

Review

Advancing Genetic Disorder Detection: Integrating Nanomaterial-Enhanced Biosensors with Genetic Markers

Tanushri Talla¹, Hiteshree Dirisala², Deepti Niranjani³, Sanjay Gadadas⁴, Snigdha Sujith⁵, Nitya Mandowara⁶

¹Liberty High School, 15250 Rolater Rd, United States of America

²South Windsor High School, 161 Nevers Rd, United States of America

³East Chapel Hill High School, 500 Weaver Dairy Rd, United States of America

⁴Woodbridge Academy Magnet School, 1 Convery Blvd, United States of America

⁵South Forsyth High School, 585 Peachtree Pkwy., United States of America

⁶South Brunswick High School, 750 Ridge Rd, United States of America

Abstract

Genetic disorders pose significant challenges in health care because of the more nuanced and costly methods that prolong patient treatment and recovery times. In addition, to ensure a more accurate diagnosis, the process for the detection of this disease can be quite complex and requires excessive testing and counseling, such as hereditary testing. Given these challenges, a new option has arisen in recent decades: nanomaterial-enhanced biosensors. These diagnostic methods are cutting edge and stand out from traditional methods in many areas, some of which include sensitivity, selectivity, and stability. Among other nanomaterials, gold nanoparticles (AUNPs), carbon nanotubes (CNTs), graphene (GR), and quantum dots (QDs) stand out in terms of their performance metrics and are the most promising for the field. Thus, they are examined in depth in this paper. AUNPs enable visible color changes for genetic disorder detection through DNA hybridization, CNTs have high sensitivity and conductivity for detecting genetic mutations, GR provides exceptional electrical conductivity and biocompatibility for various biosensing utilizations, and QDs allow for precise and accurate diagnostics owing to their light-emitting properties. Nanomaterial biosensor technology has greatly improved in the field of genetics, including innovations in wireless technology and advancements in faster and more specific disease detection. These findings have helped significantly improve the diagnosis of health conditions. Even with all of these benefits, there are still issues with sensitivity, stability, biocompatibility, nonspecific binding, a low dynamic range, and high costs. Other major obstacles are ethical concerns, such as data privacy. Nanomaterial-based biosensors undoubtedly can change the game in regard to diagnosing and treating genetic conditions, but additional research must be done to improve the cost, applicability, and reliability.

*Corresponding author: Sanjay Gadadas

Email addresses:

tanushri.talla.1@gmail.com (Tanushri Talla), kanadhanyu@gmail.com (Hiteshree Dirisala), deeptiniranjani@gmail.com (Deepti Niranjani), sanjaygadadas@gmail.com (Sanjay Gadadas), saritha.s.radha@gmail.com (Snigdha Sujith), nityamandowara24@gmail.com (Nitya Mandowara)

Received: 16-08-2024; Accepted: 27-08-2024; Published: 25-12-2024



Copyright: © The Author(s), 2024. Published by JKLST. This is an **Open Access** article, distributed under the terms of the Creative Commons Attribution 4.0 License (<http://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution and reproduction in any medium, provided the original work is properly cited.

Keywords

Nanomaterials, Nanoparticles, Biosensors, Biocompatibility, Biomarkers, Genetic Markers, Genetic Disorders

1. Introduction

Before the emergence of biosensors, analytes were typically detected through more traditional laboratory procedures, such as spectroscopy, chromatography, and mass spectrometry. For example, in 1928, Raman spectroscopy emerged as a potential analytical laboratory technique. This procedure involves lasers that are used to visualize the composition of cells and tissues. Although the Raman spectroscopy technique is still used today, the need for a more technological device has drawn more attention [1]. Since biosensors were first created to detect blood oxygen, their use has grown immensely because of their remarkable ability to detect diseases. An appropriately structured biosensor is not only user friendly but also noninvasive and provides point-of-care health. In addition, the biosensor market has accumulated almost \$40 billion as of 2022, which further proves the need to integrate them into the genetic disease domain [2].

Biosensors have become essential devices across various industries, particularly because of their ability to harness biological signals and translate them into electrical signals. Their history traces back to the early 1960s. This was when the “father of biosensors” Leland C. Clark Jr developed the first enzyme electrode. In 1975, the first commercial biosensor was developed by Yellow Spring Instruments (YSI). [3] The field has now grown into a still undiscovered but multifunctional area of research to help our medical industry. Over the last few decades, biosensors have significantly improved, especially in the medical field. They have increased sensitivity and response rates, which in turn increase the speed and quality of diagnosis and treatment.

Biosensors play a large role in being effective methods for diagnosing certain conditions or detecting the presence of a target molecule. Compared with traditional methods, these sensors have many advantages in terms of cost and accuracy. Because of these benefits, they can be more widely used to diagnose different diseases or defects through an accurate approach. [3,4] Specifically, with respect to genetic disorders, biosensors can play an important role in detecting analytes, from specific proteins encoded in genes to the actual genes themselves. Owing to their ability to efficiently integrate and detect DNA, proteins, and other analytes, they can be very useful in providing new and novel diagnoses for certain diseases [6].

When discussing the various subtypes of nanoparticles, three major types have been identified: gold nanoparticles (AuNPs), carbon nanotubes (CNTs), and graphene (GR). Each nanoparticle possesses distinct attributes, which allows for

certain advantages in the field of biosensor applications [4].

Biosensors work in various ways with the help of different materials and actions. Biosensors are made up of three main parts: a bioreceptor, a transducer, and an electronic system. A receptor is able to recognize the biological reactions related to the target. There are a few different types that use enzymes, antibodies, nucleic acids, and cells. The transducer uses the biological interaction between the device mechanism and the human body to create a signal. Biosensors can be divided into different categories on the basis of their sensing properties, such as electrochemical, optical, and thermal properties. For example, thermal methods detect temperature changes, whereas optical methods are more focused on absorbance. Finally, the electronic system of biosensors includes all the small parts that make the device work, such as amplifiers, processors, and display visuals. These take the signals made in the transducer and help them become understandable for someone to help with the issue. These parts of a biosensor work through the processes of recognition, transduction, signal processing, and display. Recognition is what the biosensor does when it binds to the target. Transduction occurs when the biosensor sends the signal and switches it to a readable format. Signal processing occurs when the transducer is weak and therefore in need of an amplifier to achieve a stronger signal and detection process. Finally, the display is the visual effect used to help understand the situation, problem, etc. [7].

