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Lab-on-a chip: nanobiosensors for point-of-care diagnostics

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ABSTRACT

Introduction: Growing demand for fast, sensitive and simple diagnostic tools are driving the innovation of nanobiosensors, for point-of-care application. By combining state-of-the-art biosensing technologies and micro-scale platforms, they facilitate rapid in situ analyses of disease biomarkers for infectious diseases, cancer, and a wide range of diseases. There are several new modified nanomaterial-based biosensors (including modified graphene, carbon nanotubes, quantum dots and noble metals nanoparticles) that could offer desired sensitivity and specificity, combined with microfluidic and wireless systems.
Objectives: The present paper aims to review the technical aspects of the new generation of biosensors and its potential uses in point-of-care evidence-based diagnostics.
Methodology: A literature search was conducted across PubMed, ScienceDirect, and MDPI, focusing on peer-reviewed articles from 2010 to 2024, with priority given to studies from 2019–2024. A total of 63 articles were identified; 47 were included in this review, and 16 were excluded based on relevance.
Results: We provide examples of the clinical relevance of these tools from pathogen detection as well as oncology. The use of nanobiosensing for decentralized/point-of-care/personalized health care has great potential even in the context of remaining challenges including standardization practices and biofouling related problems, especially when multidisciplinary innovations are united.
Conclusions: In conclusion, although challenges such as standardization and biofouling still persist, the future of nanobiosensors as a key component in personalized and decentralized healthcare is promising, especially when driven by interdisciplinary collaborations.

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RESUMO

Introdução: A crescente necessidade por ferramentas de diagnóstico rápidas, sensíveis e de fácil utilização está a impulsionar a inovação das tecnologias de nanobiossensores, especialmente para aplicações em pontos de cuidado. Ao integrar tecnologias avançadas de deteção com plataformas em microescala, esses dispositivos possibilitam análises rápidas e in situ de biomarcadores de doenças, incluindo doenças infeciosas e cancros. Estudos recentes destacam o desenvolvimento de biossensores baseados em nanomateriais modificados (como grafeno modificado, nanotubos de carbono, "quantum dots" e nanopartículas de metais nobres) que oferecem maior sensibilidade e especificidade. Esses sensores são frequentemente combinados com sistemas microfluídicos e tecnologias sem fio, representando uma nova geração de ferramentas diagnósticas inteligentes.
Objetivos: O presente artigo tem como objetivo analisar os aspetos técnicos da nova geração de biossensores e as suas potenciais utilizações em diagnósticos baseados em evidência no local de atendimento.
Metodologia: Foi realizada uma busca abrangente na literatura científica utilizando as bases de dados PubMed, ScienceDirect e MDPI, considerando artigos publicados entre 2010 e 2024, com ênfase no período de 2019 a 2024. Um total de 63 artigos foram identificados; desses, 47 foram incluídos nesta revisão e 16 foram excluídos com base em critérios de relevância.
Resultados: Fornecemos exemplos da relevância clínica desses dispositivos, tanto na deteção de patógeneos quanto na oncologia. O uso de nanobiossensores para cuidados de saúde descentralizados, personalizados e em pontos de cuidado apresenta grande potencial, mesmo diante de desafios persistentes, como a padronização e os problemas relacionados com o "biofouling"—especialmente quando há integração de inovações multidisciplinares.
Conclusões: Em conclusão, embora desafios como a padronização e o "biofouling" ainda persistam, o futuro dos nanobiossensores como componente-chave na saúde personalizada e descentralizada é promissor, especialmente quando impulsionado por colaborações interdisciplinares.

