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# Nano Technology Based Bio Sensor for Early Disease Diagnosis

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**Abstract:** The accurate and rapid diagnosis of viral and other infectious diseases has become a global healthcare priority due to the increasing burden of emerging and re-emerging pathogens. Early detection is essential for timely treatment, effective disease management, and prevention of widespread transmission. Biosensors have emerged as powerful diagnostic platforms because of their ability to provide rapid, sensitive, specific, and cost-effective detection compared with conventional laboratory-based techniques. This systematic review evaluates recent advancements in biosensor technologies for the detection of infectious diseases, following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Particular emphasis is placed on nanotechnology-enabled biosensors, which exploit the unique physicochemical properties of nanomaterials, including their high surface-to-volume ratio, excellent electrical conductivity, enhanced optical characteristics and customizable surface chemistry. These features significantly improve the sensitivity, selectivity, and overall analytical performance of biosensing platforms. The review discusses various biosensor types based on their signal transduction mechanisms, including electrochemical, optical, piezoelectric, thermal, and mass-based biosensors, highlighting their principles, recent innovations and clinical applications. Furthermore, the expanding role of biosensors in point-of-care diagnostics, disease surveillance, personalized medicine and public health is examined. Despite remarkable technological progress, several challenges remain, including sensor stability, reproducibility, large-scale manufacturing, regulatory approval and integration with digital healthcare systems. The review also explores the incorporation of artificial intelligence, Internet of Things (IoT), smartphone-based platforms, and wearable biosensors to enable real-time disease monitoring and remote healthcare delivery. Overall, next-generation biosensors demonstrate significant potential to transform infectious disease diagnostics by enabling faster, more accessible and highly accurate detection, thereby supporting improved clinical decision-making and global health preparedness.

**Keywords:** Biosensors; Nano biosensors; Viral Diseases; Infectious Disease Detection; Nanotechnology; Nanomaterials; Early Diagnosis; Disease Biomarkers; Electrochemical Biosensors; Optical Biosensors; Diagnostic Technology; Personalized Medicine; PRISMA; Rapid Detection; Point-of-Care Diagnostics.

## Introduction

Infectious diseases have been a persistent challenge to global health, contributing to significant morbidity and mortality worldwide. The early and accurate detection of such diseases is critical in curbing their spread and ensuring timely treatment interventions. However, early diagnosis is often difficult or impossible without an appropriate means of detecting small differences in the patient's physiology. Histopathology is the gold standard for the diagnosis of many diseases but also requires an expert practitioner and introduces an element of subjectivity to disease diagnosis (Uckermann et al., 2014). Likewise, medical imaging is commonly used in disease diagnosis but cannot easily detect early-stage disorders, which often affect tissues on scales too small to be resolved by the imaging technique. Standard biochemical assays are now employed for the diagnosis of tuberculosis, HIV, hepatitis, Escherichia coli enteritis, and many other pathological conditions. The first biosensor, designed for the detection of glucose, was introduced in 1962 by Clark and Lyons (Rapp et al., 2010). Also called an "enzyme electrode," it was a biosensor of the amperometric type. Biosensors can be classified according to their recognition element (e.g., enzymes, antibodies, nucleic acids), output type (e.g., optical, electrical, mechanical), detection principle (e.g., surface plasmon resonance (SPR) based, surface-enhanced Raman spectroscopy (SERS) based, quartz crystal microbalance (QCM) based), or intended use (in vivo or ex vivo).There are challenges in cancer detection. Fuel cell developments have influenced portable device development. Molecular level detection refinement is still needed. Biosensors have a biologically derive sensitive biological component or biosensing element such as antibodies or enzymes that generates a signal proportional to the concentration of an analyte which can be used for early screening of diseases .Following are a few categorizations of biosensors:

1. Optical Biosensors:
    a. Fiber Optical Biosensors.
    b. Reflective Optical Biosensors.
    c. Sensors based on Fluorescence Excitation.
    d. Sensors based on Evanescent Light Wave.
    e. Sensors based on Surface Plasmon Resonance.
    f. Sensors Based on Surface Enhanced Raman.
    g. Acoustic Wave Sensors.
    h. Infrared Sensors.
2. Electrochemical Biosensors:
    a. Amperometric Biosensors (current measuring).
    b. Potentiometric.
    c. Conductometric (resistance measuring).
3. Non-Invasive Biosensor:
    a. Optical reflectometry / photoplethysmography (monitoring heart rate, blood level, etc).
    b. Thermal parameters.
    c. Microwaves.
    d. Electric field (detecting skin temperature, acidity, etc).
4. Miniaturized Biosensors:
    a. Stand Alone (fully portable).
    b. Integrated (lab-on-chip).