This review discusses the usage and functions of various biosensors and their associated nanomaterials. We also aim to explore how certain nanomaterials may be more effective than others are and how these materials can be applied to create new and novel biosensors for more accurate detection of analytes. Finally, we delve deeper into the limitations of existing models in terms of their sensitivity, stability, and biocompatibility.

2. Discussion

2.1. Nanomaterial mechanism of action

Nanomaterials are substances in which at least one dimension of a substance is between 1 and 100 nanometers. Generally, nanomaterials can be classified on the basis of five factors: size, origin, structural composition, diameter, and toxicity [8]. Size refers to the scale of the material, typically measured in nanometers (nm), with dimensions ranging from 0D (zero-dimensional) to 3D (three-dimensional) structures;

origin refers to either the organic or artificial nature of the substance; structure composition can be carbon-based, organic, inorganic, or composite; diameter refers to the length of the nanomaterial pore being micro, meso-, or macroporous; and toxicity refers to either fiber-like nanoparticles, persistent granular nanoparticles, or CMAR nanoparticles (carcinogenic, mutagenic, asthma genic, or reproductive toxins) [9]. Among this variety of classifications, commonly used nanomaterials

include gold nanoparticles (AuNPs), carbon nanotubes (CNTs), graphene (GR), and photonic crystals (PCs) [4]. The unique properties of nanomaterials offer numerous applications, particularly in the field of nanomedicine [10]. The characteristics of nanoparticles have made them especially popular in the biosensing sphere. Nanomaterials play a key role in the efficiency of biosensors, providing increased sensitivity and assisting in the detection of analytes [11].

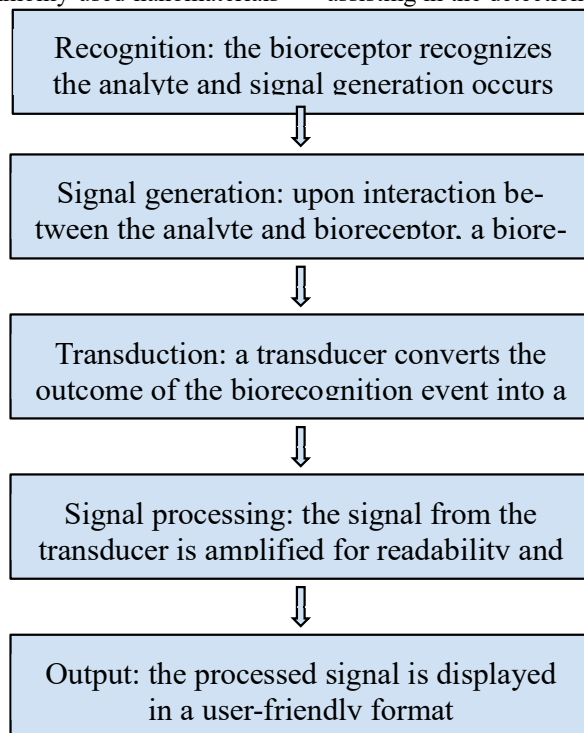


Figure 1. Biosensing mechanism of action.

2.2. Types of nanomaterials

2.2.1. Gold Nanoparticles (AuNPs)

Nanoparticles of gold, often known as AuNPs, have nanoscale dimensions that range from one to a hundred nanometers in diameter. Their minute size allows them to be directly attached to particular cells and biomolecules existing within tissues. There are a few methods for synthesizing AuNPs, but the most widely used method is the Turkevich process developed by Turkevich in 1951, which is based on the reduction of HAuCl₄ by citrate in water [12]. Gold nanoparticles have many applications in detecting genetic diseases. Single-stranded DNA probes complementary to the target DNA sequences of interest are attached to AuNP surfaces. These DNA probes can accurately hybridize with the target sequences, thus enabling selective detection. Additionally, selective hybridization is only possible owing to the ability of these DNA probes to accurately hybridize with the target sequences.

When exposed to the target DNA, these AuNPs functionalized with a DNA probe induce hybridization between the DNA probes and the target DNA in the sample, which leads to the aggregation of AuNPs. This causes a shift in the localized surface plasmon resonance (LSPR) peak of the AuNPs, resulting in a visible color change from red to purple or blue. Thus, this alteration can be easily detected by an unaided eye or simple optic tools. In addition, gold nanoparticles are used as biomarkers for the detection of infectious pathogens, cancers, and cardiac conditions. [13].

2.2.2. Carbon nanotubes (CNTs)

Carbon nanotubes (CNTs) take the form of cylindrical structures, which are composed of carbon atoms arranged in patterns that resemble hexagons. CNTs can be visualized as rolls of graphene sheets when carbon atoms bond together to form a continuous cylindrical shape. Depending on the number of graphene layers, a CNT may have different structural forms. [14]. Genetic disorders can be identified in several

ways, including via the use of carbon nanotubes. Thus, researchers have employed the electrical characteristics of these nanotubes to identify a particular gene mutation that causes hereditary hemochromatosis, a condition characterized by excess iron deposition in body tissues. This technique is fascinating for advancing label-free electrical technologies because, in this case, the detector and the detected species-DNA molecules are approximately the same size [15].

2.2.3. Quantum Dots (QDs)

Quantum dots (QDs) are nanostructures capable of trapping electrons in zero dimensions. They can be considered three-dimensional quantum wells but are confined if they are zero-dimensional [12]. Quantum dots can be used for detecting many medical disorders. Proteins and nucleic acids are examples of specific biomolecules to which quantum dots can be functionalized for binding. A surface coating is selected for a target molecule to identify and quantify certain biomarkers for cancer and infectious diseases; this helps in the implementation of extremely targeted and sensitive diagnostics that may aid in the follow-up and early diagnosis of the disease [16].

