**Chapter**

# Applications of Cutting-Edge Biosensors in Healthcare and Biomedical Research

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**Abstract**

Biosensors are remarkable devices that convert biological reactions to chemical compounds into measurable signals, allowing for specific detection of target analytes. The classification of biosensors is based on the type of bioreceptor or transducer used. They have diverse applications in environmental monitoring, detection of toxins, pharmaceuticals, prosthetics, biotechnology, and biomedical engineering, with a crucial role in monitoring soil, water, and food quality. In the field of health and biomedicine, biosensors have undergone significant advancements in diagnosis and treatment of diseases by providing highly accurate results. This chapter focuses on the advancements and applications of biosensors in various biotechnological domains.

**Keywords:** biosensor, measurable signal, specific detection, target analyte, bioreceptor, wearable biosensor

## 1. Introduction

A biosensor is a device that converts a biological response to a chemical molecule into signals with optical, thermal, or electrical properties, according to the definition provided by the International Union of Pure and Applied Chemistry (IUPAC). The biological response is achieved by specific biochemical reactions accompanied by isolated enzymes, tissues, immune systems, organelles, or cells. From this perspective, it is possible to characterize a biosensor with three main components: (i) a biological recognition system (bioreceptor) that selectively detects the chemical compound and possesses an appropriate binding site, (ii) a transducer that converts biochemical/physicochemical interactions resulting from specific binding into measurable signals, and (iii) a signal processing system that detects changes in electrical current, mass, temperature, or optics based on their intensity and translates them into information that is interpretable. While biosensors are classified based on the type of bioreceptor, such as DNA, enzyme, glucose, and cholesterol biosensors, a significant classification is also made based on the type of transducer utilized. This type of classification includes electrochemical, acoustic, piezoelectric, thermometric, magnetic biosensors, as well as optical biosensors. In **Figure 1**, the schematic of the fundamental principles of biosensors is given. Biosensors find extensive applications in monitoring the quality of soil–water–food triangle, environmental monitoring, detection of toxins in

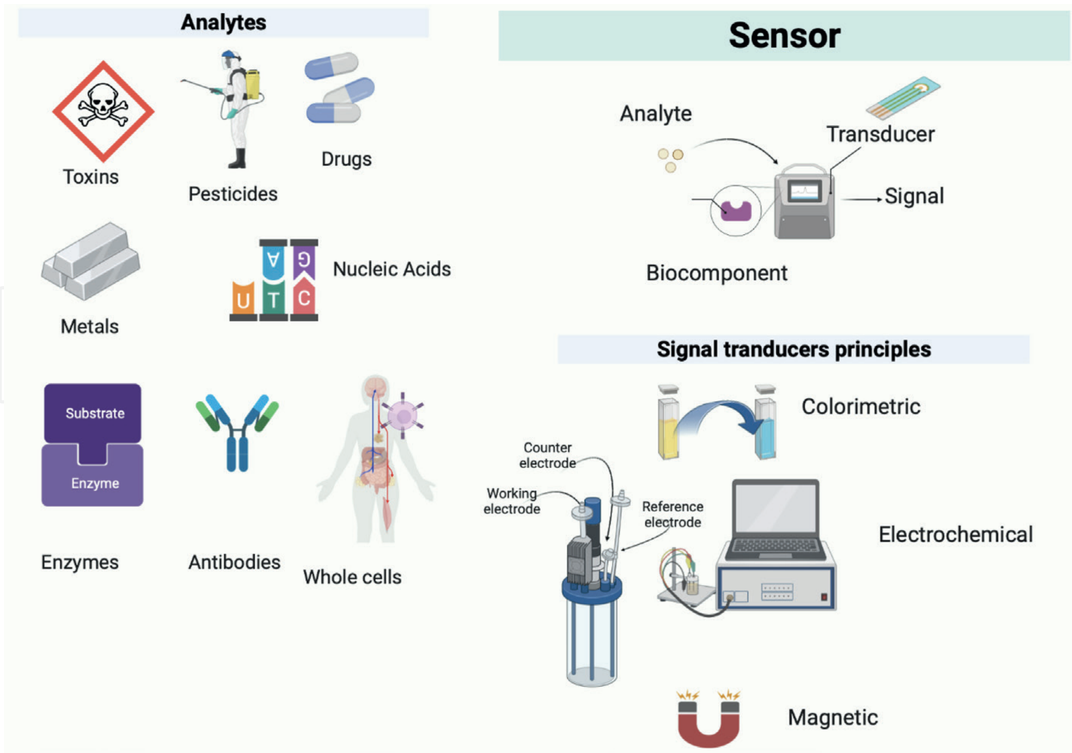


**Figure 1.**
*The schematic of the fundamental principles of biosensor.*

defense, pharmaceutical industry, prosthetic devices, biotechnology, and biomedical engineering. They play a crucial role in diagnosing and treating diseases, as evident from the growing number of articles in the literature. This section of the book focuses on significant advancements in health and biomedicine achieved through the use of biosensors in recent years. It covers the current potential applications, limitations, and future prospects of biosensors in these fields.

