Paper Type: Original Article

Nanomaterial Based Biosensors for Disease Detection: A Review

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Citation:

Abstract

The advent of nanotechnology has revolutionized biosensing, enabling the development of highly sensitive, rapid, and portable diagnostic platforms. This review comprehensively examines advancements in nanomaterial-based biosensors for detecting a broad range of diseases, including infectious diseases, cancers, neurodegenerative disorders, and cardiovascular conditions. Leveraging unique properties of nanomaterials such as graphene, Carbon Nanotubes (CNTs), metal nanoparticles, and MXenes, these biosensors achieve exceptional analytical performance, often detecting biomarkers at femtomolar to attomolar concentrations. We discuss the operational principles of electrochemical, optical, and Field-Effect Transistor (FET)-based biosensors, emphasizing their applications in Point Of Care (POC) diagnostics. Despite significant progress, challenges persist in clinical validation, reproducibility, stability, and large-scale manufacturing. The review concludes by highlighting future trends, including multiplexed detection, integration with Artificial Intelligence (AI), and the development of sustainable and wearable sensor platforms.

Keywords: Nanomaterial-based biosensors, Disease detection, Point-of-care diagnostics, Electrochemical sensors, Optical biosensors, Artificial intelligence.

1 | Introduction

Early and accurate diagnosis is a cornerstone of effective healthcare, significantly reducing morbidity, mortality, and healthcare costs. According to the Global Burden of Disease (GBD) Study 2023, published in 2025, Non Communicable Diseases (NCDs) such as cancer, Cardiovascular Diseases (CVDs), and neurodegenerative disorders account for the majority of the global disease burden, with Disability Adjusted Life Years (DALYs) increasingly dominated by late-stage diagnoses [1]. Delayed detection exacerbates outcomes; for instance, early-stage cancer diagnosis can improve five-year survival rates dramatically (e.g., up to 98% for stage 1 breast cancer versus <30% for stage 4), while timely identification of cardiovascular biomarkers prevents acute events like heart attacks. Similarly, in infectious diseases and neurodegenerative conditions like Alzheimer's, early intervention is critical for better management and quality of life.

Conventional diagnostic techniques, such as Enzyme Linked Immunosorbent Assay (ELISA), Polymerase Chain Reaction (PCR), and culture based methods, are often constrained by their time consuming protocols, need for specialized equipment and trained personnel, and high costs [1], [2]. These limitations are particularly pronounced in resource-limited settings and during outbreaks, as highlighted by the COVID-19 pandemic, which underscored the urgent need for rapid, decentralized testing. In response, nanomaterial-based biosensors have emerged as powerful alternatives, offering the potential for rapid, sensitive, and low-cost detection of disease biomarkers directly at the Point Of Care (POC) [3]. The global POC diagnostics market is projected to grow at a Compound Annual Growth Rate (CAGR) of approximately 8-9% from 2025 to 2030, driven by the demand for accessible and real-time diagnostics. These biosensors incorporate nanomaterials like graphene, Gold Nanoparticles (AuNPs), Quantum Dots (QDs), Carbon Nanotubes (CNTs), and emerging materials such as MXenes to enhance signal transduction, increase surface area for bioreceptor immobilization, improve selectivity, and boost overall sensor stability and sensitivity often achieving detection limits in the femtomolar to attomolar range [4]. This review synthesizes findings from recent publications (primarily 2020-2025) to provide a detailed overview of the design, functionality, and applications of these advanced biosensing platforms across various medical fields, including infectious diseases, cancers, neurodegenerative disorders, and cardiovascular conditions. We also address key hurdles to their clinical translation and commercialization, such as reproducibility, stability, and regulatory challenges, while highlighting future perspectives like multiplexed detection and integration with Artificial Intelligence (AI).

2 | Fundamental Nanomaterials and Their Properties

The exceptional performance of nanomaterial-based biosensors is rooted in the unique intrinsic properties of the nanomaterials employed (*Fig. 1*).

2.1 | Carbon-Based Nanomaterials

Graphene and its derivatives, such as Graphene Oxide (GO) and Reduced Graphene Oxide (rGO), are highly valued for their excellent electrical conductivity, large specific surface area, and remarkable mechanical strength, rendering them ideal for electrochemical and Field-Effect Transistor (FET)-based sensors [5], [6]. CNTs enable efficient electron transfer due to their one-dimensional structure, whereas carbon CQDs provide tunable fluorescence and low toxicity, making them particularly suitable for optical biosensing platforms [7], [8].