## HISTORY

The history of nanotechnology-based biosensors is the result of two fields evolving together. Their integration has greatly improved the early detection of disease by making diagnostic devices more sensitive, faster, and portable.

1. Development of Biosensors (1960s-1970s)
    - In 1962, Leland C. Clark Jr. developed the first biosensor, known as the Clark oxygen electrode.

- This invention laid the foundation for modern biosensor by combining a biological sensing element detector.
- During the 1970s, enzyme-based biosensors, especially glucose biosensors for diabetes monitoring, became widely used.

2. Emergency of Nanotechnology (1980s-1990s)
   - In 1974, Norio Taniguchi introduced the term "nanotechnology"
   - During the 1980s and 1990s, scientists developed nanomaterials such as nanoparticles, carbon nanotubes, and quantum dots.
   - These materials showed unique electrical, optical, and chemical properties that made them ideal for biosensing applications.
3. Integration of Nanotechnology with Biosensors (2000s)
   - In the early 2000s, researchers began incorporating nanomaterials into biosensors.
   - Gold nanoparticles, graphene, carbon nanotubes, and quantum dots significantly improved sensor performance.
   - These nano biosensors achieved:
     - Higher sensitivity
     - Better selectivity
     - Faster response times
     - Lower limits of detection
     - Miniaturization and portability
4. Advances in Early Disease Diagnosis (2010s)
   - Nanotechnology-based biosensors were increasingly applied to detect:
     - Cancer biomarkers
     - Cardiovascular disease markers
     - Infectious disease
     - Neurological disorders

These biosensors enabled diagnosis from very small biological samples such as blood, saliva, urine, and tears.

5. Recent Developments (2020-Present)
   - The COVID-19 pandemic accelerated the development of rapid nanobiosensors for virus detection.
   - Current research focuses on:
     - Wearable biosensors
     - Smartphone-integrated diagnostic devices
     - Artificial intelligence-assisted biosensing
     - Lab-on-a-chip and point-of-care testing
     - Multiplex biosensors capable of detecting multiple disease biomarkers simultaneously

## SIGNIFICANCE

Nanotechnology-based biosensors have transformed disease diagnosis by enabling early, accurate, and cost-effective detection. They are becoming increasingly important in personalized medicine, home-based healthcare, and point-of-care diagnostics.

## PLAN

The plan for nanotechnology-based biosensors in early disease diagnosis focuses on integrating advanced nanomaterials, such as gold nanoparticles, graphene, and quantum dots, with biological recognition elements to achieve ultra-sensitive, rapid, and point-of-care detection of disease biomarkers at microscopic concentrations.

## DESIGN AND MATERIALS

**Nanomaterials:** Utilizing carbon nanotubes, graphene, and metal nanoparticles for a high surface-to-volume ratio that magnifies electrical and optical signals.

**Bioreceptors:** Attaching specific antibodies, DNA strands, or enzymes to nanomaterials to selectively trap target disease molecules like a lock and key**.**

**Signal Amplification:** Converting microscopic biological bindings into measurable electronic, colorimetric, or fluorescent readouts.

## DIAGNOSTIC APPLICATION GOALS

**Infectious Diseases:** Detecting viral antigens or pathogen DNA rapidly without waiting for slow culture growth**.**

**Cancer and Tumours:** Identifying trace tumour biomarkers and genetic mutations at early, treatable stages using surface-enhanced Raman spectroscopy (SERS).

**Chronic and Neurodegenerative Conditions:** Monitoring glucose levels continuously or spotting early brain plaque proteins like amyloid-beta.

