

Review

Carbon nanomaterial-based electrochemical sensor in biomedical application, a comprehensive study

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Abstract: Recently, carbon nanocomposites have garnered a lot of curiosity because of their distinctive characteristics and extensive variety of possible possibilities. Among all of these applications, the development of sensors with electrochemical properties based on carbon nanocomposites for use in biomedicine has shown as an area with potential. These sensors are suitable for an assortment of biomedical applications, such as prescribing medications, disease diagnostics, and biomarker detection. They have many benefits, including outstanding sensitivity, selectivity, and low limitations on detection. This comprehensive review aims to provide an in-depth analysis of the recent advancements in carbon nanocomposites-based electrochemical sensors for biomedical applications. The different types of carbon nanomaterials used in sensor fabrication, their synthesis methods, and the functionalization techniques employed to enhance their sensing properties have been discussed. Furthermore, we enumerate the numerous biological and biomedical uses of electrochemical sensors based on carbon nanocomposites, among them their employment in illness diagnosis, physiological parameter monitoring, and biomolecule detection. The challenges and prospects of these sensors in biomedical applications are also discussed. Overall, this review highlights the tremendous potential of carbon nanomaterial-based electrochemical sensors in revolutionizing biomedical research and clinical diagnostics.

Keywords: carbon nanocomposites; sensitivity; selectivity; low detection limits; detecting biomolecules; monitoring physiological parameters; diagnosing diseases; electrochemical sensors

1. Introduction

Because electrochemical sensors can identify and measure the different biochemicals present in human fluid, they are essential in biomedical applications. It provides excellent sensitivity and selectivity for identifying target analytes and can quickly and precisely identify certain compounds or biomarkers in complex biological samples. Because of this, electrochemical sensors' sensitivity and selectivity make them useful instruments for monitoring and diagnosing diseases early on [1–5]. As known, the electrochemical sensors provide rapid analysis, delivering real-time results within minutes or seconds, which is essential in critical medical situations for timely diagnosis and treatment decisions [6–8]. Thus, it eliminates the step of sending

samples to a clinical laboratory and delays the late medical interventions. In addition, electrochemical sensors are often cost-effective compared to traditional laboratory-based analytical techniques, making them accessible in resource-limited settings [9,10].

Multiplexed analysis can be made possible by designing the electrochemical sensors to detect numerous analytes at once. This is another potential feature. This function is very helpful for biomarker profiling, as the combination of several biomarkers can yield more thorough diagnostic data [11,12]. In terms of long-term monitoring, the electrochemical sensors can be integrated into implantable or wearable devices for long-term monitoring of physiological parameters or drug delivery. This allows continuous monitoring of patient health and therapeutic efficacy over extended periods, providing valuable insights for personalized medicine and treatment optimization [13,14]. Thus, electrochemical sensors have diverse applications in biomedicine, including disease diagnosis, drug discovery, monitoring of therapeutic interventions, environmental monitoring, and biosecurity. Their versatility allows them to be adapted for various biomedical needs.

In short, electrochemical sensors offer high sensitivity, selectivity, rapid analysis, and versatility, making them indispensable tools in biomedical applications. They have the potential to revolutionize medical diagnostics, patient monitoring, and personalized medicine by providing accurate, real-time, and cost-effective solutions.

2. Instrumentation of electrochemical sensors

Electrochemical sensors are widely used for detecting and quantifying various analytes in fields such as environmental monitoring, healthcare, and industrial processes. The instrumentation of electrochemical sensors typically involves several key components and techniques. The basic setup of an electrochemical sensor consists of an electrochemical cell. This cell typically includes an electrode system, which consists of a working electrode, a reference electrode, and a counter electrode. The analyte of interest interacts with the working electrode surface, leading to an electrochemical reaction. To control and measure the electrical potential or current during electrochemical measurements, a potentiostat or galvanostat is used. These instruments provide a stable potential or current to the working electrode and maintain it at the desired value throughout the experiment. Potentiostats are commonly used for most electrochemical measurements. The reference electrode is a stable electrode with a known and constant potential. It provides a reference point for measuring the potential at the working electrode. Common reference electrodes include silver/silver chloride (Ag/AgCl) and saturated calomel electrode (SCE). The counter electrode completes the electrical circuit in the electrochemical cell. It compensates for the current flowing through the working electrode during the electrochemical reaction. Common counter electrodes are made of materials such as platinum, graphite, or gold. The electrochemical signal generated at the working electrode is typically small and requires amplification and conditioning for accurate measurement. Signal amplifiers and filters are used to enhance the signal-to-noise ratio and remove unwanted noise or interference. A data acquisition system is used to collect and process the output from the electrochemical sensor. It typically includes analog-to-digital converters (ADCs)

to convert the analog electrochemical signal into a digital format, which can be further processed and analyzed by a computer or microcontroller. Electrochemical sensors often require calibration to establish a relationship between the measured signal and the analyte concentration. Calibration involves measuring the sensor response with known concentrations of the analyte and creating a calibration curve. Standardization ensures the accuracy and reliability of the sensor measurements by using certified reference materials. In recent years, there has been a trend toward miniaturizing electrochemical sensors and integrating them with portable or wearable devices. This allows for on-site and real-time monitoring of analytes in various applications, including point-of-care diagnostics and environmental sensing. In **Figure 1**, the instrumentation of an electrochemical sensor is illustrated.

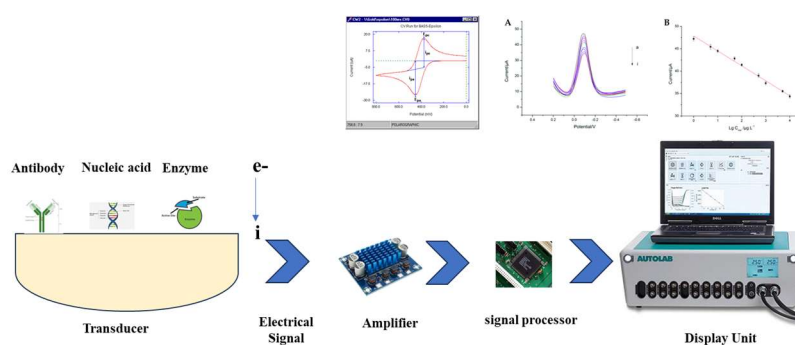


Figure 1. Instrumentation of electrochemical sensor.

3. Reagent and biomolecules for electrochemical sensing

Electrochemical sensors utilize specific reagents and biomolecules to facilitate the detection and quantification of analytes. The choice of reagents and biomolecules depends on the nature of the analyte and the sensing mechanism employed. Enzymes are widely used in electrochemical sensors due to their high catalytic activity and specificity. They can be immobilized on the electrode surface or incorporated into the sensor matrix. Examples include glucose oxidase for glucose sensing, lactate oxidase for lactate sensing, and cholinesterase for acetylcholine sensing [15–17]. Antibodies or antibody fragments (e.g., monoclonal antibodies) are used in immunosensors for the detection of specific antigens or biomarkers. The antibodies are immobilized on the electrode surface or on nanoparticles that are subsequently captured by the electrode. This allows for highly specific recognition and measurement of target analytes [18,19]. Besides this, DNA or RNA probes are employed in nucleic acid sensors for the detection of specific DNA sequences or RNA molecules. Probes can be designed to hybridize with the target sequence, leading to changes in the electrochemical signal. Various strategies, such as hybridization chain reaction (HCR) or strand displacement amplification (SDA), can be used to enhance the sensitivity of nucleic acid sensors [20,21]. Moreover, Redox mediators are small molecules that facilitate the transfer of electrons between the electrode and the analyte, enhancing the electrochemical signal. Examples include ferrocene derivatives, methylene blue, and quinones. Redox mediators can be incorporated into the sensor system to mediate the electrochemical reaction and amplify the signal [22,23]. Reducing or oxidizing agents can be added to the sensor system to modulate the electrochemical reaction or enhance

the signal. For example, in amperometric glucose sensors, a reducing agent (e.g., ascorbic acid) can be added to minimize interference from other electroactive species [24,25]. In addition, electrochemical sensors often require buffer solutions to maintain a stable pH and optimize the electrochemical reactions. Common buffer systems include phosphate-buffered saline (PBS), Tris-HCl, or acetate buffers. The buffer composition and pH are chosen based on the requirements of the specific electrochemical reaction and the stability of the biomolecules involved [26,27].