2.2.4. Graphene (GR)

Graphene (GR) is a two-dimensional single layer of carbon atoms intrinsically arranged in a honeycomb lattice [17]. The chemical properties of graphite include intermolecular forces between the sheets, which determine the physical qualities of the graphene sheets in the bulk. Each individual carbon atom in a single layer of graphene is covalently bonded to neighboring carbon atoms through sigma and pi bonds [17]. This strong carbon-carbon bonding allows graphene to be equipped with rare mechanical, electrical, physical, thermal, and optical properties. Graphene, specifically graphene oxide (GO), is applicable for tissue engineering because of its colloidal stability and hydrophilicity via H-bonding. In addition, the larger surface area of graphene allows for modifiable surface chemistry, which can be manipulated for biomedical applications such as biosensing, bioimaging, and regenerative medicine [17]. Graphene has the potential to function as a sensor for the human body. Biosensors based on graphene provide specific identification of biomolecules such as DNA, proteins, and metabolites. These sensors can be incorporated into tools for disease detection, tracking biomarkers, and conducting point-of-care testing. The exceptional electrical conductivity, extensive surface area, and compatibility with living organisms make graphene an excellent foundation for advancing biosensing technologies in the future [18].

2.3. Performance Metrics of Existing Models

Although biosensors have many benefits over traditional methods in terms of cost, problems may arise in the sensitivity,

stability, and biocompatibility of these models. Every biosensor has a limit of detection (LOD) for detecting a minimum concentration of analyte, which determines its sensitivity [1]. In a biosensor designed by Sahoo et al., the minimum concentration of glucose that could be detected was -36.25 nm/mL (mg/mL) [21]. A lower detection limit allows biosensors to obtain higher accuracy in detecting smaller amounts of biological analytes.

Another similar performance metric of biosensors is selectivity, which refers to the ability of a biosensor to differentiate between different analytes and attach only to the target analyte [23]. Certain areas where this may be needed include the bloodstream, where there are a variety of substances for possible detection. In these cases, the analyte should be singled out and accurately detected. In a biosensor developed by Gao et al., multiple components collaborate to detect bacteria in human blood for effectively diagnosing infectious diseases. The biosensor is capable of differentiating between molecules in the bloodstream and the target analyte, bacteria [24]. Especially in regard to electrochemical enzyme biosensors, solutions for improving selectivity may include incorporating support biosensors or sensing systems with more than one enzyme [23].

Stability is another factor that is used to determine the quality and robustness of biosensors. [25]. The properties of this metric include how long a biosensor remains viable without maintenance, how well it can be used repeatedly, and how continuously it performs and sustains the signal for a duration of time [26]. For example, regarding the first characteristic, a conducting polymer electrolyte biosensor developed by Arslan et al. was determined to have a shelf life of 25 days before it became nonfunctional. The same biosensor was also found to have high stability throughout 30 repeated uses, although the activity decreased by 20% by the fifth use. After this measurement, the relative activity of the biosensor remained stable at approximately 80% for the remaining 25 trials [27]. In another glucose-detecting enzyme-based biosensor designed by Mei et al., the addition of silicon dioxide (SiO_2) significantly improved the stability of the biosensor. Without SiO_2 , a loss of enzyme led to poor stability, as the biosensor was unable to consistently detect the analyte [28].

Finally, biocompatibility refers to how well a biosensor functions in cooperation with the host in which it was implemented [29]. Two types of biocompatibility are mechanical and immune. Mechanical biocompatibility refers to how physically compatible a biosensor is and mainly addresses larger wearable biosensors rather than nanomaterial biosensors. Certain characteristics that might influence this type of compatibility include comfort, size, and weight. Immune biocompatibility refers to how cooperative the biosensor is with the host's immune system and whether it is able to prevent it from being targeted. A significant area of biosensor design remains considering that a biosensor will not function if it is under attack

by the host's defense mechanisms [30]. Together, both types of biocompatibility play a large role in whether biosensors can

be used in a practical setting in different hosts, so research in this field is extremely important

Nanomaterial	Structure	Properties
Gold nanoparticles (AuNPs)	Spherical, core-shell	Large surface-to-volume ratio, low toxicity, excellent biocompatibility [19], Increased detection in low concentrations of analyte [4]
Carbon nanotubes (CNTs)	Cylindrical, rolled-up graphene	High tensile strength, relatively elastic, can withstand high temperatures, good thermal conductors [20]
Quantum Dots (QDs)	Spherical, core-shell	Semiconductors, tunable composition, high brightness, small size, high quantum yield [21]
Graphene (GR)	Honeycomb Honey-comb shape structure	Large surface area, strong catalytic activity, excellent thermal conductivity, good electrical properties, and electron mobility [22]

Table 1. Structures and properties of various nanomaterials

2.4. Applications of Biosensors

At present, biosensors serve the role of precisely detecting specific biomarkers. Specifically, the diversification of these applications is widespread over a wide variety of subsets. Dengue fever, for example, is activated by the complementary dengue virus (DENV), hindering a particular RNA strip. The effects of dengue infections can be lethal to some extent; however, a targeted cure does not exist for the virus. Fortunately, there have been some developments in addressing this disparity with the utilization of biosensors, particularly in DENV detection. Such a biosensor does exist, and its chemical components of palladium and platinum are combined to offer more favorable characteristics for identifying the DENV genetic analyte [23]. Detection methods can range from electronic, optical, and microarray methods. Moreover, their functions are significant. BiodetectTM is one such nanosensor that aids in identifying hereditary mutation biomarkers through electronic detection. In optical detection, gold nanoparticles are primarily responsible for the ability of biosensors to specifically target and image the surface through oscillation. Fingerprint identification through nucleic acids is performed through microarrays. These tools specifically target DNA, mRNA, cDNA, and other minuscule molecules [31]. In addition, biosensors are becoming increasingly notable in the cancer field because of their sensitive and rapid ability to detect biological analytes. Various types of biosensors—piezoelectric, optical, and electrochemical—have been used to detect breast cancer, lung cancer, and prostate cancer [32]. In particular, electrochemical-based biosensors have been utilized for analyzing tumor formation and development. They identify and

differentiate between localized tumor cells and normal cells, which leads to the proper diagnosis of unrestricted growth [33]. Biosensors have also proven to be significant in antibacterial research, especially as a medium to combat the spread of bacterial resistance. These particular biosensors utilize laborious methods to detect antibacterials for further developments in bacterial resistance [34].

