Nevertheless, problems as signal perturbation are exist in CNTs-based biosensors due to the presence of residual metal catalysts [25]. With all aforementioned aspects, nanohybrids formed by the combination of graphene and/or CNTs structures might play a vital role in the design of advanced biosensors, and compensation of disadvantages of both materials by forming a composite structure from them would overcome these problems and the detection could be maximized. Taking advantage of the cooperation created by the composite structure of MONs, graphene, and CNTs, it seems indispensable to provide an improved signal amplification and to prepare advanced bioaffinity strategies, resulting in development of improved biosensing devices to meet future requirements. Hence, within the scope of this review, it has been focused on recently realized MONs, graphene and CNTs-based biosensors. Moreover, the critical role of using these nanomaterials, not alone, but also together, in the production of biosensors with superior properties obtained by their combination has been discussed. By evaluating future expectations and challenges, we would like to put forward an alternative perspective for further studies.

Metal Oxides Nanostructures-Based Biosensors

Metal oxides (MOs) have been an essential candidates for sensor applications since initial biosensor studies in 1954 [26, 27]. MOs can be synthesized in various nanomorphologies such as NPs [28, 29], nanofibers [30], nanospheres (NSs) [31], nanorods [32], nanotubes and nanowires (NWs) [33], nanosheets [34, 35]. Besides morphological versatility, MONs offer some advantages: high surface/volume ratio, nontoxicity, good biocompatibility, chemical stability, excellent selectivity, electron and phonon limitation, high catalytic efficiency, and strong adsorption ability, physicochemical interface features [36–40]. Additionally, MONs can be produced via relatively easy and cost-effective methods such as radio frequency (RF) magnetron sputtering [41–43], thermal evaporation [44, 45], plasma-enhanced chemical vapor deposition (PECVD) [46, 47], molecular beam epitaxy [48], and solgel technique [49], electrochemical deposition process [50], and hydrothermal method [51]. These significant features have made MONs one of the most desired materials for biomedical applications and biosensor market. Publications on MONs from 2010 to 2020 were analyzed and are presented in Fig. 2 with a pie chart presented as the distribution of biomedical applications of MONs.

On the other hand, predominantly in recent years, various MONs such as ZnO, Fe_3O_4, CuO, NiO, TiO_2, MgO have been continuously produced as versatile and functional biosensors for a long time [44, 52]. Among the MONs, ZnO and Fe_3O_4, due to their widespread applications, are considered to be prominent members in biosensor construction [53, 54].

ZnO Nanostructures

ZnO nanostructures play an extensive role in the fabrication of novel nanostructured biosensors due to their unique properties including high isoelectric point (IEP ~ 9,5) [55], wide band-gap, useful electron communication feature, high chemical stability, good biocompatibility, and piezoelectricity. Especially, its high isoelectric point clearly explains why ZnO is the most prevalent metal oxide employed for biosensing technologies. Additionally, ZnO can be utilized in all clinical or nonclinical applications since it is environmentally friendly and safe material [53, 54, 56]. For instance, Akhtar et al. [57] developed a reagent-less optical biosensor based on the mechanism of fluorescence enhancement for the amyloid detection in the diagnosis of neurodegenerative diseases like Alzheimer's disease and insulin-dependent type II diabetes by utilizing flower-like ZnO nanostructures which have a greater surface area. Besides, ZnO nanoflower has been reported to be a good performance-enhancing material that provides a faster and cost-effective amyloid biosensor [57]. Further, a glucose biosensor using ZnO nanorod-based field-effect transistor (FET) related to wearable continuous glucose monitoring application for individuals with diabetes was fabricated by Zong and Zhu [54] via hydrothermal method. They

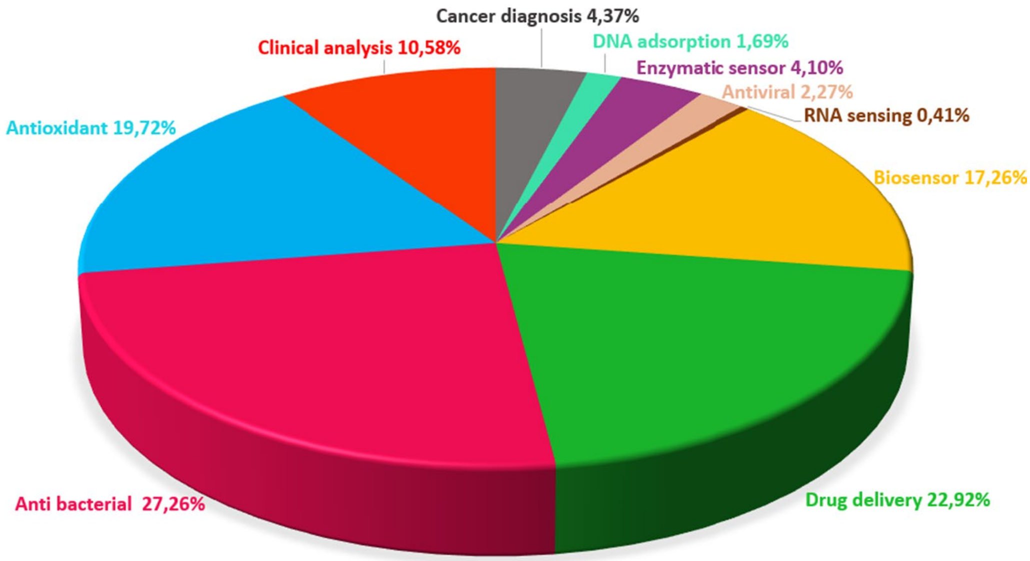

Fig. 2 Pie chart showing the distribution of MONs in biomedical applications

achieved high-performance biosensor with a high sensitivity of 1.6 mA/μM cm^2 with a tiny sensing area of 180 μm^2 and a detection limit of 1 μM under the favor of the large surface-to-volume ratio of ZnO nanorods [54]. Sahyar et al. [58] developed a new Ag-doped ZnO NPs-based biosensor for early detection of meat spoilage. As a result of their analysis with an enzyme xanthine oxidase (XO)-modified electrode (nanoAg-ZnO/polypyrrole (PPy)/pencil graphite electrode), they stated that the enzyme biosensor they obtained showed high selectivity with 0.03μA/mM sensitivity and 0.07 μM low detection limit [58].

In another study, Yue et al. [59], successfully developed an ideal dopamine (DA) biosensor based on Au NPs-ZnO nanocone-arrays/graphene foam electrodes. In their characterizations, they proved that the electrode they modified has a high sensitivity (4.36 μA μM^{-1}) and a low detection limit (0.04 μM, S/N = 3) in detecting DA. Furthermore, they reported that the ZnO nanocone-based electrode exhibited excellent selectivity, good reproducibility, and stability under uric acid (UA) interference. They also emphasized that the electrode has tremendous potential in medicine and health care [59]. In the same year, Qian et al. developed an electrochemical glucose detector using ZnO NPs. The sensor consists of a CeO_2 nanowhisker decorated with ZnO NPs, and they stated that the ZnO/CeO_2 nanocomposite structure has an extensive surface area, nontoxicity, and high electrocatalytic activity. The nanocomposite showed an extraordinary performance for detecting glucose with a linear range of 0.5–300 μM and a limit of detection (LOD) of 0.224 μM (40 ppb). They also emphasized that the nanocomposite sensor showed an excellent linear relationship between current signal intensity and glucose concentration ($R^2 = 0.99944$) [60]. Another glucose biosensor was developed by Rafiee et al. [61] by combining graphene nanoplatelets (GNPs), known for their high conductivity and chemical stability, and ZnO NWs, known to be sensitive to glucose. In their study, they modified the structure of the device like a glucose biosensor by synthesizing ZnO NWs on thin films of GNPs in three different concentrations (0.5, 1, and 2 mg), defined as GNP1, GNP2, and GNP3. The system showed that the dual effect of ZnO NWs and GNPs led to the perfect improvement for an efficient glucose biosensor. For instance, they noted that for low glucose concentrations, the device's response increased as the amount of graphene in solution increased, and the sensor response time decreased with an increase in the number of GNPs. Moreover, they reported that long-term stability, namely consistent resistance to concentration relation, an important criterion for an ideal biosensor, was observed in samples modified with GNPs after exposure to 30 mg/dL glucose over 30 days. Consequently, they presented an ideal glucose biosensor with useful features: response time of 5 s, a detection range of 0.003–30,000 mg/dL, and long-term electrical stability [61]. In addition to these studies, some other recent studies using different ZnO nanostructures for the detection of various enzymes are given in Table 1.

Table 1 Selected recent biosensor studies based on nanomaterials including ZnO nanostructures

Nanomaterials and morphology	Types of biosensors	LOD	Sensitivity	Linear detection range	Analyte detected	Applications	References
ZnO nanoflower	Optical fluorescence	2.76 μg	1.388 mg/ml	-	Amyloids	Neurodegenerative disorders (Alzheimer, diabetes)	Akhtar et al. [57]
CuO-modified ZnO nanorods (NRs)	Electrochemical Amperometric	0.40 μM	2961.7μA mM^{-1} cm^{-2}	0.001–8.45 mM	Glucose	Diabetes	Ahmad et al. [62]
ZnO NRs	Electrochemical-Potentiometric	NR	164.4 mV/decades	1 μM–10 mM	Glucose	Diabetes	Wahab et al. [63]
ZnO NRs	FET	1 μM	1.6 mA/(μM-cm^2)	-	Glucose	Diabetes	Zong et al. [54]
Cu-doped ZnO NPs	Electrochemical Impedimetric	10^{-9} M	0.06 μF	10^{-9} M-10^{-5} M	Glucose	Diabetes	Mahmoud et al. [64]
$ZnO/CuO/Co_3O_4$ NPs	Electrochemical	9.7 ± 0.5 pM	36.98 μA μM^{-1} cm^{-2}	0.05 nM–0.05 mM	Melamine	Food safety	Alam et al. [65]
ZnO Nanotube	Optical-Fluorescence	70 μM	3.5%·mM^{-1}	0.1–15 mM	Glucose	Diabetes	Mai et al. [66]
ZnO nanosheets	FET	210 nM	0.27 mA/M/cm^2	10 nM–1 mM	Formaldehyde	Life protection	Kim et al. [67]
CNT-embedded ZnO nanofiber	Electrochemical	5.368 zM	21.61 (KΩ μg^{-1} mL^{-1}) cm^{-2}	10 zM^{-1} μM	Atrazine	Environmental protection	Supraja et al. [68]
ZnO NWs/Graphene nanoplates	Electrochemical	0.003 mg/dL	–	0.003–30,000 mg/dL	Glucose	Diabetes	Rafiee et al. [61]
Flower-like ZnO nanosheets/Graphene	Electrochemical	0.0093 μM,	–	0.02–216 μM	Epinephrine	Clinical applications	Zhu et al. [69]
ZnO NRs/Carbon fibers	Electrochemical	0.45 fg/mL	6.09 μA/(g/mL)	1 fg/mL–1 μg/mL	Cortisol	Medical textile industry	Madhu et al. [70]
RuO_2 doped ZnO NPs	Electrochemical Amperometric	96.0 ± 5.0 pM	5.42 μA μM^{-1} cm^{-2}	0.1 nM–0.01 mM	l-glutamic acid	Food safety	Alam et al. [71]
ZnO quantum dots/BiOI nanoflower	Photoelectrochemical	3.3 pM	–	0.01- 500 nM	Histone acetyltransferase	Clinical applications	Chen et al. [72]

Considering the current studies shown in Table 1, it can be expressed that ZnO structures produced through numerous methods with varying morphologies, and it continues to be widely used due to its ease in integration into composite structures. Production alternatives and morphological versatility, as well as forming nanocomposite and nanohybrid structures with other nanomaterials, especially with carbon nanostructures, offer an extraordinary potential to ZnO structures in terms of meeting the expected properties with full efficiency in an ideal biosensor.