### A typical biosensor consists of three fundamentals

### The biorecognition element

The biorecognition element, also known as the bioreceptor, is responsible for the specific and selective interaction with the target analyte (i.e., the substance to be detected, such as glucose, troponin, or cancer biomarkers). This elements mimics the biological recognition process and is key to ensuring specificity and accuracy

### The transducer

The transducer converts the recognition event into a measurable signal. This conversion is the cornerstone of biosensing because biological interactions themselves are not directly measurable (e.g., binding of glucose to an enzyme). The transducer translates this event into an electrical, optical, thermal, or mechanical signal.

### Signal processor and display unit

After the signal is generated by the transducer, it needs to be processed, digitized, and interpreted for the user. This role of the signal processor, which may include microcontrollers, amplifiers, analog-to-digital converters (ADC), and software algorithms.

### Detection of specific cancer biomarkers using nano biosensors

### Circulating Tumour DNA (ctDNA)

Circulating tumour DNA comprises small fragments of DNA released into the bloodstream by tumour cells. These fragments carry genetic mutations characteristic of cancer, making ctDNA a valuable biomarker for early cancer detection. To overcome these obstacles, electrochemical biosensors with high sensitivity and specificity have been created. (e.g. the possibility for early cancer diagnosis was established by a biosensor that used gold-coated magnetic nanoparticles to detect ctDNA at concentrations as low).

### Protein biomarkers

Certain proteins function as biomarkers for different types of cancer. Cancer antigen 125 (CA-125) is linked to ovarian cancer, but prostate-specific antigen (PSA) is frequently linked to prostate cancer. Nano biosensors employing aptamers short, single-stranded DNA or RNA molecules that can bind to specific targets have been designed to detect these proteins with high specificity. (e.g. have been developed for the detection of CA-125, achieving low limits of detection and demonstrating potential for early-stage cancer diagnosis).

### 1. Enzymatic activity

Altered enzyme levels can indicate the presence of cancer. Nanozymes nanomaterials with enzyme-like activities have been incorporated into biosensors to detect such enzymatic changes. These nanozyme-based biosensors offer advantages over natural enzymes, including higher stability, lower cost, and the ability to function under a broader range of conditions. (e.g. nanozyme-based apt sensors have been developed to detect tumour biomarkers, combining the specificity of aptamers with the catalytic activity of nanozymes to enhance detection sensitivity).

### 2. Exosomes

Exosomes are small extracellular vesicles released by cells, containing proteins, lipids, and nucleic acids. Tumour-derived exosomes carry molecular signatures reflective of their parent cancer cells, making them valuable biomarkers for cancer detection. Nano biosensors have been developed to detect these exosomes in bodily fluids, offering a non-invasive approach to cancer diagnosis. For instance, biosensors utilizing nanomaterials have been designed to capture and detect exosomes with high sensitivity, facilitating early detection and monitoring of cancer progression

### Cancer-specific biosensors

### Breast Cancer

A biosensor developed using molybdenum trioxide and poly-taurine nanofilms demonstrated effective detection of HER2 in serum samples, a key biomarker for breast cancer. Nano biosensors detect HER2, CA15-3, and BRCA mutations. Electrochemical and optical biosensors integrated with AuNPs or graphene have demonstrated high sensitivity in detecting these markers from blood or saliva.

### Lung Cancer

Paper-based biosensors utilizing metal organic frameworks and gold nanorods have been designed to detect volatile organic compounds in exhaled breath, serving as non-invasive indicators of lung cancer.

### Oral Cancer

Nanotechnology-enabled biosensors have demonstrated significant potential for cancer diagnosis by enabling the rapid, sensitive, and specific detection of biomarkers such as DNA mutations, proteins, mRNAs, and salivary biomarkers. Nanomaterials including carbon nanotubes, quantum dots, and gold nanoparticles have substantially enhanced biosensor performance through improved signal amplification and analytical sensitivity. Despite these advancements, most biosensors are designed to detect a single biomarker, whereas accurate cancer diagnosis often requires multiplex biomarker profiling due to the heterogeneous nature of the disease. Furthermore, the clinical translation of optical biosensors remains limited by challenges such as photobleaching, background interference, and nanoparticle-associated toxicity. Variability in biological sample types, including serum, plasma, saliva, and urine, also affects reproducibility and cross-platform comparisons. Future research should prioritize standardized protocols, multiplex detection platforms, and clinically validated biosensors to improve diagnostic accuracy and facilitate routine clinical implementation.