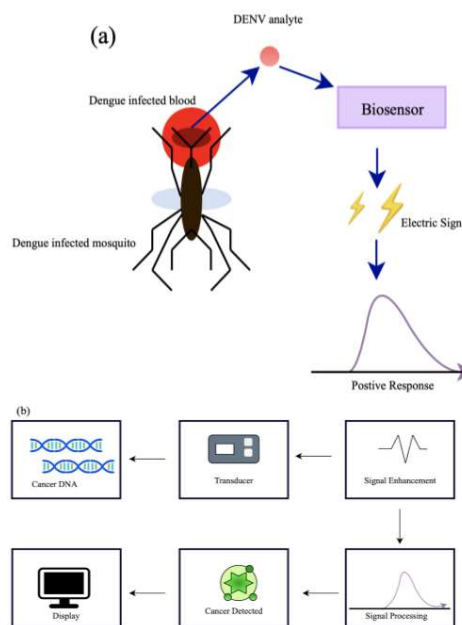


Figure 2. (a) Biosensor applied for dengue virus detection. (b) Cancer application steps of a biosensor.

2.4. Advancements in nanomaterial biosensors

The nanotechnology domain has undergone many remarkable advancements, especially with respect to nanomaterials such as carbon nanotubes, graphene, quantum dots, and gold nanoparticles[6]. In addition, the growing demand for point-of-care technologies (POCTs) has led biosensors to expand to include blood, DNA, contamination, saliva, and pathogen detection. Premises of artificial intelligence and cyber-physical means have been recently integrated into the nanobiosensor field. Moreover, nanobiosensors have served as a great advantage to healthcare practitioners and scientists in detecting proteins, enzymes, biomarkers, and nucleic acid chains in a variety of diseases and illnesses [35].

Recently, there has been great momentum in the evolution of diagnostic strategies, which has allowed healthcare officials to gain more insight into and knowledge of the pathways of inexplicable diseases. Specifically, issues associated with traditional biosensors, low sensitivity, and specificity have been slowly resolved with the utilization of nanomaterials. Potential modifications and advances in biosensors lie in miniaturizing the device, reducing the time in analysis, and improving the efficiency of detection and sensitivity [36].

Biosensors have also improved their sensing properties. Some biosensors have recently emerged with fluorescent technology to better sense abnormalities in the body. This design is particularly useful for monitoring food and environmental quality because of its high selectivity and sensitivity. Additionally, some biosensors use nanoparticles to increase signal strength by taking advantage of the high surface area of these materials. Recent diagnostics have even used the rise of AI technology to incorporate it into biosensor technology to improve disease detection and diagnosis. Furthermore, the selectivity of biosensors has increased, ensuring that only invasive molecules in the body trigger a response [37].

Increasing the biosensor response time is crucial for an efficient working model. Advances have been made to generate quicker signals and faster responses. For example, many biosensors now use nanostructured surfaces, which lead to quicker binding events and thus faster detection. Other biosensors have also used different numbered electrode configurations, which results in faster and more precise responses, leading to quicker identification. Crosslinking enzymes and proteins is another recent innovation that strengthens attachment within the biosensor, increasing its speed. Owing to their highly targeted signal triggers, fluorescent-based optical biosensors also provide shorter response times. [38]

Overall, nanomaterial biosensors have significantly improved in their ability to detect diseases, provide rapid responses, and utilize wireless technology for broader

applications. These advancements are crucial for enhancing diagnostic practices and making biosensors more versatile, cost-effective, and user friendly. Continued research and development in this field will further enhance the capabilities of nanomaterial biosensors, offering better health solutions for everyone.

2.5. Limitations and Ethical Considerations

Biosensors are organized into three types: single use, intermittent use, and continuous use. Single use makes up most of the commercial market. It is easy to use and not very precise, and the cost per use is very high, reaching up to \$50. Intermittent use has moderate complexity in operation and performs outstandingly. They come with a significant upfront cost, ranging from \$1000 to \$10,000 per instrument. However, they offer good precision and accuracy, with a moderate cost relative to the data rate. Finally, continuous use is very easy. However, it performs poorly and has poor accuracy despite offering good precision. On the upside, they come with a low cost relative to the data rate [39]. This finding indicates that the most widely used biosensor type, which has the best overall performance, is also the most expensive, which limits its accessibility for many.

Another limitation that comes with the use of biosensors is nonspecific binding (NBS). Since biosensors detect substances through physical or chemical measurements, they can sometimes run into the problem of unintended reactions, which can result in false readings. While antibodies are commonly used to overcome this, they sometimes do not work well when attached to certain surfaces [40].

Furthermore, specific biosensors, such as transcription-based biosensors, have limitations, such as slow response times and insufficient dynamic ranges. Because of the various steps taken through a cell, transcription-based biosensors have slow response times. Because of the many steps taken, transcription-based biosensors have a slow response time. These steps include chemical signals that activate transcription factors (TFs), which then trigger processes such as making RNA and proteins, causing delays. TFs also need to move into the nucleus and attach to DNA, which takes time. The dynamic range of these specific biosensors is also inadequate because they struggle to detect analytes across a wide range of concentrations, meaning that they sometimes miss detecting low levels of analytes or become overwhelmed by high levels, leading to inaccurate readings. Because of the narrow detection range, the range of biosensors in different environments is limited [41].