2.2 | Noble Metal Nanoparticles

Gold (AuNPs) and silver nanoparticles (AgNPs) exhibit strong Localized Surface Plasmon Resonance (LSPR), which is widely exploited in colorimetric assays and Surface-Enhanced Raman Scattering (SERS)-based sensors for rapid visual detection or ultrasensitive analysis [9], [10]. Their excellent biocompatibility and facile surface functionalization with biomolecules (e.g., antibodies, aptamers, or DNA) further enhance their versatility in biosensing applications [11].

2.3 | Other Emerging Nanomaterials

Two-Dimensional (2D) materials such as MXenes and Black Phosphorus (BP) (phosphorene) offer high surface-to-volume ratios and tunable electronic properties, showing great promise for next-generation sensors [2], [12]. However, the oxidative instability of BP under ambient conditions remains a significant challenge that requires further stabilization strategies [12]. Magnetic nanoparticles, particularly iron oxide (Fe_3O_4), are frequently employed for magnetic separation and preconcentration of targets in complex biological matrices,

thereby improving detection limits and reducing matrix interference [9]. Despite their advantages, careful consideration of potential toxicity (as discussed in Section 5.4) is essential for clinical translation.
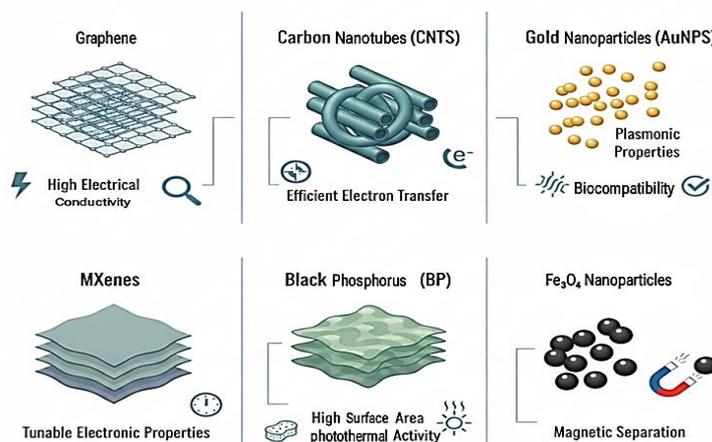

Fig. 1. Schematic overview of major nanomaterials used in biosensors, including Graphene, CNTs, AuNPs, MXenes, BP, and Fe3O4 nanoparticles, highlighting their key properties.

3 | Biosensing Platforms and Transduction Mechanisms

3.1 | Electrochemical Biosensors

Electrochemical biosensors are among the most prevalent due to their high sensitivity, portability, and potential for miniaturization. For instance, a 3D-printed porous gold micropillar electrode coated with rGO nanoflakes was functionalized with SARS-CoV-2 antigens, enabling label-free detection of specific antibodies in human plasma within 10–12 seconds using Electrochemical Impedance Spectroscopy (EIS) [13]. In another approach, a nanochannel-based sensor was developed for Alzheimer's Disease (AD) biomarker detection by optimizing antibody-antigen charge interactions at different pH levels to maximize channel blockage, thereby enhancing the electrochemical signal [14]. Non-enzymatic sensors and those employing Molecularly Imprinted Polymers (MIPs) have also been developed for metabolites such as glucose and cholesterol, offering improved stability compared to traditional enzyme-based sensors [15].
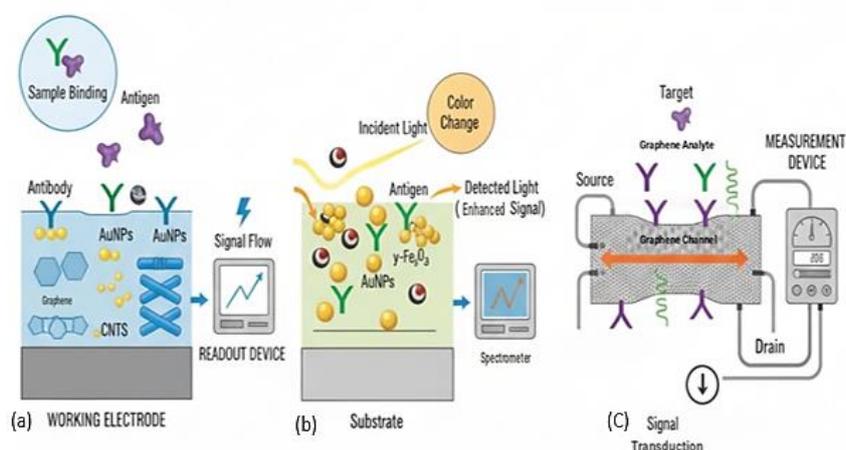
3.2 | Optical Biosensors

