

Developments in Nanomaterials Applied to Biosensing

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Abstract

In recent years, the application and development of nanomaterials in the field of biosensors has become a hot topic in scientific research. With their unique physical and chemical properties, such as size effect, surface effect, and quantum effect, nanomaterials provide new research ideas and technical approaches for the development of biosensor technology. This paper systematically overviews the main types of nanomaterials and biosensors, and introduces in detail the preparation methods and key physical properties of various nanomaterials, including plasmonic nanomaterials, carbon-based nanomaterials, metal-organic frameworks, etc. On this basis, this paper focuses on summarizing the latest research progress of nanomaterials in the field of biosensors in recent years, specifically involving four key application directions: disease screening and diagnosis, drug residue detection, material performance optimization, and environmental monitoring. By systematically sorting out and looking forward to the cutting-edge applications of nanomaterials in the field of biosensors, it aims to provide valuable references for researchers in related fields and bring new inspiration to the basic research and application development of nanomaterials in the future.

Keywords

Nanomaterials, biosensing, disease diagnosis, environmental monitoring, research progress.

1. Introduction

Nanomaterials are material systems composed of crystalline or amorphous ultrafine particles at the nanoscale (1-100 nm) as structural units. Such materials have been widely applied in the field of biosensors due to their high detection sensitivity, excellent environmental stability, good biocompatibility, efficient analytical capability, and high specificity [1]. The unique physicochemical properties and biocompatibility of nanomaterials significantly expand the application dimensions of biosensing technologies.

Compared with traditional material systems, nanomaterials exhibit significant advantages in core performance indicators such as precise quantitative analysis of biomarkers, simultaneous multi-target detection, in vivo real-time monitoring, and signal cascade amplification through the synergistic effect of quantum confinement and ultra-high specific surface area. For special application scenarios such as wearable sensing, nanomaterials effectively overcome the inherent shortcomings of traditional materials, which are significantly rigid and insufficiently flexible, providing a key technical pathway for the innovative design of flexible electronic devices. Although nanomaterials surpass traditional systems in functional characteristics, their large-scale manufacturing processes and long-term service stability still need to draw on the industrialisation experience of traditional material systems [2].

This paper systematically reviews the latest research progress and technical challenges of nanomaterials in the field of biosensing and proposes targeted optimisation strategies, aiming

to provide a theoretical basis for the technological development of nanomaterials, with a view to deeply exploring their potential value in biosensing applications.

2. Types of Nanomaterials and Biosensors

Table 1 mainly introduces four types of nanomaterials commonly used in biosensing applications. For each type of material, representative substances are listed, and the core characteristics of the four materials are briefly described along with typical applications. By comparing the four types of materials in the table, the application scenarios and roles of different materials are analysed.

Table 1. Common types of nanomaterials in the field of biosensing

Material category	Representative Substances	Core features	Typical Applications and Effects
Plasma Nanomaterials	Gold nanostructures (such as gold nanoprism AuTNPs), silver nanostructures	Localised surface plasmon resonance (LSPR) effect, optical signal enhancement	Detection of SARS-CoV-2 spike protein, detection limit reduced to 0.01 ng/mL, sensitivity increased 100-fold compared to conventional ELISA [3]
Carbon-based Nanomaterials	Carbon nanotubes (CNTs), graphene, carbon dots (CDs)	Carbon nanotubes exhibit high conductivity and large specific surface area (>500 m ² /g) Carbon dots exhibit low toxicity and tunable fluorescence	Carbon nanotubes can be used in electrochemical sensors with detection limits reaching fM level, and can be employed to construct molecular sieves with separation efficiency 50% higher than traditional chromatography[4]. Carbon dots can be used for biological thiol detection, enabling a 'fluorescence switch' response [5].
Metal-Organic Frameworks (MOFs)	ZIF-8, MIL-100(Fe)	Ultra-high specific surface area (up to 1500 m ² /g), tunable pore size	Encapsulation of functional molecules through biomineralisation, providing both targeted delivery and signal amplification, showing significant effect in in vivo imaging [3].
Functional Mimicking Nanomaterials	Nanozymes (such as Pt NPs), molecularly imprinted polymers (MIPs)	Nanozymes exhibit enzyme-like catalytic activity MIPs possess specific recognition sites ('lock-and-key' mechanism)	Catalytic efficiency of nanozymes exceeds 50 times that of natural enzymes. MIPs maintain high selectivity even in complex samples [6].