Fe_3O_4 Nanostructures

In recent years, Fe_3O_4 nanostructure has aroused much interest in many promising applications, including biosensors, drug delivery, cell separation, and pharmacy, thanks to its superior properties such as good biocompatibility, low toxicity, superparamagnetism, catalytic activity, and the ease of preparation and modification process. Magnetic Fe_3O_4 NPs are appropriate for the immobilization of desired biomolecules such as enzymes [73–76] due to simple separation ability from the medium by its magnetic nature [77]. Fe_3O_4 magnetic NPs and their derivatives have been extensively used in biosensor technology, and various attractive studies have been discussed in the literature [75, 78]. In this context, Sanaeifar et al. [75] designed a new electrochemical biosensor for glucose detection. They evaluated the electrochemical performance of the nanocomposite prepared by dispersing Fe_3O_4 magnetic NPs, which were produced via the co-precipitation method in polyvinyl alcohol (PVA). They reported that Fe_3O_4 NPs in the PVA matrix, having excellent catalytic properties against immobilized glucose oxidase, increased the electron transfer rates between the enzyme and the electrode surface. The bioelectrode that prepared could measure glucose in the range of 5×10^{-3} to 30 mM with a sensitivity of 9.36 μA mM^{-1} and displayed a detection limit of less than 8 μM [75]. Dong et al. [79] developed Ag/Fe_3O_4 core–shell NSs-based sensors, produced via simple solvothermal approach, to be used in the detection of hydrazine for environmental protection. They reported that the high-performance hydrazine sensor has a 2 s response time, a linear range of 0.25–3400 μm, a sensitivity of 270 μA mM^{-1} cm^{-2}, and a detection limit of 0.06 μM. Comparing the figures, a hydrazine sensor that is far superior to other sensors in the literature developed [79].

In another study, Sriram et al. [80] developed Fe_3O_4 NSs/reduced graphene oxide (rGO) nanocomposite to detect UA in urine and blood serum samples. As a result of their electrochemical analysis, Fe_3O_4 NSs/reduced graphene oxide (rGO) nanocomposites, with high stability and repeatability, showed an excellent electrochemical reduction peak. Moreover, they emphasized that the linear range of the UA sensor they developed was between 0.02 and 783.6 μM, and the LOD was 0.12 nM [80]. Likewise, a new biosensor for DA detection by combining graphene oxide (GO) and Fe_3O_4 was developed by Cai et al. [81]. In their study, they successfully synthesized Fe_3O_4/GO/pristine graphene (PG) ternary composite by dispersion and co-precipitation methods. Later, they deposited the nanocomposite on to the working electrode, glassy carbon electrode (GCE), by dropping technique. The highest peak current is recorded for Fe_3O_4/GO/PG structures in cyclic voltammograms (CVs). Similarly, they reported that the highest peak current in DA presence belongs to Fe_3O_4/GO/PG/GCE sample. They also highlighted an increase in the peak current for the Fe_3O_4/GO/PG/GCE sample due to increased DA concentration. Finally Cai et al. stated that the electrochemical sensor could effectively be used in DA detection [81]. Some representative studies on Fe_3O_4 nanostructures as a biosensor component are given in Table 2.

Despite their superior properties, magnetic Fe_3O_4 nanostructures have restrictive problems in biosensor and biological applications. Due to their high surface energy, chemical reactivity, and strong magnetic interactions, they are incredibly prone to agglomeration, creating difficulties in stabilizing Fe_3O_4 magnetic nanostructures. To overcome this problem, the surface of Fe_3O_4 nanostructures is coated with the polymer layers [95]. However, coating the surface with the polymer may decrease efficiency in terms of electrochemical biosensor applications. Thus, in stabilizing magnetic Fe_3O_4 nanostructures, biomolecules such as genes, cells, enzymes, proteins, and other essential nanostructures (graphene, CNTs, quantum dots, NPs, etc.) can be used. Therefore, it can be predicted that complex nanohybrid and nanocomposite systems based on magnetic Fe_3O_4 nanostructures will become a phenomenon in producing new generation biosensors in the future.

After all, MOs-based biosensors incorporating various nanostructures present unique and novel functions in practical and industrial applications. Nanostructures of MOs strongly impact devising highly sensitive, rapid, and stable biosensors due to their peerless properties. Besides, each kind of nanostructures and oxides of metals include its advantages. Hence, new advancements in sensing devices are likely to take place in biotechnology. Additionally, it is seen that nanocarbon structures have been given much space in recent studies, and MOs are used together with them. Therefore, the second part of this work will focus on the two most commonly used nanocarbon (graphene and CNTs) in biosensors.

Graphene and Its Derivatives-Based Biosensors

Graphene is one of the most popular allotropes of carbon, just like graphite, CNTs, fullerene, diamond. It is a two-dimensional layer of sp^2-hybridized carbon atoms. After the discovery of graphene by Geim and Novoselov, it has drawn huge attention worldwide in various disciplines such as transparent electrodes, energy storage, drug delivery, biosensors, supercapacitors, batteries, and catalysis [96, 97]. Graphene as many other nanomaterials can be synthesized by top-down (mechanical exfoliation, chemical exfoliation, and chemical synthesis) and bottom-up methods (pyrolysis, epitaxial growth, chemical vapor deposition (CVD)) [97]. Different production methods lead to the presence of numerous graphene-like materials such as graphene, GQDs, GO, rGO, graphene nanoribbons (GNRs), nanomesh, nanosheets [98]. The frequently used derivatives are shown in Fig. 3.

Graphene has good thermal conductivity (5000 W/mK), high electron mobility in room temperature (250,000 cm^2/V s), large surface area (2630 m^2/g), high modulus of elasticity (21 T Pa), and good electrical conductivity [99]. Furthermore, the atomic thickness of the graphene sheets and their high surface area provides material sensitivity against the changes in conditions. Thus, graphene's surface features, in which every atom can be directly contacted, make it sensitive to the environment. Therefore, it is an excellent candidate for sensor applications in comparison to the other materials [, , 4, 100, 101]. The last decade studies related to graphene and its derivatives were analyzed and are presented in Fig. 102 with a pie chart that presented the distribution of biomedical applications of graphene. It can be stated that researchers mostly focus on the field of biosensors due to the features of graphene mentioned above.

As mentioned in the first section, some biosensors are prepared by combining graphene and graphene derivatives with MONs. In this part of the review, we focus on biosensors based on graphene and its derivatives. A general representation and mechanism of graphene-based biosensors are shown in Fig. 5. Here, analytes interacting with the functional group (s) on

Table 2 Selected recent biosensor studies based on nanomaterials with Fe_3O_4 nanostructures

Nanomaterials and Morphology	Types of biosensor	LOD	Sensitivity	Linear detection range	Analyte detected	Applications	References
Fe_3O_4 NPs	Electrochemical-Amperometric	8 µM	9.36µA mM^{-1}	5×10^{-3}–30 mM	Glucose	NR	Sanaeifar et al. [75]
Fe_3O_4/Graphene/Pt flowers nanocomposite	Electrochemical Amperometric	1.58 µM	6.875 µA/mM	0.1 ~ 2.4 mM	H_2O_2	Clinical and nonclinical applications	Zhao et al. [82]
Fe_3O_4/rGO nanocomposite	Electrochemical	106.5 µA mM^{-1}	2.645 µA mM^{-1}	0.5–10 mM	Glucose	Diabetes	Wang et al. [83]
Fe_3O_4/CNTs/PPy/Pd NPs	Electrochemical	1.417×10^{-9} M	–	2.247×10^{-9} M–2.752×10^{-7} M	Triclosan	Clinical and nonclinical applications	Zheng et al. [84]
Fe_3O_4/Graphene/Chitosan	Electrochemical Voltammetric	0.08 µM	–	0.4–2.0 µM	Ammonium	Environmental protection	Yu et al. [85]
Hollow magnetic Pt/Fe_3O_4/C NSs	Electrochemical Amperometric	0.43 µM	48.8 nA μM^{-1} cm^{-2}	0.5–60 µM	Sarcosine	Prostate cancer	Yang et al. [86]
Graphene quantum dots (GQDs)/Fe_3O_4/MoS_2 nanosheets	Optical Fluorescence	1.19 nM	–	2–64 nM	Epithelial cell adhesion molecule	Cancer diagnosis	Cui et al. [87]
Fe_3O_4/Au core–shell NPs	Optical Colourimetric	2 µM	–	5.0–70.0 µM	Catechol	Environmental protection	Karami et al. [88]
Cyclodextrin (CD)/Multi-walled carbon nanotubes (MWCNTs) Fe_3O_4/Chitosan/MWCNTs	Electrochemical Amperometric	19.30 µM	23.59 µA mM^{-1} cm^{-2}	40 µM– 1.04 mM	Glucose	Diabetes	Peng et al. [89]
PtTi/GO/Fe_3O_4/MWCNTs-Fe_3O_4 nanocomposite	Electrochemical Aptasensor	25.3 pg mL^{-1}	–	0.05–100 ng mL^{-1}	Penicillin	Clinical applications	Guo et al. [90]
Methylcellulose/GO/Fe_3O_4 nanocomposite hydrogel	Electrochemical Potentiometric	0.17 µM	0.9093 µA/µM	0.5–140 µM	UA	Clinical applications	Sohouli et al. [91]
Fe_3O_4/Au nanoflowers	Surface-enhanced Raman scattering (SERS) Aptasensor	0.40 pg·mL^{-1}	–	0.0001–100 ng·mL^{-1}	Aflatoxin B1	Food safety and quality	He et al. [92]
Fe_3O_4 Nanoroses/Mesoporous GO sheets	Electrochemical	0.1 mM	1183.6 µA·mM^{-1} ·cm^{-2}	0.1–16 mM	Glucose	Food and biomedical industry	Yao et al. [93]
PPy-coated Fe_3O_4/MWCNTs	Electrochemical	0.0230 µM	-	21.3–201 µM	Atorvastatin	Clinical applications	Tavousi et al. [94]

the graphene surface, and electrochemical, optical, or other outputs can be obtained based on this interaction [96, 97, 103]. For instance, Mani et al. [104] developed a ternary nanobiocomposite based on rGO nanoribbons/MWCNTs/chitosan for sensitive and selective detection of H_2O_2 and NO_2^-. They explored the beneficial properties of the biosensor in contact lens cleaning solution and meat sample. They reported