Introduction

Innovative diagnostic systems, specially point-of-care (POC) devices, are currently essential components in personalised medicine due to their compactness, affordability, portability, and user-friendliness. POC testing enables biomarker detection near the patient, which is vital for accurate and timely disease diagnosis, monitoring, and management. These systems facilitate early detection and support rapid clinical decisions and interventions, improving patient outcomes.[1]

Biosensing has developed into a highly adaptable technology, specially over the past few decades, evolving alongside advancements in environmental monitoring and biomedical diagnostics. Modern biosensors offer several advantages over traditional biosensors used in many POC devices, including miniaturisation, real-time analyte detection, portability, and suitability for mass production. This makes them suitable for monitoring rapid physiological changes and enabling the early detection of disease.[2]

Biosensors detect specific chemical or biological compounds and convert reactions into electronic signals. This allows for fast and precise assessments essential for modern medical diagnostics. Various materials, such as silver and graphene, have been studied as sensitive elements in these sensors.[3] Continued innovations in biosensing technologies will drive the development of next-generation POC diagnostic tools, creating a new landscape of accessible and personalised healthcare solutions.[1] This review aims to explore recent advances in biosensors for POC diagnostics.

Methodology

This review was conducted to explore and analyse the recent advancements in nanobiosensors for diagnostic applications. The review follows a narrative review methodology, focusing on synthesising scientific findings.

A comprehensive search of peer-reviewed articles was performed using scientific databases such as PubMed, ScienceDirect, and MDPI. The search included publications from 2010 to 2024, with priority given to articles published between 2019 and 2024, to ensure the inclusion of the most recent and relevant studies in the rapidly evolving field of nanobiosensors.

The search yielded a total of 63 papers. Of those 47 were included and 16 excluded based on relevance.

The inclusion criteria were: studies describing the design, optimization, or application of biosensors, articles published in English, studies that demonstrate diagnostic relevance, particularly for infectious diseases, cancer, or genetic biomarkers, review papers and original research articles, studies involving electrochemical, optical, or label-free detection, studies involving nanomaterials in sensor architecture, papers with quantitative performance metrics such as limit of detection (LOD), sensitivity, selectivity, response time, and stability.

The exclusion criteria were articles limited to environmental or food safety applications with no medical relevance, patents, editorials, non-peer-reviewed conference proceedings, outdated studies with no novel contribution to the current understanding, and articles published more than 10 years ago.

Results

1. Biosensors

Professor Leland Charles Clark Jr. developed the first biosensor instrument in 1956.[4] It was initially designed to measure oxygen levels in blood.[5] A biosensor is an analytical device that integrates a biological element with a physicochemical sensor, allowing for the quantitative or semi-quantitative detection of biological phenomena.[4] Usually, biosensors identify biological components such as DNA, RNA, proteins, and pathogenic cells.[5]

1.1. Principles of Operation

The fundamental principle of biosensors is to convert a biophysical or biochemical interaction between a biologically sensitive element (comprising various biological substances) and the target analyte into measurable signals.

A physicochemical reaction occurs when the biologically sensitive element interacts with the analyte. The changes during these physicochemical reactions can be detected and converted into measurable signals, such as electrical, optical, and thermal, and then processed and finally quantified.[4]

A biosensor typically has three major elements:

- A bioreceptor is a natural particle or element capable of recognising and binding to a specific analyte.[5] Normally, a bioreceptor is an antibody, enzyme, DNA/RNA, aptamer, or microorganism.[6,7] When the bioreceptor and analyte interact, they induce physicochemical changes in properties such as pH, temperature, mass, charge, or light emission.[8] The specificity of the bioreceptor ensures that only the targeted analyte generates the signal.[9]
- The transducer is the component that converts the bioreceptor recognition event into a measurable signal.[5,7] The biosensor detects changes in the bioreceptor-analyte interaction and translates them into detectable signals.[10] Transducers may operate through electrochemical, optical, thermal, electronic, or gravitational mechanisms.[7] Depending on the type of sensor, the signals produced by the transducers can be electrical (voltage, current, or impedance) or optical (fluorescence or absorbance). The generated signals are proportional to the amount of analyte.[8]
- The reader device processes and interprets the signals generated by the transducer.[5,7] It comprises an amplifier, a microprocessor, and a display, which enable the conversion of unprocessed data into meaningful information for analysis.[10] This component produces the output measurement, often in the form of a concentration reading or a qualitative indicator of the presence of the analyte.[4]