## 2. Healthcare applications of biosensors

The main objective in promoting, presenting, and researching healthcare services is to assess the health status, detect the early and advanced stages of diseases, and monitor treatment progress through noninvasive methods. To achieve this goal, three essential conditions must be met: specific biomarkers to differentiate between normal and infected states, noninvasive monitoring approaches for these biomarkers, and techniques to identify and differentiate them. Early-stage detection is vital for patient's survival and favorable prognosis. This criticality necessitates the development of highly sensitive and specialized methods. The three diseases with the highest incidence, impact, prevalence, and mortality rate worldwide are diabetes, cardiac diseases, and cancer. Biosensors are rapidly emerging as crucial research areas, particularly for these three diseases. They provide advantages such as rapid response times, user-friendliness, affordability, and the ability to create simple and disposable devices suitable for mass production [1]. This section presents the latest research findings on the application of biosensors in diagnosing and treating diseases such as parasitic malaria, dementia, Alzheimer's, and infections, in addition to the mentioned diseases.

### 2.1 Biosensor applications for diabetes

Diabetes mellitus (diabetes) is a chronic metabolic illness that harms the body because blood sugar levels are too high. The prevalence of type 2 diabetes, which is more prevalent in adults, has increased globally. On the other hand, type 1 diabetes affects a sizable proportion of the population and is linked to a high risk of mortality. Tragically, the frequency of the condition and the number of persons receiving diabetes diagnoses are both increasing [2]. Affordable medical care, including insulin, is crucial for diabetic individuals' survival. Regular glucose monitoring is essential, but current testing products often cause discomfort and dissatisfaction. The development of a reliable, noninvasive device or technique for the identification and treatment of diabetes is long overdue. Glucose sensors, which detect glucose levels in the subcutaneous fat, are now readily available as compact and minimally invasive devices [3]. Long-term stability, oxygen isolation, miniaturization, user-friendly operation, and biological compatibility are key characteristics of *in vivo* blood glucose sensors. The main requirement has been ensuring long-term biocompatibility, which restricts the usage of *in vivo* glucose sensors to short time periods. Sensor sensitivity is compromised by the migration of low molecular weight compounds across the outer membrane of the polymeric sensor. To address this issue, advances in microdialysis or ultrafiltration technology are employed in conjunction with glucose-detecting biosensors [4].

To monitor their blood glucose levels, diabetes patients rely on glucose test strips. However, existing test strips often suffer from cost and durability limitations. In response, scientists have created an electrical sensor constructed from paper that has been molecularly imprinted with glucose recognition sites. This sensor demonstrates good accuracy in detecting glucose concentrations in solutions derived from bovine blood, as indicated by its calibration graph. By addressing the shortcomings of traditional test strips, this nonenzymatic glucose biosensor has the potential to reduce medical expenses and enhance accessibility in underserved areas [5]. In a separate study, scientists have created a paper chip for glucose detection in saliva using a smartphone. This chip combines luminol-encapsulated metal–organic frameworks and glucose oxidase (GOx) on filter paper, exhibiting a color change from purple to brown in the presence of glucose. Leveraging the image processing capabilities of smartphones, this chip enables fast and accurate quantification of glucose, particularly benefiting individuals with color vision impairments. Its simple design, affordability, and compatibility with mobile devices make it a precise and user-friendly tool for evaluating glucose levels [6]. Another work used a three-dimensional (3D) porous graphene aerogel and glucose oxidase (GOx) to create an enzymatic electrochemical microfluidic biosensor. Excellent selectivity, stability, and a linear detection range of 1 mM to 18 mM ($R^2$: 0.991) were all displayed by the biosensor. This biosensor has a low limit of detection (LOD: 0.87 mM) and successfully monitors glucose levels in serum samples, which has tremendous promise for enhancing prevention of diabetes and clinical diagnosis [7]. For the detection of glucose and saccharides, a self-healing smart hydrogel sensor with boronate ester linkages has been created. The sensor demonstrates strong identification ability and a wide determination range for glucose by leveraging the optical capabilities of a photonic crystal and the regenerative qualities of the hydrogel. The self-healing feature of the sensor increases reliability while reducing the cost of the measurement procedure. The sensor has promise for early diabetes screening despite its weak selectivity for monosaccharides [8]. In 2021, the development of copper(I) halide and copper(II) oxide nanoparticles (CuBr@CuO