Table 2 introduces three common types of biosensing technologies, including sensing detection principles and core technologies, and lists relevant application examples, comparing the application differences among the three biosensing technologies.

Table 2. Common Types of Biosensing Technologies

Technical Category	Detection Principle	Core Technology/Materials	Typical Applications and Effects
Optical Sensing Technology	Detection achieved via changes in plasmon resonance, fluorescence emission or Raman scattering	Surface-enhanced Raman Scattering (SERS), Upconversion Nanoparticles (UCNPs)	SERS applied to '4N-in-1' substrates (including nanopillars, nanocrack networks, etc.) enhances signal by 50 times, can be reused more than 20 times, with single-molecule sensitivity [7]. UCNPs can be applied in near-infrared excitation, enhancing tissue penetration depth and reducing biological background interference [8].
Electrochemical Sensing Technology	Quantification of target analytes through changes in electrical signals (current, impedance) at electrode surfaces	Niobium Carbide MXene (Nb_4C_3), MOF / Carbon Nanotube	Composite Electrodes MXene-modified paper-based electrodes for detecting cardiac troponin I (cTnI), detection limit 0.04 ng/mL, biodegradable, aiding point-of-care testing (POCT) [8]. MOF / Carbon Nanotube composite electrodes (e.g., MIL-100 (Fe)/AuNPs_MWCNTs) applied to lower bisphenol A (BPA) detection limit [7].
Bioaffinity-based Sensing Technology	Relies on specific molecular recognition mechanisms (antibody-antigen, nucleic acid hybridisation, etc.)	Nanobodies (NanoBiT), DNA Nanostructures (tetrahedra, nanoflowers)	Nanobody technology can split luciferase fragments (SmBiT/LgBiT) to reconstruct signals, detecting oesophageal cancer marker FGL1, sensitivity 86.67%, specificity 100% [9]. DNA nanostructures capture molecules through spatially precise arrangement, enhancing exosome detection accuracy [4].

3. Methods and Characteristics of Nanomaterial Preparation

3.1. Nanomaterial Preparation Methods

Table 3 lists three different nanomaterial preparation methods, mainly introducing the preparation principles and common techniques, and analysing the advantages and disadvantages of each method. The third preparation method is not merely a simple material fabrication but involves surface modification of the existing material to enhance the functionality and applicability of the nanomaterials.

Table 3. Common Methods for Preparing Nanomaterials

Synthesis Strategy Category	Core Principles	Typical Methods	Method Features and Applications
Top-Down Approach	Breaking bulk materials into nanostructures through physical or chemical methods	Laser Ablation	Preparation of gold nanoparticles with uniform size (± 2 nm deviation), but at a higher cost.
		HF Etching Method	Synthesis of MXene (e.g., Nb ₄ C ₃), retains layered structure and high conductivity, suitable for flexible electrodes [8].
Bottom-Up Approach	Constructing nanostructures by self-assembly of atoms/molecules	Hydrothermal/Solvothermal Methods	Main technique for synthesising MOFs (e.g., ZIF-8), 48-hour reactions can yield 200 nm crystals, pore size precisely controlled by ligand length [3][7].
		Biomimetic Method	Utilizing protein or DNA templates to guide inorganic material growth.
Surface Functionalisation and Modification	Enhances biocompatibility and selectivity of nanomaterials	Covalent Modification (e.g., carboxylation of CNT surfaces)	Increases hydrophilicity, facilitates antibody immobilisation
		Non-Covalent Modification (e.g., π - π stacking adsorption of nucleic acid probes)	Avoids damaging the conductivity of carbon nanotubes [4].

3.2. Characteristics of Nanomaterials

3.2.1. Small Size Effect (1 - 100 nm)

When the size of a material is reduced to the nanoscale range, its physicochemical properties undergo significant changes. This effect is mainly reflected in the following two aspects: Firstly, nanomaterials have an extremely high specific surface area. Recently, P research team constructed molecular-level folded sheet structures consisting of hydrated silicon-oxygen tetrahedra by improving the classical sol-gel method (Stober). This structure, due to its unique open framework, possesses an exceptionally high specific surface area, greatly increasing the number of surface adsorption sites [10]. Secondly, when the size of a material approaches or falls below certain physical characteristic lengths, such as the electron mean free path or exciton Bohr radius, the periodic boundary conditions of the crystal are disrupted, leading to abrupt changes in the material's acoustic, optical, electrical, magnetic, and thermal properties. Compared with non-nanoscale metals, the melting points of metal nanoparticles are significantly lowered; when the diameter of the metal powder reaches 10 nm, the melting point drops to 940 °C, and further decreases to 5 nm, the melting point will reduce to 830 °C, while the optical absorption coefficient is greatly enhanced and the surface plasmon resonance frequency shifts [11]. These characteristics have important applications in fields such as military stealth technology, microwave-absorbing materials, and optical coatings.