4. Role of carbon nanomaterials in electrochemical sensor development

The creation of electrochemical sensors greatly benefits from the use of carbon nanomaterials. Its remarkable mechanical, chemical, and electrical characteristics make it an excellent choice for applications involving electrochemical sensing. Due to its huge reactive surface area and strong electrical conductivity, it can move electrons efficiently and has increased sensitivity. The performance of conventional electrodes can be enhanced by using carbon nanomaterials as modifiers or by directly integrating them into the electrode structure [28,29]. Besides this, it can serve as excellent support for electro-catalysts in electrochemical sensors. The high surface area and good mechanical stability of carbon nanomaterials enhance the catalyst's activity and stability, leading to improved sensor performance [30,31]. In addition, carbon nanomaterials can act as electrochemical sensing platforms themselves. Carbon nanomaterials can be utilized to amplify the electrochemical signals generated during electrochemical sensing processes. A schematic setup of an electrochemical sensor is demonstrated in **Figure 2**.

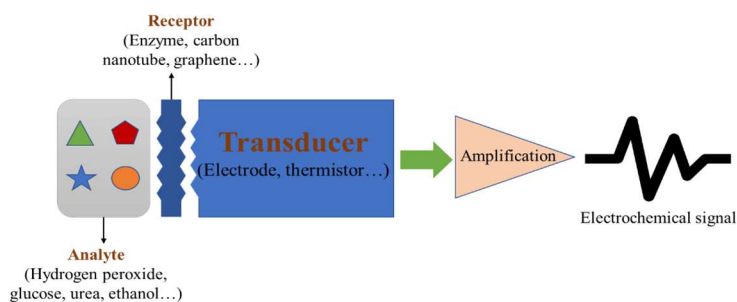


Figure 2. Schematic diagram of an electrochemical sensor.

Thus, this signal amplification approach improves the electrochemical sensor's sensitivity, enabling the detection of trace analytes [32,33]. On the other hand, the carbon nanomaterials can be tailored to exhibit selective interactions with target analytes, enabling the development of highly specific electrochemical sensors. Functionalization of the carbon nanomaterial surface with specific receptors, such as antibodies, enzymes, or molecular imprints, allows for the selective recognition and detection of target molecules in complex samples [34,35]. Therefore, carbon nanomaterials have revolutionized the field of electrochemical sensing by providing enhanced sensitivity, excellent electrical conductivity, versatile functionalization, stability, and integration capabilities. Ongoing research continues to explore new synthesis and functionalization techniques, as well as innovative sensor designs, to

further optimize the properties of carbon nanomaterials and expand their applications in various fields, including environmental monitoring, healthcare diagnostics, and food safety.

5. Types of carbon nanomaterials

There are several types of carbon nanomaterials, each with unique structures and properties.

5.1. Carbon nanotubes (CNTs)

Carbon nanotubes are cylindrical structures made of rolled-up graphene sheets. They can be classified as single-walled (SWCNTs) or multi-walled (MWCNTs) depending on the number of graphene layers. CNTs possess excellent mechanical strength, high electrical conductivity, and large surface area. Various types of carbon nanotubes are illustrated in **Figure 3**. They are widely used in various applications as electronics, energy storage, and composite materials.

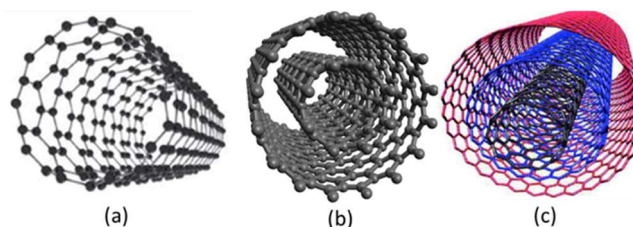


Figure 3. Structure. **(a)** single-walled carbon nanotube (SWCNT); **(b)** double-walled carbon nanotube (DWCNT); **(c)** multi-walled carbon nanotube (MWCNT).

Thus, carbon nanotubes can serve as excellent transducers in electrochemical sensors due to their unique electrical properties. When CNTs are functionalized or modified with specific biomolecules or receptors, they can selectively recognize and bind to target analytes, such as disease-specific biomarkers or molecules indicative of a particular disease [36–38]. Thus, the unique properties of carbon nanotubes, including their high sensitivity, excellent electrical conductivity, electrochemical activity, and compatibility with functionalization and integration, make them highly valuable for electrochemical sensing applications. Ongoing research aims to further optimize the properties of CNTs, explore new synthesis and functionalization techniques, and develop innovative sensor designs for enhanced performance and broader application domains.

5.2. Graphene

A further important aspect of the carbon nanomaterial family is graphene, which is a substance made up of just a single layer of carbon atoms organized in a two-dimensional in nature honeycomb lattice. The structure of graphene is shown in **Figure 4**. It is a highly conductive, flexible, and incredibly thin material. Because of its remarkable mechanical, electrical, and thermal features, ranging graphene receives application throughout a variety of fields, including medicinal devices, electronics, sensors, and energy storage. To achieve high selectivity and specificity towards the target biomarker, graphene-based electrochemical sensors can be functionalized with

particular receptors, such as antibodies, aptamers, or molecularly imprinted polymers. Functionalization lowers false-positive or false-negative readings by enabling the sensor to distinguish between the target biomarker and other interfering species present in the sample. Graphene, like carbon nanotubes, can be used in sensor arrays to allow for the simultaneous multiplexed detection of several biomarkers. An array of graphene-based sensors can be functionalized with distinct receptors for various biomarkers, enabling simultaneous analysis and thorough illness diagnosis [39–42]. The application of graphene in electrochemical sensing has shown great promise, and ongoing research aims to further optimize its properties, explore new fabrication techniques, and develop innovative sensor designs. Graphene-based electrochemical sensors have the potential to revolutionize fields such as environmental monitoring, healthcare diagnostics, food safety, and many other areas where sensitive and selective detection of analytes is crucial.

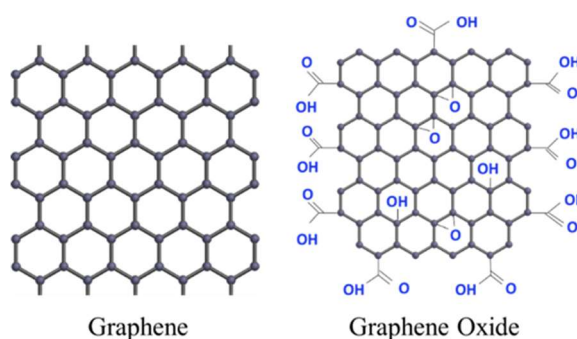


Figure 4. Structure of graphene and graphene oxide.

5.3. Graphene oxide (GO)

Graphene oxide is derived from graphene by introducing oxygen-containing functional groups. The structure of graphene oxide is shown in **Figure 4**. GO exhibits good dispersibility in water and other solvents, making it easier to process and functionalize. It is used in various fields, including sensors, membranes, drug delivery systems, and composites [43,44]. Thus, the application of graphene oxide in electrochemical sensors has shown great promise in various fields, including environmental monitoring, healthcare diagnostics, and food safety. Ongoing research is focused on further optimizing the properties of GO-based sensors [45,46] and exploring new applications in areas such as energy storage, wearable devices, and point-of-care diagnostics.

5.4. Carbon nanofibers (CNFs)

Carbon nanofibers are elongated structures composed of graphene sheets stacked together in a fibrous form. The structure of carbon nanofiber is illustrated in **Figure 5**. They can be produced through various methods, including chemical vapor deposition and electrospinning. CNFs possess high mechanical strength, electrical conductivity, and thermal stability. They find applications in composite materials, energy storage, and sensors. Therefore, carbon nanofibers offer a range of advantages for electrochemical sensing applications, including high surface area, excellent conductivity, versatile functionalization, and compatibility with other materials

[47,78]. Ongoing research aims to further optimize the properties of CNFs, explore new synthesis techniques, and develop innovative sensor designs for various analytical applications.