NPs) on Cu foils has revolutionized electrocatalytic glucose detection. This electrode has a low overpotential, a wide linear range, and remarkable electrocatalytic activity. Furthermore, a strong link between blood glucose levels has been confirmed by validation trials utilizing salivary samples. Because of this, the noninvasive glucose monitoring system using the NP-based electrode has tremendous potential for use by diabetic patients [9]. Salivary glucose levels in diabetics can be detected noninvasively with a toothbrush containing an amperometric biosensor. In a study by Liu et al., the sensor electrodes, made of carbon graphite and Ag/AgCl inks, demonstrated successful glucose detection within a concentration range of 0.18 mM to 5.22 mM in less than 5 minutes. This discovery holds intriguing possibilities for advancing healthcare and introducing innovative toothbrush sensors [10]. Particularly in the case of diabetes, early disease detection, ongoing monitoring, and rapid diagnosis are essential for individualized care. Visual inspection tests, low-cost analysis, and individualized home testing have all been transformed by portable biosensors made of nano/microscale materials. Salivary trace glucose can now be detected noninvasively using an extremely sensitive minisensor. Thanks to the strong electrocatalytic ability and electron transfer rate of the 3D nanostructured CuO nanoflake array, it exhibits exceptional sensitivity and resolution at low glucose concentrations [11]. This small sensor holds tremendous potential for noninvasive glucose monitoring in saliva for diabetic patients, offering a broad linear range, excellent sensitivity, LOD, and the ability to distinguish between people with diabetes and healthy individuals. Point-of-care (PoC) health services offer diagnostics and vaccinations in a sterile environment. PoC testing improves patient satisfaction and glucose control, benefiting diabetes management. Glucose sensors utilizing chitosan-capped ZnS-doped Mn nanoparticles provide fast and accurate detection. Among the tested materials, chitosan-capped ZnS-doped Mn at 1% weight demonstrates superior sensitivity, selectivity, and stability [12].

### 2.2 Biosensor applications for cardiovascular diseases

Cardiovascular diseases (CVDs), which account for 17.9 million fatalities annually, are the leading cause of death worldwide. Research on cardiovascular disease relies mostly on biosensors that gauge cholesterol levels. Cholesterol oxidase (ChOx) and cholesterol esterase (ChEt) are frequently used in these biosensors as sensor components, allowing for the measurement of both free cholesterol and total cholesterol. An effective method for precisely determining cholesterol levels in the system is electrochemical transducers. MicroRNA-21 (miRNA-21), a biomarker linked to cardiovascular disorders, has been investigated as a potential target for a carbon nanodot-based biosensor. The carbon nanodots (CNDs) that were employed in the biosensor were created using a quick and eco-friendly process. The CNDs had advantageous optical and surface characteristics that made them co-reactant agents in the electrochemiluminescent process of the biosensor. The biosensor immobilized a complementary polynucleotide on a single-use gold electrode to achieve sensitive detection of miRNA-21. The approach was straightforward and did not need any difficult labeling steps, allowing for the immediate detection of miRNA-21 in serum specimens from cardiac patients [13]. Exosomal miRNAs are potential indicators for detecting cardiovascular disease. Using step polymerization catalytic hairpin assembly (SP-CHA), a fresh electrochemical biosensor has been created to find exosomal miR-181. This biosensor triggers the production of increased T-shaped concatemers on the electrode surface by miR-181. The detection limit is low (7.94 fM), while the linear detection range is broad (10 fM to 100 nM). Its successful use in serum samples from healthy people and people with coronary heart disease demonstrates that it is accurate compared to qRT-PCR. This biosensor has excellent potential for the detection of exosomal miRNA in cardiovascular illness due to its long-term stability, sensitivity, usability, and cost-effectiveness [14]. In a recent study, scientists created an aptasensor with a LOD of 0.01 ng/mL that can measure troponin T (TnT) levels and diagnose myocardial infarction at an early stage. By assisting in the prevention of myocardial infarction-related mortality and the decline in the prevalence of patients with cardiac failure, this aptamer-based biosensor has the potential to have a large positive effect on healthcare. The broad use of this biosensor may also save money, speed up diagnoses, and increase the ability to identify TnT for myocardial infarction [15]. In the face of the 2019 coronavirus disease, timely detection and treatment of cardiovascular disease remain imperative for improving survival rates. To meet the growing demand for round-the-clock vital sign monitoring, healthcare providers have turned to wearable devices equipped with vital sign sensors as a vital solution. However, previous technologies faced significant challenges, primarily due to high power consumption. This sensor captures essential vital indicators such as blood sugar, pulse, and oxygen levels, all while consuming minimal power. Its lightweight and compact design allows for seamless integration into flexible wristbands. By monitoring the subtle movements of the radial artery, this sensor provides accurate and continuous noninvasive measurements. The implications of this technology are far-reaching, holding tremendous promise for integrating telehealth into our daily lives and advancing the field of wearable technology [16].