## METHODS

### Inclusion Criteria

- Studies that evaluated bio-sensors for detecting infectious disease in clinical, laboratory, or point-of-care settings.
- Research focusing on the sensitivity, specificity, and reliability of biosensor-based diagnostic methods.
- Peer-reviewed articles published in English between 2015 and 2024.
- Studies incorporating novel biosensor technologies, including nanomaterials, microfluids, and AI-driven diagnostics.

### Exclusion Criteria

- Studies focusing on biosensors for non-infectious disease.

- Articles lacking experimental validation or clinical application.
- Review articles, opinion pieces, and editorials.
- Non-English language studies.

### Study Selection Process

The study selection was conducted through a three-stage screening process:

1. **Title screening:** Initial article screening was based on the articles' titles. At this stage, irrelevant studies were excluded.
2. **Abstract review:** The abstracts from the remaining articles were evaluated according to our selection criteria.
3. **Full-Text Assessment:** Retrieved full-text articles that fufilled the eligibility criteria were evaluated in depth-, and studies that met the final inclusion criteria were selected for inclusion in the review.

Inter-rater reliability was assessed by measuring the level of general agreement between the independent reviewers using Cohen's Kappa coefficient and yielded a value of 0.85, reflecting high concordance between reviewers.

### Data Extraction

An extraction from for collecting relevant data from each included study was designed in a structure.
The data points extracted included the following:

- Study design and setting.
- Technique used (electrochemical, optical, nanomaterial, etc.)
- Infectious disease targeted.
- Sensitivity, specificity, and detection limit.
- Advantages and limitations.
- Translational potential.

### Quality Assessment

Data were extracted and assessed for the quality of included studies using the QUADAS-2 (Quality Assessment of Diagnostic Accuracy Studies) tool. Studies were assessed in 4 domains:

1. **Patient Selection**: Appropriateness of participant recruitment.
2. **Index Test**: Adequacy of biosensor performance evaluation.
3. **Reference Standard**: Comparison with conventional diagnostic methods.
4. **Flow and Timing**: Completeness of follow-up data.

### Future Trends

The future trends of nano technology-based biosensors for early disease diagnosis are promising, with significant advancements in sensitivity, accuracy, and real-time monitoring capabilities. Some key trends to expect:

- **Multiplexed Biomarker Detection**: Nano-biosensors are being developed to enable multiplexed biomarker detection with high sensitivity and precision, allowing for real-time, high-throughput, and personalized health monitoring.
- **Integration with Microfluidics**: The integration of microfluidics with nano-biosensors is enhancing sensor performance through precise sample processing, reduced reagent use, and simultaneous biomarker detection.
- **Adaptive AI Algorithms**: The role of adaptive AI algorithms in individualizing diagnostics to diverse patient groups while addressing key ethical and regulatory considerations is becoming increasingly important.