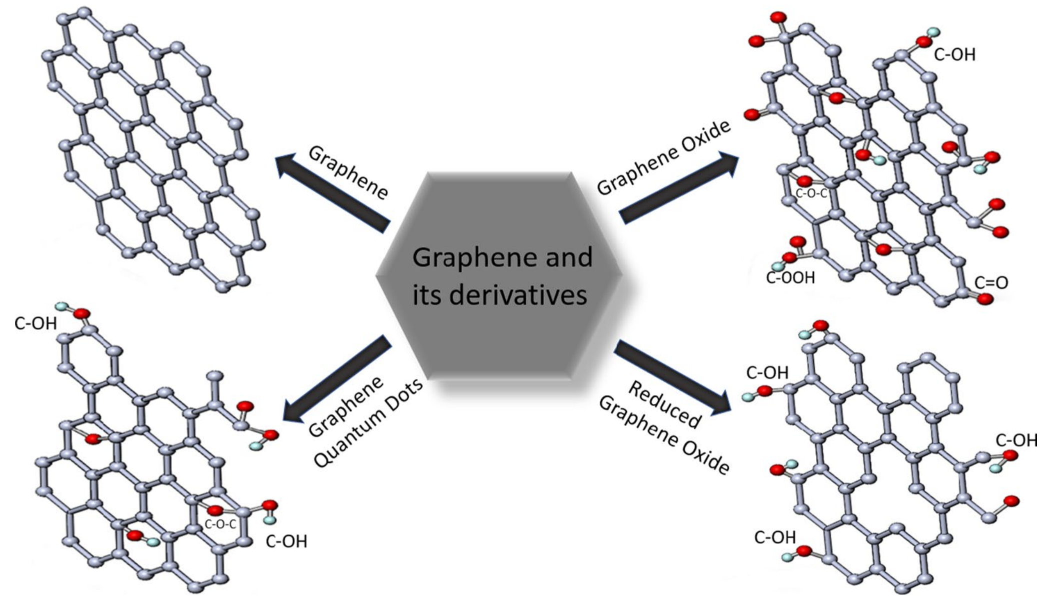

Fig. 3 Structure of most popular graphene-based materials

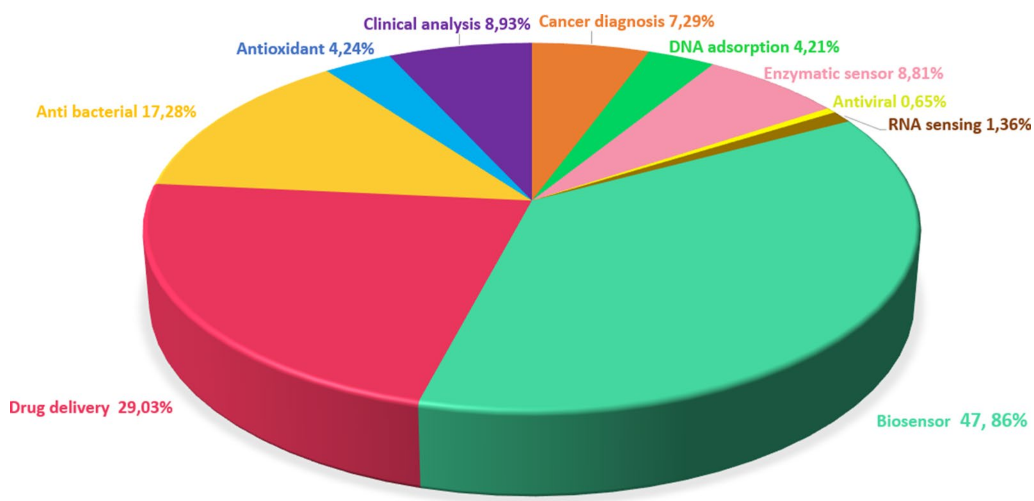

Fig. 4 Pie chart showing the distribution of graphene in biomedical applications

that for H_2O_2, the nanobiocomposite-based sensor had a sensitivity of 0.616 μAμM^{-1} cm^{-2}, the detection limit of 1 nm, and a linear range of 0.001–1625 μM, while these values for NO_2^-, 0.643 μAμM^{-1} cm^{-2}, 10 nm, and 0.01–1350 μM, respectively. Thus, they proved that the graphene-based sensor could be used effectively in medical applications and food safety [104]. Another graphene-based H_2O_2 sensor was prepared by Yin et al. [105]. In their study, Yin and colleagues synthesized conductive three-dimensional (3D) graphene aerogels (GA) decorated with Ni_3N NPs using the hydrothermal method. As a result of their characterization, they showed that the Ni_3N/GA composites they obtained could be applied not only for H_2O_2 but also for glucose determination. They reported that the Ni_3N/GA-based electrode, in the determination of H_2O_2, demonstrated high electrochemical performance as the detection range of 5 μM–75.13 mM, the sensitivity of 101.9 μAmM^{-1} cm^{-2}, and a low detection limit of 1.80 μM. Moreover, for glucose determination, they emphasized

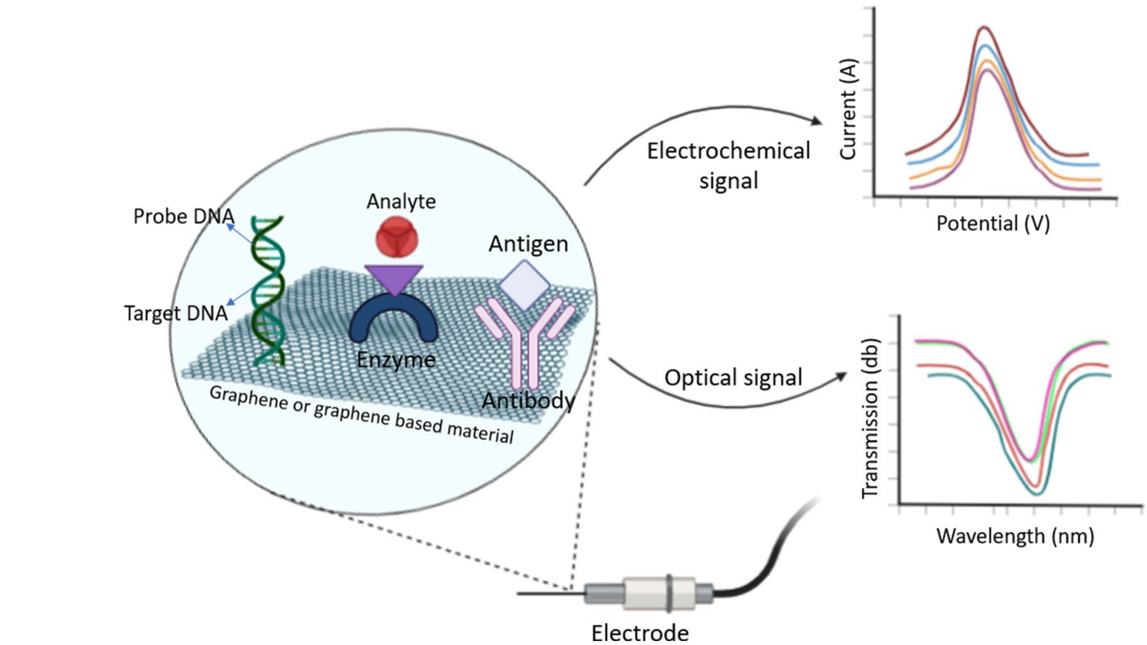

Fig. 5 Representation of graphene-based biosensors and its mechanism

that the designed electrode has a detection range of 0.1–7645.3 µM, a detection limit of 0.04 µM, and a sensitivity of 905.6 µA mM^{-1} cm^{-2} [105].

It can be said that recently there has been intense interest in graphene-based biosensors for the practical detection of glucose Table 3. For instance, Đurđić et al. [106] successfully synthesized a single-use biosensor based on Bi_2O_3-decorated GNRs by co-precipitation. As a result of their characterization, they proved that the sensor they obtained had a detection limit of 0.07 mM, a linear range of 0.28–1.70 mM, and a sensitivity of 64.81 µA/$mMcm^2$. Thus, they proposed that the graphene-based sensor could detect glucose in blood serum and urine samples reproducible and stable [106]. In the same year, a useful glucose biosensor was successfully designed by the single-pot hydrothermal synthesis of a 3D nitrogen-doped porous graphene hydrogel (NHGH) with $NiCo_2O_4$ nanoflowers (NHGH/$NiCo_2O_4$) by Lu and team. They modified the GCE with the nanocomposite they obtained and evaluated the modified electrode's electrochemical performance in determining glucose. Firstly, they received CVs in 0.1 M NaOH solution, with a scan rate of 50 mV s^{-1}, to examine the electrochemical catalytic performance. They reported that the NHGH/GCE has an increased oxidation peak current of 0.5 V than the weak anodic peak current of bare GCE. Moreover, in their study, they observed that the redox peak pair is visible, which indicates that the electrochemical activity of NHGH/$NiCo_2O_4$/GCE is highest compared to other electrodes. They attributed this improvement to graphene's extended surface area, good conductivity, and Co and Ni's redox reactions. In addition, they showed the electrochemical catalytic performances of the electrodes in the 5.0 mM glucose addition. They interpreted NHGH/$NiCo_2O_4$/GCE with the highest peak current at 0.5 V as a clear indication that glucose oxidation could be better catalyzed than other electrodes due to the dual effect of $NiCo_2O_4$ and NHGH. They also reported that the peak currents increased linearly with increasing glucose concentration and the NHGH/$NiCo_2O_4$-based glucose sensor exhibited a broad linear relationship between peak current and glucose concentration in the range of 5 µM–2.6 mM and 2.6 mM–10.9 mM, respectively. Also, they emphasized that NHGH/$NiCo_2O_4$/GCE has a high sensitivity (2072 µA mM^{-1} cm^{-2}) and a low detection limit (0.39 µM). As a result, they suggested using for a precise determination of glucose in real blood samples [107].

As seen in Table 3, graphene and its derivatives have become an indispensable building block for biosensor applications, because of its excellent properties. Considering the studies performed recently Table 3, it is remarkable that graphene and its derivatives are used in hybrid nanostructures with MONs to improve biosensors' sensitivity and reproducibility. Additionally, MONs/graphene synergy should be evaluated to obtain multifunctional biosensors and achieve high electrocatalytic activity. Moreover, graphene can be easily combined with other

Table 3 Selected recent biosensor studies based on graphene and its derivatives

Nanomaterials and Morphology	Types of biosensors	LOD	Sensitivity	Linear detection range	Analyte detected	Applications	References
rGO/Ni/ZnO NRs arrays	Electrochemical Amperometric	0,15 µM	2030 µA mM^{-1} cm^{-2}	0.5 µM–1.11 mM	Glucose	Clinical applications	Mazaheri et al. [108]
GO/MoS_2 aerogel	Electrochemical	0.29 mM	3.36 µA/mM	2–20 mM	Glucose	Clinical and nonclinical applications	Jeong et al. [109]
Graphene flakes/Ni	Electrochemical	1 µM	2213 µA mM^{-1} cm^{-2}	1–1150 µM	Glucose	Clinical diagnosis	Wu et al. [110]
rGO/Au and Pt alloy NPs	Electrochemical	5 µm	48 µA/mM cm^2	50 mV/s–150 mV/s	Glucose	Medical Textile Industry	Xuan et al. [111]
GO	Optical Fiber	-	0,24 nm/mM = 1,33 nm/(mg/ml)	-	Glucose	Bioengineering applications	Jiang et al. [112]
rGO/Ni NPs/Gelatin methacryloyl (GelMA)	Electrochemical	0.005 µM = 5 nm	0.056 $mAmM^{-1}$	0.15 µM-10 mM	Glucose	Clinical and nonclinical applications	Darvishi et al. [113]
Chemically rGO	Electrochemical Amperometric	5. 10^{-8} M	0,0040 AM^{-1}	1.5×10^{-7}–3.0×10^{-6} M	H_2O_2	Medical applications	Nieto et al. [114]
GO/Ag/Au NPs	Electrochemical	0,001 µg/ml	0.084 µA m/cm^2 µg/ml	0.01 – 5000 µg/mL	Cholesterol	Clinical diagnosis	Huang et al. [115]
Graphene/Poly Diphenylamine (PDPA)/Phosphotungstic acid (PTA)	Electrochemical Amperometric	0.1 µM	1.085 µA/µM cm^2	1–13 µM	Urease	Electrocatalytic applications	Muthusankar et al. [116]
Graphene/MoS_2/TiO_2/SiO_2 layers	Surface plasmon resonance	-	82.83 Deg-RIU^{-1}	-	Formalin	Food safety	Hossain et al. [117]
N-Doped Graphene/Polyaniline (PANI)/DNA-Functionalized CNTs	Electrochemical	14 nM	–	0.02-1 µM	DA	Molecular diagnosis	Keteklahijani et al. [118]
Monolayer graphene/Au NPs	Electrochemical	0.1 nM	–	0.0005–5000 µM	Glucose	Diabetes	Yuan et al. [119]
NiO-N-doped carbon/rGO microspheres	Electrochemical	70.9 nM	4254µAmM^{-1} cm^{-2}	0.5 µM – 20.0 µM	Glucose	Food analysis and clinical diagnosis	Zhang et al. [34, 35]
Ionic liquid-functionalized graphene/CNTs	Electrochemical	3.99×10^{-7} mol/L	53.89 µA mmol/L^{-1} cm^{-2}	0.004–5 mmol/L	Glucose	Diabetes	Zou et al. [120]
GO nanofibers/Cu nanoflower-decorated Au NPs	Electrochemical	0.018 µM	–	0.001–0.1 mM	Glucose	Clinical applications	Baek et al. [121]
GO/NiO Films/Au NPs	Electrochemical	7.64 µM	57.16 mV/decade	0.01 mM–100 mM	Urease	Clinical and nonclinical applications	Nien et al. [122]

Table 3 (continued)

Nanomaterials and Morphology	Types of biosensors	LOD	Sensitivity	Linear detection range	Analyte detected	Applications	References
Thermally rGO	Electrochemical Amperometric	0.02 mM	2.3 ± 0.1 μA cm^{-2} mM^{-1}	0.2–12.0 mM	Urease	Medical Technologies	Razumiene et al. [123]
GNPs/graphitized nanodiamond	Electrochemical	0.005 mg/mL	806.3 μA(mg mL^{-1})$^{-1}$ $cm^{-2)}$	0.1–0.9 mg/mL	Urease	Food analysis	Kumar et al. [124]

nanocarbons such as CNTs. Therefore, rich edge density and highly beneficial edge defects for creating enzymatic biosensors can be obtained.