Optical biosensors provide label-free, real-time monitoring and are often highly versatile. A notable example is a dual-mode plasmonic biosensor that combined LSPR with a photothermal effect for SARS-CoV-2 detection. This design utilized a laser to generate localized heat on gold nanoislands upon target binding, amplifying the signal and significantly improving specificity [16]. Colorimetric assays exploiting the peroxidase-mimetic activity of γ-Fe_2O_3 nanoparticles have been developed, wherein the presence of viral antigens inhibits the catalytic reaction, resulting in a measurable color change [17]. Furthermore, theoretical studies have proposed SPR biosensors incorporating layers of TiO_2 and MXene, predicting extremely high sensitivity for virus detection [18].

3.3 | Field-Effect Transistor Biosensors

FET biosensors functionalized with nanomaterials offer exceptional sensitivity and real-time electrical readouts. A groundbreaking graphene-based FET biosensor was functionalized with antibodies against the SARS-CoV-2 spike protein, enabling direct detection of the virus in clinical nasopharyngeal swab samples within minutes [19]. To overcome challenges in graphene functionalization, one study employed gas-phase-synthesized AuNPs as anchors for DNA aptamers, resulting in a Graphene Field-Effect Transistor (GFET) capable of attomolar-level detection and single-nucleotide polymorphism discrimination [20]. These

platforms are particularly promising for POC diagnostics due to their potential for miniaturization and seamless integration with electronic devices (*Fig. 2* and *Table 1*).

Fig. 2. Schematic representation of main biosensing platforms; a. Electrochemical, b. Optical (LSPR/SERS), and c. Field-effect transistor biosensors, showing sample binding, signal transduction, and role of nanomaterials.

Table 1. Systematic comparison of major biosensing platforms.

Biosensing Platform	Transduction Mechanism	Strengths	Limitations	Instrumentation Requirement	POC Suitability
Electrochemical	Current/voltage/impedance changes upon biomolecular recognition	High sensitivity, low cost, portable, easy miniaturization	Matrix interference, surface fouling, requires optimized electrode modification	Very low	Excellent
Optical (LSPR, SERS, fluorescence, photothermal)	Change in optical response upon target binding	Ultra-high sensitivity, real-time, label-free detection	Requires lasers or optical benches; relatively expensive	Medium–high	Moderate
FET	Conductance modulation in the semiconductor channel caused by biomolecule charges	Extremely fast response, ultra-low LOD (even aM), ideal for integration with electronics	Complex fabrication, challenging functionalization, susceptible to environmental noise	Medium	Excellent
Colorimetric	Visible color change due to nanoparticle aggregation or catalytic reactions	Simple, low-cost, instrument-free, user-friendly	Lower sensitivity than FET/optical sensors; qualitative or semi-quantitative	Very low	Excellent

4 | Applications in Diagnosing Major Diseases

4.1 | Infectious Diseases

The COVID-19 pandemic served as a major catalyst for the rapid development of nanomaterial-based biosensors. Numerous platforms have been developed for detecting SARS-CoV-2 RNA, antigens, and antibodies with unprecedented speed and sensitivity [13], [16], [19]. Beyond COVID-19, a noninvasive electrochemical biosensor has been designed for detecting Helicobacter pylori antigens directly in saliva, providing a comfortable alternative to invasive biopsies [21]. Comprehensive reviews have also highlighted the efficacy of noble metal nanomaterials and carbon-based sensors for detecting a range of respiratory viruses, including influenza and MERS-CoV [9], [22].