- **Sustainability and Cost-effectiveness**: There is a growing focus on the sustainable of nano-biosensors and the development of cost-effective diagnostic solutions.
- **Addressing Nano-toxicology Challenges**: Research is ongoing to overcome nano-toxicology challenges that may limit the application of nano-biosensor in biological systems. These trends indicate a strong potential for nano technology-based biosensor to play a crucial role in the future of disease diagnosis and personalized healthcare.
- **Wearable and Flexible Biosensors:** Nanotechnology-enabled wearable devices will continuously monitor biomarkers in sweat, saliva, tears, or interstitial fluid. These biosensors will allow real-time health monitoring and early detection of chronic diseases such as diabetes, cardiovascular disorders, and cancer.
- **Lab-on-a-Chip and Microfluidic Technologies:** Combining nanomaterials with microfluidic systems will enable automated sample preparation, detection, and analysis on a single miniaturized platform. These systems will reduce sample volume, cost, and testing time while improving diagnostic efficiency.
- **CRISPR-Based Nano biosensors:** CRISPR-Cas systems integrated with nanomaterials will enable highly specific detection of genetic mutations and infectious pathogens. These biosensors are expected to revolutionize precision diagnostics for viral diseases, inherited disorders, and cancer.
- **Ultra-Early Disease Detection:** Next-generation nano biosensors will detect diseases at extremely low biomarker concentrations (femtomolar to Atto molar levels). Earlier diagnosis will improve treatment outcomes for cancer, neurodegenerative diseases, cardiovascular disorders, and infectious diseases.
- **Commercialization and Clinical Translation:** Future research will focus on improving reproducibility, standardization, scalability, and regulatory approval. Large-scale manufacturing and cost-effective production will promote widespread clinical adoption.
- **Non-Invasive Diagnostics:** Future biosensors will increasingly utilize saliva, urine, breath, sweat, and tears instead of blood samples. This approach will improve patient comfort and facilitate frequent health monitoring.
- **Personalized and Precision Medicine:** Nano biosensors will support individualized treatment by monitoring patient-specific biomarkers and therapeutic responses. Continuous biomarker monitoring will enable personalized disease management and optimized treatment strategies.
- **Point-of-Care (POC) Diagnostics:** Portable, user-friendly biosensors will provide rapid diagnostic results outside conventional laboratories. Integration with smartphones will enable immediate data analysis and remote healthcare services, particularly in rural and resource-limited settings.

**Results of Nanotechnology-Based Biosensors for Early Disease Diagnosis**

The development of nanotechnology-based biosensors has significantly improved the early diagnosis of various diseases by providing rapid, highly sensitive, and accurate detection of disease biomarkers. The major findings reported in recent studies are.

**Enhanced Sensitivity**: Nanomaterials such as gold nanoparticles, graphene, carbon nanotubes, quantum dots, and MXenes greatly enhance signal amplification. These biosensors can detect biomarkers at femtomolar ($10^{-15}$ M) or even Atto molar ($10^{-18}$ M) concentrations, enabling disease detection at very early stages.

**High Specificity:** Functionalization of nanomaterials with antibodies, aptamers, nucleic acids, or molecularly imprinted polymers enables selective recognition of target biomarkers. This minimizes cross-reactivity and reduces false-positive and false-negative results.

**Rapid Detection:** Nanotechnology-based biosensors provide results within minutes, compared to conventional laboratory techniques that may require several hours or days. Rapid diagnosis is particularly valuable for infectious diseases and emergency clinical settings.

**Improved Diagnostic Accuracy:** Enhanced sensitivity and specificity contribute to higher diagnostic accuracy. Early identification of disease biomarkers facilitates timely clinical intervention and improves patient outcomes.

**Detection of Multiple Biomarkers:** Advanced nano biosensors can simultaneously detect multiple biomarkers in a single sample. Multiplex detection improves disease classification and diagnostic reliability.

**Low Sample Volume:** Only a small amount of blood, saliva, urine, tears, or sweat is required for analysis. This makes testing less invasive and more convenient for patients.

**Point-of-Care Applications:** Portable biosensors enable rapid diagnosis outside centralized laboratories. These devices are particularly useful in remote and resource-limited healthcare settings.

### Application Across Multiple Diseases:

Nano biosensors have demonstrated excellent performance in detecting:

- Cancer biomarkers (e.g., PSA, CEA, HER2)
- Viral infections (COVID-19, dengue, influenza, HIV, hepatitis)
- Cardiovascular biomarkers (troponin, BNP)
- Diabetes biomarkers (glucose, HbA1c)
- Neurological disease biomarkers (amyloid-β, tau protein)

**Cost-Effectiveness:** Miniaturized sensor platforms reduce reagent consumption and testing costs**.** Large-scale production of nanomaterials is expected to further improve affordability.

**Potential for Personalized Medicine**: Continuous monitoring of disease biomarkers supports individualized treatment decisions and real-time assessment of therapeutic response.

Nanotechnology-based biosensors have demonstrated substantial improvements in the early diagnosis of diseases by combining high sensitivity, excellent specificity, rapid response times, and portability. Their ability to detect extremely low concentrations of biomarkers, perform multiplex analysis, and operate with minimal sample volumes makes them promising alternatives to conventional diagnostic methods. Although challenges related to long-term stability, reproducibility, standardization, and regulatory approval remain, continued advancements in nanomaterials and biosensor design are expected to facilitate broader clinical adoption and improve global healthcare outcomes.