Carbon Nanotubes-Based Biosensors

CNT's, discovered by Iijima in 1991, can be conceived as the formation of a graphene layer into a cylinder. CNTs can be categorized in general two types as single-walled carbon nanotubes (SWCNTs) Fig. 6a and MWCNTs Fig. 6b [125]. The diameter and wrapping angle determine the physical features of the CNTs by chirality and the (n, m) index [126–128]. According to the (n,m) index, CNTs can exhibit metal or semiconductor behavior [129–132],depending on chirality, SWCNTs may be classified in three different ways: (1) $m = n$ is the armchair nanotube Fig. 6c, (2) $n > m$ and if $m = 0$ is the chiral nanotube Fig. 6d, and $m = 0$ is the zig-zag nanotube Fig. 6e. CNTs display the semiconductive behavior in their nature, but for a given (n, m) SWNT, when $(2n + m)/3$ is an integer, the CNTs will be metallic. Thus, it can be claimed that all armchair nanotubes are metallic [130]. Therefore, the ability to control chirality during production means to control the electronic features of CNTs, which provides a great advantage in biosensor applications. Several different methods have been proposed to synthesize CNTs in recent years. However, there are three main synthesis techniques (arc discharge, laser ablation, and CVD for CNTs production [133].

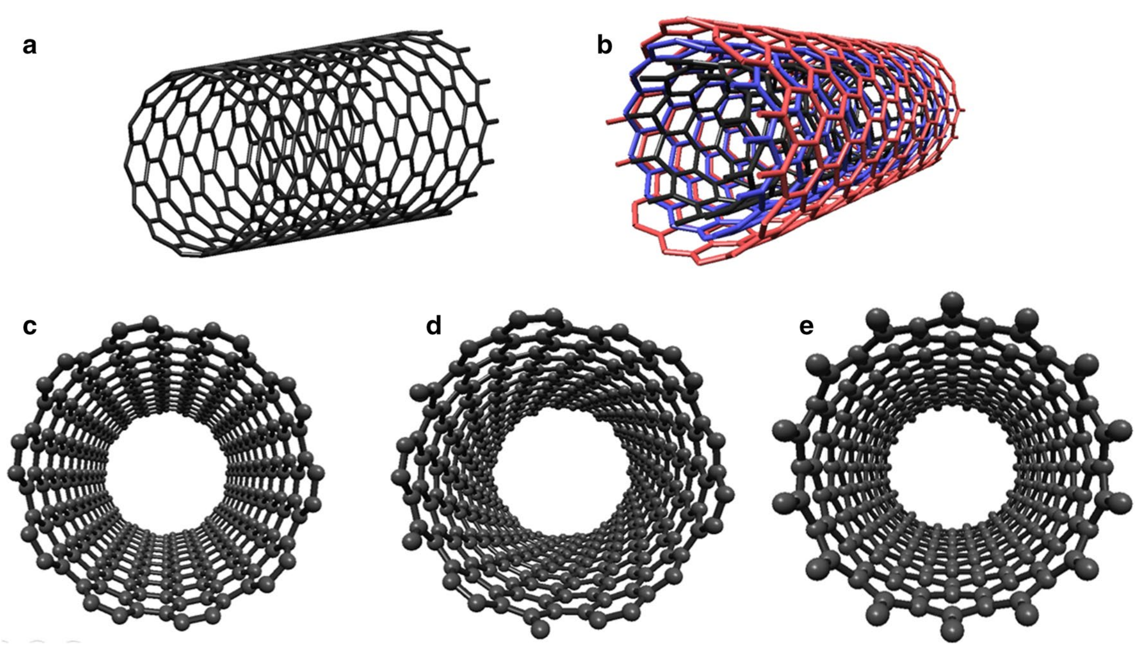

Fig. 6 The classification of the CNTs of **a** SWCNT, **b** MWCNT; Schematic representation of three typical types of SWCNTs **c** Armchair (10, 10), **d** Chiral (13, 6), and **e** Zigzag (14, 0)

Compared to arc-discharge and laser ablation methods, CVD is the most effective method for simple and cost-effective controlling the chirality of CNTs [133, 134].

The ends and sidewalls of the CNTs can be easily modified by the addition of virtually any desired chemical species. CNTs can be excellent transducers in nanoscale sensors owing to their significant sensitivity. Additionally, CNTs have very favorable properties for transmitting electrical signals generated upon recognition of a target and therefore play an essential role in the final development of enzyme-based biosensors [135]. Moreover, CNTs with small size, fast response times, and excellent electrochemical properties are equal or superior to most other electrodes with their ions, metabolites, and protein biomarkers [136]. As a result of their unique tubular nanostructures with extensive length and diameter ratios, CNTs are desirable materials in applying electrochemical biosensors due to their excellent electrochemical stability, great mechanical flexibility, rapid electron transport, and unique thermal conductivity [137, 133]. CNTs are also widely used in tissue engineering and drug delivery systems to improve electrical and mechanical features after being functionalized to ensure their biocompatibility and conjugated with organic compounds or metallic NPs. [138]. Studies on CNTs from 2010 to 2020 were analyzed and are presented in Fig. 7 as a pie chart that shows the distribution of biomedical applications of CNTs.

CNTs, as with graphene and its derivatives, also make important contributions to the development of biosensors with higher sensitivity and selectivity by hybridizing with MONs. Researchers have recently focused on the production and characterization of new nanobiosensors that can combine the unique properties of CNTs with the superior properties of metal NPs. For instance, Rahman et al. [139] designed the Fe_3O_4-decorated CNTs based 3-methoxyphenyl (3-MP) biosensor for environmental protection applications. Fe_3O_4/CNTs nanocomposites synthesized by wet-chemical method and coated the nanocomposite on the GCE surface as a thin layer. Then, they evaluated the electrochemical performance of the modified electrodes by I-V characterization and reported that the Fe_3O_4/CNT-based electrode showed a wide detection range (90.0 pM–90.0 mM), low detection limit (1.0 pM), and high sensitivity (9×10^{-4} μA μM^{-1} cm^{-2}) in detecting dangerous phenol [139]. Similarly, for environmental protection, MWCNT/TiO_2/chitosan-based biosensor was developed by Fotouhi et al. [140] to detect dihydroxy benzene isomers released into the environment from the chemical and pharmaceutical industries. Fotouhi et al. reported that they performed the simultaneous determination of hydroquinone (HQ), catechol (CC), and resorcinol (RS), causing pollution in real water samples by the MWCNTs-based sensor. Additionally, they indicated the detection limits ($S/N=3$) of HQ, CC and RS, as 0.06 μmol d m^{-3}, 0.07 μmol d m^{-3}, and 0.52 μmol d m^{-3}, and the linear response ranges are between 0.4–276.0 μmol d m^{-3}, 0.4–159.0 μmol d m^{-3}, and 3.0–657 μmol d m^{-3}, respectively [140].

Besides environmental protection, biosensor designs of CNTs for clinical applications have recently become extremely interesting Table 4. For instance, Zhu et al. [141] obtained the buckypaper containing two layers: purified SWCNTs and SWCNTs decorated with NiO, by helium arc discharge method. Later, as a result of their analysis to evaluate its electrochemical performance, they showed that glucose biosensor

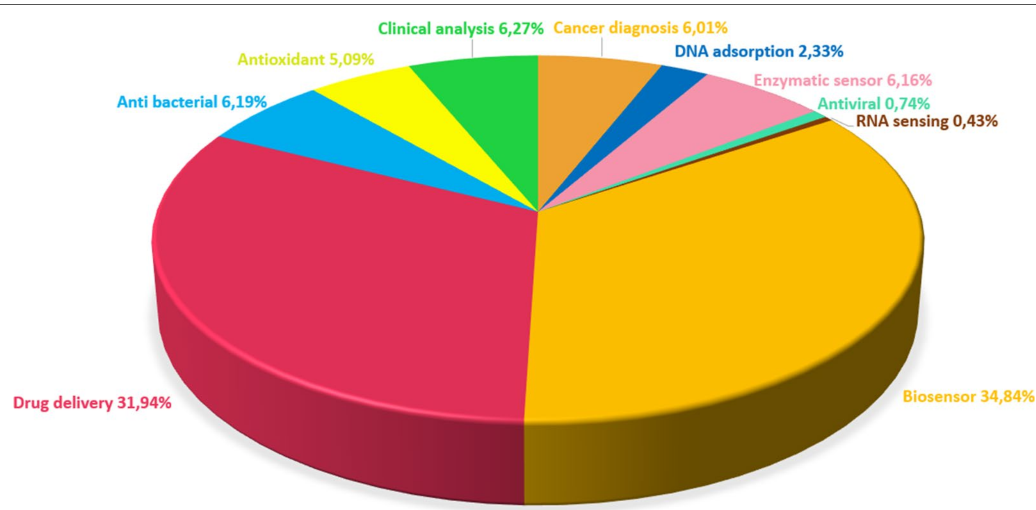

Fig. 7 Pie chart showing the distribution of CNTs in biomedical applications

Table 4 Selected recent biosensor studies based on CNTs

Nanomaterials and morphology	Types of biosensors	LOD	Sensitivity	Lineer detection range	Analyte detected	Applications	References
CNTs/Dendrimer-encapsulated Pt nanoclusters	Electrochemical Non-enzymatic	0.8 μM	987.5 μA mM^{-1} cm^{-2}	0.003–0.4 mM	H_2O_2	Clinical applications	Liu and Ding [144]
CNTs/Pd-Co NPs	Electrochemical Non-enzymatic	0.3 μM	–	1 μM–1.11 mM	H_2O_2	Clinical and nonclinical analysis	Huang et al. [145]
		1 μM	75.4 μA mM^{-1} cm^{-2}	10 μM–2.4 mM	Glucose	Diabetes	
CNTs/mucin composite	Electrochemical Amperometric	3 μM	0.44 ± 0.01 mA M^{-1}	0.002–3.2 mM	Glucose	Diabetes	Comba et al. [146]
MWCNTs/Graphene/Poly(diallyl dimethyl ammonium chloride) (PDADMAC)	Electrochemical	4.40 μM	–	5–50 μM	UA/Hypoxanthine	Clinical applications	Si et al. [147]
CNTs/Co_3O_4/TiO_2	Photoelectrochemical	0.16 μM	0.3 μAmM − 1 cm − 2	0–4 mM	Glucose	Diabetes	Çakıroğlu and Özacar [148]
CNTs/NiO/Poly(3,4-ethylenedioxythiophene) (PEDOT)	Electrochemical	0.026 μM 0.063 μM 0.210 μM	7.36 μA $μM^{-1}$ cm^{-2} 3.04 μA $μM^{-1}$ cm^{-2} 0.92 μA $μM^{-1}$ cm^{-2}	0.03–20 μM 0.3–35 μM 1–41 μM	DA Serotonin Tryptophan	Clinical applications	Sun et al. [149]
CNTs/$ZnFe_2O_4$	Colorimetric	0.58 μM	–	0.8–250 μM	Glucose	Diabetes	Wang et al. [150, 151]
MWCNTs/GQDs/Au NPs/Chitosan	Electrochemiluminescence	64 nM	–	0.1–5000 μM	Glucose	Diabetes	Wang et al. [150, 151]
MWCNTs/CdO NPs	Electrochemical	4.0 pM	25.7911 μA μM cm^{-2}	0.01 nM–0.1 mM	M-tolyl hydrazine hydrochloride	Environmental safety	Rahman et al. [152]
MWCNTs/PANI	Electrochemical	10 μM	0.38 μA mM^{-1} cm^{-2}	10–50 μM	Urease	Disease diagnosis	Bao et al. [153]
CNTs/ZnO NWs	Electrochemical Amperometric	3.3 ng/μl	–	3.3 ng/μl-3.3 mg/μl	Urine albumin	Medical applications	Tabatabaei et al. [154]
MWCNTs/Fe_3O_4/PANI	Electrochemical Amperometric	67 μM	–	1.0–25.0 mM	Urease	Food analysis	Singh et al. [155]
MWCNTs/AuNPs/PPy	Electrochemical Impedimetric	0.1×10^{-3} M	10.12 μA mM^{-1} cm^{-2}	2×10^{-3}–8×10^{-3} M	Cholesterol	Clinical applications	Alagappan et al. [156]
MWCNTs/$Ni(OH)_2$	Electrochemical	0.095 μmol L^{-1}	–	0.5–26 μmol L^{-1}	Folic acid (vitamin B_9)	Food safety	Winiarski et al. [157]
Carboxylated SWCNTs/Molecularly imprinted polymer (MIP)/Chitosan	Electrochemical	0.025 ng mL^{-1}	–	0.04–7.6 ng mL^{-1}	Semicarbazide	Food safety	Yu et al. [158]
MWCNTs/GQDs	Electrochemical	0.87 nM	–	0.005–100.0 μM	DA	Clinical applications	Huang et al. [159]