Aptamers are crucial for biosensors because they allow themselves to bind strongly to specific targets, are stable, and can be easily synthesized. However, limitations have also been

found in the use of aptamers. An aptamer is a short DNA or RNA sequence that specifically binds to target molecules, but identifying them can be difficult. The long and frequent SELEX selection process requires multiple cycles of binding, splitting, and amplification, which is very time-consuming and results in the loss of candidates during the process [42]. Moreover, riboswitches also pose limitations in biosensors. Riboswitches are RNA switches that turn genes on or off when they encounter certain molecules. Riboswitches are composed of two parts: an aptamer that binds to molecules and a response domain that generates a signal. Unlike regular biosensors, in riboswitches, the response domain is a part of the aptamer sequence. When the aptamer sequence binds to a molecule, it changes shape, affecting the response domain and generating a signal. However, which aptamers work best for riboswitches is still uncertain, which makes the process tricky [43].

Although biosensors provide significant advancements in health monitoring and diagnosis, privacy and data security remain ethical concerns. Biosensors are devices that detect and record biological data, such as glucose levels and heart rates, into electronic files that may be sent wirelessly or via wires. These records contain private health information that can be accessed by unauthorized parties if appropriate security measures are not implemented. Furthermore, problems regarding discrimination and data misuse are raised by the usage of personal health information by insurers, employers, and other parties. As biosensors become more common, these ethical issues become even more pressing. [44].

2.6. Barriers to Biocompatibility

In the present review, we highlight various types of biosensors and their applications in the field of nanotechnology. The specific characteristics of biosensors and their sensitivity, stability, and biocompatibility have since been explored.

A sensor may work efficiently in the laboratory; however, its application in living organisms results in a much more complex environment. This could culminate in issues of biocompatibility, stability, and sensitivity. While the detection limit may be the most significant of the aforementioned limitations, as it pertains to how effective a biosensor can be, there is still much opportunity for research to overcome it [3].

Another issue to work on is selectivity, and different biosensors should be able to separate their counterparts to detect compounds. Selectivity is a major area for improvement, as different biosensors must be able to distinguish between their respective analytes to detect the compounds. Stability also remains a possible area for investigation, as biosensors should be resistant to degradation in their designated environment, whether on their own or after attaching to the analyte [23].

2.7. Nanomaterials and Genetic Disorder Detection

Currently, nanomaterials are crucial for developing biosensors, particularly those that identify genetic diseases. Genetic disorders, including sickle cell anemia, Huntington's disease, and cystic fibrosis, are caused by mutations in an individual's DNA. These illnesses must be identified early and precisely to be effectively handled. In this way, nanomaterials greatly improve the functionality of biosensors. Owing to their superior electrical flow and ability to interact with the body, gold nanoparticles (AuNPs) increase the sensitivity and specificity of sensors. Because of their high fluorescence, quantum dots (QDs) are useful for tracking and tagging genetic markers. The high surface area and excellent electron mobility of graphene (GR) allow rapid and precise detection of genetic mutations.

Nanomaterial biosensors have multiple ways to detect genetic disorders, but most of these methods involve DNA in procedures such as DNA hybridization. In a study by Han et al., for example, an electrochemical DNA biosensor composed of carbon nanotube-gold nanoparticle nanoclusters for signal amplification was developed. The combination of these two nanomaterials significantly improved the detection limit to 5.2 fM [45]. Sensors such as this one provide a promising approach to DNA detection and genetic disorder diagnosis, as they combine the best properties of each nanomaterial used. Because genetic disorders can be detected only at the molecular level when abnormalities are diagnosed in the absence of symptoms, biosensors are particularly useful in this case. Nanomaterials working with other components of the sensor can identify changes in DNA sequences or detect the absence or presence of a key molecule. Compared with conventional methods, which are able to molecularly interact with other substrates, nanomaterial biosensors prove their superiority in diagnosing genetic disorders.

Gold nanoparticles, or AUNPs, have many benefits when placed in a biosensor that is specifically designed for detecting genetic disorders. Because of the large surface area of AUNPs, their ability to attach to DNA is great. They then stick to specific DNA sequences because they are coated with matching DNA probes. When they find their target DNA, they clump together, changing color visibly. This color change is easy to observe with the naked eye or basic tools. Therefore, gold nanoparticles provide an effective way to identify genetic disorders quickly.

Carbon nanotubes (CNTs) have also emerged as another compelling nanomaterial for use in genetic disorder detection. Owing to their rolled-up carbon structure, electrons move easily along their length, making them highly conductive. Their small size also increases their sensitivity to changes in their surroundings because of the development of special quantum effects. By observing changes in conductivity caused when

DNA with these mutations interacts with CNTs, scientists can identify specific genetic problems, making CNTs promising nanomaterials for use in the detection of genetic disorders.

Graphene, also referred to as GR, has many properties that make it highly beneficial for detecting genetic disorders through biosensing. Owing to the structure and arrangement of carbon atoms in the hexagonal lattice, electrons can move freely across the graphene sheet, leading to excellent electrical conductivity. Furthermore, graphene is a two-dimensional material with a high specific surface area and is good at interacting with biomolecules, making it able to be used as a biosensor without poisoning organisms. This would permit the identification of DNA, proteins, and other biomolecules that could, in principle, be useful for the diagnosis of a disease or to follow a biomarker. Quantum dots (QDs) also have many properties that can help in detecting genetic disorders. Their ability to release light in a variety of colors depending on their size gives clear detection signals. Their brightness and long-lasting light emission produce strong and dependable signals during imaging. The broad absorption and limited light emission range of QDs allow for the simultaneous detection of many targets. When functionalized to bind to certain biomolecules, such as proteins and nucleic acids, QDs can target and recognize specific genetic sequences. QDs can discover and measure biomarkers linked with genetic diseases by covering their surfaces with a target molecule-specific surface. This results in extremely specific and sensitive diagnostics, allowing for early and precise diagnosis of genetic disorders. Thus, QDs improve the ability to diagnose genetic disorders. Together, these nanomaterials increase the precision and speed of genetic disorder detection, making all of them ideal for use in biosensors. However, with the reputation of AuNPs as a top contender for biocompatibility and previous success in similar biosensing technologies, gold nanomaterials are likely the best option for designing biosensors to detect genetic markers.