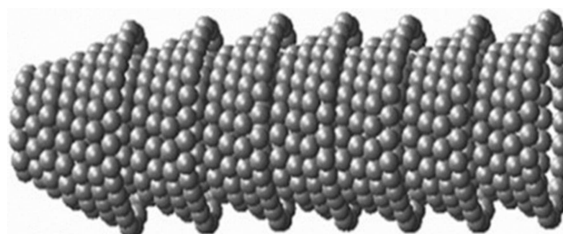


Figure 5. Structure of carbon nanofiber.

5.5. Fullerenes

Fullerenes are closed-cage carbon molecules with a hollow spherical or ellipsoidal structure. The most well-known fullerene is C₆₀, also called buckminsterfullerene or Buckyball. Fullerenes exhibit unique electronic and optical properties and have applications in electronics, photovoltaics, and biomedical research. Thus, fullerene, specifically C₆₀ (buckminsterfullerene), has shown promising potential for various electrochemical sensor applications. While fullerene-based sensors are not as extensively studied as other carbon nanomaterials like graphene or carbon nanotubes, they offer unique properties that make them attractive for certain sensing applications. Here are some potential applications of C₆₀ as an electrochemical sensor [49–51]. While the use of C₆₀ as an electrochemical sensor is still an active area of research, its unique properties, including redox activity, electron transfer kinetics, stability, and the ability to detect reactive species, make it an intriguing material for certain sensing applications. Further research and development are needed to explore and optimize the potential of C₆₀-based electrochemical sensors and to understand their performance characteristics in various sensing scenarios. The larger C₇₀ molecule, similar to C₆₀, belongs to the fullerene family. It resembles the ellipsoidal cage structure of a rugby ball. The structures of C₇₀ and C₆₀ fullerene are shown in **Figure 6b,c**. A fullerene C₇₀ cube is used for sensing volatile aromatic solvent vapors [52,53].

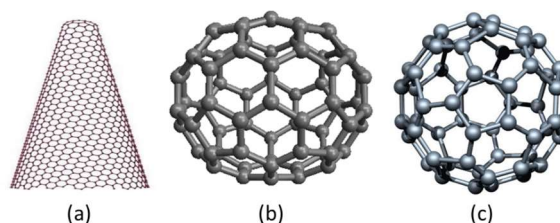


Figure 6. Structure. (a) carbon nanohorn; (b) C₇₀ fullerene; (c) C₆₀ fullerene.

5.6. Carbon dots

Carbon dots are small carbon nanoparticles with sizes typically less than 10 nanometers. They exhibit strong fluorescence properties and can be easily functionalized. As illustrated in **Figure 7**, CDs are comprised of graphene quantum dots, carbon quantum dots, carbon nanodots, and carbonized polymer dots. These dots

are categorized based on the particular characteristics of their carbon core structure, surface groups, and properties [54].

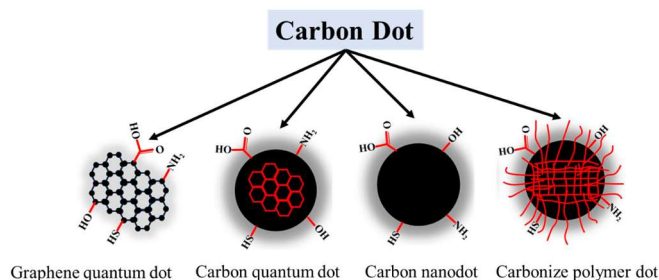


Figure 7. Classification of carbon dots.

Carbon dots find applications in bioimaging, optoelectronics, and sensing. Therefore, carbon dots as electrochemical sensors are an active area of research, with ongoing efforts focused on optimizing their properties, exploring new synthesis techniques, and developing innovative sensing strategies. The unique characteristics of CDs, including their electrochemical activity, high surface area, sensitivity, and versatility, make them attractive for a wide range of electrochemical sensing applications [55–57].

5.7. Carbon nanohorns

Carbon nanohorns (CNHs) are unique carbon nanostructures that have gained significant attention in various fields, including electrochemical sensor applications. CNHs are three-dimensional, hollow, horn-shaped carbon nanoparticles with a high surface area and unique electronic properties. The structure of carbon nanohorn is shown in **Figure 6a**. These properties make them promising candidates for sensor development, particularly in electrochemical sensing [58,59]. Ongoing research and development in this field aim to further optimize the performance of CNH-based sensors and explore new applications in sensing and detection.

6. Carbon nanomaterial-based electrochemical sensors

Due to its special qualities, which include strong electrical conductivity, a huge surface area, and exceptional chemical stability, carbon nanomaterials have demonstrated significant potential in the field of electrochemical sensors, as was previously mentioned. Their ability to efficiently transport electrons and offer a large surface area for analyte adsorption makes them excellent choices for sensing applications. A summary of the electrochemical sensors that have been developed utilizing various carbon nanomaterials is presented in **Table 1**. Applications for carbon nanomaterial-based electrochemical sensors are numerous and include food safety, industrial process control, healthcare diagnostics, and environmental monitoring [60,61]. Target analytes can be detected swiftly, cautiously, and exquisitely attributable to the distinctive characteristics of carbon nanomaterials. The goal of ongoing research is to further improve the performance of these sensors by the integration of cutting-edge signal transduction techniques, the optimization of carbon nanomaterial manufacturing, and the investigation of novel functionalization procedures.

Table 1. Carbon nanomaterials based modified electrochemical sensors [62].

Modified electrode	Drug	Method	Linear range	Limit of detection
MWNT-COOH/GCE	6-mercaptopurine	Amperometry	-	-
MWNT-COOH/GCE	6-mercaptopurine	Amperometry	0.4–100 μM	0.2 μM
SWNT-DCP/GCE	Epirubicin	Linear sweep voltammetry	0.05–50 μM	0.02 μM
CNT-CTAB/GCE	Daunorubicin	Cyclic voltammetry	20–500 nM	10 nM
MWCNT/GCE	Enrofloxacin Ciprofloxacin	Linear sweep voltammetry	2.0–780.0 μM	0.5 μM
MWCNT/GCE	Ciprofloxacin	Linear sweep voltammetry	40–1000 μM	6.0 μM
MWCNT/GCE	Gatifloxacin	Differential pulse voltammetry	21.3–1700 μM	4.5 nM
Ag NPs/MWCNTs-COOH/GCE	Adriamycin	Differential pulse voltammetry	8.2–19 nM	1.7 nM
Cyclodextrin-Gr NS/GCE	Doxorubicin Methotrexate	Differential pulse voltammetry	10 nM–0.2 μM	0.1 nM
MWCNTs/CPE	6-Mercaptopurine	Linear sweep voltammetry	0.5–900 μM	0.1 μM
O-MWNTs/GCE	Methotrexate	Differential pulse voltammetry	0.1–8.0 μM	0.015 μM
Q-MWNTs/GCE	Methotrexate	Amperometry	0.01–20 mg/L	0.2 $\mu\text{M/L}$
dsDNA-modified PPyMWCNTs/PGE	6-Mercaptopurine	Differential pulse voltammetry	0.2–100 μM	0.08 μM
CQDs/GCE	Etoposide	Differential pulse voltammetry	0.02–10.0 μM	0.005 μM
GQD/GCE	Doxorubicin hydrochloride	Differential pulse voltammetry	0.018–3.600 μM	0.016 μM
GQD/GCE	Doxorubicin hydrochloride	Differential pulse voltammetry	0.018–3.60 μM	0.016 μM
MWCNT/GCE	6-Mercaptopurine	Linear sweep voltammetry	0.5–3.0 μM	8.41 nM
MWCNT/Pt E	Doxorubicin	Cyclic voltammetry	0.2–4.0 $\mu\text{M/mL}$	0.002 $\mu\text{M/mL}$
DNA/SWCNTs/PPy/PGE	Ciprofloxacin	Differential pulse voltammetry	0.008–30.0 μM	4 nM
CB/B-CD/SPE	Flutamide	Differential pulse voltammetry	0.05–158.3 μM	0.016 μM
MWCNTs/GCE	Dacarbazine	Differential pulse voltammetry	0.4–2500 nM	0.12 nM
MWCNT-PUFIX/HF-PGE	Capecitabine Erlotinib	Differential pulse voltammetry	7.70–142.00 μM	0.11 μM
N-rGO-CS/Au	Doxorubicin	Differential pulse voltammetry	0.010–15 μM	10 nM
CNPs/N/GCE	Azathioprine	Cyclic voltammetry	0.2–50 μM	80 μM
NDG/CS/GCE	Azathioprine	Cyclic voltammetry	0.2–100 μM	65 μM

7. Working principles of electrochemical sensors

The cornerstone for the functioning of electrochemical sensors is the principle of converting an electrical signal from a chemical signal, such as the presence or concentration of an analyte. Usually, they are made up of an electrode/electrolyte system that aids in the electrochemical reactions necessary for sensing. These comprise the general working principles of electrochemical sensors; however, they might differ based on the particular design and configuration as:

7.1. Potentiometric sensors

Potentiometric sensors measure the potential difference (voltage) between two or more electrodes in an electrochemical cell. The potential difference is related to the concentration of the analyte under investigation. These sensors typically employ ion-selective electrodes (ISEs), such as pH electrodes or ion-specific electrodes, that selectively respond to specific ions in the solution. The potential difference generated

by the ISE is measured and correlated with the analyte concentration using a calibration curve.

