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The Application of Electrochemical Nanosensors in Biomedical Detection

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Abstract. Electrochemical nanosensors are at the forefront of biomedical detection, combining the extraordinary properties of nanomaterials with the precision and speed of electrochemical sensing. These innovative sensors open the door to highly sensitive, selective, fast, and affordable miniaturized bioanalysis, holding great promise for improving disease diagnosis, health tracking, and medical research. This review captures the latest progress and emerging directions in electrochemical nanosensors for biomedical use. It offers a structured overview of diverse nanomaterials—including metal nanoparticles, carbon-based structures like graphene and nanotubes, and functional composites—and explains how they boost sensor performance through enhanced interfaces, faster electron transfer, and catalytic effects. The article also explores real-world applications, ranging from the early detection of cancers and heart diseases via biomarkers to continuous health monitoring using wearable technology. Finally, it addresses current obstacles such as signal interference and reproducibility, while pointing toward future advances in AI coupling, new materials, and scalable production.

Keywords: nanomaterials, electrochemical sensors, biomedical detection, early disease diagnosis, health monitoring

1. Introduction

For any healthcare system, prompt and precise diagnosis is a vital pillar supporting effective disease control, progression monitoring, and the alleviation of multifaceted strain on patients and society. Early detection is therefore essential, given that it dictates clinical strategy and is fundamental to achieving superior health results [1]. Driven by this understanding, the medical community now sees that timely intervention in disease progression is fundamentally contingent upon advanced biomedical detection methodologies. Consequently, developing efficient methods for non-invasive, fast, and cost-effective cancer detection represents an urgent priority. The field of biomedical detection—particularly its capacity for early disease identification and diagnostic precision—has thus evolved into a major research frontier.

Electrochemical biosensors have gained significant research interest in cancer biomarker detection, attributed to their rapid analytical response, minimal sample consumption, and exceptional sensitivity. Actionable analyte targets include circulating cells, metabolites, protein antigens, carbohydrate antigens, and nucleic acids. Nanotechnology facilitates the nanoscale

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modification of electrode surfaces, improving sensing performance. Biofunctional nanomaterials offer high surface area and biocompatibility, effectively transporting signaling molecules and transducing signals at electrodes. Common materials like nanowires, nanotubes, nanocubes, and nanooctahedra are used to build various sensors. The convergence of nanotechnology and nanomedicine is gaining increasing attention in biosensing [2].

Therefore, this review primarily focuses on elucidating recent applications of electrochemical nanosensors in addressing challenges within the biomedical detection field. It details the characteristics of nanomaterials, their advantages in electrochemical sensing, their roles in biomedical applications, and future perspectives. It aims to provide a reference for further optimization of electrochemical nanosensors in biomedical detection.

2. Nanomaterial structural properties

The nanoscale dimensions of nanomaterials confer unique properties—including high surface area, electrical conductivity, catalytic activity, chemical stability, and tunable optical properties—that make them particularly effective for electrochemical sensors, enhancing sensitivity, selectivity, and performance [3].

2.1. Metal nanomaterials

Gold nanoparticles serve as highly efficient electrocatalysts for a diverse range of electrochemical reactions. Electrodes modified with these nanoparticles exhibit multiple advantages, including enhanced diffusion of electroactive species, high selectivity, superior catalytic activity, and an improved signal-to-noise ratio (S/N) [4].

These beneficial properties align with the general merits of metallic nanomaterials—such as high density of molecular immobilization sites and excellent conductivity—further enabling effective anchoring of biorecognition elements and facilitating electron transfer.

In this context, Chen and co-workers developed a simple and economical method for fabricating gold-based electrochemical nanosensors, achieving an ultra-low detection limit of 32.5 pM for arsenic ions (As^{3+}) [5].