### 2.3 Biosensor applications for cancer

Many low- and middle-income nations lack the resources needed to adequately manage this cost, which prevents numerous cancer patients worldwide from having adequate access to prompt and effective treatment and diagnosis. Cancer testing with biosensors offers helpful and profitable procedures. Compared to microarray or proteome analysis, it is more rapid, simpler to use, more affordable, and less technically complex. Still, additional technological developments are needed for protein-based biosensors. Multiple marker analysis by multi-array sensors would improve the diagnosis of cancer. To detect biomarkers, antibodies are frequently used as molecular recognition molecules. There have been numerous successful biosensor studies for cancer diagnosis, one of which utilized an ultrasensitive DNA electrochemical biosensor. This biosensor employed a carbon paste electrode amplified with ZIF-8 and 1-butyl-3-methylimidazolium methanesulfonate to detect the anticancer drug mitoxantrone in aqueous solutions. By exploiting the interaction between mitoxantrone and guanine bases of ds-DNA, as confirmed through docking research, the biosensor exhibited robust catalytic effects and precise determination capabilities. With a LOD of 3.0 nM, it successfully detected mitoxantrone across a wide concentration range of 8.0 nM to 110 M. Furthermore, the biosensor demonstrated excellent recovery results for detecting mitoxantrone in injectable samples [17]. Pharmacological investigations have brought attention to viscumin, a plant-derived protein with potential applications in cancer treatment. In a recent study, scientists utilized a 9-mer peptide sequence as a template to create a molecularly imprinted polymer. Under the influence of ultraviolet light, the functional monomer formed hydrogen bonds with the epitope, resulting in the polymer's structure. Subsequently, the epitope was extracted from the polymer surface using a solution of acetic acid and sodium dodecyl sulfate (SDS). When evaluated in blood plasma and urine, the nano-biosensor exhibited selectivity [18].

It would be ideal to apply self-powered biosensors to the delivery of pharmaceuticals. In related work, a targeted medication delivery system and a glucose-$O_2$ fuel cell-based biosensor were successfully combined. This resulted in a small, self-sustaining drug delivery model with self-diagnosis and evaluation capabilities. The biosensor also functions as a component of evaluation, tracking the effectiveness of treatment by examining drug-induced apoptosis cells in therapeutic cancer therapy [19]. In a recent work, utilizing methotrexate (MTX) as a model system, an analytical method for detecting an anticancer treatment in whole blood was developed. In order to facilitate redox cycling, the electrode surface of the biosensor used a unique modified carbon nanotube. Due to the cooperative action of the nitrogen-CNT, this composite displayed excellent electrical conductivity and catalytic activity. With low LOD (45 nM), a broad detection range (0.01–540 M), excellent selectivity, and long-term stability for MTX detection, the modified screen-printed electrodes (SPE) with WP/N-CNT demonstrated impressive performance, making it ideal for efficient and mobile MTX detecting, even in blood samples [20].

### 2.4 Biosensor applications for Parkinson's disease

Parkinson's disease (PD) is a degenerative brain condition that causes a variety of nonmotor difficulties, including cognitive decline, mental disorders, sleep disturbances, and sensory disturbances, in addition to motor symptoms like slow activity, shaking hands, strength, and difficulties with balance. Communication, activity, and general well-being of life are all further negatively affected by motor dysfunctions including muscular weakness and spasms. Because of their gradual nature, these signs frequently result in limitations and rising healthcare costs. Biosensors technical advancements open up new diagnostic approaches for PD with the use of a novel platform that enables accurate, reliable, and versatile identification to be achieved with little trouble and discomfort for patients. A rapid and precise miRNA biosensor was developed using the target-triggered three-way junction (3-WJ), terminal deoxynucleotide transferase (TDT)/Nt.BspQI, and activated copper nanoparticles (Cu NPs). The biosensor successfully detected target miRNAs down to a minimal detection limit of 1 fM at 1.75 h [21]. By examining whole blood RNA samples from patients with Parkinson's disease, its applicability was proven. Additionally, a label-free liquid crystal biosensor based on DNA aptamer was created for sensitive alpha-synuclein detection, enabling early Parkinson's disease diagnosis and offering a flexible detection platform [22]. Alpha-synuclein can be detected in serum samples using a surface plasmon resonance (SPR) biosensor that has been created utilizing magnetite nanoparticles ($Fe_3O_4$ NPs) and matched antibodies. The sensitivity of the SPR is greatly improved by depositing $Fe_3O_4$ NPs on the surface of Au at a high density, enabling a detection limit of 5.6 fg $mL^{-1}$, 20.000-fold lower than commercial Enzyme-linked immunosorbent assay (ELISA). A highly sensitive and specific method for the early diagnosis of Parkinson's disease was proven using the SPR sensor, which allowed for the accurate quantification of -syn in diluted serum samples [23]. In another study, Sonuç et al. developed a highly sensitive electrochemical neurobiosensor by utilizing an electrode doped with a nanocomposite of multiwalled carbon nanotubes (MWCNT) and gold nanoparticles (AuNP). This nanostructure-based electrode was employed to detect DJ-1, a protein responsible for mitigating oxidative stress and managing mitochondrial dysfunction in Parkinson's disease.