7.2. Amperometric sensors

Amperometric sensors detect the current generated by an electrochemical reaction at an electrode surface. The current is proportional to the concentration of the analyte. These sensors usually consist of a working electrode, a reference electrode, and sometimes a counter electrode. The working electrode is typically modified with a catalyst or specific molecules that facilitate the electrochemical reaction of the analyte. When the analyte comes into contact with the working electrode, it undergoes an oxidation or reduction reaction, resulting in the generation of a current that is measured and correlated with the analyte concentration.

7.3. Voltammetric sensors

Voltammetric sensors involve the measurement of the current as a function of the applied potential (voltage) at an electrode. These sensors utilize techniques such as cyclic voltammetry, differential pulse voltammetry, or square wave voltammetry. The potential is scanned over a specific range, and the resulting current response provides information about the analyte concentration. Voltammetric sensors are commonly used for the detection of redox-active species or for studying the electrochemical behavior of analytes.

7.4. Impedimetric sensors

Impedimetric sensors track variations in the electrode-electrolyte interface's impedance, or frequency-dependent resistance, in response to analyte interaction. Usually, these sensors use highly surface-area electrodes or certain surface treatments to increase sensitivity. The electrical characteristics of the electrode-electrolyte interface, such as capacitance or charge transfer resistance, change in the presence of the analyte and are measured in order to ascertain the analyte concentration.

8. Fabrication methods of electrochemical sensor

The fabrication of electrochemical sensors involves several key steps, including the selection of materials, electrode preparation, immobilization of sensing elements, and assembly of the sensor. Here is a general overview of the fabrication process:

8.1. Material selection

The first step is to select suitable materials for the sensor components. This includes choosing appropriate electrode materials, such as metals (e.g., gold, platinum), carbon-based materials (e.g., graphite, carbon nanotubes), or conductive polymers. The selection depends on factors such as the target analyte, desired sensitivity, and compatibility with the chosen fabrication techniques.

8.2. Electrode preparation

The electrodes can be prepared through various techniques, such as physical deposition, screen printing, or lithography. For example, metal electrodes can be

fabricated by depositing a thin layer of the metal onto a substrate using techniques like sputtering or evaporation. Carbon-based electrodes can be prepared by screen printing a carbon ink onto a substrate or by directly growing carbon nanomaterials on the electrode surface.

8.3. Surface modification

Surface modification is often performed to enhance the sensitivity and selectivity of the sensor. This can involve functionalizing the electrode surface with specific molecules or nanoparticles. Functionalization can be achieved through self-assembled monolayers (SAMs), electrodeposition, or chemical modification techniques. The functionalized surface allows for the immobilization of sensing elements or recognition elements that interact with the target analyte. The surface of nanotubes can be functionalized in different ways as illustrated in **Figure 8**.

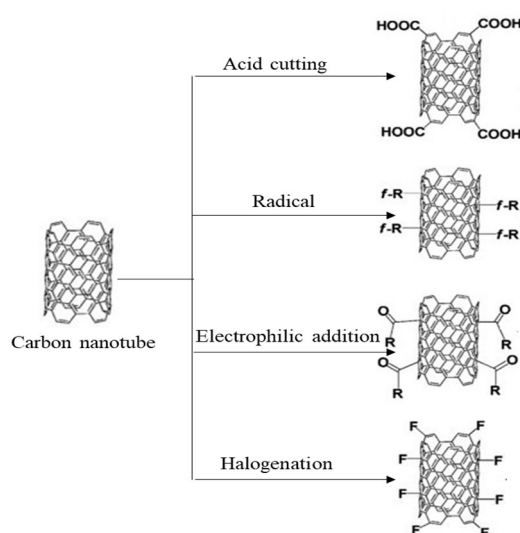


Figure 8. Surface functionalization of carbon nanotubes.

8.4. Immobilization of sensing elements

Sensing elements, such as enzymes, antibodies, or DNA probes, are immobilized onto the electrode surface to enable the selective detection of the target analyte. Immobilization techniques can include physical adsorption, covalent attachment, or entrapment within a polymer matrix. The immobilization method should ensure the stability and activity of the sensing element while allowing for efficient analyte interaction.

8.5. Sensor assembly

Once the electrode and sensing elements are prepared, the sensor is assembled. This typically involves placing the prepared electrode into a suitable housing or cell that allows for the introduction of the analyte and the connection to measurement equipment. The assembly can include additional components, such as reference electrodes or counter electrodes, depending on the sensor design.

8.6. Sensor characterization and testing

After fabrication, the sensor needs to be characterized and tested to evaluate its performance. This includes calibrating the sensor response, determining the detection limit, assessing the selectivity, and evaluating the stability and reproducibility of the sensor. Various electrochemical techniques, such as cyclic voltammetry or amperometry, are commonly used for characterization and testing.

9. Biomedical applications of electrochemical sensor

Electrochemical sensors have found numerous applications in the field of biomedicine due to their ability to provide sensitive and selective detection of various biomolecules and analytes. Here are some key biomedical applications of electrochemical sensors:

9.1. Detection of biomolecules

The detection of biomolecules, such as proteins, DNA, and other analytes, is frequently accomplished through the use of electrochemical sensors. Thus, there are electrochemical sensors that can identify DNA using a variety of approaches, such as amplification and DNA hybridization. The particular binding between a DNA probe that has been mounted on the sensor surface and its complementary target DNA sequence is what drives DNA hybridization-based sensors. A change in the electrochemical signal, such as a change in voltage or current, is caused by the hybridization event and can be monitored to determine whether the target DNA is present or concentrated [48–50]. Additionally, it could detect proteins using a variety of methods, including immunosorbent assays involving enzymes (ELISAs) and antibody-based tests. Target proteins in the sample attach to particular antibodies that have been permanently selected on the sensor surface in antibody-based sensors. Protein identification is made conceivable by the binding event, which causes a modification in the electrochemical signal. Enzyme-labeled antibodies that react with the target protein to produce an electrochemical signal are used in ELISA-based electrochemical sensors [63–66]. In addition, enzymatic activity, which is frequently employed to quantify the presence of particular biomolecules, can be detected by electrochemical sensors. Immobilized enzymes that have been immobilized that catalyze particular reactions with the target analyte are used in enzyme-based sensors. An electrochemical signal, such as a shift in potential or current, has been generated by the enzymatic process and can be evaluated for determining the quantity of the target biomolecule [67–69]. Aptamers, which are short single-stranded DNA or RNA molecules, can bind to target molecules with high specificity. Electrochemical sensors can be functionalized with aptamers, allowing for the selective detection of various analytes, including small molecules, proteins, and toxins. The binding of the target analyte to the aptamer leads to changes in the electrochemical signal, enabling sensitive and specific detection [70–72]. In addition, electrochemical sensors can be integrated with nucleic acid amplification techniques, such as polymerase chain reaction (PCR) or loop-mediated isothermal amplification (LAMP), to enhance the sensitivity of DNA or RNA detection [73–75]. These amplification techniques produce

multiple copies of the target nucleic acid sequence, which can be detected by the electrochemical sensor.