3.2.2. Quantum Size Effect

When the size of nanomaterials approaches or is smaller than the electron de Broglie wavelength, the electronic energy levels near the Fermi level change from continuous states to discrete states. This quantisation effect significantly widens the band gap, leading to a series of unique physical properties, including sensitive absorption of infrared radiation, sharp quantum resonance peaks, and non-linear temperature dependence of specific heat. When copper particles reach the nanoscale, the material loses its conductivity, yet typically, insulating silica particles begin to conduct when their size reaches 20 nm [12]. Ferroelectric materials lose their ferroelectricity and become paraelectric, and some materials that originally lack piezoelectric properties may exhibit piezoelectric effects. These characteristics have important application prospects in fields such as quantum dot light-emitting devices and infrared detectors.

3.2.3. Surface Effects

In nanomaterials, the proportion of surface atoms increases sharply as the size decreases. Surface atoms have a large number of unsaturated coordination sites, and when their proportion increases dramatically, their chemical activity is significantly enhanced. This enhancement effect is reflected in the catalysis of reactions, for example, the catalytic efficiency of nano-gold catalysts for CO oxidation reactions is 10 to 100 times higher than that of traditional catalysts [13]. The material's tendency to self-ignite is also markedly increased, and its ability to adsorb and react with gas molecules is enhanced. These characteristics give nanomaterials enormous potential applications in fields such as catalytic chemistry, energy storage, and gas sensing.

3.2.4. Macroscopic Quantum Tunnelling Effect

This effect refers to the phenomenon where certain macroscopic physical quantities, such as magnetisation intensity and superconducting current, can traverse potential barriers considered insurmountable by classical theory. This effect has significant theoretical and practical value: on one hand, it determines the ultimate information storage density of magnetic storage media; on the other hand, it also sets quantum physical boundaries for the miniaturisation of microelectronic devices. This effect is of crucial importance in research on quantum computing, high-density storage devices, and other fields.

4. Recent Advances in Biosensing

4.1. Disease Screening and Diagnosis

In recent years, biosensing has made significant progress in disease screening and diagnosis, with the development of various highly sensitive detection systems and their effective application in clinical diagnostics. The team from the Chinese Academy of Agricultural Sciences developed the DNA@ZIF-8@Protein NPs system, which uses the principle of rolling circle amplification (RCA) triggered by APE1 enzyme to achieve precise imaging of endogenous apurinic/apyrimidinic endonuclease 1 (APE1), lowering the detection limit to 0.0005 U/mL, thereby directly enhancing sensitivity by several tens of times. To reduce background interference, the research team utilised the pH-responsive properties of MOFs to precisely release probes in tumour tissues [14]. Li developed the FGL1 biosensor, which utilised the structural characteristics of NanoBiT-nanobody to achieve fluorescence enzyme fragment reconstitution, obtaining an AUC of 0.7880 in serum testing of 96 oesophageal cancer patients, with an AUC of 0.8286 for early-stage patients. In combined detection experiments, FGL1 and CEA increased the AUC to 0.8847, which is crucial for early diagnosis of oesophageal cancer [9].

4.2. Drug Residue Detection

The latest developed drug detection sensors have further improved detection sensitivity and accuracy, and have been applied in the detection of actual samples and disease-related

biomarkers. Sedeeq and others developed an optical fibre sensor based on graphene oxide/chitosan (GOCH) composites and surface plasmon resonance (SPR) technology for high-sensitivity detection of amlodipine (AML). By optimising the sensing region and nanocomposite coating, the sensor achieved a sensitivity of 2315.2 nm/ μM and a binding affinity of 60.12 μM^{-1} , with a detection limit of 25 nM, and was successfully applied in actual sample detection [15]. Carbon dot (CDs)- Hg^{2+} ion pair probes quantitatively detect biothiols via a fluorescence recovery mechanism. After Hg^{2+} quenches the fluorescence of carbon dots, biothiols (such as cysteine) dissociate from the complex due to strong affinity with Hg^{2+} , and the fluorescence recovery intensity is proportional to the concentration. This technology provides a convenient detection method for neurodegenerative diseases such as Alzheimer's disease [16].