Another notable nanomaterial is silver nanoparticles, which have also garnered significant attention in the field of biosensing due to their tunable size, narrow size distribution, and exceptional properties such as strong surface-enhanced Raman scattering (SERS) activity and high catalytic efficiency [4]. For example, Sebastian et al. employed a microwave-assisted approach to synthesize Ag nanoparticles, demonstrating their capability in detecting Hg(II) ions with a detection limit as low as 2.1×10^{-6} M [6]. Furthermore, incorporating Ag nanoparticles into various matrices—including metal oxides, silicate networks, polymers, graphene, nanofibers, and dendrimers—has been shown to enhance sensing stability and functionality. A study by Kariuki et al. illustrated this through the development of an electrochemical sensor based on poly(amic) acid-embedded Ag nanoparticles (PAA–Ag NPs) for nitrobenzene detection [7]. The sensor exhibited a wide linear detection range of 10–600 mM, a detection limit of 1.68 mM, and high sensitivity (7.88 mA mM^{-1}), along with excellent selectivity against other nitroaromatic compounds.

In short, gold and silver nanoparticles act as powerful enhancers for electrochemical sensors. Gold enables exceptional sensitivity for detecting traces of toxins like arsenic, while silver's versatility shines when combined with other materials to create robust and selective sensors. Ultimately, these nanomaterials provide the fundamental tools to build more accurate and practical sensing devices for the future.

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2.2. Carbon-based nanomaterials

Carbon-based nanomaterials (CBNs), defined by their nanoscale dimensions and primarily composed of carbon, exhibit a unique combination of advantageous properties such as excellent electrical and thermal conductivity, remarkable chemical stability, tunable optical characteristics, and high mechanical strength [8]. Commonly used CBNs include graphene and its derivatives, carbon nanotubes, carbon dots, nanodiamonds, as well as fullerenes.

The discovery of buckminsterfullerene (C_{60}) in 1985 marked the emergence of the first fullerene, a stable molecular form of carbon even in the gaseous state. Its structure—comprising 20 hexagons and 12 pentagons forming a spherical soccer ball-like shape with 60 vertices—has earned it the widely recognized name "buckyball". Besides C_{60}, other structural variants such as C_{70}, C_{76}, C_{78}, as well as smaller analogues like C_{28} and C_{36}, have also been identified. As a zero-dimensional nanomaterial, C_{60} crystallizes in a face-centered cubic (FCC) lattice with (111) and (200) crystal planes at room temperature, transitioning to a graphite-like structure above 677 °C [9].

Graphene, a single layer of carbon atoms derived from graphite, is another prominent CBN noted for its ultrahigh theoretical specific surface area and exceptional charge carrier mobility. However, its tendency to aggregate through van der Waals and π–π interactions often leads to property degradation. Functionalization is frequently employed to improve dispersion and biocompatibility, yielding derivatives such as graphene oxide (GO), doped graphene, and graphene quantum dots, which are highly relevant for sensor applications [10].

2.3. Other nanomaterials

Although metallic and carbon-based nanomaterials dominate research hotspots in the field of electrochemical biosensors, other functional nanomaterials increasingly demonstrate significant scientific value and clinical potential by virtue of their irreplaceable physicochemical properties and application advantages. For example, semiconductor quantum dots generate size-dependent optoelectronic characteristics through quantum confinement effects, with their broad excitation/narrow emission spectra providing unique signal outputs for multimodal sensing; metal oxide nanomaterials integrate dual functionalities of magnetic separation and electrocatalysis, significantly enhancing detection reliability in complex biological samples; conducting polymer nanoparticles effectively promote electron transfer processes through redox-active sites.

Among these, magnetic Fe_3O_4 nanoparticles—categorized as metal oxide nanomaterials—serve as core magnetic materials for biomedical electrochemical sensors. Their value is reflected in three aspects: the nanoscale structure provides high specific surface area and superparamagnetism, supporting efficient magnetic enrichment of trace targets in complex biological samples; through core-shell structure design, conductivity and catalytic activity are simultaneously enhanced, significantly improving electron transfer efficiency; when serving as enzyme carriers, individual particles achieve substantial signal amplification effects, providing novel strategies for highly sensitive detection.