1.2. Advantages of biosensors

Biosensors offer a highly selective, sensitive, and cost-effective method for detecting target analytes, capable of performing real-time analysis without complex sample preparation. Their portability and ability for in-situ use make them especially valuable POC diagnostics.[9]

Beyond medical applications, biosensors are used in disease monitoring, food safety, environmental assessment, drug discovery, forensics, and biomedical research. Their main function involves converting biological interactions into measurable electrical signals, ensuring accurate detection of tiny molecular changes.[11]

Recent innovations, such as smartphone-integrated nano-biosensors, have further improved POC testing, offering a quick and accessible alternative to traditional methods, which often face speed, complexity, and cost issues.[5] Biosensors also excel in real-time data collection, providing a clear advantage over conventional microbiological methods.[6]

1.3. Major classification of biosensors

Biosensors can be divided into two groups: those based on the bioreceptor and those based on the transducer.[4]
a) Transducer-based classification can be optical, electrochemical, or mechanical biosensors.[8,9]
b) Bioreceptor-based classification includes enzyme-based biosensors, whole-cell-based biosensors, and Nucleic Acid-Based Biosensors. [10,11]

1.3.1. Classification based on the bioreceptors

Based on biorecognition, this classification principle can differentiate between biosensors that rely on catalysis and those based on non-catalytic reactions.

In biosensors based on catalytic reactions, the analyte (in this case, an enzyme, microorganism, or whole cell is used as a bioreceptor)[4] must produce a new biochemical reaction product through its interaction with other substances under study.

In biosensors based on non-catalytic reactions, the receptor is irreversibly linked to the analyte under investigation, and no new biochemical product is generated to measure it. In this type of biosensor, the analyte can be an antibody, cell receptor, DNA, or RNA.[8]

- Enzyme-Based Biosensors: These biocatalytic enzyme biosensors utilise enzymes to accelerate specific chemical reactions. This technology enhances discrimination among analytes and increases the sensitivity of detection. It also relies on an interaction between the enzymes and their targets to achieve precise combined actions.[7] Due to their remarkable catalytic efficiency, enzymes have become central to biosensors, yielding impressive results across various fields. For instance, this type of sensor has been employed in molecular science, life science, drug discovery, clinical diagnosis, and fundamental research into medical and biological aspects of life.[12]

- Whole-Cell-Based Biosensors: Living cells function as versatile biosensors, serving as the primary component for sensing, transducing, detecting, and quantifying specific analytes. Cellular processes can transform chemical or physical information into measurable signals. The operation of whole-cell biosensors depends on the metabolic regulation of living cells, which maintain stable recognition and transduction signals, allowing them to stay in balance even under challenging external conditions. Their main advantages include simplicity, cost-efficiency, and adaptable production. Because the sensing elements are cells capable of replication, this reduces the need for external resources. External signal amplification systems are unnecessary because cells have innate mechanisms to replicate DNA and divide themselves.[13]

Most biosensor platforms typically need extraction and purification, which can be expensive and slow. Conversely, whole-cell biosensors with living cells skip these steps because the recognition elements- such as antibodies, enzymes, or reporter proteins- are produced inside the cell. Common organisms used include bacteria, fungi, algae, protozoa, and viruses. These self-sustaining species grow quickly, are easy to cultivate, and suit large-scale industrial use as well as small lab tests. Whole-cell biosensors can identify a wide range of analytes such as organic compounds, heavy metals, and biological molecules. They facilitate the creation of flexible, highly sensitive tests by utilising endogenous metabolic pathways or genetic circuits to amplify responses. These biosensors have been successfully applied across various fields, with potential uses in detecting pollutants, identifying microbial contaminants, and assessing drug toxicity.[8]

- Nucleic Acid-Based Biosensors: Small alterations in nucleic acid sequences, such as single-nucleotide polymorphisms (SNPs), can dramatically influence biological and clinical outcomes, affecting an individual's susceptibility to disease and their response to therapies.[14]

Due to these alterations, nucleic acids are the most studied and important biomarkers in biomolecular analysis, since they are involved in gene expression.[15]