The neurobiosensor showed a LOD of 0.5 fg $mL^{-1}$ and range of 4.7–4700 fg $mL^{-1}$. With its ability for selective determination, the biosensor shows potential for identifying DJ-1 protein in cerebrospinal fluid (CSF) and saliva [24]. In 2022, Fan et al. developed a minimally invasive biosensor based on a flexible differential microneedle array (FDMA) to accurately monitor the dynamic concentration of levodopa (L-Dopa) in PD patients and lower the risk of consequences. The FDMA biosensor, which has two functional electrodes, has great anti-interference performance when it comes to separating out interfering chemicals from L-Dopa. A viable solution for continuous and less invasive monitoring of L-Dopa levels in PD patients, the biosensor shows a wide linear dynamic range, good sensitivity, and long-term stability [25]. Anthocyanins, pigments known as flavonoid present in fruits and vegetables, were studied for their effects on amyloid fibrils linked to neurodegenerative diseases such as Parkinson's and Alzheimer's diseases. Using total-internal-reflection-fluorescence microscopy (TIRFM), they were able to directly observe how anthocyanins broke down amyloid beta (Abeta) fibrils. The findings showed that the number of hydroxyl groups in the anthocyanin's six-membered ring B determines the disassembly activity of Abeta fibrils, with delphinidin-3-galactoside having the maximum disassembling activity. This study emphasizes the significance of hydroxyl groups and shows how TIRFM-QCM can be used to investigate chemical interactions with amyloid fibrils [26].

### 2.5 Biosensory applications for Alzheimer's

Dementia is a collection of brain disorders causing progressive and severe loss of cerebral disorders, including memory, thinking, behavior, and emotions. It can affect anyone regardless of social class, gender, ethnicity, or location, with a higher prevalence among older individuals.

With the developing R&D studies, researchers developed a surface plasmon resonance imaging (SPRi)-based biosensor to evaluate extracellular vesicles (EVs) in plasma samples from Alzheimer's disease (AD) patients and normal individuals, successfully identifying and identifying EV populations formed by various cell types. The quantity and particular traits of the EV populations were significantly different in AD patients and healthy controls, according to comparisons between their EV profiles [27]. For the development of specific therapy approaches, the noninvasive early detection of AD biomarkers is vital. For this reason, Researchers have successfully developed highly flexible nanopillar-based electrochemical biosensors with a significantly large surface area by depositing gold on a polyurethane substrate. The biosensors were made biocompatible through the utilization of a self-assembled monolayer of thiol chemistry, enabling the effective immobilization of antibodies. Notably, these biosensors exhibited exceptional electrochemical performance, demonstrating consistent and reliable detection of beta-amyloid with a sensitivity of 0.14 ng $mL^{-1}$ and outstanding repeatability. These findings highlight the tremendous potential of the nanopillar-based immunoelectrochemical biosensor as a robust and promising platform for point-of-care diagnostics [28].

### 2.6 Biosensor applications for various diseases

Biosensor development for diagnosing various diseases, including COVID-19, coronary artery disease, diabetes, cancer, dementia, Parkinson's disease, malaria, and infection, is the focus of extensive research (coronary artery disease, diabetes, cancer, dementia, Parkinson's disease have already been discussed earlier in this text).