9.2. Disease diagnosis

In the detection and monitoring of cancer, infectious diseases, and other medical disorders, electrochemical sensors have demonstrated considerable promise in the field of disease diagnostics. It may be useful in the early identification and treatment of cancer. Prostate-specific antigen (PSA) for prostate cancer and carcinoembryonic antigen (CEA) for colorectal cancer are two examples of specific biomarkers that they can identify. Electrochemical sensors can provide important information for cancer screening, diagnosis, and treatment response monitoring by detecting the concentration of these biomarkers in patient samples [76–78]. Besides this, electrochemical sensors are also employed for the rapid and sensitive detection of infectious agents, including bacteria, viruses, and parasites. By targeting specific nucleic acid sequences or antigens associated with the pathogens, electrochemical sensors can identify infections such as HIV, hepatitis, malaria, and respiratory infections. These sensors offer the potential for point-of-care testing, enabling early diagnosis and timely treatment [79–81]. In addition, electrochemical sensors are commonly used for continuous glucose monitoring in diabetes management. By measuring glucose levels in body fluids, such as blood or interstitial fluid, electrochemical sensors provide real-time information about glucose concentration. This helps individuals with diabetes to monitor and manage their blood sugar levels, ensuring proper insulin administration and dietary adjustments [82,83]. It is also employed for the detection of cardiac biomarkers, such as troponin, creatine kinase-MB (CK-MB), and brain natriuretic peptide (BNP). These biomarkers are indicative of heart damage or dysfunction and are used in the diagnosis of acute myocardial infarction (heart attack), heart failure, and other cardiac conditions [83–86]. Thus, electrochemical sensors can provide rapid and sensitive measurements of these biomarkers, aiding in early diagnosis and risk assessment. Moreover, electrochemical sensors can be used for genetic disease screening, such as detecting mutations or variations in specific genes associated with inherited disorders. By incorporating DNA probes or aptamers specific to the target genetic sequence, electrochemical sensors can identify genetic mutations and variations linked to diseases like cystic fibrosis, sickle cell anemia, and genetic predisposition to certain cancers [87–88]. Again more, electrochemical sensors have applications in the diagnosis and monitoring of neurological disorders. They can measure neurotransmitters, such as dopamine and serotonin, in the central nervous system, providing insights into conditions like Parkinson's disease, depression, and schizophrenia. It can also detect biomarkers associated with neurodegenerative diseases, such as Alzheimer's and Huntington's diseases [89–91].

9.3. Electrochemical biosensing in drug delivery

The use of biosensors in drug delivery systems to track and regulate different medication administration parameters is known as “biosensing in drug delivery”. Medication delivery can be tailored and optimized with the help of biosensors, which

can offer real-time data on medication release, drug concentration, physiological parameters, and patient reaction. Drug release from delivery methods like implants, patches, or nanoparticles can be tracked using biosensors. Biosensors ensure the intended therapeutic impact by providing feedback on the release profile through the incorporation of sensing devices that react to changes in medication concentration or release kinetics. The drug delivery mechanism can be improved or the dosage can be changed with the use of this information [92,93]. Drug monitoring, Biosensors can measure drug concentrations in biological fluids, such as blood or interstitial fluid, enabling the monitoring of drug levels in real-time. This information helps in maintaining therapeutic drug concentrations within the desired range, ensuring efficacy while minimizing side effects or toxicity [94–96]. Besides this, biosensors can be designed to detect specific drugs or drug classes using various sensing mechanisms, including enzymatic reactions, immunoassays, or affinity-based interactions. Moreover, it can be integrated into drug delivery systems to monitor relevant physiological parameters. For example, biosensors can measure parameters such as pH, temperature, oxygen levels, or biomarkers indicative of disease progression or treatment response. This information can be used to optimize drug delivery parameters or trigger drug release in response to specific physiological cues. In addition, biosensors can be coupled with drug delivery systems to create closed-loop or feedback control systems. Biosensors continuously monitor drug concentrations or physiological parameters and provide feedback to control drug delivery rates or adjust dosing algorithms in real-time. This enables personalized and adaptive drug delivery, ensuring optimal therapeutic outcomes [97,98].

10. Challenges and future perspectives of electrochemical sensors

Because of their special qualities and possible uses, carbon-based electrochemical sensors—such as carbon nanotubes (CNTs) and graphene—have drawn a lot of interest. But they also have to deal with some difficulties. Because of their high electrical conductivity and huge surface area, carbon-based sensors frequently show great sensitivity. However, achieving consistent and reproducible sensor performance can be challenging due to variations in material properties and fabrication techniques. Future research aims to optimize sensor performance by developing standardized fabrication processes, improving material quality, and enhancing the understanding of surface interactions and electrochemical properties. Selectivity is a crucial aspect of sensor performance, as it determines the ability to distinguish the target analyte from interfering species. Thus, carbon-based sensors may suffer from non-specific adsorption or interference from other components present in complex samples. Future efforts focus on surface functionalization, selective modification, and integration with specific recognition elements (e.g., antibodies or aptamers) to enhance selectivity and mitigate interference effects.

Long-term stability is a challenge for carbon-based sensors, as they can be susceptible to fouling, surface contamination, or material degradation over time. Researchers are exploring surface modification techniques, protective coatings, and encapsulation strategies to improve the stability and longevity of carbon-based sensors, especially in harsh or dynamic environments. Scalability of carbon-based

sensors for mass production is an important consideration for their practical applications. Challenges exist in translating lab-scale fabrication techniques to scalable manufacturing processes while maintaining sensor performance and consistency. Future research aims to develop cost-effective and scalable manufacturing methods for carbon-based sensors, including roll-to-roll printing, solution processing, and other high-throughput techniques. Integration of carbon-based sensors into compact, portable devices or wearable systems is a key area of development. Miniaturization of these sensors requires addressing challenges related to electronics integration, power management, and device packaging. Future perspectives involve advancements in flexible electronics, wireless communication, and microfabrication techniques to enable the seamless integration of carbon-based sensors into various form factors.

Carbon-based sensors have the potential for multifunctionality and multimodal sensing by combining their electrochemical properties with other sensing modalities, such as optical or mechanical sensing. Integrating multiple sensing mechanisms can provide complementary information and enhance overall sensor performance. Future research focuses on developing hybrid sensor platforms that combine carbon-based materials with other functional materials or transduction principles for multimodal sensing capabilities. As with any technology, environmental considerations are important for carbon-based electrochemical sensors. Efforts are being made to develop eco-friendly and sustainable fabrication processes, minimize the use of hazardous materials, and explore recycling or disposal strategies for sensor devices.

11. Conclusion

In conclusion, carbon-based electrochemical sensors offer unique properties and tremendous potential for various applications. These sensors exhibit high sensitivity, a large surface area, excellent electrical conductivity, and can be functionalized to enhance selectivity. However, they also face challenges such as achieving consistent and reproducible sensor performance, addressing selectivity and interference issues, ensuring stability and longevity, enabling scalable manufacturing, facilitating integration and miniaturization, and considering environmental sustainability. Despite these challenges, ongoing research and technological advancements are paving the way for the future of carbon-based electrochemical sensors. Efforts are focused on optimizing sensor performance through standardized fabrication processes, improving material quality, and understanding surface interactions. Selectivity is being enhanced through surface functionalization, selective modification, and integration with recognition elements. Stability and longevity are being improved through surface modification techniques and protective coatings. Scalable manufacturing methods are being developed to enable mass production, and integration into compact, portable devices and wearable systems is being pursued. Multifunctionality and multimodal sensing capabilities are being explored by combining carbon-based materials with other sensing modalities. Additionally, environmental considerations, such as eco-friendly fabrication processes and recycling strategies, are being addressed.