## DISCUSSION

Nanotechnology-based biosensors have emerged as one of the most promising diagnostic technologies for the early detection of diseases due to their exceptional sensitivity, specificity, and rapid response. This review highlights the significant advancements in nanomaterials and biosensor platforms that have enabled the detection of disease biomarkers at extremely low concentrations, facilitating diagnosis before the onset of clinical symptoms. Compared with conventional diagnostic techniques such as enzyme-linked immunosorbent assay (ELISA), polymerase chain reaction (PCR), and imaging-based methods, nanotechnology-based biosensors offer faster analysis, reduced sample requirements, portability, and the potential for point-of-care testing.

Recent studies demonstrate the successful application of nanotechnology-based biosensors in the diagnosis of a wide range of diseases, including cancer, cardiovascular diseases, diabetes, neurodegenerative disorders, and infectious diseases such as COVID-19, dengue, influenza, hepatitis, and HIV. Their ability to detect circulating tumour DNA, microRNAs, proteins, metabolites, and viral nucleic acids has significantly improved early disease identification and disease monitoring. Multiplex biosensor platforms capable of simultaneously detecting multiple biomarkers have further enhanced diagnostic accuracy by providing comprehensive disease profiles.

The integration of nanotechnology with artificial intelligence (AI), machine learning, CRISPR-based molecular diagnostics, the Internet of Medical Things (IoMT), and wearable electronics represents a major future direction. AI-assisted biosensors can improve data interpretation, reduce diagnostic errors, and support personalized medicine by enabling predictive disease analysis and continuous patient monitoring. Combining nanotechnology with lab-on-a-chip and microfluidic platforms is expected to

produce fully automated diagnostic systems that are rapid, affordable, and suitable for decentralized healthcare.

The findings indicate that nanotechnology-based biosensors have significantly advanced the field of early disease diagnosis by providing highly sensitive, specific, rapid, and cost-effective diagnostic solutions. Continued interdisciplinary collaboration among nanotechnology, biotechnology, materials science, engineering, and clinical medicine will be essential to overcome existing limitations and facilitate the translation of these innovative biosensors from laboratory research to routine clinical applications. Their successful implementation has the potential to transform modern healthcare by enabling earlier diagnosis, timely therapeutic intervention, personalized treatment, and improved patient outcomes while reducing the global burden of disease.

## CONCLUSION

The integration of nanotechnology with portable biosensor platforms marks a transformative leap in the early detection and management of non-communicable disease (NCDs), particularly diabetes, cardiovascular disease, and cancer. Nanotechnology-based biosensors have emerged as a promising and transformative approach for the early diagnosis of diseases due to their exceptional sensitivity, specificity, rapid response, and ability to detect biomarkers at very low concentrations. Early identification of NCDs remains a challenge, particularly because many conditions develop asymptomatically. This review highlights that nano-invasive biomarker detection. Their capacity to function non-invasively through a variety of bodily fluids and their incorporation into wearable technology and cell phones are well-suited to support early intervention and personalized health monitoring, especially when integrated with wearable and mobile technologies. The incorporation of advanced nanomaterials, such as gold nanoparticles, graphene, carbon nanotubes, quantum dots, MXenes, and metal-organic frameworks, has significantly enhanced biosensor performance by improving signal amplification, biocompatibility, and detection accuracy. These advancements have enabled the reliable detection of biomarkers associated with cancer, infectious diseases, cardiovascular disorders, neurological conditions, and metabolic diseases at their earliest stages, thereby facilitating timely intervention and improving patient outcomes.

In conclusion, nanotechnology-based biosensors represent the next generation of diagnostic technologies for early disease detection. Their unique combination of high analytical performance, rapid detection, and potential for decentralized healthcare makes them valuable tools for improving disease management and reducing healthcare costs. Continued interdisciplinary research, technological innovation, and successful clinical translation are expected to accelerate their adoption in routine medical practice, ultimately contributing to more accurate, accessible, and personalized healthcare worldwide.

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