As a result, nucleic acid-based biosensors have become ideal tools, especially when accompanied by a low occurrence genetic mutation.[16]

Nucleic acid biosensors, or genosensors, combine a nucleic acid molecule used as biorecognition element and a transducer that translates the recognition of the molecular event into an output signal.[17]

Nevertheless, the applications of nucleic acid-based biosensors are relatively restricted in practice because nucleic acids are sensitive to environmental factors such as temperature and pH and can be easily cleaved by nucleases or restriction enzymes.[18]

Due to their high thermal resistance and low immunogenicity, aptamer-based biosensors have emerged as a leading technology in nucleic acid-based cellular engineering techniques for disease detection.[18]

- Aptamers, which are short, single-stranded synthetic nucleic acid sequences (primarily DNA or RNA, and occasionally peptides), have been selected to bind with high affinity and specificity to a diverse array of target molecules, from small metabolites, proteins and nucleic acids, to whole cells.[19] [20.] [21] Aptamers bind to targets through electrostatic interactions, hydrophobic forces, or complementary 3D structures.[18]

High sensitivity, specificity, and versatile aptasensors are of particular value for biomedical research and key importance for environmental monitoring, food safety, and agricultural work.[21]

1.3.2. Classification based on Transducers

These biosensors are classified into electrochemical, optical, and mechanical types based on the transducers they employ. [4,8]

- Optical Biosensors: Optical biosensors detect and measure specific analytes by interacting light with matter. These interactions can lead to absorption, fluorescence, refractive index changes, and reflection.[4] The biorecognition element must be connected to a suitable optical transduction system to convert the biological response into an optical signal.

While this occurs, rapid and intense changes in the properties of electromagnetic radiation take place, such as intensity, wavelength, phase, amplitude, frequency, and polarisation. These changes often provide a direct measure of the analyte's concentration.[8]

The main benefit of these biosensors is their ability to detect reactions in real-time and quantitatively without the need for analyte labelling. They are also highly sensitive and specific. These devices incorporate different biological recognition elements- such as enzymes, antibodies, aptamers, tissue, and even whole cells- to achieve specific interactions with target molecules.

Optical fibers are frequently used as transduction elements. Detection methods include colourimetry, absorption, fluorescence, or luminescence, depending on the selected detection strategy application.[5]

Optical biosensors have a lower noise-to-signal ratio, strong resistance to external disturbances, and greater flexibility in conducting multiplexed, non-invasive measurements compared to electrochemical biosensors.[4] Their fast detection speeds, low cost, and ease of use in on-site testing make them ideally suitable for clinical diagnostics, environmental monitoring, food safety and biological applications research.[5]

Besides their efficiency in detecting large bacterial cultures, optical biosensors are also crucial in identifying chemical and biological contaminants. Their simplified operation system, quick reaction times, and strong analytical capabilities make them among the most important tools in modern bioanalytic systems.[6]

- Electrochemical Biosensors: Electrochemical biosensors serve as the basis for various other types of biosensors. They have been employed for the longest periods, have the widest range of applications, and have achieved the greatest success in research endeavours. Their operating principle is based on converting biochemical phenomena into measurable electrical signals, which can be utilised to detect a wide range of analytes.[4]

Organic recognition components, such as antibodies or enzymes, are typically attached to electrodes using biochemical modification techniques. When these elements bind with a specific target molecule in a suspension, they trigger a biochemical reaction, which is then converted into an electrical signal through the electrode.[4]

The formation of a signal in electrochemical biosensors is usually based on redox reactions during a specific reaction between the analyte and the biorecognition element.[5]

The signal can be measured as voltage, impedance, or capacitance, depending on the transduction type.[9] Potentiometry, amperometry, and conductometry are the most used techniques for reading these signals.[5]

Due to their low cost, high sensitivity, portability, and ease of miniaturisation, electrochemical biosensors offer advantages over other methods in clinical diagnostics, food quality control, and environmental monitoring.[6]

Moreover, their ability to detect analytes quickly and directly, relying on the direct electrochemical response at the contact point between analyte and sensor, has made them essential tools in POC applications and decentralised settings.[8]

The remarkable achievements in nanotechnology have enabled the creation of new electrochemical biosensors utilising various nanomaterials, including carbon-based materials, metallic nanoparticles, and quantum dots.