Table 4 (continued)

Nanomaterials and morphology	Types of biosensors	LOD	Sensitivity	Lineer detection range	Analyte detected	Applications	References
MWCNTs/Co-based Metal organic framework (MOFs)/Au NPs	Electrochemical	0.4 μM	0.223 μA μM^{-1}	1–1000 μM	Nitrite	Environmental safety	Lei et al. [160]
SWCNTs	Electrochemical Field-effect transistor	0.01 mM	0.4–0.6 μA/mM	0.01–2 mM	Glucose	Clinical and nonclinical applications	Pandey et al. [161]
SWCNTs/Pt–Pd NiO NPs	Electrochemical	3.0 nM 0.1 μM	0.2267 μA/μM	0.008–350 μM 0.5–330 μM	Daunorubicin Tamoxifen	Clinical applications	Alizadeh et al. [162]
CNTs/Pt NPs/Au: Ru NPs	Electrochemical Amperometric	0.068 mM	0.2347 nA/(μM mm^2)	1 – 10 mM	Glucose	Prediabetes and diabetes	Nguyen et al. [163]
MWCNTs/CoS NPs	Electrochemical	5 μM	15 mA M^{-1} cm^{-2}	8 μM-1.5 mM	Glucose	Diabetes	Li et al. [164]
CNTs/peptide-decorated Au NPs	Electrochemical	6 pg/mL	–	0.01–1000 ng/nL	Matrix metalloproteinase-7	Cancer diagnosis	Palomar et al. [165]
CNTs/Fe_3O_4 NPs/rGO	Electrochemical Amperometric	0.54 μM	–	1 – 50 μM	Antipsychotic drug trifluoperazine	Medical applications	Ognjanovic et al. [166]

has a broad linear range (0.1–9 mM), high sensitivity (2701 μA mM^{-1} cm^{-2}), and fast response time (< 2.5 s) [141]. Barthwal and Singh [142] designed a ZnO/MWCNTs nanocomposite biosensor to detect urea in their study. They indicated that the ZnO/MWCNTs-based sensor has the highest detection characteristics compared to the ZnO and MWCNTs-based sensor. Also, they emphasized that the nanocomposite's sensitivity containing 2% MWCNTs is less than 10 s, and the detection limit is 10 ppm [142]. In the same year, Guan et al. successfully developed a CNTs-based hybrid nanocomposite as an electrochemical biosensor for simultaneous high-sensitivity detection of DA and UA. In their study, they reported that the most extensive ($\Delta E_p = 144$ mV) and highest oxidation current was observed in the electrode modified with CNTs-based nanohybrid. Additionally, they investigated the simultaneous detection of DA and UA in nanohybrid-modified GCE via differential pulse voltammetry (DPV). They showed that the anodic peak current response of the nanohybrid/GCE increased linearly due to the increase in DA concentration. Also, they obtained a similar observation for the UA concentration. They emphasized that the concentration range for both target analytes is 2–150 μM. As a result, they reported that the limit of DA and UA detection values was 0.37 μM and 0.61 μM, respectively [143].

Studies on increasing the efficiency of CNTs-based biosensors in different application areas by hybridizing with MONs and graphene and graphene derivatives and improving their properties are of great interest Table 4. The higher electrochemical activity and higher conductivity of nanohybrid structures designed with CNTs-based electrochemical sensors can be considered a result of the inherent properties of CNTs. On the other hand, one of the features that limit the use of CNTs in biosensor applications is that they are not dissolved in most solvents. Also, it has low biocompatibility and, in some cases, toxicity. To overcome these problems, combining different functional groups on the surface and end caps of CNTs with MONs, and applying surface modifications can be considered as a solution.

Additionally, due to the integration of CNTs with graphene and its derivatives, it is possible to create more active sites for biomolecules due to strong binding interactions. Another advantage of CNTs/graphene hybrid structure is that it allows biosensors to respond in a shorter time due to their higher electron transfer rate. Thus, in the next generation of biosensors to be developed in the future, it seems inevitable to achieve high sensitivity and selectivity, simultaneous target biomolecule detection by benefiting from the dually effect of CNTs with MONs or other nanocarbons such as graphene and its derivatives.

Conclusion and Outlook

Biosensors and bioelectrodes play a crucial role in environmental monitoring, food safety, the medical textile industry, drug discovery and analysis, clinical and nonclinical applications. With the recent COVID-19 pandemic, fast responsive, reusable, cheap and highly selective biosensors became crucial for the fight against infectious diseases to be taken under control. For the design of a biosensor, the material used in transducer component and to functionalize transducer surfaces has an explicit effect on the results with aforementioned properties obtained from a biosensor. Within this frame, for the improvement of the properties of these devices, nanomaterials have been extensively used and their expanded surface area, ability to adapt to the surface modifications for the use of any type of analyte, and such extraordinary nanosize-dependent properties brought them one-step ahead unprecedently in the production of an ideal biosensor.

With this motivation, this paper presents an overview on recent developments in hybrid nanosystems created by the combined use of MONs, graphene, and CNTs. Numerous efforts have been made to create biosensors with improved sensitivity and selectivity to detect biomolecules with the help of these nanostructures. Obviously, apart from each of these materials' unique characteristics, the multiple effect of hybrid design of them is a key point in obtaining a higher performance biosensor. Combining these nanostructures to create a hybrid design improves the biosensor's electrocatalytic activity, its electron transfer rate, and enables more active sites to allow two or more biomolecules to be detected, simultaneously. It also meets other desired functions expected from an ideal biosensor, such as stability, long shelf life, repeatability, wide measuring range, fast response time for next-generation biosensor applications. However, there are compelling factors in combining these three trending nanomaterials, such as the control on agglomeration tendency, cytotoxicity, the choice of the right concentration, and the extensive optimization of conditions to improve purity and these materials better integration with each other. Therefore, there are still open allowance for improvements to be made for the preparation of nanomaterials and their composite structures. Furthermore, for an onsite diagnosis of an analyte, having a major impact for biosensors for medical applications, it is important to have a quick and reliable result in a cost-effective way. For this purpose, nanomaterials used in biosensors might be modified to facilitate diagnosis with more delicate sensing especially for the biomarkers of some diseases with a very minute concentration at their early stages. For gaining and improving such features, graphene, CNTs and MONs, should be produced with minimum catalyst impurities, high crystallinity, and in massive amounts in a cost-effective way. They should also be engineered for their density of states and the structure of bonds for tailoring a better electron transport properties. Within this review, a combination of nanostructures that help to develop an accurate 'future biosensor' mechanism was proposed and expectations as sensitivity, superior selectivity, low limit of detection, real-time sensing with multi-functional properties were summarized.

Abbreviations

1D: One-dimensional; 3D: Three-dimensional; CD: Cyclodextrin; CVD: Chemical vapor deposition; CVs: Cyclic voltammograms; DA: Dopamine; DNA: Deoxyribonucleic acid; DPV: Differential pulse voltammetry; FET: Field-effect transistor; GCE: Glassy carbon electrode; GelMA: Gelatin methacryloyl; GNPs: Graphene nanoplatelets; GNRs: Graphene nanoribbons; GO: Graphene oxide; GQDs: Graphene quantum dots; LOD: Limit of detection; MIP: Molecularly imprinted polymer; MOFs: Metal organic frameworks; MOs: Metal oxides; MWCNTs: Multi-walled carbon nanotubes; NHGH: Nitrogen-doped porous graphene hydrogel; NPs: Nanoparticles; NRs: Nanorods; NSs: Nanospheres; NWs: Nanowires; PANI: Polyaniline; PDADMAC: Poly(diallyl dimethyl ammonium chloride); PDPA: Poly Diphenylamine; PECVD: Plasma-enhanced chemical vapor deposition; PEDOT: Poly(3,4-ethylenedioxythiophene); PG: Pristine graphene; PPy: Polypyrrole; PTA: Phosphotungstic acid; PVA: Polyvinyl alcohol; RF: Radio frequency; rGO: Reduced graphene oxide; SERS: Surface-enhanced Raman scattering; SWCNTs: Single-walled carbon nanotubes; UA: Uric acid; XO: Xanthine oxidase.

Authors' Contributions

AA was the lead author he designed, organized, wrote and edited most of the manuscript. HG assisted and she helped with writing and editing each parts of the manuscript. BB wrote certain parts, helped with edition of the manuscript. EOA wrote certain parts, helped with edition of the manuscript. AY wrote certain parts, helped with edition of the manuscript. SG wrote certain parts, helped with edition of the manuscript. FG wrote certain parts, helped with edition of the manuscript. ME wrote certain parts, helped with edition of the manuscript. All authors read and approved the final manuscript.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

Availability of Data and Materials

Not applicable.

Declarations

Competing interests

The authors declare that they have no competing interests.

Author details

[1] Department of Engineering Sciences, Izmir Katip Çelebi University, 35620 Izmir, Turkey. [2] Department of Nanoscience and Nanotechnology, Izmir Katip Çelebi University, 35620 Izmir, Turkey. [3] Department of Nanoscience and Nanoengineering, Dokuz Eylul University, 35390 Izmir, Turkey. [4] Department of Material Science and Engineering, Izmir Katip Çelebi University, 35620 Izmir, Turkey. [5] Department of Metallurgical and Materials Engineering, Dokuz Eylul University, 35390 Izmir, Turkey.

Received: 20 January 2021 Accepted: 30 March 2021
Published online: 20 April 2021

References

1. Mavrogiannis N, Crivellari F, Gagnon ZR (2016) Label-free biomolecular detection at electrically displaced liquid interfaces using interfacial electrokinetic transduction (IET). Biosens Bioelectron 77:790–798