3. The principles and performance breakthroughs of nanoscale construction in electrochemical sensors

The working principle of electrochemical nanosensors is established upon specific electrochemical transformation processes (such as oxidation and reduction reactions) of target analytes occurring at the working electrode surface. When analyte substances in biological samples diffuse to the

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electrode interface, their electron transfer process generates quantitatively detectable current or potential signals. The intensity of these signals exhibits a distinct correlation with substance concentration, thereby enabling precise analysis of the target.

The field of biosensors was initiated in 1962 with the development of the first-generation glucose oxidase (GOx) biosensor. Remarkably, the GOx sensor remains the most prevalent type today, despite multiple generations of enhancements introduced since the 1960s. A key advantage of such electrochemical biosensors is their low complexity and cost, largely attributable to their compatibility with inexpensive microelectronic manufacturing processes and straightforward integration with standard electronic readout systems [11].

Compared to conventional sensors, the core breakthrough of nanotechnology lies in achieving performance leaps through three synergistic mechanisms: Firstly, interface enhancement utilizes the high-surface-area structures constructed by nanomaterials (e.g., noble metal particles, carbon nanotubes) to significantly increase reaction site density, while enabling directional immobilization of biorecognition probes through surface modifications; Secondly, the electron transfer enhancement mechanism leverages the synergistic acceleration of electron transfer kinetics by combining the local field effects of metallic nanostructures with the delocalized electron properties of carbon-based materials; Finally, the catalytic cascade amplification effect employs nanozymes to mimic natural enzymatic activity for substrate conversion, generating exponentially responsive electrochemical signals. This unique combination of nanoconfinement effects and multifunctional integrated design empowers the sensors with single-molecule-level detection capabilities, providing transformative tools for biomedical diagnostics.

4. Core scenarios for biomedical testing

4.1. Molecular marker detection and early disease diagnosis

Biomarkers represent significant biochemical indicators of physiological states, utilized to predict the onset or progression of diseases. Their detection facilitates forecasting disease development trajectories. Crucially, early biomarkers are essential for early disease diagnosis and serve as vital tools for diagnosis and staging [12].

Cancer stands as a foremost cause of global mortality; 2020 estimates documented approximately 9.9 million deaths and 18.1 million new cases worldwide [13]. Consequently, early cancer detection is critically important, yet conventional diagnostic approaches remain inefficient. This underscores an urgent clinical need for novel detection methodologies. Nanobiosensors serve as non-invasive analytical platforms capable of multiplexed biomarker quantification in complex biological samples. These systems achieve trace-level detection with exceptional specificity and sensitivity, enabling simultaneous monitoring of single or multiple cancer biomarkers. This capability advances early-stage cancer identification and preventative interventions.

Notably, atherosclerosis and its disabling sequelae account for the predominant cause of global mortality. Substantial evidence accumulated in recent decades highlights inflammation's pivotal role in atherogenesis. This inflammatory paradigm closely associates with the clinical relevance of highly sensitive C-reactive protein (hsCRP)—an established cardiovascular biomarker [14,15]. Consequently, hsCRP is indispensable for early diagnosis, cardiovascular risk stratification, and therapy monitoring, thus functioning as a critical indicator of inflammatory processes propelling atheroma progression. Accurately measuring hsCRP level requires detection tools with extreme sensitivity and high efficiency. Clinicians urgently need better tools for efficient hsCRP monitoring. Electrochemical sensors enhanced with nanomaterials now deliver major performance

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improvements through multiple synergistic mechanisms. Noble metal nanoparticles like gold or platinum boost detection signals. They harness plasmonic effects and catalytic properties to amplify readings. Carbon-based materials such as graphene and carbon nanotubes maximize antibody loading capacity. Their ultrahigh surface area also accelerates reactions at optimized interfaces. Magnetic core-shell composites selectively concentrate targets from complex samples. This is achieved through magnetic handling technology. Porous frameworks precisely trap biomarker molecules. Their size-exclusion filters capture specific targets while built-in electroactive groups generate detection signals. Together, these innovations achieve unprecedented sensitivity. They reliably detect hsCRP below the critical cardiovascular risk cutoff. This breakthrough makes clinical testing significantly faster and more precise.