These nanomaterials increase the sensor's surface area and improve electron transfer efficiency and biocompatibility. Consequently, these modifications result in a device with higher sensitivity, lower detection limits, and greater operational stability.[10]

- Mechanical Biosensors: Inside the human body, there are a multitude of mechanical stimuli, such as pressure, pulse, strain, etc.[22] The measurement of these mechanical stimuli enables a broad range of important applications, including, precise monitoring of vital signs such as pulse rate, blood pressure and body motion, which are essential for real-time health assessment and early disease detection.

Mechanical sensors are typically categorised into four groups based on the specific mechanical stimuli they detect. These four groups are pressure sensors, strain sensors (or gauges), shear sensors, and vibration sensors. Although these sensors detect different forms of mechanical stimuli, their operation normally involves the same two steps.[23]

First, the mechanical stimulus induces a deformation in the sensor's structure. Then, those changes lead to a measurable variation in the sensor's electrical properties such as capacitance, resistance and output voltage.[22,23]

These two core operation principles govern the primary performance parameters of the mechanical sensors, including sensitivity, dynamic range, selectivity toward specific deformation modes, response time, signal linearity, and hysteresis.[23]

Mechanical biosensors generally leverage characteristics that scale favorably as device dimensions are reduced. The ability to be displaced or deformed greatly increases with the reduction of its dimension; this is called the mechanical compliance of a device. Enhanced force responsivity at the microscale opens new possibilities for detecting the subtle forces involved in biological interactions.

Furthermore, miniature fluidic mechanical devices achieve rapid response times, allowing the observation of biological processes in fluids in very short periods.[24]

2. Nanoparticle-based Biosensors

Recent advances in nanoscience and nanotechnology have resulted in a new generation of bioreceptors based on nanomaterials (NMs).[7]

These nanomaterials function as bioreceptors and transducers, enhancing the sensitivity, specificity, and overall performance of biosensing platforms.[25]

Nanomaterials such as graphene, carbon nanotubes (CNTs), noble metal nanoparticles (NPs), and quantum dots (QDs) have demonstrated superior transduction capabilities, enabling highly efficient signal generation and detection mechanisms. They exhibit excellent signal transduction ability and hold the promise of high-performance signal generation and detection mechanism.[7]

Nanosensors sometimes cannot detect events at the nanoscale level. They often require bulk instruments to be integrated into a complete sensing system. However, progress has been made in this area when electrodes could be manufactured into smaller nanoscale detectors. These devices' quick response capability and very low power requirements enable on-site monitoring, and contamination can be detected rapidly.[26]

The sensitivity, response speed, and overall performance of nanobiosensors have significantly improved through nanostructures such as nanorods, nanotubes, nanowires, thin films, and nanoparticles. They are well-suited for on-site applications because they perform efficiently with minimal energy to achieve rapid detection responses.[27]

3. Nanoparticles

3.1. Quantum Dots (QDs)

Quantum Dots(QD) are nanoparticle crystals that exhibit both conductive and insulative behaviours. They are distinguished by their unique electronic and optical properties, which depend on their size. When exposed to UV radiation, they emit visible light, with the wavelength of this emitted light inversely related to the size of the quantum dot.

QD of smaller dimensional sizes exhibited larger band gaps. Consequently, QD will emit increasingly higher energy due to the quantum confinement effect. That accounts for the inverse relationship.[26]

QD are smaller than ten nanometres in diameter. Recent advances in biosensing technologies have increased interest in nanocrystals due to their excellent optical properties-high photostability, tunable emission spectra, and narrow emission bandwidths. They are well-suited for enhancing the performance of biosensors.

QD also demonstrate effective charge carrier transport, aiding signal amplification in sensing platforms.[28] This characteristic allows QD to operate with a variety of biomolecules, including proteins and oligonucleotides.