4.2 | Cancer Diagnostics

Early detection of cancer is critical for improving treatment outcomes and patient survival. Nanomaterial-based biosensors have demonstrated remarkable performance in identifying cancer-specific biomarkers. For breast cancer, sensors targeting BRCA1 and BRCA2 genes have achieved detection limits in the attomolar range using electrochemical and optical methods [23]. In oral cancer diagnostics, graphene-based electrochemical biosensors functionalized with nanocomposites such as ZnO-rGO have been employed to detect salivary biomarkers like IL-8 and CYFRA-21-1 with high specificity [24]. The adoption of aptasensors, which utilize nucleic acid aptamers instead of antibodies, has gained significant traction due to their enhanced stability, reproducibility, and lower production costs [25].

4.3 | Neurodegenerative and Cardiovascular Diseases

Early diagnosis of AD is being advanced by biosensors capable of detecting key biomarkers such as Tau protein and amyloid-β in blood and cerebrospinal fluid. Optical sensors leveraging nanomaterials for signal amplification have shown particular promise in this area [26]. In CVD diagnostics, the detection of biomarkers like Cardiac Troponin I (cTnI) and N-Terminal pro-Brain Natriuretic Peptide (NT-proBNP) is essential for timely intervention. Advanced nanomaterial-based aptasensors and electrochemical platforms have been developed to quantify these biomarkers at clinically relevant concentrations, with some achieving sensitivities in the fg/mL range *Table 2* [27], [28].

Table 2. Systematic comparison of nanomaterials and biosensing platforms by disease area.

Disease Area	Biomarker Type	Preferred Nanomaterial	Biosensor Platform	Key Advantage	Reference
Infectious Diseases (COVID-19, Influenza)	Viral RNA / Antigen	Graphene, AuNPs	FET, Electrochemical	Ultra-sensitive, point-of-care detection	[13], [16], [19]
Cancer (Breast, Oral)	Proteins / Genes (BRCA1/2, IL-8, CYFRA-21-1)	Graphene, ZnO-rGO, AuNPs	Electrochemical, Optical	Atto molar detection, multiplexing possible	[23], [24]
Neurodegenerative (Alzheimer's)	Tau, Amyloid-β	CNTs, GO	Electrochemical, Optical	Early detection, label-free	[14], [26]
Cardiovascular (CVD)	cTnI, NT-proBNP	AuNPs, CNTs, Aptamer-modified nanomaterials	Electrochemical, Aptasensors	High specificity, fg/mL detection	[27], [28]
Helicobacter pylori	Antigens in saliva	Fe3O4, AuNPs	Electrochemical	Noninvasive, rapid	[21]

5 | Challenges and Limitations

Despite the impressive analytical performance demonstrated in laboratory and research settings, the path to widespread clinical adoption remains fraught with significant challenges.

5.1 | Analytical and Manufacturing Hurdles

A major limitation is the lack of comprehensive long-term stability and batch-to-batch reproducibility data. The synthesis and functionalization of nanomaterials are often complex processes that are difficult to standardize for mass production [4], [5]. Furthermore, many sensor fabrication protocols involve multiple steps and are not easily scalable, hindering commercial viability.

5.2 | Clinical and Regulatory Translation

There is a notable scarcity of extensive validation studies involving large, diverse clinical cohorts. Most reported studies rely on spiked buffer solutions or a limited number of patient samples [1]. The complex matrix of biological fluids (e.g., blood, saliva, plasma) can cause significant interference, compromising sensor accuracy and reliability [21]. Navigating regulatory pathways for approval as clinical diagnostic tools remains a substantial hurdle [22].

5.3 | Material and Practical Considerations

Certain nanomaterials, such as BP, suffer from inherent stability issues, degrading upon exposure to air and water [8]. The potential toxicity and long-term environmental impact of some nanomaterials also require thorough investigation [29]. Additionally, many highly sensitive platforms depend on sophisticated and expensive readout instrumentation, which limits their deployment as low-cost POC devices [16].