3. Conclusion

In the domain of biosensors, electrochemical biosensors have gained immense attention. This is evident through the high number of publications on the topic of “electrochemical biosensors”. Although already advanced, these biosensors have a large scope for further technical modifications. Another area within the field of electrochemical biosensors is wearable biosensors. This has paved the path for their integration into athletic sports. Recently, research has been conducted to create polymers specifically designed to provide flexibility and strength for new wearable biosensors. In addition, the detection-based mechanism within biosensors takes into account sweat, saliva, and other bodily fluids as analytes to circumvent the painful process of acquiring blood serum [46]. Another area that electrochemical biosensors have grasped is

communication technology. Especially after the COVID-19 pandemic, hybrid sensors that can be used to monitor patient health became crucial. Although research is still being done into creating hybrid biosensors, the potential has proven that there is great scope for creating at-home testing kits [46]. Biosensors are modern-day technologies that convert organic responses into quantifiable, measurable signals used in many specific fields. They have a large range of programs, and even as their ability is promising and assisting in studies, biosensors additionally face tremendous limitations. There are many exciting applications of biosensors. The integration of technology, consisting of Bluetooth-enabled transportable gadgets, makes remote records series and health tracking simpler. Moreover, creating biosensors with several features can result in quicker reaction times and more thorough diagnostic records. Another important advancement is the introduction of environmentally friendly and electricity-efficient designs, making biosensors more reachable because of decreased resource requirements [38][47].

However, despite their ability, biosensors have several drawbacks. Their unreliability may cause inconsistent balance and reproducibility, which is an enormous problem in addition to their quick lifespan. Economic problems are also associated with the high cost and complexity of biosensor production, which restricts its use and accessibility [48]. While biosensors have substantial capacity throughout multiple domain names, addressing their modern boundaries is crucial for destiny improvement and advancement. Continued research and innovation will lead to massive enhancements, helping to overcome existing challenges and contributing to the evolution of this generation.

While a multitude of topics have been covered in this review paper, nanomaterial-based biosensors are an extensive field, and many still remain to be discovered. This paper specifically highlights the uses of AuNP-, CNT-, QD-, and GR-based biosensors, but other emerging nanomaterials for use in this field include magnetic nanobeads and nanodiamonds. However, since the first four materials are the most promising, more research has been performed on them, but not as much research has been dedicated to the remaining materials. With an increasing need for technological advancements in detecting biological markers, biosensors have emerged. Biosensors have increased in their ability to detect various analytes, especially in biological disorders. They have also played a pivotal role in the integrative laboratory field. Biosensors have been deemed to provide great advancements in precision and more inclusive accessibility for different types of diagnostic practices.

Blending the artificial intelligence domain with mobile biosensors also allows applications to reach the level of detecting chronic diseases. For example, machine learning can assist in combining and interpreting data from different biosensors to identify patient diseases where a multistep diagnosis is

necessary. In these cases, the data from two or more biosensors can be combined to diagnose the disorder in a single step [49]. In addition, the genetic disorder platform would greatly benefit from the highly advanced chip technology utilized for detecting DNA mutations within the blood. More developments and technological growth in biosensors will allow for early detection and more fulfillment in healthcare corporations [50]. In conclusion, the exploration of nanomaterial-based biosensors, as demonstrated in various studies, underscores their transformative potential in advancing diagnostic practices, including pathogen detection and glucose sensing, thereby paving the way for significant improvements in healthcare and environmental monitoring [51] [52] [53] [54] [55].

Author Contributions

T.T., H.D., D.N., S.G., S.S., and N.M. conceptualized the topic; T.T., H.D., D.N., S.G., S.S., and N.M. developed the methodology; T.T., H.D., D.N., S.G., and N.M. worked on visualization; T.T., H.D., D.N., S.G., S.S., and N.M. wrote the article; T.T., H.D., D.N., S.G., and N.M. led project administration; T.T., H.D., D.N., and S.G. reviewed and edited the paper.

Conflicts of interest

The authors declare that they have no competing financial interests or conflicts of interest.