QD used in biosensors hold great promise for numerous biomedical fields, such as tumor diagnosis, gene therapy, and biomarker detection for viral diagnosis. QD can be utilised in advanced diagnostics because of their rapid, sensitive, and specific detection of pathogenic viruses.[27]

3.2 Carbon-Based Nanomaterials

3.2.1 Graphene

Graphene is regarded as an ideal material for sensor applications. Due to its exceptional electrical conductivity, low charge carrier resistance, and high surface-to-volume ratio, it has propelled progress in nanotechnology.

Graphene is made up of a single sheet of carbon atoms organised in a hexagonal pattern. This structure allows for an extremely quick and highly responsive reaction to external stimuli.[28]

Graphene is typically synthesised by mechanically exfoliating graphite. Its flexibility in terms of sheet size, oxidation level, and structure makes it suitable for a wide range of biosensing applications.[26]

Graphene-based nanocomposites are gaining interest as future sensor materials. Graphene is particularly ideal for this purpose due to its high specific surface area, excellent mechanical elasticity, and distinctive optical and magnetic properties.

Its electrochemical characteristics and the ability to modify its functional properties have facilitated the development of highly sensitive and specific sensors.[29]

3.2.2. Carbon nanotubes

Due to their distinctive thermal, electrical, chemical, and mechanical characteristics, Carbon Nanotubes (CNT) are now among the main focuses of scientific research.[27]

These elongated tubular nanomaterials, usually 1-2 nm in diameter, behave like metals or semiconductors depending on their diameter and chirality.

The structure of a CNT resembles a rolled-up graphite sheet, and its remarkable cylindrical form results from this. They belong to a class of materials that are highly versatile due to their outstanding physical and chemical stability, superior mechanical strength, low surface fouling, low overpotential, high thermal conductivity, notable electrocatalytic activity, and high aspect ratio (surface-to-volume).[30]

Consequently, CNT appear in their original form but also act as components in composite materials for many practical applications.[31]

In biology, CNT are widely used as one-dimensional nanomaterials in biosensors, diagnostics, and tissue engineering.

Biosensors using CNT have proven especially valuable, for instance, in enabling highly sensitive electrochemical detection of analytes in healthcare, environmental monitoring, industry, and food quality.

They can be used to monitor glucose levels or to identify biomolecules such as fructose, galactose, cancer biomarkers, cells, microorganisms and DNA.[8]

3.3. Silica nanoparticles

Silica nanoparticles (SiNP) have emerged as highly versatile nanomaterials with significant potential for biomedical and bioanalytical applications. Their distinct physical and chemical properties, including a large specific surface area, controllable pore and particle sizes, and surface silanol groups (Si–OH) that are easily functionalised, enable the attachment of various bioactive substances.[27]

As inorganic materials, SiNP exhibit exceptional stability under harsh thermal, chemical, and biological conditions, including temperature fluctuations, exposure to organic solvents, and acidic environments.[32]

Their colloidal stability, ease of synthesis and production, and scalability further demonstrate their functional versatility. Under specific experimental conditions, SiNP can effectively stabilise and protect various molecular cargos without compromising their functionality.[33]

3.4. Noble metal nanoparticles

Nanoparticles of noble metals (AuNP, AgNP, CuNP, PtNP, and PdNP) exhibit unique electrical and optical properties primarily due to their localized surface plasmon resonance (LSPR) phenomena, which result in broad absorption bands within the visible region of the electromagnetic spectrum. These characteristics can make them ideal for many scientific and technological applications.

These advanced functions pertain to the controlled synthesis of nanomaterials, allowing precise manipulation of their facets, size, and shape. The structural characteristics of noble metal nanoparticles influence their chemical reactivity, stability, and interaction with light.[30,31] These inherent properties render noble metal nanostructures ideal as sensing probes for biomedical and environmental applications.