4.2. Disease surveillance and health assessment

Nanosensors are indispensable for continuous health monitoring and personalized medicine, delivering real-time data to enable prompt medical interventions. These devices monitor glucose levels in diabetes management, assess cardiovascular status, and track infectious diseases. Their adaptability provides rapid precision, facilitating responsive and efficient medical solutions [16].

For example, the analysis of molecular abnormalities in biomarkers (e.g., miRNA) within biopsy or resected specimens facilitates tumor burden assessment and perioperative treatment optimization. Conventional methods for such analyses often face limitations in speed and sensitivity. Here, nanomaterial-functionalized electrochemical biosensors integrated with nucleic acid probes demonstrate significant advantages: they selectively capture targets and rapidly convert concentration gradients into measurable reporter signals via electron transfer mechanisms. This approach enables highly efficient biomarker quantification with enhanced sensitivity and accelerated readout times [17].

Recent advances in wearable electrochemical biosensors have opened new avenues for on-body continuous biomarker monitoring, enabling personalized, real-time, and preventative healthcare [18]. For the majority of elderly populations, specific health vulnerabilities necessitate real-time monitoring systems. Wearable devices enable continuous tracking of multiple real-time health parameters, serving as critical tools for acquiring comprehensive health data. Nanosensors integrated into these devices substantially enhance detection sensitivity and specificity, thereby improving the accuracy and reliability of collected data [19]. The integration of nanomaterials has revolutionized wearable health and environmental sensing technologies. Leveraging exceptional surface-to-volume ratios, superior conductivity, and tunable optical properties, these materials enable precise monitoring of physiological parameters (body temperature, heart rate, biomarkers) and environmental factors (air/water quality). Nanomaterial-based sensors offer mechanical compliance through stretchability, breathability, and flexibility, ensuring wearing comfort and seamless daily integration. Coupled with wireless communication and data analytics, this platform delivers personalized health insights, early disease detection, and continuous surveillance capabilities [20].

5. Current challenges and future prospects

Electrochemical biosensors have gained significant popularity due to their versatility (capable of detecting various biological and non-biological substances), exceptional sensitivity, and rapid detection capabilities. Consequently, they are attracting substantial attention in the fields of medicine and clinical diagnostics. However, their practical application still faces multiple challenges: Due to the diversity and complexity of the samples, matrix interference occurs; instability and low

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reproducibility result from batch-to-batch variations in nanomaterials and fluctuations in biomolecular activity; as well as difficulties in scaling up nanomaterial synthesis and sensor manufacturing processes while controlling costs [21].

Despite these hurdles, ongoing research continues to drive innovations aimed at overcoming current limitations. Future development will prioritize three strategic directions: integrated advances in artificial intelligence, machine learning, nanotechnology, and nanoelectronics to enable transformative intelligent nanobiosensors meeting global market demands; development of ultrasensitive sensing materials with enhanced biorecognition capabilities; and advancement of scalable manufacturing technologies to overcome current fabrication barriers [22]. These synergistic efforts will accelerate commercialization while addressing critical performance and production challenges.

6. Conclusion

Electrochemical nanosensors are reshaping the landscape of biomedical detection, offering a powerful and versatile platform that combines high sensitivity, miniaturization, and cost-effectiveness. By harnessing the unique properties of nanomaterials—from noble metals and carbon nanostructures to functional composites—these sensors have dramatically improved our ability to detect diseases early, monitor health in real time, and support personalized medical solutions. Despite exciting progress, challenges such as signal interference, reproducibility, and scalable production remain. Yet, the future looks promising. With ongoing integration of artificial intelligence, advanced materials, and scalable fabrication technologies, electrochemical nanosensors are poised to transition from laboratory innovation to real-world impact. They hold the potential not only to advance diagnostic precision but also to make healthcare more accessible, proactive, and human-centered.

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