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References

1. Lu H, He B, Gao B. Emerging electrochemical sensors for life healthcare. *Engineered Regeneration*. 2021; 2: 175-181. doi: 10.1016/j.engreg.2021.12.002
2. Sinha K, Uddin Z, Kawsar HI, et al. Analyzing chronic disease biomarkers using electrochemical sensors and artificial neural networks. *TrAC Trends in Analytical Chemistry*. 2023; 158: 116861. doi: 10.1016/j.trac.2022.116861
3. Tanisclass S, Arshad MKM, Gopinath SCB. Graphene-based electrochemical biosensors for monitoring noncommunicable disease biomarkers. *Biosensors and Bioelectronics*. 2019; 130: 276-292. doi: 10.1016/j.bios.2019.01.047
4. Haque S, Yasir M, Ciocan S, et al. Enzymatic Fuel Cells and Biosensors. In: Ghangrekar MM, Duteanu NM, Surampalli RY, Zhang TC (editors). *Microbial Electrochemical Technologies*. Wiley - VCH GmbH; 2023. pp. 467-494. doi: 10.1002/9783527839001.ch19
5. Haque S, Nasar A, Duteanu N, et al. Carbon based-nanomaterials used in biofuel cells – A review. *Fuel*. 2023; 331: 125634. doi: 10.1016/j.fuel.2022.125634
6. Simoska O, Stevenson KJ. Electrochemical sensors for rapid diagnosis of pathogens in real time. *The Analyst*. 2019; 144(22): 6461-6478. doi: 10.1039/c9an01747j
7. Min J, Sempionatto JR, Teymourian H, et al. Wearable electrochemical biosensors in North America. *Biosensors and Bioelectronics*. 2021; 172: 112750. doi: 10.1016/j.bios.2020.112750
8. Campuzano S, Barderas R, Moreno-Casbas MT, et al. Pursuing precision in medicine and nutrition: the rise of electrochemical biosensing at the molecular level. *Analytical and Bioanalytical Chemistry*. 2023; 416(9): 2151-2172. doi: 10.1007/s00216-023-04805-5
9. Umapathi R, Ghoreishian SM, Rani GM, et al. Review—Emerging Trends in the Development of Electrochemical Devices for the On-Site Detection of Food Contaminants. *ECS Sensors Plus*. 2022; 1(4): 044601. doi: 10.1149/2754-2726/ac9d4a
10. Zhang W, Wang R, Luo F, et al. Miniaturized electrochemical sensors and their point-of-care applications. *Chinese Chemical Letters*. 2020; 31(3): 589-600. doi: 10.1016/j.ccl.2019.09.022
11. Pakchin PS, Nakhjavani SA, Saber R, et al. Recent advances in simultaneous electrochemical multi-analyte sensing platforms. *TrAC Trends in Analytical Chemistry*. 2017; 92: 32-41. doi: 10.1016/j.trac.2017.04.010
12. Zhu C, Yang G, Li H, et al. Electrochemical Sensors and Biosensors Based on Nanomaterials and Nanostructures. *Analytical Chemistry*. 2014; 87(1): 230-249. doi: 10.1021/ac5039863
13. Teymourian H, Parrilla M, Sempionatto JR, et al. Wearable Electrochemical Sensors for the Monitoring and Screening of Drugs. *ACS Sensors*. 2020; 5(9): 2679-2700. doi: 10.1021/acssensors.0c01318
14. Lu T, Ji S, Jin W, et al. Biocompatible and Long-Term Monitoring Strategies of Wearable, Ingestible and Implantable Biosensors: Reform the Next Generation Healthcare. *Sensors*. 2023; 23(6): 2991. doi: 10.3390/s23062991
15. Rossi LM, Quach AD, Rosenzweig Z. Glucose oxidase? magnetite nanoparticle bioconjugate for glucose sensing. *Analytical and Bioanalytical Chemistry*. 2004; 380(4): 606-613. doi: 10.1007/s00216-004-2770-3
16. Madden J, Vaughan E, Thompson M, et al. Electrochemical sensor for enzymatic lactate detection based on laser-scribed graphitic carbon modified with platinum, chitosan and lactate oxidase. *Talanta*. 2022; 246: 123492. doi: 10.1016/j.talanta.2022.123492
17. Singh AP, Balayan S, Hooda V, et al. Nano-interface driven electrochemical sensor for pesticides detection based on the acetylcholinesterase enzyme inhibition. *International Journal of Biological Macromolecules*. 2020; 164: 3943-3952. doi: 10.1016/j.ijbiomac.2020.08.215
18. Teepruksapun K, Hedström M, Mattiasson B. A Sensitive Capacitive Biosensor for Protein a Detection Using Human IgG Immobilized on an Electrode Using Layer-by-Layer Applied Gold Nanoparticles. *Sensors*. 2021; 22(1): 99. doi: 10.3390/s22010099
19. Razzino CA, Serafin V, Gamella M, et al. An electrochemical immunosensor using gold nanoparticles-PAMAM-nanostructured screen-printed carbon electrodes for tau protein determination in plasma and brain tissues from Alzheimer patients. *Biosensors and Bioelectronics*. 2020; 163: 112238. doi: 10.1016/j.bios.2020.112238
20. Wu Y, Arroyo-Currás N. Advances in nucleic acid architectures for electrochemical sensing. *Current Opinion in Electrochemistry*. 2021; 27: 100695. doi: 10.1016/j.coelec.2021.100695
21. Wang DX, Wang J, Wang YX, et al. DNA nanostructure-based nucleic acid probes: construction and biological applications. *Chemical Science*. 2021; 12(22): 7602-7622. doi: 10.1039/d1sc00587a

22. Gao X, Dong S, Fu L, et al. Use of Triangular Silver Nanoplates as Low Potential Redox Mediators for Electrochemical Sensing. *Analytical Chemistry*. 2021; 93(6): 3295-3300. doi: 10.1021/acs.analchem.0c05342
23. Mayall RM, Marengo AJ, Kilgore M, et al. Ultrasensitive Detection of Surface-Confined Redox Molecules by Mediation-Based Amplification. *ChemElectroChem*. 2021; 8(10): 1873-1880. doi: 10.1002/celec.202100369
24. Nishitani S, Sakata T. Enhancement of Signal-to-Noise Ratio for Serotonin Detection with Well-Designed Nanofilter-Coated Potentiometric Electrochemical Biosensor. *ACS Applied Materials & Interfaces*. 2020; 12(13): 14761-14769. doi: 10.1021/acsami.9b19309
25. Hassan MH, Vyas C, Grieve B, et al. Recent Advances in Enzymatic and Non-Enzymatic Electrochemical Glucose Sensing. *Sensors*. 2021; 21(14): 4672. doi: 10.3390/s21144672
26. Manjakkal L, Szwagierczak D, Dahiya R. Metal oxides based electrochemical pH sensors: Current progress and future perspectives. *Progress in Materials Science*. 2020; 109: 100635. doi: 10.1016/j.pmatsci.2019.100635
27. Beaver K, Dantanarayana A, Minteer SD. Materials Approaches for Improving Electrochemical Sensor Performance. *The Journal of Physical Chemistry B*. 2021; 125(43): 11820-11834. doi: 10.1021/acs.jpcc.1c07063
28. Porto LS, Silva DN, de Oliveira AEF, et al. Carbon nanomaterials: synthesis and applications to development of electrochemical sensors in determination of drugs and compounds of clinical interest. *Reviews in Analytical Chemistry*. 2020; 38(3). doi: 10.1515/revac-2019-0017
29. Asadian E, Ghalkhani M, Shahrokhian S. Electrochemical sensing based on carbon nanoparticles: A review. *Sensors and Actuators B: Chemical*. 2019; 293: 183-209. doi: 10.1016/j.snb.2019.04.075
30. Cho IH, Kim DH, Park S. Electrochemical biosensors: perspective on functional nanomaterials for on-site analysis. *Biomaterials Research*. 2020; 24(1). doi: 10.1186/s40824-019-0181-y
31. Yan Y, Miao J, Yang Z, et al. Carbon nanotube catalysts: recent advances in synthesis, characterization and applications. *Chemical Society Reviews*. 2015; 44(10): 3295-3346. doi: 10.1039/c4cs00492b
32. Zhou C, Zou H, Sun C, et al. Recent advances in biosensors for antibiotic detection: Selectivity and signal amplification with nanomaterials. *Food Chemistry*. 2021; 361: 130109. doi: 10.1016/j.foodchem.2021.130109
33. Cho IH, Lee J, Kim J, et al. Current Technologies of Electrochemical Immunosensors: Perspective on Signal Amplification. *Sensors*. 2018; 18(2): 207. doi: 10.3390/s18010207
34. Zamora-Gálvez A, Morales-Narváez E, Mayorga-Martinez CC, et al. Nanomaterials connected to antibodies and molecularly imprinted polymers as bio/receptors for bio/sensor applications. *Applied Materials Today*. 2017; 9: 387-401. doi: 10.1016/j.apmt.2017.09.006
35. Mahmoudpour M, Ezzati Nazhad Dolatabadi J, Torbati M, et al. Nanomaterials and new biorecognition molecules based surface plasmon resonance biosensors for mycotoxin detection. *Biosensors and Bioelectronics*. 2019; 143: 111603. doi: 10.1016/j.bios.2019.111603
36. Pasinszki T, Krebsz M, Tung TT, et al. Carbon Nanomaterial Based Biosensors for Non-Invasive Detection of Cancer and Disease Biomarkers for Clinical Diagnosis. *Sensors*. 2017; 17(8): 1919. doi: 10.3390/s17081919
37. Fahmy HM, Abu Serea ES, Salah-Eldin RE, et al. Recent Progress in Graphene- and Related Carbon-Nanomaterial-based Electrochemical Biosensors for Early Disease Detection. *ACS Biomaterials Science & Engineering*. 2022; 8(3): 964-1000. doi: 10.1021/acsbiomaterials.1c00710
38. Pineda S, Han Z, Ostrikov K. Plasma-Enabled Carbon Nanostructures for Early Diagnosis of Neurodegenerative Diseases. *Materials*. 2014; 7(7): 4896-4929. doi: 10.3390/ma7074896
39. Gan T, Hu, S. Electrochemical sensors based on graphene materials. *Microchimica Acta*. 2011; 175: 1-19. doi: 10.1007/s00604-011-0639-7S
40. Li SJ, Xing Y, Wang GF. A graphene-based electrochemical sensor for sensitive and selective determination of hydroquinone. *Microchimica Acta*. 2011; 176(1-2): 163-168. doi: 10.1007/s00604-011-0709-x
41. Terse-Thakoor T, Badhulika S, Mulchandani A. Graphene based biosensors for healthcare. *Journal of Materials Research*. 2017; 32(15): 2905-2929. doi: 10.1557/jmr.2017.175
42. Coroş M, Pruneanu S, Stefan-van Staden RI. Review—Recent Progress in the Graphene-Based Electrochemical Sensors and Biosensors. *Journal of The Electrochemical Society*. 2019; 167(3): 037528. doi: 10.1149/2.0282003jes
43. Ahmad H, Fan M, Hui D. Graphene oxide incorporated functional materials: A review. *Composites Part B: Engineering*. 2018; 145: 270-280. doi: 10.1016/j.compositesb.2018.02.006