2. Clark LC Jr, Wolf R, Granger D, Taylor Z (1953) Continuous recording of blood oxygen tensions by polarography. J Appl Physiol 6(3):189–193
3. Clark L, Lyons C (1962) Electrode systems for continuous monitoring in cardiovascular surgery. Ann N Y Acad Sci 102(29):29–45
4. Updike SJ, Hicks GP (1967) The enzyme electrode. Nature 214(5092):986–988
5. Wang J (2008) Electrochemical glucose biosensors. Chem Rev 108(2):814–825
6. Farka Z, Juřík T, Kovář D, Trnková L, Skládal P (2017) Nanoparticle-based immunochemical biosensors and assays: recent advances and challenges. Chem Rev 117(15):9973–10042
7. Thévenot DR, Toth K, Durst RA, Wilson GS (2001) Electrochemical biosensors: recommended definitions and classification. Biosens Bioelectron 16(1–2):121–131
8. Taylor R, Coulombe S, Otanicar T, Phelan P, Gunawan A, Lv W, Rosengarten G, Prasher R, Tyagi H (2013) Small particles, big impacts: a review of the diverse applications of nanofluids. J Appl Phys 113(1):1
9. Nayl AA, Abd-Elhamid AI, El-Moghazy AY, Hussin M, Abu-Saied MA, El-Shanshory AA, Soliman HMA (2020) The nanomaterials and recent progress in biosensing systems: a review. Trends Environ Anal Chem e00087
10. Sha R, Badhulika S (2020) Recent advancements in fabrication of nanomaterial based biosensors for diagnosis of ovarian cancer: a comprehensive review. Microchim Acta 187(3):1–15
11. Gergeroglu H, Yildirim S, Ebeoglugil MF (2020) Nano-carbons in biosensor applications: an overview of carbon nanotubes (CNTs) and fullerenes (C 60). SN Appl Sci 2(4):1–22
12. Nunes D, Pimentel A, Gonçalves A, Pereira S, Branquinho R, Barquinha P, Fortunato E, Martins R (2019) Metal oxide nanostructures for sensor applications. Semicond Sci Technol 34(4):43001
13. Kumar S, Bukkitgar SD, Singh S, Singh V, Reddy KR, Shetti NP, Venkata Reddy C, Sadhu V, Naveen S (2019) Electrochemical sensors and biosensors based on graphene functionalized with metal oxide nanostructures for healthcare applications. ChemistrySelect 4(18):5322–5337
14. Yang H, Xu W, Liang X, Yang Y, Zhou Y (2020) Carbon nanotubes in electrochemical, colorimetric, and fluorimetric immunosensors and immunoassays: a review. Microchim Acta 187(4):1–18
15. Lu D, Zhang Y, Lin S, Wang L, Wang C (2013) Synthesis of PtAu bimetallic nanoparticles on graphene–carbon nanotube hybrid nanomaterials for nonenzymatic hydrogen peroxide sensor. Talanta 112:111–116
16. Sheng Q, Wang M, Zheng J (2011) A novel hydrogen peroxide biosensor based on enzymatically induced deposition of polyaniline on the functionalized graphene–carbon nanotube hybrid materials. Sens Actuators B Chem 160(1):1070–1077
17. Khalil I, Rahmati S, Julkapli NM, Yehye WA (2018) Graphene metal nanocomposites—recent progress in electrochemical biosensing applications. J Ind Eng Chem 59:425–439
18. Xiao F, Li Y, Zan X, Liao K, Xu R, Duan H (2012) Growth of metal–metal oxide nanostructures on freestanding graphene paper for flexible biosensors. Adv Func Mater 22(12):2487–2494
19. Parnianchi F, Nazari M, Maleki J, Mohebi M (2018) Combination of graphene and graphene oxide with metal and metal oxide nanoparticles in fabrication of electrochemical enzymatic biosensors. Int Nano Lett 8(4):229–239
20. Bollella P, Fusco G, Tortolini C, Sanzò G, Favero G, Gorton L, Antiochia R (2017) Beyond graphene: electrochemical sensors and biosensors for biomarkers detection. Biosens Bioelectron 89:152–166
21. Reina G, González-Domínguez JM, Criado A, Vázquez E, Bianco A, Prato M (2017) Promises, facts and challenges for graphene in biomedical applications. Chem Soc Rev 46(15):4400–4416
22. Song Y, Luo Y, Zhu C, Li H, Du D, Lin Y (2016) Recent advances in electrochemical biosensors based on graphene two-dimensional nanomaterials. Biosens Bioelectron 76:195–212
23. Zhu Z (2017) An overview of carbon nanotubes and graphene for biosensing applications. Nano-Micro Letters 9(3):25
24. Mathur RB, Singh BP, Pande S (2016) Carbon nanomaterials: synthesis, structure, properties and applications. Taylor & Francis
25. Mohd Yazid SNA, Md Isa I, Abu Bakar S, Hashim N, Ab Ghani S (2014) A review of glucose biosensors based on graphene/metal oxide nanomaterials. Anal Lett 47(11):1821–1834
26. Comini E (2016) Metal oxide nanowire chemical sensors: innovation and quality of life. Mater Today 19(10):559–567
27. Hassanpour S, Baradaran B, Hejazi M, Hasanzadeh M, Mokhtarzadeh A, de la Guardia M (2018) Recent trends in rapid detection of influenza infections by bio and nanobiosensor. TrAC Trends Anal Chem 98:201–215
28. Agostoni V, Horcajada P, Noiray M, Malanga M, Aykaç A, Jicsinszky L, Vargas-Berenguel A, Semiramoth N, Daoud-Mahammed S, Nicolas V (2015) A "green" strategy to construct non-covalent, stable and bioactive coatings on porous MOF nanoparticles. Sci Rep 5(1):1–7
29. George JM, Antony A, Mathew B (2018) Metal oxide nanoparticles in electrochemical sensing and biosensing: a review. Microchim Acta 185(7):358
30. Mondal K, Sharma A (2016) Recent advances in electrospun metal-oxide nanofiber based interfaces for electrochemical biosensing. RSC Adv 6(97):94595–94616
31. Santos L, Silveira CM, Elangovan E, Neto JP, Nunes D, Pereira L, Martins R, Viegas J, Moura JJG, Todorovic S (2016) Synthesis of WO3 nanoparticles for biosensing applications. Sens Actuators B Chem 223:186–194
32. Dong S, Tong M, Zhang D, Huang T (2017) The strategy of nitrite and immunoassay human IgG biosensors based on ZnO@ ZIF-8 and ionic liquid composite film. Sens Actuators B Chem 251:650–657
33. Liu A (2008) Towards development of chemosensors and biosensors with metal-oxide-based nanowires or nanotubes. Biosens Bioelectron 24(2):167–177
34. Zhang B, Wang H, Xi J, Zhao F, Zeng B (2020) In situ formation of inorganic/organic heterojunction photocatalyst of WO3/Au/polydopamine for immunoassay of human epididymal protein 4. Electrochim Acta 331:135350
35. Zhang Y, Liu Y-Q, Bai Y, Chu W, Sh J (2020) Confinement preparation of hierarchical NiO-N-doped carbon@ reduced graphene oxide microspheres for high-performance non-enzymatic detection of glucose. Sens Actuators B Chem 309:127779
36. Cañas-Carrell JE, Li S, Parra AM, Shrestha B (2014) Metal oxide nanomaterials: health and environmental effects. In Health and environmental safety of nanomaterials. Elsevier, pp 200–221
37. Hernández-Cancel G, Suazo-Dávila D, Medina-Guzmán J, Rosado-González M, Díaz-Vázquez LM, Griebenow K (2015) Chemically glycosylation improves the stability of an amperometric horseradish peroxidase biosensor. Anal Chim Acta 854:129–139
38. Khan MM, Adil SF, Al-Mayouf A (2015) Metal oxides as photocatalysts. Elsevier
39. Scognamiglio V, Antonacci A, Arduini F, Moscone D, Campos EVR, Fraceto LF, Palleschi G (2019) An eco-designed paper-based algal biosensor for nanoformulated herbicide optical detection. J Hazard Mater 373:483–492
40. Song H, Zhang Y, Wang S, Huang K, Luo Y, Zhang W, Xu W (2020) Label-free polygonal-plate fluorescent-hydrogel biosensor for ultrasensitive microRNA detection. Sens Actuat B Chem 306:127554
41. Asrami PN, Tehrani MS, Azar PA, Mozaffari SA (2017) Impedimetric glucose biosensor based on nanostructure nickel oxide transducer fabricated by reactive RF magnetron sputtering system. J Electroanal Chem 801:258–266
42. Mozaffari SA, Rahmanian R, Abedi M, Amoli HS (2014) Urea impedimetric biosensor based on reactive RF magnetron sputtered zinc oxide nanoporous transducer. Electrochim Acta 146:538–547
43. Singh SP, Arya SK, Pandey P, Malhotra BD, Saha S, Sreenivas K, Gupta V (2007) Cholesterol biosensor based on rf sputtered zinc oxide nanoporous thin film. Appl Phys Lett 91(6):63901
44. Solanki PR, Kaushik A, Agrawal VV, Malhotra BD (2011) Nanostructured metal oxide-based biosensors. NPG Asia Mater 3(1):17
45. Umar A, Rahman MM, Hahn Y-B (2009) MgO polyhedral nanocages and nanocrystals based glucose biosensor. Electrochem Commun 11(7):1353–1357
46. Vasudev MC, Anderson KD, Bunning TJ, Tsukruk VV, Naik RR (2013) Exploration of plasma-enhanced chemical vapor deposition as a method for thin-film fabrication with biological applications. ACS Appl Mater Interfaces 5(10):3983–3994
47. Yang W, Wolden CA (2006) Plasma-enhanced chemical vapor deposition of TiO2 thin films for dielectric applications. Thin Solid Films 515(4):1708–1713