References

- [1] Oshima, Y., et al. (2023). Practices, potential, and perspectives for detecting predisease using Raman spectroscopy. *International Journal of Molecular Sciences (Online)*, 24(15), 12170–12170. <https://doi.org/10.3390/ijms241512170>.
- [2] Zubair, M., Wang, S., & Ali, N. (2021). Advanced approaches to breast cancer classification and diagnosis. *Frontiers in Pharmacology*, 11. <https://doi.org/10.3389/fphar.2020.632079>.
- [3] Bhalla, N., Jolly, P., Formisano, N., & Estrela, P. (2016). Introduction to biosensors. *Essays In Biochemistry*, 60(1), 1–8. <https://doi.org/10.1042/ebc20150001>.
- [4] Su, H., et al. (2017). Nanomaterial-based biosensors for biological detections. *Advanced Health Care Technologies*, Oct. 03. <https://www.dovepress.com/nanomaterial-based-biosensors-for-biological-detections-peer-reviewed-fulltext-article-AHCT>.
- [5] Feng, Y., et al. (2018). The applications of promoter-gene-engineered biosensors. *Sensors*, 18(9), 2823–2823. <https://doi.org/10.3390/s18092823>.
- [6] Malik, S., et al. (2023). Nanomaterials-based biosensor and their applications: A review. *Heliyon*, 9(9), e19929–e19929. <https://doi.org/10.1016/j.heliyon.2023.e19929>.
- [7] Tetyana, P., Shumbula, P. M., & Njengele-Tetyana, Z. (2021). *Biosensors: Design, Development and Applications*. IntechOpen. Available: <https://www.intechopen.com/chapters/76543>.
- [8] Mekuye, B., & Abera, B. (2023). Nanomaterials: An overview of synthesis, classification, characterization, and applications. *Nano Select*, 4(8). <https://doi.org/10.1002/nano.202300038>.
- [9] Bratovic, A. (2019). Different applications of nanomaterials and their impact on the environment. *International Journal of Material Science and Engineering*, 5(1), 1–7. <https://doi.org/10.14445/23948884/ijmse-v5i1p101>.
- [10] Mehrotra, P. (2016). Biosensors and their applications – A review. *Journal of Oral Biology and Craniofacial Research*, 6(2), 153–159. <https://doi.org/10.1016/j.jobcr.2015.12.002>.
- [11] Herizchi, R., Abbasi, E., Milani, M., & Akbarzadeh, A. (2014). Current methods for synthesis of gold nanoparticles. *Artificial Cells, Nanomedicine, and Biotechnology*, 44(2), 596–602. <https://doi.org/10.3109/21691401.2014.971807>.
- [12] Merck. (2024). NMR chemical shifts of impurities charts. *Merck*, 1(1). Available: <https://www.sigmaaldrich.com/MX/en/technical-documents/technical-article/genomics/cloning-and-expression/blue-white-screening>.
- [13] Szabó, A., Perri, C., Csató, A., Giordano, G., Vuono, D., & Nagy, J. B. (2010). Synthesis methods of carbon nanotubes and related materials. *Materials*, 3(5), 3092–3140. <https://doi.org/10.3390/ma3053092>.
- [14] *Carbon Nanotube Transistor Can Detect Genetic Mutations*. (2006). phys.org. <https://phys.org/news/2006-01-carbon-nanotube-transistor-genetic-mutations.html>.
- [15] Joglekar, P. V., Mandalkar, D. J., Nikam, M. A., Pande, N. S., & Dubal, A. (2019). Review article on quantum dots: Synthesis, properties and application. *International Journal of Research in Advent Technology*, 7(1), 510–515. <https://doi.org/10.32622/ijrat.712019113>.
- [16] Kandhola, G., et al. (2023). Nanomaterial-based scaffolds for tissue engineering applications: A review on graphene, carbon nanotubes and nanocellulose. *Tissue Engineering and Regenerative Medicine*, 20(3), 411–433. <https://doi.org/10.1007/s13770-023-00530-3>.
- [17] Han, Q., et al. (2021). Graphene biodevices for early disease diagnosis based on biomarker detection. *ACS Sensors*, 6(11), 3841–3881. <https://doi.org/10.1021/acssensors.1c01172>.
- [18] Yeh, Y.-C., Creran, B., & Rotello, V. M. (2012). Gold nanoparticles: Preparation, properties, and applications in bionanotechnology. *Nanoscale*, 4(6), 1871–1880.

- <https://doi.org/10.1039/c1nr11188d>.
- [19] Eatemadi, A., et al. (2014). Carbon nanotubes: Properties, synthesis, purification, and medical applications. *Nanoscale Research Letters*, 9(1), 393. <https://doi.org/10.1186/1556-276x-9-393>.
 - [20] Abdellatif, A. A., Younis, M. A., Alsharidah, M., Al Rugaie, O., & Tawfeek, H. M. (2022). Biomedical applications of quantum dots: Overview, challenges, and clinical potential. *International Journal of Nanomedicine, Volume 17*, 1951–1970. <https://doi.org/10.2147/ijn.s357980>.
 - [21] Singh, S., Hasan, M. R., Sharma, P., & Narang, J. (2022). Graphene nanomaterials: The wondering material from synthesis to applications. *Sensors International*, 3, 100190. <https://doi.org/10.1016/j.sintl.2022.100190>.
 - [22] Gupte, P., Dhingra, K., & Saloni. (2024). Precision gene editing strategies with CRISPR-Cas9 for advancing cancer immunotherapy and Alzheimer's disease. *Journal of Knowledge Learning and Science Technology*, 3(4), 11–21. <https://doi.org/10.60087/jklst.v3.n4.p1>.
 - [23] Gao, J., et al. (2017). A multiplex electrochemical biosensor for bloodstream infection diagnosis. *SLAS Technology*, 22(4), 466–474. <https://doi.org/10.1177/2211068216651232>.
 - [24] Bucur, B., Purcarea, C., Andreescu, S., & Vasilescu, A. (2021). Addressing the selectivity of enzyme biosensors: Solutions and perspectives. *Sensors*, 21(9), 3038. <https://doi.org/10.3390/s21093038>.
 - [25] Panjan, P., Virtanen, V., & Sesay, A. M. (2017). Determination of stability characteristics for electrochemical biosensors via thermally accelerated aging. *Talanta*, 170, 331–336. <https://doi.org/10.1016/j.talanta.2017.04.011>.
 - [26] Arslan, A., Kuralp, S., Toppare, L., & Bozkurt, A. (2006). Novel conducting polymer electrolyte biosensor based on poly(1-vinyl imidazole) and poly(acrylic acid) networks. *Langmuir*, 22(6), 2912–2915. <https://doi.org/10.1021/la0530539>.
 - [27] Mei, L., Yang, Y., Li, J., Shang, S., & Fu, X. (2023). A SiO₂ hybrid enzyme-based biosensor with enhanced electrochemical stability for accuracy detection of glucose. *International Journal of Analytical Chemistry*, 2023, 1–8. <https://doi.org/10.1155/2023/6620613>.
 - [28] Gill, A., Lillie, G., Farace, G., & Vadgama, P. (2005). Biocompatible interfaces for biosensors. *International Journal of Environmental Analytical Chemistry*, 85(9–11), 699–725. <https://doi.org/10.1080/03067310500155129>.
 - [29] Lu, T., Ji, S., Jin, W., Yang, Q., Luo, Q., & Ren, T.-L. (2023). Biocompatible and long-term monitoring strategies of wearable, ingestible and implantable biosensors: Reform the next generation healthcare. *Sensors (Basel, Switzerland)*, 23(6), 2991. <https://doi.org/10.3390/s23062991>.
 - [30] Aljabali, A. A. A., et al. (2020). Application of nanomaterials in the diagnosis and treatment of genetic disorders. *Springer*. https://doi.org/10.1007/978-981-15-4802-4_7.
 - [31] Pourmadadi, M., et al. (2022). Properties and applications of graphene and its derivatives in biosensors for cancer detection: A comprehensive review. *Biosensors*, 12(5), 269. <https://doi.org/10.3390/bios12050269>.
 - [32] Singh, P., Pandit, S., Mokkalapati, V. R. S. S., Garg, A., Ravikumar, V., & Mijakovic, I. (2018). Gold nanoparticles in diagnostics and therapeutics for human cancer. *International Journal of Molecular Sciences*, 19(7), 1979. <https://doi.org/10.3390/ijms19071979>.
 - [33] Wang, X., Li, F., & Guo, Y. (2020). Recent trends in nanomaterial-based biosensors for point-of-care testing. *Frontiers in Chemistry*, 8. <https://doi.org/10.3389/fchem.2020.586702>.
 - [34] Reder-Christ, K., & Bendas, G. (2011). Biosensor applications in the field of antibiotic research—A review of recent developments. *Sensors*, 11(10), 9450–9466. <https://doi.org/10.3390/s111009450>.
 - [35] Kulkarni, S., Dhingra, K., & Verma, S. (2024). Applications of CMUT technology in medical diagnostics: From photoacoustic to ultrasonic imaging. *International Journal of Science and Research (IJSR)*, 13(6), 1264–1269. <https://www.ijsr.net/archive/v13i6/SR24619062609.pdf>.
 - [36] Naresh, V., & Lee, N. (2021). A review on biosensors and recent development of nanostructured materials-enabled biosensors. *Sensors*, 21(4), 1109. <https://doi.org/10.3390/s21041109>.
 - [37] Sadana, A. (2005). Market size and economics for biosensors. In *Fractal Binding and Dissociation Kinetics for Different Biosensor Applications* (pp. 265–299). <https://doi.org/10.1016/B978-044451945-0/50014-5>.
 - [38] Ferrigno, P. K. (2016). Nonantibody protein-based biosensors. *Essays In Biochemistry*, 60(1), 19–25. <https://doi.org/10.1042/ebc20150003>.
 - [39] Tellechea-Luzardo, J., Stiebritz, M. T., & Carbonell, P. (2023). Transcription factor-based biosensors for screening and dynamic regulation. *Frontiers in Bioengineering and Biotechnology*, 11. <https://doi.org/10.3389/fbioe.2023.1118702>.
 - [40] Carpenter, A., Paulsen, I., & Williams, T. (2018). Blueprints for biosensors: Design, limitations, and applications. *Genes*, 9(8), 375. <https://doi.org/10.3390/genes9080375>.
 - [41] Han, S., Liu, W., Zheng, M., & Wang, R. (2020). Label-free and ultrasensitive electrochemical DNA biosensor based on urchinlike carbon nanotube-gold nanoparticle nanoclusters. *Analytical Chemistry*, 92(7), 4780–4787. <https://doi.org/10.1021/acs.analchem.9b03520>.
 - [42] A.v, L., T.v, T., & L.v, G. (2013). Aptamers: Problems, solutions, and prospects. *Acta Naturae (англоязычная версия)*,