Due to their optical properties, surface stability, and compatibility with biological molecules, they are attractive candidates for surface implementation and integration into biosensing platforms. These advantages become particularly valuable with the increasing demand for highly sensitive and selective diagnostic applications, as modifying the surface with a wide range of biomolecules is easier.[28]

3.4.1. Silver nanoparticles

Due to their unique antimicrobial qualities and effectiveness against various microorganisms—including bacteria, fungi, and viruses—silver nanoparticles (AgNP)have garnered considerable interest in biomedical research.[26]

They range in size from 1 to 100 nanometres, and their high surface-to-volume ratio enhances their biological interaction properties by altering the chemical, physical, and biological characteristics of the nanoparticles. This property makes them more relevant for biomedical applications. This nanometer-scale enables them to operate and perform functions in medical applications.[16]

Furthermore, owing to their high biocompatibility, excellent surface-enhanced Raman scattering (SERS) performance, electrical conductivity, and ability to amplify electrochemical signals, AgNP have seamless integration with biosensing technology.[8]

The compatibility of AgNP with other nanometal structures, such as gold nanoarrays, supports the development of next-generation biosensors.[27]

3.4.2. Gold nanoparticles

Gold nanoparticles (AuNP) are highly promising for biosensor applications due to their unique optical, electrical, and physical properties.[8]

Their characteristic color varies based on shape, size, and aggregation level, making detection systems highly sensitive when analytes are present.

Moreover, AuNP enable quick direct electron transfer between electrodes and electroactive species, making them an ideal material for developing optical and electrochemical biosensors.[12]

They are also adaptable to various applications. AuNP, with their biocompatibility and non-toxic nature, are widely used in virus detection, drug delivery, diagnostic development, and new therapies.[26,27] The coatings of AuNP are commonly utilised in SEMs (scanning electron microscopes), enhancing electron conductivity and improving image quality.[30]

AuNP are a type of noble metal that stand out in biomedical research due to their straightforward synthesis methods, chemical stability, excellent catalytic activity, and diverse possibilities for forming nanocomposites. As agents, they are essential in emerging fields such as biosensors or medical treatments.

4. FET-based Biosensors

FET-based biosensors are important in life sciences since they provide direct, real-time, and highly sensitive identification of specific biomolecules without requiring any labels.[34]

Field-effect transistor (FET)-based biosensors, or bioFET as commonly referred to, are a novel subclass of electrical biosensors distinguished by their mechanisms of action, offering several advantages over conventional systems. They are widely applied in electronic biosensing and show much lower detection limits than impedance-based electrochemical biosensors.[35] Their sensitivity, responsiveness, ability to be scaled down in size, and capability to be used without labels make them suitable for next-generation medical diagnostic devices, especially for POC testing[36] They are used in the selective detection of biological molecules. A sensor includes multiple components: a source electrode, a drain electrode, a gate, a semiconductor channel, and a dielectric insulator.[37]

Discussion

The rising demand for quick, cost-effective, and reliable diagnostic solutions at or near the point of care is transforming modern healthcare. POC diagnostics have the potential to significantly improve clinical outcomes by enabling real-time, immediate decision-making. Biosensors are gaining attention in this context due to their high sensitivity, rapid response, and compact, integrated design. Overall, the studies reviewed demonstrate how biosensors are advancing various clinical fields, including oncology, infectious disease management, and pandemic response.

Biosensor platforms are used to detect disease biomarkers at extremely low concentrations for cancer diagnostics. For instance, a polycrystalline-SiNW-FET biosensor, functionalized with magnetic graphene composites, achieved a detection limit of just 6.7 pg/mL for the bladder cancer biomarker apolipoprotein A-II (APOA2).[38] Similarly, Li et al.[39] developed CMOS-compatible, high-density SiNW-array FETs capable of detecting circulating tumour DNA (ctDNA) with an attomolar level of 10 aM, maintaining high specificity and functionality in human serum.[39] These examples demonstrate the promising role of biosensors in early cancer detection and non-invasive monitoring in point-of-care settings. Identifying pathogens associated with infectious diseases represents the actual value of biosensors. Wei et al.[40] and Ma et al.[41] developed bio-barcode-enhanced SiNW-FET platforms to detect *Mycobacterium tuberculosis* DNA with femtomolar (78.5 fM) LOD using enzymatic signal amplification. The system enabled fast and sensitive detection directly from extracts, highlighting the potential of biosensor detection systems in low-resource settings lacking conventional diagnostic infrastructure.