44. Hayyan M, Abo-Hamad A, AlSaadi MA, et al. Functionalization of graphene using deep eutectic solvents. *Nanoscale Research Letters*. 2015; 10(1). doi: 10.1186/s11671-015-1004-2
45. Li J, Kuang D, Feng Y, et al. A graphene oxide-based electrochemical sensor for sensitive determination of 4-nitrophenol. *Journal of Hazardous Materials*. 2012; 201-202: 250-259. doi: 10.1016/j.jhazmat.2011.11.076
46. Qian L, Thiruppathi AR, Elmahdy R, et al. Graphene-Oxide-Based Electrochemical Sensors for the Sensitive Detection of Pharmaceutical Drug Naproxen. *Sensors*. 2020; 20(5): 1252. doi: 10.3390/s20051252
47. Zhang L, Yin M, Wei X, et al. Recent advances in morphology, aperture control, functional control and electrochemical sensors applications of carbon nanofibers. *Analytical Biochemistry*. 2022; 656: 114882. doi: 10.1016/j.ab.2022.114882
48. Jahromi Z, Mirzaei E, Savardashtaki A, et al. A rapid and selective electrochemical sensor based on electrospun carbon nanofibers for tramadol detection. *Microchemical Journal*. 2020; 157: 104942. doi: 10.1016/j.microc.2020.104942
49. Kurbanoglu S, Cevher SC, Toppare L, et al. Electrochemical biosensor based on three components random conjugated polymer with fullerene (C60). *Bioelectrochemistry*. 2022; 147: 108219. doi: 10.1016/j.bioelechem.2022.108219
50. Paukov M, Kramberger C, Begichev I, et al. Functionalized Fullerenes and Their Applications in Electrochemistry, Solar Cells, and Nanoelectronics. *Materials*. 2023; 16(3): 1276. doi: 10.3390/ma16031276
51. Gakhar T, Rosenwaks Y, Hazra A. Fullerene (C60) functionalized TiO₂ nanotubes for conductometric sensing of formaldehyde. *Sensors and Actuators B: Chemical*. 2022; 364: 131892. doi: 10.1016/j.snb.2022.131892
52. Bai J, Sun C, Jiang X. Carbon dots-decorated multiwalled carbon nanotubes nanocomposites as a high-performance electrochemical sensor for detection of H₂O₂ in living cells. *Analytical and Bioanalytical Chemistry*. 2016; 408(17): 4705-4714. doi: 10.1007/s00216-016-9554-4
53. Lin X, Xiong M, Zhang J, et al. Carbon dots based on natural resources: Synthesis and applications in sensors. *Microchemical Journal*. 2021; 160: 105604. doi: 10.1016/j.microc.2020.105604
54. Xu D, Lin Q, Chang H. Recent Advances and Sensing Applications of Carbon Dots. *Small Methods*. 2019; 4(4). doi: 10.1002/smt.201900387
55. Carli S, Lambertini L, Zucchini E, et al. Single walled carbon nanohorns composite for neural sensing and stimulation. *Sensors and Actuators B: Chemical*. 2018; 271: 280-288. doi: 10.1016/j.snb.2018.05.083
56. Zhang R, Fu K, Zou F, et al. Highly sensitive electrochemical sensor based on Pt nanoparticles/carbon nanohorns for simultaneous determination of morphine and MDMA in biological samples. *Electrochimica Acta*. 2021; 370: 137803. doi: 10.1016/j.electacta.2021.137803
57. Qureshi A, Kang WP, Davidson JL, et al. Review on carbon-derived, solid-state, micro and nano sensors for electrochemical sensing applications. *Diamond and Related Materials*. 2009; 18(12): 1401-1420. doi: 10.1016/j.diamond.2009.09.008
58. Yang Y, Yang X, Yang Y, et al. Aptamer-functionalized carbon nanomaterials electrochemical sensors for detecting cancer relevant biomolecules. *Carbon*. 2018; 129: 380-395. doi: 10.1016/j.carbon.2017.12.013
59. Lv MM, Fan SF, Wang QL, et al. An enzyme-free electrochemical sandwich DNA assay based on the use of hybridization chain reaction and gold nanoparticles: application to the determination of the DNA of *Helicobacter pylori*. *Microchimica Acta*. 2019; 187(1). doi: 10.1007/s00604-019-3999-z
60. Santhanam M, Algov I, Alfonta L. DNA/RNA Electrochemical Biosensing Devices a Future Replacement of PCR Methods for a Fast Epidemic Containment. *Sensors*. 2020; 20(16): 4648. doi: 10.3390/s20164648
61. Zhang L, Su W, Liu S, et al. Recent Progresses in Electrochemical DNA Biosensors for MicroRNA Detection. *Phenomics*. 2022; 2(1): 18-32. doi: 10.1007/s43657-021-00032-z
62. Mazouz Z, Mokni M, Fourati N, et al. Computational approach and electrochemical measurements for protein detection with MIP-based sensor. *Biosensors and Bioelectronics*. 2020; 151: 111978. doi: 10.1016/j.bios.2019.111978
63. Vanova V, Mitrevska K, Milosavljevic V, et al. Peptide-based electrochemical biosensors utilized for protein detection. *Biosensors and Bioelectronics*. 2021; 180: 113087. doi: 10.1016/j.bios.2021.113087
64. Yakoh A, Pimpitak U, Rengpipat S, et al. Paper-based electrochemical biosensor for diagnosing COVID-19: Detection of SARS-CoV-2 antibodies and antigen. *Biosensors and Bioelectronics*. 2021; 176: 112912. doi: 10.1016/j.bios.2020.112912
65. Ranallo S, Bracaglia S, Sorrentino D, et al. Synthetic Antigen-Conjugated DNA Systems for Antibody Detection and Characterization. *ACS Sensors*. 2023; 8(7): 2415-2426. doi: 10.1021/acssensors.3c00564
66. Coronado-Apodaca KG, González-Meza GM, Aguayo-Acosta A, et al. Immobilized Enzyme-based Novel Biosensing System for Recognition of Toxic Elements in the Aqueous Environment. *Topics in Catalysis*. 2023; 66(9-12): 606-624. doi: 10.1007/s11244-023-01786-8