48. Ogata K, Koike K, Tanite T, Komuro T, Yan F, Sasa S, Inoue M, Yano M (2003) ZnO and ZnMgO growth on a-plane sapphire by molecular beam epitaxy. J Cryst Growth 251(1–4):623–627
49. Rathinamala I, Jeyakumaran N, Prithivikumaran N (2019) Sol-gel assisted spin coated CdS/PS electrode based glucose biosensor. Vacuum 161:291–296
50. Sayyed SG, Mahadik MA, Shaikh AV, Jang JS, Pathan HM (2019) Nano-metal oxide based supercapacitor via electrochemical deposition. ES Energy Environ 3(4):25–44
51. Zhou Y, Yang L, Li S, Dang Y (2017) A novel electrochemical sensor for highly sensitive detection of bisphenol A based on the hydrothermal synthesized Na-doped WO3 nanorods. Sens Actuators B Chem 245:238–246
52. Rahman M, Ahammad AJ, Jin J-H, Ahn SJ, Lee J-J (2010) A comprehensive review of glucose biosensors based on nanostructured metal-oxides. Sensors 10(5):4855–4886
53. Mokhtarzadeh A, Eivazzadeh-Keihan R, Pashazadeh P, Hejazi M, Gharaatifar N, Hasanzadeh M, Baradaran B, de la Guardia M (2017) Nanomaterial-based biosensors for detection of pathogenic virus. TrAC, Trends Anal Chem 97:445–457
54. Zong X, Zhu R (2018) ZnO nanorod-based FET biosensor for continuous glucose monitoring. Sens Actuators B Chem 255:2448–2453
55. Beitollahi H, Tajik S, Nejad FG, Safaei M (2020) Recent advances in ZnO nanostructure-based electrochemical sensors and biosensors. J Mater Chem B 8(27):5826–5844
56. Tak M, Gupta V, Tomar M (2015) A highly efficient urea detection using flower-like zinc oxide nanostructures. Mater Sci Eng C 57:38–48
57. Akhtar N, Metkar SK, Girigoswami A, Girigoswami K (2017) ZnO nano-flower based sensitive nano-biosensor for amyloid detection. Mater Sci Eng C 78:960–968
58. Sahyar BY, Kaplan M, Ozsoz M, Celik E, Otles S (2019) Electrochemical xanthine detection by enzymatic method based on Ag doped ZnO nanoparticles by using polypyrrole. Bioelectrochemistry 130:107327
59. Yue HY, Zhang HJ, Huang S, Lu XX, Gao X, Song SS, Wang Z, Wang WQ, Guan EH (2020) Highly sensitive and selective dopamine biosensor using Au nanoparticles-ZnO nanocone arrays/graphene foam electrode. Mater Sci Eng C 108:110490
60. Qian J, Wang Y, Pan J, Chen Z, Wang C, Chen J, Wu Z (2020) Non-enzymatic glucose sensor based on ZnO–CeO2 whiskers. Mater Chem Phys 239:122051
61. Rafiee Z, Mosahebfard A, Sheikhi MH (2020) High-performance ZnO nanowires-based glucose biosensor modified by graphene nanoplates. Mater Sci Semicond Process 115:105116
62. Ahmad R, Tripathy N, Ahn M-S, Bhat KS, Mahmoudi T, Wang Y, Yoo J-Y, Kwon D-W, Yang H-Y, Hahn Y-B (2017) Highly efficient non-enzymatic glucose sensor based on CuO modified vertically-grown ZnO nanorods on electrode. Sci Rep 7(1):1–10
63. Wahab HA, Salama AA, El Saeid AA, Willander M, Nur O, Battisha IK (2018) Zinc oxide nano-rods based glucose biosensor devices fabrication. Res Phys 9:809–814
64. Mahmoud A, Echabaane M, Omri K, El Mir L, Chaabane RB (2019) Development of an impedimetric non enzymatic sensor based on ZnO and Cu doped ZnO nanoparticles for the detection of glucose. J Alloys Compd 786:960–968
65. Alam MM, Asiri AM, Uddin MT, Islam MA, Awual MR, Rahman MM (2019) One-step wet-chemical synthesis of ternary ZnO/CuO/Co 3 O 4 nanoparticles for sensitive and selective melamine sensor development. New J Chem 43(12):4849–4858
66. Mai HH, Tran DH, Janssens E (2019) Non-enzymatic fluorescent glucose sensor using vertically aligned ZnO nanotubes grown by a one-step, seedless hydrothermal method. Microchim Acta 186(4):245
67. Kim E-B, Seo H-K (2019) Highly sensitive formaldehyde detection using well-aligned zinc oxide nanosheets synthesized by chemical bath deposition technique. Materials 12(2):250
68. Supraja P, Singh V, Vanjari SRK, Singh SG (2020) Electrospun CNT embedded ZnO nanofiber based biosensor for electrochemical detection of Atrazine: a step closure to single molecule detection. Microsyst Nanoeng 6(1):1–10
69. Zhu D, Ma H, Zhen Q, Xin J, Tan L, Zhang C, Wang X, Xiao B (2020) Hierarchical flower-like zinc oxide nanosheets in-situ growth on three-dimensional ferrocene-functionalized graphene framework for sensitive determination of epinephrine and its oxidation derivative. Appl Surf Sci 526:146721
70. Madhu S, Anthuuvan AJ, Ramasamy S, Manickam P, Bhansali S, Nagamony P, Chinnuswamy V (2020) ZnO nanorod integrated flexible carbon fibers for sweat cortisol detection. ACS Appl Electron Mater 2(2):499–509
71. Alam MM, Uddin MT, Asiri AM, Awual MR, Fazal MA, Rahman MM, Islam MA (2020) Fabrication of selective l-glutamic acid sensor in electrochemical technique from wet-chemically prepared RuO2 doped ZnO nanoparticles. Mater Chem Phys 251:123029
72. Chen Y, Zhou Y, Yin H, Li F, Li H, Guo R, Han Y, Ai S (2020) Photoelectrochemical biosensor for histone acetyltransferase detection based on ZnO quantum dots inhibited photoactivity of BiOI nanoflower. Sens Actuat B Chem 307:127633
73. Çevik E, Şenel M, Baykal A (2013) Potentiometric urea biosensor based on poly (glycidylmethacrylate)-grafted iron oxide nanoparticles. Curr Appl Phys 13(1):280–286
74. Kaushik A, Solanki PR, Ansari AA, Sumana G, Ahmad S, Malhotra BD (2009) Iron oxide-chitosan nanobiocomposite for urea sensor. Sens Actuators B Chem 138(2):572–580
75. Sanaeifar N, Rabiee M, Abdolrahim M, Tahriri M, Vashaee D, Tayebi L (2017) A novel electrochemical biosensor based on Fe3O4 nanoparticles-polyvinyl alcohol composite for sensitive detection of glucose. Anal Biochem 519:19–26
76. Yang L, Ren X, Tang F, Zhang L (2009) A practical glucose biosensor based on Fe_3O_4 nanoparticles and chitosan/nafion composite film. Biosens Bioelectron 25(4):889–895
77. Mohamed SA, Al-Harbi MH, Almulaiky YQ, Ibrahim IH, El-Shishtawy RM (2017) Immobilization of horseradish peroxidase on Fe3O4 magnetic nanoparticles. Electron J Biotechnol 27:84–90
78. Pang Y, Wang C, Wang J, Sun Z, Xiao R, Wang S (2016) Fe3O4@ Ag magnetic nanoparticles for microRNA capture and duplex-specific nuclease signal amplification based SERS detection in cancer cells. Biosens Bioelectron 79:574–580
79. Dong Y, Yang Z, Sheng Q, Zheng J (2018) Solvothermal synthesis of Ag@ Fe3O4 nanosphere and its application as hydrazine sensor. Colloids Surf A 538:371–377
80. Sriram B, Govindasamy M, Wang S-F, Ramalingam RJ, Al-Lohedan H, Maiyalagan T (2019) Novel sonochemical synthesis of Fe3O4 nanospheres decorated on highly active reduced graphene oxide nanosheets for sensitive detection of uric acid in biological samples. Ultrason Sonochem 58:104618
81. Cai L, Shang Y, Jiang X (2020) Synthesis of Fe_3O_4/graphene oxide/pristine graphene composite and its application in electrochemical sensor. J Phys Conf Ser 1622(1):12096
82. Zhao X, Li Z, Chen C, Wu Y, Zhu Z, Zhao H, Lan M (2017) A novel biomimetic hydrogen peroxide biosensor based on pt flowers-decorated Fe_3O_4/graphene nanocomposite. Electroanalysis 29(6):1518–1523
83. Wang Y, Liu X, Xu X, Yang Y, Huang L, He Z, Xu Y, Chen J, Feng Z (2018) Preparation and characterization of reduced graphene oxide/Fe3O4 nanocomposite by a facile in-situ deposition method for glucose biosensor applications. Mater Res Bull 101:340–346
84. Zheng J, Zhang M, Ling Y, Xu J, Hu S, Hayat T, Alharbi NS, Yang F (2018) Fabrication of one dimensional CNTs/Fe3O4@ PPy/Pd magnetic composites for the accumulation and electrochemical detection of triclosan. J Electroanal Chem 818:97–105
85. Yu L, Zhang Q, Jin D, Xu Q, Hu X (2019) A promising voltammetric biosensor based on glutamate dehydrogenase/Fe3O4/graphene/chitosan nanobiocomposite for sensitive ammonium determination in PM2. 5. Talanta 197:622–630
86. Yang Q, Li N, Li Q, Chen S, Wang H-L, Yang H (2019) Amperometric sarcosine biosensor based on hollow magnetic Pt–Fe_3O_4@ C nanospheres. Anal Chim Acta 1078:161–167
87. Cui F, Ji J, Sun J, Wang J, Wang H, Zhang Y, Ding H, Lu Y, Xu D, Sun X (2019) A novel magnetic fluorescent biosensor based on graphene quantum dots for rapid, efficient, and sensitive separation and detection of circulating tumor cells. Anal Bioanal Chem 411(5):985–995
88. Karami C, Taher MA (2019) A catechol biosensor based on immobilizing laccase to Fe3O4@ Au core-shell nanoparticles. Int J Biol Macromol 129:84–90

89. Peng L, Luo Y, Xiong H, Yao S, Zhu M, Song H (n.d.) A novel amperometric glucose biosensor based on Fe3O4-chitosan-β-cyclodextrin/MWCNTs nanobiocomposite. Electroanalysis
90. Guo W, Umar A, Alsaiari MA, Wang L, Pei M (2020) Ultrasensitive and selective label-free aptasensor for the detection of penicillin based on nanoporous PtTi/graphene oxide-Fe_3O_4/MWCNT–Fe_3O_4 nanocomposite. Microchem J 158:105270
91. Sohouli E, Khosrowshahi EM, Radi P, Naghian E, Rahimi-Nasrabadi M, Ahmadi F (2020) Electrochemical sensor based on modified methylcellulose by graphene oxide and Fe_3O_4 nanoparticles: Application in the analysis of uric acid content in urine. J Electroanal Chem 877:114503
92. He H, Sun D-W, Pu H, Huang L (2020) Bridging Fe3O4@ Au nanoflowers and Au@ Ag nanospheres with aptamer for ultrasensitive SERS detection of aflatoxin B1. Food Chem 324:126832
93. Yao X, Liu T, Xie Y, Chu Z, Jin W (2020) In situ-forming magnetic Fe_3O_4 nanoroses on defect-controllable mesoporous graphene oxide for enzyme-mimic sensing. Ind Eng Chem Res 59(40):17934–17943
94. Tavousi, A., Ahmadi, E., Mohammadi-Behzad, L., Riahifar, V., & Maghemi, F. (2020). Sensitive electrochemical sensor using polypyrrole-coated Fe3O4 core-shell nanoparticles/multiwall carbon nanotubes modified graphite electrode for atorvastatin analysis. *Microchemical Journal*, 105159.
95. Antarnusa G, Suharyadi E (2020) A synthesis of polyethylene glycol (PEG)-coated magnetite Fe_3O_4 nanoparticles and their characteristics for enhancement of biosensor. Mater Res Express 7(5):56103
96. Jin Z, Owour P, Lei S, Ge L (2015) Graphene, graphene quantum dots and their applications in optoelectronics. Curr Opin Colloid Interface Sci 20(5–6):439–453
97. Movlaee K, Ganjali MR, Norouzi P, Neri G (2017) Iron-based nanomaterials/graphene composites for advanced electrochemical sensors. Nanomaterials 7(12):406
98. Ghany NAA, Elsherif SA, Handal HT (2017) Revolution of Graphene for different applications: state-of-the-art. Surf Interfaces 9:93–106
99. Papageorgiou DG, Kinloch IA, Young RJ (2017) Mechanical properties of graphene and graphene-based nanocomposites. Prog Mater Sci 90:75–127
100. Afsahi S, Lerner MB, Goldstein JM, Lee J, Tang X, Bagarozzi DA Jr, Pan D, Locascio L, Walker A, Barron F (2018) Novel graphene-based biosensor for early detection of Zika virus infection. Biosens Bioelectron 100:85–88
101. Justino CIL, Gomes AR, Freitas AC, Duarte AC, Rocha-Santos TAP (2017) Graphene based sensors and biosensors. TrAC Trends Anal Chem 91:53–66
102. Novoselov KS, Fal VI, Colombo L, Gellert PR, Schwab MG, Kim K (2012) A roadmap for graphene. Nature 490(7419):192–200
103. Nag A, Mitra A, Mukhopadhyay SC (2018) Graphene and its sensor-based applications: a review. Sens Actuators A 270:177–194
104. Mani V, Govindasamy M, Chen S-M, Chen T-W, Kumar AS, Huang S-T (2017) Core-shell heterostructured multiwalled carbon nanotubes@ reduced graphene oxide nanoribbons/chitosan, a robust nanobiocomposite for enzymatic biosensing of hydrogen peroxide and nitrite. Sci Rep 7(1):1–10
105. Yin D, Bo X, Liu J, Guo L (2018) A novel enzyme-free glucose and H2O2 sensor based on 3D graphene aerogels decorated with Ni3N nanoparticles. Anal Chim Acta 1038:11–20
106. Đurđić S, Vukojević V, Vlahović F, Ognjanović M, Švorc L', Kalcher K, Mutić J, Stanković DM (2019) Application of bismuth (III) oxide decorated graphene nanoribbons for enzymatic glucose biosensing. J Electroanal Chem 850:113400. https://doi.org/10.1016/j.jelechem.2019.11340
107. Lu Z, Wu L, Zhang J, Dai W, Mo G, Ye J (2019) Bifunctional and highly sensitive electrochemical non-enzymatic glucose and hydrogen peroxide biosensor based on NiCo2O4 nanoflowers decorated 3D nitrogen doped holey graphene hydrogel. Mater Sci Eng, C 102:708–717
108. Mazaheri M, Aashuri H, Simchi A (2017) Three-dimensional hybrid graphene/nickel electrodes on zinc oxide nanorod arrays as non-enzymatic glucose biosensors. Sens Actuators B Chem 251:462–471
109. Jeong J-M, Yang M, Kim DS, Lee TJ, Choi BG (2017) High performance electrochemical glucose sensor based on three-dimensional MoS2/graphene aerogel. J Colloid Interface Sci 506:379–385
110. Wu H, Yu Y, Gao W, Gao A, Qasim AM, Zhang F, Wang J, Ding K, Wu G, Chu PK (2017) Nickel plasma modification of graphene for high-performance non-enzymatic glucose sensing. Sens Actuators B Chem 251:842–850
111. Xuan X, Yoon HS, Park JY (2018) A wearable electrochemical glucose sensor based on simple and low-cost fabrication supported micro-patterned reduced graphene oxide nanocomposite electrode on flexible substrate. Biosens Bioelectron 109:75–82
112. Jiang B, Zhou K, Wang C, Sun Q, Yin G, Tai Z, Wilson K, Zhao J, Zhang L (2018) Label-free glucose biosensor based on enzymatic graphene oxide-functionalized tilted fiber grating. Sens Actuators B Chem 254:1033–1039
113. Darvishi S, Souissi M, Kharaziha M, Karimzadeh F, Sahara R, Ahadian S (2018) Gelatin methacryloyl hydrogel for glucose biosensing using Ni nanoparticles-reduced graphene oxide: an experimental and modeling study. Electrochim Acta 261:275–283
114. Nieto CHD, Granero AM, Lopez JC, Pierini GD, Levin GJ, Fernández H, Zon MA (2018) Development of a third generation biosensor to determine hydrogen peroxide based on a composite of soybean peroxidase/chemically reduced graphene oxide deposited on glassy carbon electrodes. Sens Actuators B Chem 263:377–386
115. Huang Y, Tan J, Cui L, Zhou Z, Zhou S, Zhang Z, Zheng R, Xue Y, Zhang M, Li S (2018) Graphene and Au NPs co-mediated enzymatic silver deposition for the ultrasensitive electrochemical detection of cholesterol. Biosens Bioelectron 102:560–567
116. Muthusankar E, Ponnusamy VK, Ragupathy D (2019) Electrochemically sandwiched poly (diphenylamine)/phosphotungstic acid/graphene nanohybrid as highly sensitive and selective urea biosensor. Synth Met 254:134–140
117. Hossain MB, Rana MM, Abdulrazak LF, Mitra S, Rahman M (2019) Graphene-MoS_2 with TiO_2SiO_2 layers based surface plasmon resonance biosensor: numerical development for formalin detection. Biochem Biophys Rep 18:100639
118. Keteklahijani YZ, Sharif F, Roberts EPL, Sundararaj U (2019) Enhanced sensitivity of dopamine biosensors: an electrochemical approach based on nanocomposite electrodes comprising polyaniline, nitrogen-doped graphene, and DNA-functionalized carbon nanotubes. J Electrochem Soc 166(15):B1415
119. Yuan Y, Wang Y, Wang H, Hou S (2019) Gold nanoparticles decorated on single layer graphene applied for electrochemical ultrasensitive glucose biosensor. J Electroanal Chem 855:113495
120. Zou L, Wang S, Qiu J (2020) Preparation and properties of a glucose biosensor based on an ionic liquid-functionalized graphene/carbon nanotube composite. New Carbon Mater 35(1):12–19
121. Baek SH, Roh J, Park CY, Kim MW, Shi R, Kailasa SK, Park TJ (2020) Cu-nanoflower decorated gold nanoparticles-graphene oxide nanofiber as electrochemical biosensor for glucose detection. Mater Sci Eng, C 107:110273
122. Nien Y-H, Su T-Y, Chou J-C, Lai C-H, Kuo P-Y, Lin S-H, Lai T-Y, Rangasamy M (2020) Investigation of flexible arrayed urea biosensor based on graphene oxide/nickel oxide films modified by au nanoparticles. IEEE Trans Instrum Meas 70:1–9
123. Razumiene J, Gureviciene V, Sakinyte I, Rimsevicius L, Laurinavicius V (2020) The synergy of thermally reduced graphene oxide in amperometric urea biosensor: application for medical technologies. Sensors 20(16):4496
124. Kumar V, Kaur I, Arora S, Mehla R, Vellingiri K, Kim K-H (2020) Graphene nanoplatelet/graphitized nanodiamond-based nanocomposite for mediator-free electrochemical sensing of urea. Food Chem 303:125375
125. Gupta S, Murthy CN, Prabha CR (2018) Recent advances in carbon nanotube based electrochemical biosensors. Int J Biol Macromol 108:687–703
126. Kataura H, Kumazawa Y, Maniwa Y, Umezu I, Suzuki S, Ohtsuka Y, Achiba Y (1999) Optical properties of single-wall carbon nanotubes. Synth Met 103(1–3):2555–2558
127. Odom TW, Huang J-L, Kim P, Lieber CM (2000) Structure and electronic properties of carbon nanotubes. ACS Publications, London
128. Wilder JWG, Venema LC, Rinzler AG, Smalley RE, Dekker C (1998) Electronic structure of atomically resolved carbon nanotubes. Nature 391(6662):59–62
129. Dresselhaus G, Riichiro S (1998) Physical properties of carbon nanotubes. World Scientific, Singapore
130. Dresselhaus MS, Dresselhaus G, Eklund PC (1996) Science of fullerenes and carbon nanotubes: their properties and applications. Elsevier