The urgency for rapid and affordable diagnostics is particularly evident in the case of COVID-19, where identifying asymptomatic individuals and curbing local transmission is crucial. One study proposes the use of cholesteric liquid crystal biosensor platforms as a one-step, wash-free, and rapid detection method for the SARS-CoV-2 virus, considering the limitations of antibody-based serological tests. Cholesteric liquid crystals have the potential to revolutionize healthcare by providing efficient and rapid diagnostic capabilities for various disorders [29]. For the purpose of diagnosing SARS-CoV-2, a quick, inexpensive, and reliable paper-based electrochemical sensor chip has been created. Using gold nanoparticles (AuNPs) coated with certain antisense oligonucleotides (ssDNA), the sensor specifically targets the viral nucleocapsid phosphoprotein. These probes can be read with a handheld device and are immobilized on a paper-based electrochemical substrate. The SARS-CoV-2 RNA may be detected by the biosensor with a LOD of 6.9 copies $mL^{-1}$ without the need for amplification, and findings are available in 5 minutes. Its capability to accurately identify between positive and negative samples with approximately 100% accuracy, sensitivity, and specificity was proven in clinical testing on COVID-19-positive patients and healthy individuals [30]. A highly sensitive biosensor for sensing SARS-CoV-2 has been developed using CRISPR-Cas12a technology. This biosensor utilizes the disaggregation of gold nanoparticles and resulting color changes caused by the degradation of single-stranded DNA triggered by SARS-CoV-2 nucleic acids. The color change can be easily observed by the naked eye or using a smartphone with a Color Picker App. The biosensor demonstrated excellent sensitivity, detecting as low as 1 copy $muL^{-1}$ of SARS-CoV-2 without any interference from other substances. It successfully detected the SARS-CoV-2 gene in synthetic vectors, SARS-CoV pseudoviruses, and RNA without cross-reactivity [31]. For rapid SARS-CoV-2 detection in saliva, a label-free biosensor has been created. It utilizes a brand-new chemical formulation and reusable electrochemical sensor chips. The sensor has a short response time of 5 minutes and gives a quantitative measurement of viral load. With a LOD of 200 pM and 500 pM, respectively, it can find the virus in both phosphate buffer saline and human saliva. A COVID-19 pseudovirus has been successfully found using the sensor in an electrolyte solution. Overall, it demonstrates potential as a practical and reliable approach for identifying and tracking COVID-19 [32]. In a study by Xiao et al., an antibody chip biosensor is introduced as a rapid and automated method for detecting antibiotic residues in milk and pork. The biosensor immobilizes particular antibiotic conjugates on disposable chips using 3D polymer slides. Monoclonal antibodies and a fluorescence-based detection device enable the simultaneous detection of various antibiotics. With detection limits that are below maximum residue limits, the biosensor exhibits great sensitivity. The approach exhibits good precision and accuracy and requires little sample preparation. This biosensor provides an important quality control method for identifying antibiotic residues in food generated from animals [33]. Growing public health concerns include drug trafficking, particularly at ports, airports, and border crossing points. Detecting trace amounts of small drug residues presents a challenge. However, through the innovative use of fluorescently labeled antibodies and a monolithic affinity column, a highly sensitive immunosensor has been developed to address this issue. It takes less than 3 minutes to complete the assay and can detect cocaine at a limit of 23 pM within 90 seconds. The sensor may also detect as little as 300 pg. of cocaine using surface wipe sampling. One of the quickest and most accurate cocaine detectors available is this immunosensor, which provides measurement that is nearly continuous [34].

## 3. Biosensors adapting to developing technology

Biosensors have been essential in improving the early detection, diagnosis, and treatment of many disorders. Fortunately, ongoing research is opening the door for more optimistic advancements in fields including wireless communication, 2D materials, nanotechnology, flexible electronics, and e-textiles. These developments are assisting in the creation of biosensors that keep up with the quick progress in technology. Compared to conventional biosensors, nanobiosensors, which mix nanotechnology and biosensors, offer greater sensitivity. Gold nanoparticles (AuNPs) have demonstrated potential for identifying certain targets inside of cells. However, creating remotely operable gold detection technology is still difficult. A new AuNP-capped cage fluorescence biosensor that uses controlled-release and cyclic enzymatic amplification that is supported by exonuclease III (Exo III) and activated by adenosine triphosphate (ATP) was recently introduced in a study. Through DNA hybridization, AuNPs are used in this system to seal the pores of Au nanocages (AuNCs) that have been loaded with rhodamine B (RhB) molecules. The RhB fluorescent molecules are released in the presence of ATP for detection with the aid of Exo III. The biosensor exhibits an outstanding LOD as low as 0.88 nM and a broad linear detection range for ATP. It also distinguishes itself from analogs because of its remarkable selectivity for ATP. This technique has a huge potential for usage in the biomedical industry as a practical and extremely sensitive biosensor [35].