67. Bucur B, Purcarea C, Andreescu S, et al. Addressing the Selectivity of Enzyme Biosensors: Solutions and Perspectives. *Sensors*. 2021; 21(9): 3038. doi: 10.3390/s21093038
68. Cavalcante FTT, de A. Falcão IR, da S. Souza JE, et al. Designing of Nanomaterials-Based Enzymatic Biosensors: Synthesis, Properties, and Applications. *Electrochem*. 2021; 2(1): 149-184. doi: 10.3390/electrochem2010012
69. Ziółkowski R, Jarczewska M, Górski Ł, et al. From Small Molecules toward Whole Cells Detection: Application of Electrochemical Aptasensors in Modern Medical Diagnostics. *Sensors*. 2021; 21(3): 724. doi: 10.3390/s21030724
70. Onaş AM, Dascălu C, Raicopol MD, et al. Critical Design Factors for Electrochemical Aptasensors Based on Target-Induced Conformational Changes: The Case of Small-Molecule Targets. *Biosensors*. 2022; 12(10): 816. doi: 10.3390/bios12100816
71. Mahmoudpour M, Karimzadeh Z, Ebrahimi G, et al. Synergizing Functional Nanomaterials with Aptamers Based on Electrochemical Strategies for Pesticide Detection: Current Status and Perspectives. *Critical Reviews in Analytical Chemistry*. 2021; 52(8): 1818-1845. doi: 10.1080/10408347.2021.1919987
72. Wang Z, Li P, Cui L, et al. Integration of nanomaterials with nucleic acid amplification approaches for biosensing. *TrAC Trends in Analytical Chemistry*. 2020; 129: 115959. doi: 10.1016/j.trac.2020.115959
73. Chen Y, Qian C, Liu C, et al. Nucleic acid amplification free biosensors for pathogen detection. *Biosensors and Bioelectronics*. 2020; 153: 112049. doi: 10.1016/j.bios.2020.112049
74. Wang Z yue, Li P, Cui L, et al. Integration of nanomaterials with nucleic acid amplification approaches for biosensing. *TrAC Trends in Analytical Chemistry*. 2020; 129: 115959. doi: 10.1016/j.trac.2020.115959
75. Bertok T, Bertokova A, Hroncekova S, et al. Novel Prostate Cancer Biomarkers: Aetiology, Clinical Performance and Sensing Applications. *Chemosensors*. 2021; 9(8): 205. doi: 10.3390/chemosensors9080205
76. Zhang W, Xiao G, Chen J, et al. Electrochemical biosensors for measurement of colorectal cancer biomarkers. *Analytical and Bioanalytical Chemistry*. 2021; 413(9): 2407-2428. doi: 10.1007/s00216-021-03197-8
77. Dowlatshahi S, Abdekhodaie MJ. Electrochemical prostate-specific antigen biosensors based on electroconductive nanomaterials and polymers. *Clinica Chimica Acta*. 2021; 516: 111-135. doi: 10.1016/j.cca.2021.01.018
78. Menon S, Mathew MR, Sam S, et al. Recent advances and challenges in electrochemical biosensors for emerging and re-emerging infectious diseases. *Journal of Electroanalytical Chemistry*. 2020; 878: 114596. doi: 10.1016/j.jelechem.2020.114596
79. Brazaca LC, dos Santos PL, de Oliveira PR, et al. Biosensing strategies for the electrochemical detection of viruses and viral diseases – A review. *Analytica Chimica Acta*. 2021; 1159: 338384. doi: 10.1016/j.aca.2021.338384
80. Cesewski E, Johnson BN. Electrochemical biosensors for pathogen detection. *Biosensors and Bioelectronics*. 2020; 159: 112214. doi: 10.1016/j.bios.2020.112214
81. Karyakin AA. Glucose biosensors for clinical and personal use. *Electrochemistry Communications*. 2021; 125: 106973. doi: 10.1016/j.elecom.2021.106973
82. Lipińska W, Grochowska K, Siuzdak K. Enzyme Immobilization on Gold Nanoparticles for Electrochemical Glucose Biosensors. *Nanomaterials*. 2021; 11(5): 1156. doi: 10.3390/nano11051156
83. Shinde R, Juwarwala I, Modi V, et al. Chandarana C. Utility of cardiac biomarkers and biosensors for diagnosis of acute myocardial infarction. *Global Translational Medicine*. 2023; 2(2): 0403. doi: 10.36922/gtm.0403
84. Zhong S, Chen L, Shi X, et al. Recent advances in electrochemical aptasensors for detecting cardiac biomarkers: A review. *Microchemical Journal*. 2023; 193: 109063. doi: 10.1016/j.microc.2023.109063
85. Kazemi Asl S, Rahimzadegan M. Recent Advances in the Fabrication of Nano-aptasensors for the Detection of Troponin as a Main Biomarker of Acute Myocardial Infarction. *Critical Reviews in Analytical Chemistry*. 2021; 53(3): 594-613. doi: 10.1080/10408347.2021.1967721
86. Aljabali AA, Obeid MA, Amawi HA, et al. Application of Nanomaterials in the Diagnosis and Treatment of Genetic Disorders. In: *Applications of Nanomaterials in Human Health*. Springer; 2020.
87. Jiang H, Xi H, Juhas M, et al. Biosensors for Point Mutation Detection. *Frontiers in Bioengineering and Biotechnology*. 2021; 9. doi: 10.3389/fbioe.2021.797831
88. Song Z, Zhou Y, Han X, et al. Recent advances in enzymeless-based electrochemical sensors to diagnose neurodegenerative diseases. *Journal of Materials Chemistry B*. 2021; 9(5): 1175-1188. doi: 10.1039/d0tb02745f
89. Karaboğa MNS, Sezgintürk MK. Biosensor approaches on the diagnosis of neurodegenerative diseases: Sensing the past to the future. *Journal of Pharmaceutical and Biomedical Analysis*. 2022; 209: 114479. doi: 10.1016/j.jpba.2021.114479

90. Brazaca LC, Sampaio I, Zucolotto V, et al. Applications of biosensors in Alzheimer's disease diagnosis. *Talanta*. 2020; 210: 120644. doi: 10.1016/j.talanta.2019.120644
91. Jampilek J, Kralova K. Advances in Drug Delivery Nanosystems Using Graphene-Based Materials and Carbon Nanotubes. *Materials*. 2021; 14(5): 1059. doi: 10.3390/ma14051059
92. Castro KPR, Colombo RNP, Iost RM, et al. Low-dimensionality carbon-based biosensors: the new era of emerging technologies in bioanalytical chemistry. *Analytical and Bioanalytical Chemistry*. 2023; 415(18): 3879-3895. doi: 10.1007/s00216-023-04578-x
93. Hassanpour S, Behnam B, Baradaran B, et al. Carbon based nanomaterials for the detection of narrow therapeutic index pharmaceuticals. *Talanta*. 2021; 221: 121610. doi: 10.1016/j.talanta.2020.121610
94. Qian L, Durairaj S, Prins S, et al. Nanomaterial-based electrochemical sensors and biosensors for the detection of pharmaceutical compounds. *Biosensors and Bioelectronics*. 2021; 175: 112836. doi: 10.1016/j.bios.2020.112836
95. Fu E, Khederlou K, Lefevre N, et al. Progress on Electrochemical Sensing of Pharmaceutical Drugs in Complex Biofluids. *Chemosensors*. 2023; 11(8): 467. doi: 10.3390/chemosensors11080467
96. Manikkath J, Subramony JA. Toward closed-loop drug delivery: Integrating wearable technologies with transdermal drug delivery systems. *Advanced Drug Delivery Reviews*. 2021; 179: 113997. doi: 10.1016/j.addr.2021.113997
97. Bhave G, Chen JC, Singer A, et al. Distributed sensor and actuator networks for closed-loop bioelectronic medicine. *Materials Today*. 2021; 46: 125-135. doi: 10.1016/j.mattod.2020.12.020
98. Cicha I, Priefer R, Severino P, et al. Biosensor-Integrated Drug Delivery Systems as New Materials for Biomedical Applications. *Biomolecules*. 2022; 12(9): 1198. doi: 10.3390/biom12091198