5.4 | Biocompatibility and Toxicity Challenges

Despite the enhanced performance of nanomaterial-based biosensors, biocompatibility and toxicity remain critical barriers to their clinical translation. The biological impact of nanomaterials varies significantly depending on their physicochemical properties, including size, shape, surface chemistry, dose, and exposure route. First, ultrasmall iron oxide nanoparticles (Fe_3O_4) pose significant risks: in mice, Fe_3O_4 nanoparticles with diameters of ~2.3 nm and ~4.2 nm induced acute toxicity at high doses due to pronounced generation of Reactive Oxygen Species (ROS), including hydroxyl radicals (·OH), particularly in the heart, leading to cardiac failure [30]. This size and dose dependent toxicity underscores the need for surface engineering or alternative designs to mitigate ROS-mediated damage. Second, Graphene Nanoplatelets (GNPs) have demonstrated sub-chronic inflammatory responses in vivo. In an intratracheal instillation study in mice (2.5 and 5 mg/kg), GNPs persisted in the lungs for up to 28 days, with inflammatory cytokine levels peaking at day 14 before gradually subsiding [29-32]. In vitro studies showed that GNPs induced autophagy and apoptosis in human Bronchial Epithelial Cells (BEAS-2B), associated with mitochondrial dysfunction and reduced ATP production [32]. Inhalation toxicity studies further revealed that GNPs with large lateral dimensions (>5 µm) triggered lung inflammation and systemic responses (e.g., in the aorta and liver), effects linked to particle size and surface reactivity [33]. Notably, a 28-day rat inhalation study (nose-only exposure) reported no dose-dependent lung pathology, suggesting a No Observed Adverse Effect Level (NOAEL) of 1.88 mg/m³ [33]. These findings emphasize the importance of controlling size, exposure route, and chronic accumulation in biosensor applications involving graphene derivatives. Third, for other 2D nanomaterials (such as MXenes and BP), biocompatibility is complex and highly dependent on exposure conditions and surface functionalization. Although detailed in vivo toxicity data for many MXenes are still emerging, early studies indicate dose-dependent effects. Mitigation strategies, such as PEGylation or other biocompatible coatings, are recommended to reduce ROS formation and enhance clearance.

Recommendations for future work

  I.   Thorough physicochemical characterization: researchers should consistently report particle size distribution, zeta potential, surface chemistry (e.g., functional groups), and degradation behavior.

 II.   Comprehensive in vitro testing: beyond simple viability assays, studies should include metrics such as ROS production, apoptosis/autophagy, cytokine release, and genotoxicity.

III.   In vivo safety studies: long-term biodistribution, clearance, immune response, organ histopathology, and dose-dependent toxicity should be systematically evaluated.

IV.   Surface design: functionalizing nanomaterials with biocompatible polymers (e.g., PEG), proteins, or biodegradable moieties to reduce toxicity.

 V.   Regulatory strategy integration: early inclusion of safety and toxicology data in sensor development to align with risk-benefit assessments for clinical use.

By addressing these biocompatibility and toxicity challenges in a rigorous and standardized manner, the field of nanomaterial-based biosensors can move more confidently toward safe and effective clinical translation.

6 | Future Perspectives and Conclusions

The future of nanomaterial-based biosensors holds immense promise, with several key trajectories poised to advance the field.

6.1 | Multiplexed Detection

Future biosensors should evolve beyond single-analyte detection toward multiplexed platforms capable of simultaneously quantifying multiple biomarkers from a single sample. This capability would provide a more comprehensive diagnostic profile, particularly for complex diseases such as cancer and cardiovascular disorders [22], [27].

6.2 | Integration with Digital Technologies

The integration of biosensors with AI, machine learning, and the Internet of Medical Things (IoMT) will facilitate real-time data analysis, remote patient monitoring, and the creation of intelligent diagnostic ecosystems [8], [15].

6.3 | Point-of-Care and Wearable Devices

The development of robust, user-friendly, and affordable POC and wearable devices remains a primary objective. Advances in miniaturization, stable bioreceptor design, microfluidics, and smartphone-compatible readouts will enable noninvasive, continuous monitoring in non-laboratory settings [4], [13].

6.4 | Sustainable and Green Nanomaterials

Increasing emphasis on eco-friendly synthesis methods and biodegradable nanomaterials will be essential to minimize environmental impact and align with sustainability goals [8].

In conclusion, nanomaterial-based biosensors represent a paradigm shift in disease diagnostics, offering unparalleled sensitivity, rapidity, and adaptability. These attributes hold the potential to democratize healthcare through early detection, personalized medicine, and decentralized testing. However, unlocking this potential requires concerted efforts from researchers, engineers, and clinicians to address challenges in reproducibility, clinical validation, biocompatibility, and scalable manufacturing. By overcoming these hurdles, nanomaterial-based biosensors are poised to become indispensable tools in the global healthcare arsenal.

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