For implantable biosensors, a novel system of co-encapsulated Pt-porphyrin in biocompatible and biodegradable carriers has been created. Using emulsification-solvent evaporation and air-driven atomization processes, polymeric nanoparticles, and nano–micro hybrid carriers were successfully created. With diameters of about 450 nm and 10 m for polylactic acid (PLA) nanoparticles and PLA-alginate nano–micro particles, respectively, these carriers showed effective encapsulation of Pt-porphyrin. Studies using fluorescent-based biosensing demonstrated a linear response for oxygen concentrations between 0 and 6 mM. These results imply that implanted glucose biosensors for effective management of blood glucose levels in diabetes may be developed using the near-infrared (NIR ) fluorophore-based carrier systems under investigation [36]. Optical nanosensors known as implantable polymer dot (Pdot) glucose transducers allow diabetic patients to monitor their blood sugar levels in real time. Hydrogen peroxide, a consequence of the oxidation of glucose, can, nevertheless, impair sensor function. A novel method for dealing with this problem includes catalase inside the sensor, resulting in an enzyme cascade that quickly breaks down hydrogen peroxide. This increases the sensor's enzymatic activity, biocompatibility, and photostability, resulting in a Pdot-GOx/CAT, a next-generation Pdot glucose transducer with increased sensing capabilities and long-term stability. This development offers hope for better continuous glucose monitoring in the treatment of diabetes [37]. Miniaturized needle electrodes and adaptable materials have been combined to create a flexible biosensing system. The method entails layer-by-layer alteration of electrodes using polyurethane semi-permeable membranes, electrochemically deposited polymers, and enzyme-doped xerogels. These biosensors exhibit sensitivity and selectivity for diseases such as sepsis, galactosemia, xanthinuria, diabetes, and preeclampsia. They can be made smaller to perform well in artificial urine or blood serum and can be wired with electrodes. Platinum nanoparticle coatings are added to improve the detection of signals. This approach has the potential to treat a variety of illnesses, making it an important tool in biosensor technology [38].

### 3.1 Paper-based biosensors

A promising method for efficiently and affordably identifying diseases is provided by paper-based analyzers. Due to their simplicity of use and interpretation, colorimetric paper-based biosensors in particular have promise for point-of-care testing (POCT). These biosensors can deliver improved colorimetric readings by adding nanomaterials thanks to special signal conversion techniques. Studies have examined the development, difficulties, and potential applications of colorimetric paper-based biosensors for pathogen detection. For the study of cortisol in sweat, a unique paper-based microfluidic device has been created. This device produces an immunosensor without the need for reagents by combining filter paper with magnetic beads. Capillary-driven flow is made possible by the microfluidic pattern, which was created using wax printing and laser cutting. Magnetic beads that have been functionalized with a monoclonal antibody enable the precise detection of cortisol. Folding the device allows for the measurement of cortisol levels in the range of 10–140 ng $mL^{-1}$ by observing the competitive interaction between the target cortisol and tagged cortisol with acetylcholinesterase. A wireless connection module is placed with the device, creating a portable cortisol detection instrument. This paper-based device's dependability has been successfully tested on a volunteer while they were riding [39]. On a disposable paper substrate, a brand-new, low-cost sensor module has been created for the instantaneous detection of uric acid. The sensor uses a capacitive measurement technique and hexagonal ZnO rods on Cu interdigitated electrodes (IDEs). Based on capacitance measurements, the uric acid content is shown on an Arduino Mega Board with an LCD screen. With great sensitivity at lower concentrations, the device shows a linear relationship between uric acid concentration (0.1 mM to 1 mM) and capacitance. By providing early screening of uric acid in actual samples, this proof-of-concept demonstrates the potential for clinical applications. A promising development is the creation of this affordable biosensor platform [40].

### 3.2 Wearable biosensors

The primary use of biological information detection technology is the detection of physiological and biochemical data, such as biomarkers, that are strongly associated to abnormalities in human tissues and organs. This technique is essential for the early clinical diagnosis and management of chronic disorders. The Internet of Things (IoT) and Big Data (BD) can be used with wearable biosensors to enable the detection, transmission, storage, and thorough analysis of human physiological and biochemical data. In frontier industries like home healthcare, chronic illness diagnosis and treatment, and personal health monitoring, this technology has incredibly broad applications and promising business prospects. Mobile devices, telemedicine, and wearable biosensors are revolutionizing clinical research. For managing diabetes, modern continuous glucose monitoring (CGM) devices provide precise interstitial glucose measurement. Smartphone apps for health are widely used for self-care and self-monitoring. To assess the effect of a synbiotic medicinal food on glucose regulation, meal-tolerance tests were performed as part of a pilot study. Over the course of 40 days, an average of 3000 data points per patient were obtained using CGM devices and a smartphone app for diet tracking. Participants expressed great satisfaction with the sensors, product, and app, and no negative incidents were noted. The need for larger research in the future is indicated by the considerable alterations in postprandial glucose response that were found in real-world settings, even though statistical significance could not be reached [41]. For noninvasive interstitial fluid (ISF) extraction and real-time glucose testing, a screen-printed iontophoretic biosensing system has been created. The technique supports glucose oxidase (GOx) immobilization by using a three-dimensional graphene aerogel paired with Prussian blue (GA@PB) as an electron mediator, improving detection sensitivity. Reverse iontophoresis-based ISF extraction is shown to be effective by utilizing an *ex vivo* model and a synthetic diffuse cell. The device detects ISF glucose with great sensitivity and accuracy in the range of 0 to 15 mM, with a detection limit of 0.26 mM. The viability of this system, which offers adaptability, biocompatibility, and promise for the development of wireless wearable biosensors for continuous blood glucose monitoring, has been tested on healthy volunteers [42].