This feature of biosensors offers a significant advantage over other validated types, as it allows them to operate without preprocessing in complex biological samples. Krivitsky et al[42] demonstrated this benefit using saturating antigen-antibody interactions within the dissociation regime. This enables the rapid detection of biomarkers in raw serum and blood in just 5 seconds under physiological conditions with Debye screening. This capability makes biosensors even more suitable for accurate POC testing because it dramatically reduces the sample preparation and turnaround time typically required by conventional POC equipment.

The COVID-19 pandemic underscored the urgent need for fast, adaptable, and precise diagnostic tools. Recently, a dual-gate oxide semiconductor thin-film transistor (DG-TFT) immunosensor was created to detect SARS-CoV-2 spike proteins at concentrations as low as 2.3 fg/ml.[43] This device exceeded the Nernst limit by utilising capacitive coupling, confirming its potential for signal enhancement with synthetic and cultured viral samples. Building on this, Park et al.[44] developed a virus-receptor-based FET biosensor using ACE2 as the recognition element, enabling SARS-CoV-2 variant-agnostic detection at levels comparable to RT-PCR (~165 copies/mL). To bypass biosafety issues, their platform used synthetic viral particles for optimisation, demonstrating that biosensors offer a versatile platform adaptable to changing diagnostic requirements. In addition, nanomaterial-functionalized FET biosensors have been used for the direct and label-free detection of SARS-CoV-2 from nasopharyngeal swabs without preprocessing[45], and SiNW-FET platforms have been used for high-specificity detection of prostate-specific antigen (PSA) from human serum.[46] These studies also validated biosensors for routine and longitudinal monitoring in addition to acute outbreaks.

Nanomaterial-enhanced biosensors offer a promising approach to managing diabetes. In a study by Sarangi et al. (2023), they developed an optical glucose sensor using ZnO nanostructures. This sensor operates through photoluminescence (PL) quenching caused by hydrogen peroxide (H_2O_2), a byproduct of glucose oxidation by glucose oxidase (GOx). Higher glucose levels generate more H_2O_2, which reduces the PL signal from the ZnO nanorods. The high sensitivity of this method and the clear connection between glucose levels and PL intensity emphasise its potential as an effective, non-enzymatic, nanomaterial-based diagnostic tool for diabetes monitoring.[47]

These biosensors demonstrate impressive performance metrics, but several challenges must be addressed before they can be widely used in clinical environments. Key obstacles include ensuring long-term stability, reproducibility across different batches, and preventing biofouling in complex biological samples.

Developing standardised fabrication procedures, implementing validated calibration methods, and establishing routes for regulatory approval are also essential steps. Despite these challenges, integrating biosensors with advanced technologies such as microfluidics, wireless communication, and machine learning offers new opportunities to tackle these issues.

The ability to detect multiple analytes simultaneously and automate signal processing could lead to future diagnostic platforms that are scalable, easy to operate, and cost-effective for both centralised and decentralised healthcare settings.

Conclusion

Nanobiosensors are advanced point-of-care diagnostic tools that allow for quick, sensitive, and highly specific detection of various biomarkers and pathogens directly at healthcare facilities. Progress in nanoscale materials like graphene, carbon nanotubes, quantum dots, and noble metal nanoparticles has resulted in highly efficient biosensors suitable for clinical diagnostics. These innovations have significantly impacted fields such as oncology and infectious disease monitoring, including pandemic response, with plans to expand their application. Their miniaturisation and integration with microfluidics enable label-free, real-time analysis, which could revolutionise healthcare in decentralised, low-resource settings. While challenges like biofouling, reproducibility, and regulation remain, combining biosensors with machine learning and wireless communication suggests a promising future for healthcare solutions. Ongoing interdisciplinary research is essential for further development and clinical implementation.

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