131. Hamada N, Sawada S, Oshiyama A (1992) New one-dimensional conductors: graphitic microtubules. Phys Rev Lett 68(10):1579
132. Mintmire JW, Dunlap BI, White CT (1992) Are fullerene tubules metallic? Phys Rev Lett 68(5):631
133. Lawal AT (2016) Synthesis and utilization of carbon nanotubes for fabrication of electrochemical biosensors. Mater Res Bull 73:308–350
134. Manawi Y, Samara A, Al-Ansari T, Atieh M (2018) A review of carbon nanomaterials' synthesis via the chemical vapor deposition (CVD) method. Materials 11(5):822
135. Wang Z, Dai Z (2015) Carbon nanomaterial-based electrochemical biosensors: an overview. Nanoscale 7(15):6420–6431
136. Gooding JJ (2005) Nanostructuring electrodes with carbon nanotubes: a review on electrochemistry and applications for sensing. Electrochim Acta 50(15):3049–3060
137. Allen BL, Kichambare PD, Star A (2007) Carbon nanotube field-effect-transistor-based biosensors. Adv Mater 19(11):1439–1451
138. Simon J, Flahaut E, Golzio M (2019) Overview of carbon nanotubes for biomedical applications. Materials 12(4):624
139. Rahman MM, Hussain MM, Asiri AM (2017) Fabrication of 3-methoxyphenol sensor based on Fe3O4 decorated carbon nanotube nanocomposites for environmental safety: Real sample analyses. PLoS ONE 12(9):e0177817
140. Fotouhi L, Dorraji PS, Keshmiri YSS, Hamtak M (2018) Electrochemical sensor based on nanocomposite of multi-walled carbon nanotubes/TiO_2 nanoparticles in chitosan matrix for simultaneous and separate determination of dihydroxybenzene isomers. J Electrochem Soc 165(5):B202
141. Zhu T, Zhang Y, Luo L, Zhao X (2019) Facile fabrication of NiO-decorated double-layer single-walled carbon nanotube buckypaper for glucose detection. ACS Appl Mater Interfaces 11(11):10856–10861
142. Barthwal S, Singh NB (2020) Urea detection by ZnO-MWCNT nanocomposite sensor. Mater Today Proc 29:749–752
143. Guan J-F, Zou J, Liu Y-P, Jiang X-Y, Yu J-G (2020) Hybrid carbon nanotubes modified glassy carbon electrode for selective, sensitive and simultaneous detection of dopamine and uric acid. Ecotoxicol Environ Saf 201:110872
144. Liu J-X, Ding S-N (2017) Non-enzymatic amperometric determination of cellular hydrogen peroxide using dendrimer-encapsulated Pt nanoclusters/carbon nanotubes hybrid composites modified glassy carbon electrode. Sens Actuators B Chem 251:200–207
145. Huang B, Wang Y, Lu Z, Du H, Ye J (2017) One pot synthesis of palladium-cobalt nanoparticles over carbon nanotubes as a sensitive non-enzymatic sensor for glucose and hydrogen peroxide detection. Sens Actuators B Chem 252:1016–1025
146. Comba FN, Romero MR, Garay FS, Baruzzi AM (2018) Mucin and carbon nanotube-based biosensor for detection of glucose in human plasma. Anal Biochem 550:34–40
147. Si Y, Park JW, Jung S, Hwang G-S, Goh E, Lee HJ (2018) Layer-by-layer electrochemical biosensors configuring xanthine oxidase and carbon nanotubes/graphene complexes for hypoxanthine and uric acid in human serum solutions. Biosens Bioelectron 121:265–271
148. Çakıroğlu B, Özacar M (2018) A self-powered photoelectrochemical glucose biosensor based on supercapacitor Co_3O_4–CNT hybrid on TiO_2. Biosens Bioelectron 119:34–41
149. Sun D, Li H, Li M, Li C, Dai H, Sun D, Yang B (2018) Electrodeposition synthesis of a NiO/CNT/PEDOT composite for simultaneous detection of dopamine, serotonin, and tryptophan. Sens Actuators B Chem 259:433–442
150. Wang C, Li J, Tan R, Wang Q, Zhang Z (2019) Colorimetric method for glucose detection with enhanced signal intensity using ZnFe 2 O 4–carbon nanotube–glucose oxidase composite material. Analyst 144(5):1831–1839
151. Wang D, Liang Y, Su Y, Shang Q, Zhang C (2019) Sensitivity enhancement of cloth-based closed bipolar electrochemiluminescence glucose sensor via electrode decoration with chitosan/multi-walled carbon nanotubes/graphene quantum dots-gold nanoparticles. Biosens Bioelectron 130:55–64
152. Rahman MM, Alam MM, Alamry KA (2019) Sensitive and selective m-tolyl hydrazine chemical sensor development based on CdO nanomaterial decorated multi-walled carbon nanotubes. J Ind Eng Chem 77:309–316
153. Bao Q, Yang Z, Song Y, Fan M, Pan P, Liu J, Liao Z, Wei J (2019) Printed flexible bifunctional electrochemical urea-pH sensor based on multiwalled carbon nanotube/polyaniline electronic ink. J Mater Sci Mater Electron 30(2):1751–1759
154. Tabatabaei MK, Fard HG, Koohsorkhi J, Arough JM (2019) High-performance immunosensor for urine albumin using hybrid architectures of ZnO nanowire/carbon nanotube. IET Nanobiotechnol 14(2):126–132
155. Singh AK, Singh M, Verma N (2020) Electrochemical preparation of Fe 3 O 4/MWCNT-polyaniline nanocomposite film for development of urea biosensor and its application in milk sample. J Food Meas Charact 14(1):163–175
156. Alagappan M, Immanuel S, Sivasubramanian R, Kandaswamy A (2020) Development of cholesterol biosensor using Au nanoparticles decorated f-MWCNT covered with polypyrrole network. Arab J Chem 13(1):2001–2010
157. Winiarski JP, Rampanelli R, Bassani JC, Mezalira DZ, Jost CL (2020) Multi-walled carbon nanotubes/nickel hydroxide composite applied as electrochemical sensor for folic acid (vitamin B9) in food samples. J Food Compos Anal 92:103511
158. Yu W, Tang Y, Sang Y, Liu W, Wang S, Wang X (2020) Preparation of a carboxylated single-walled carbon-nanotube-chitosan functional layer and its application to a molecularly imprinted electrochemical sensor to quantify semicarbazide. Food Chem 333:127524
159. Huang Q, Lin X, Tong L, Tong Q-X (2020) Graphene quantum dots/multiwalled carbon nanotubes composite-based electrochemical sensor for detecting dopamine release from living cells. ACS Sustain Chem Eng 8(3):1644–1650
160. Lei H, Zhu H, Sun S, Zhu Z, Hao J, Lu S, Cai Y, Zhang M, Du M (2020) Synergistic integration of Au nanoparticles, Co-MOF and MWCNT as biosensors for sensitive detection of low-concentration nitrite. Electrochim Acta 365:137375
161. Pandey RR, Liang J, Cakiroglu D, Charlot B, Todri-Sanial A (2020) Electrochemical glucose sensor using single-wall carbon nanotube field effect transistor
162. Alizadeh M, Azar PA, Mozaffari SA, Karimi-Maleh H, Tamaddon A-M (2020) Evaluation of Pt, Pd-doped, NiO-decorated, single-wall carbon nanotube-ionic liquid carbon paste chemically modified electrode: an ultrasensitive anticancer drug sensor for the determination of daunorubicin in the presence of tamoxifen. Front Chem 8:677
163. Nguyen TNH, Jin X, Nolan JK, Xu J, Le KVH, Lam S, Wang Y, Alam MA, Lee H (2020) Printable nonenzymatic glucose biosensors using carbon nanotube-PtNP nanocomposites modified with AuRu for improved selectivity. ACS Biomater Sci Eng 6(9):5315–5325
164. Li J, Liu Y, Tang X, Xu L, Min L, Xue Y, Hu X, Yang Z (2020) Multiwalled carbon nanotubes coated with cobalt (II) sulfide nanoparticles for electrochemical sensing of glucose via direct electron transfer to glucose oxidase. Microchim Acta 187(1):1–9
165. Palomar Q, Xu X, Selegård R, Aili D, Zhang Z (2020) Peptide decorated gold nanoparticle/carbon nanotube electrochemical sensor for ultrasensitive detection of matrix metalloproteinase-7. Sens Actuators B Chem 325:128789
166. Ognjanovic M, Stankovic DM, Jovic M, Krstic MP, Lesch A, Girault HH, Antic B (2020) Inkjet-printed carbon nanotube electrodes modified with dimercaptosuccinic acid-capped Fe_3O_4 nanoparticles on reduced graphene oxide nanosheets for single-drop determination of trifluoperazine. ACS Appl Nano Mater 3(5):4654–4662

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.