Flexible and stretchable biosensors, which can provide smooth and conformable biological-electronic interfaces for continuously gathering high-fidelity signals, are opening up a wide range of new applications. Organic thin film transistors (OTFTs) are the ideal transducers for flexible and stretchable biosensing because of their softness, inherent function of amplification, biocompatibility, simplicity of functionalization, low cost, and diversity of the device. Wearable biosensors provide a noninvasive way to continuously measure biochemical parameters, measure biochemical parameters continually, allowing for the identification of medical hazards and the prediction of physiological status. Few commercial wearable sensors can diagnose health issues through perspiration, despite the fact that they detect physical activities. With its adaptability, affordability, integration, and unobtrusiveness, electronic textile (e-textile) biosensors provide prospects in this area. There are significant challenges in the development of textile-based sensing materials, skin interfaces, and embedded data transmission. For lactate and salt detection during physical activity, a novel wearable electrochemical sweat biosensor using zinc-oxide nanowires (ZnO NWs) has been introduced. The wearable headband that houses this sweat biosensor, which is entirely integrated, accurately, and wirelessly measures human perspiration. On-body measurements during exercise show high testing accuracy and signal stability during movement [43]. Due to its breathability, flexibility, softness, and comfort, textiles present a viable substrate for the integration of wearable chemical sensors. Dry-spinning has been used to create extremely conductive, stretchable, and strain-insensitive gold fibers. These fibers can be used to make lactate-sensing electrodes for a typical three-electrode setup. Textiles can be made from these gold fibers. High sensitivity can be seen in the textile lactate biosensors. Furthermore, the sensors do not require any additional structural design to maintain their sensitivity even under the high tensile strain of up to 100%. These results demonstrate the possibility of noninvasive lactate monitoring offered by wearing smart textiles [44]. Wearable energy storage and flexible body biomolecular detection are two crucial elements for real-time monitoring of human health in a practical situation. It would be fantastic if a single wearable could be used for both energy storage and biomolecular detection. Despite recent major developments in biosensor technology, there are still a number of issues that need to be resolved before they can reach their full potential. One of these difficulties is the protracted manufacturing process for biosensors, which may prevent their general adoption. To enhance the functionality and precision of biosensors, a greater comprehension of molecular biological processes is also required. Problems with biocompatibility are also a major obstacle because it is essential for the long-term use of biosensors that they are compatible with the human body. Finally, preserving the sterility of implantable sensors is still a problem that needs to be solved in order to stop infections and guarantee their dependability. Future biosensing devices will be more effective and trustworthy if these problems are resolved through additional study and technical improvements. Exciting developments in biosensors have been made possible by the quick improvements in artificial intelligence, semiconductor technology, and 3D printing. New chances and possibilities are presented using polymeric nanoparticles in miniaturization processes, such as silicon and fiber optics. Additionally, the combination of cutting-edge 2D materials like graphene [45], borophene [46], and phosphorene [47] with biosensors has the potential to lead to sizable advancements in biotechnology and medicine. Graphene, a single layer of carbon atoms structured in a honeycomb lattice structure, borophene, a single layer of boron atoms in various configurations, and phosphorene, a single layer of phosphorus atoms arranged in a puckered honeycomb lattice, are examples of cutting-edge 2D materials that can be combined with biosensors to produce significant improvements in biotechnology and medical treatment. These outstanding 2D materials are well-suited for boosting the sensitivity and effectiveness of biosensors due to their extraordinary features like high surface-to-volume ratio, exceptional electrical conductivity, and variable band gaps. These developments will transform the way diseases are diagnosed and help save countless lives.

## 4. Conclusion

A bioreceptor, a transducer, and electronic circuitry comprising an amplifier, processor, and display make up a biosensor's three primary parts. The analyte is recognized by the bioreceptor, such as enzymes or antibodies. The transducer transforms the signal from the bioreceptor into a quantifiable form. Biosensors can make use of several energy sources, including light and charge. The electrical signal is exhibited after being amplified. Biosensors are employed in a variety of industries, including biotechnology, healthcare, agriculture, and environmental investigations. Biosensors are becoming more compact, intelligent, and adaptable thanks to technological advancements. They can be used for disease detection, environmental monitoring, food safety, and medication development. Real-time monitoring and individualized healthcare are made possible by the integration of biosensors with artificial intelligence, machine learning, and the Internet of Things. However, the simplicity, affordability, sensitivity, and accuracy of biosensors still need to be improved. It is essential to develop point-of-care diagnostics and prognostics, and biosensors can completely change how medicine is practiced. Due to ongoing research, future biosensors are expected to be increasingly effective and extensively used.

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