- 5(4), 34–43. Available: <https://cyberleninka.ru/article/n/ap-tamers-problems-solutions-and-prospects>.
- [43] Evans, R., McNamee, M., & Guy, O. (2016). Ethics, nanobi-sensors and elite sport: The need for a new governance frame-work. *Science and Engineering Ethics*, 23(6), 1487–1505. <https://doi.org/10.1007/s11948-016-9855-1>.
- [44] Singh, A., et al. (2021). Recent advances in electrochemical bi-sensors: Applications, challenges, and future scope. *Biosen-sors*, 11(9), 336. <https://doi.org/10.3390/bios11090336>.
- [45] Samal, S., Mohanty, R. P., Mohanty, P. S., Giri, M. K., Pati, S., & Das, B. (2023). Implications of biosensors and nanobiosen-sors for the eco-friendly detection of public health and agro-based insecticides: A comprehensive review. *Heliyon*, 9(5), e15848. <https://doi.org/10.1016/j.heliyon.2023.e15848>.
- [46] Flynn, C. D., & Chang, D. (2024). Artificial intelligence in point-of-care biosensing: Challenges and opportunities. *Diag-nostics*, 14(11), 1100. <https://doi.org/10.3390/diagnos-tics14111100>.
- [47] Otero, F., & Magner, E. (2020). Biosensors—Recent advances and future challenges in electrode materials. *Sensors*, 20(12), 3561. <https://doi.org/10.3390/s20123561>.
- [48] Bhalla, N., Pan, Y., Yang, Z., & Payam, A. F. (2020). Opportu-nities and challenges for biosensors and nanoscale analytical tools for pandemics: COVID-19. *ACS Nano*, 14(7), 7783–7807. <https://doi.org/10.1021/acsnano.0c04421>.
- [49] Pandya, H. J., et al. (2017). A microfluidic platform for drug screening in a 3D cancer microenvironment. *Biosensors and Bioelectronics*, 94, 632–642. <https://doi.org/10.1016/j.bios.2017.03.054>.
- [50] Safavieh, M., et al. (2017). Paper microchip with a graphene-modified silver nanocomposite electrode for electrical sensing of microbial pathogens. *Nanoscale*, 9(5), 1852–1861. <https://doi.org/10.1039/c6nr06417e>.
- [51] GhavamiNejad, P., GhavamiNejad, A., Zheng, H., Dhingra, K., Samarikhalaj, M., & Poudineh, M. (2022). A conductive hydro-gel microneedle-based assay integrating PEDOT and Ag-Pt na-noparticles for real-time, enzyme-less, and electrochemical sensing of glucose. *Advanced Healthcare Materials*, 12(1). <https://doi.org/10.1002/adhm.202202362>.
- [52] Odinotski, S., et al. (2022). A conductive hydrogel-based mi-croneedle platform for real-time pH measurement in live ani-mals. *Small*, 18(45). <https://doi.org/10.1002/smll.202200201>.
- [53] Pandya, H. J., et al. (2017). Label-free electrical sensing of bac-teria in eye wash samples: A step toward point-of-care detec-tion of pathogens in patients with infectious keratitis. *Biosen-sors and Bioelectronics*, 91, 32–39. <https://doi.org/10.1016/j.bios.2016.12.035>.