4.3. Material Performance Optimization

Through structural design and material modification, the new nanosensor significantly improves lifetime, signal enhancement, and dynamic response performance to meet the detection needs in complex scenarios. The nano-gold micro-probe developed by Nanjing Agricultural University directs ethylene oxidation towards ethanol rather than ethylene oxide by controlling the catalytic path on the gold surface, fundamentally avoiding electrode passivation. Notably, this sensor has a lifespan exceeding three months, compared with only a few days for traditional sensors, and its detection limit reaches 0.20 μM . In subsequent detection studies, the team also found that ethylene release from rice rhizosphere depends on light wavelength, with a release of 55 μM under 435 nm blue light, significantly higher than 32.5 μM under red light and 24.0 μM under green light [17]. The University of Kiel developed a '4N-in-1' plasmonic-photocatalytic substrate with structures including nanopillars and nanocrack networks that can decompose pollutants under UV light. In terms of performance enhancement, this substrate can be reused more than 20 times with no signal attenuation. Its Raman signal enhancement reaches 50 times that of traditional substrates, enabling ppt-level detection of trace pollutants in water [18]. Gao successfully fabricated a polyaniline (PANI) boric acid hydrogel sensor via electrochemical deposition, providing super-Nernstian response with a signal intensity of 77.80 mV/pH, a response time of less than 5 seconds, and a tensile strain greater than 200%, fully meeting the requirements for dynamic sweat pH monitoring [19]. These studies all propose improvements and innovations in material structure and perform certain adjustments at the interface.

4.4. Environmental Monitoring

In the field of environmental monitoring, nanomaterial sensors have also achieved high-sensitivity detection of target substances and carried out regularity analysis and mechanism studies. The L team developed an electrochemical sensor based on a MIL-100(Fe)/AuNPs_MWCNTs composite electrode, where they used the iron active centre as a catalyst to catalyse the oxidation of bisphenol A (BPA). Using this reaction, they successfully achieved a detection limit of 20 nM. The sensor also demonstrated relatively strong anti-interference capability, with interference from similar compounds being less than 4%, enabling it to effectively distinguish the target substance from structurally similar substances. Currently, the sensor has been successfully applied to detect the supernatant of human umbilical vein endothelial cells (HUVECs) cultures. The results showed that after the cells were exposed to an environment with 50 μM BPA for 6 hours, the BPA concentration in the supernatant decreased to 30.7 μM , and after 24 hours, it dropped to 15.6 μM . This result reveals the dynamic uptake pattern of pollutants by the cells [7].

5. Improvement Suggestions and Future Applications

5.1. Specificity Enhancement

Currently, the GOCH/POF amlodipine sensors only achieve a short-term RSD of less than 5%, which cannot ensure the reproducibility of detection data. The research team still needs to further validate the sensors, including experiments on long-term storage performance and continuous detection signal attenuation. On the other hand, further experiments can be conducted to verify the sensor's anti-interference capability towards other dihydropyridine drugs. Similarly, to further enhance the selectivity of the bisphenol A sensor, it is recommended to modify the electrode surface with molecular recognition materials such as molecularly imprinted polymers, specific antibodies, or aptamers.

5.2. Mechanism Exploration and Performance Verification

In the experiment, the research team verified the association of FGL1 with oesophageal cancer, but did not further explore the regulatory mechanisms of FGL1 in tumour proliferation, invasion and metastasis, and immune evasion. To understand the underlying mechanisms, gene editing technology can be used to further conduct cell and animal experiments. For the bisphenol A sensor developed by the Lorena team, the study has not yet analysed the uptake dynamics, metabolic pathways, and toxic effects of bisphenol A in different endothelial cell lines (HUVECs/HAECs). Future research could more extensively investigate the mechanisms of action of bisphenol A in supernatants and cell tissues. During the development of an enzyme-activated biosensor by Zhao, the team conducted various verification and exploratory experiments, including verifying the feasibility of RCA amplification in vitro and testing the stability and specificity of the sensor in various environments. However, the research team has not yet validated its imaging stability and detection reliability in other complex actual matrices. Testing the APE1 probe in various human-derived tumour tissue sections or body fluid samples could further expand the application of this sensor in a variety of biological samples.

6. Conclusion

In recent years, research on nanomaterials in the field of biosensing has developed rapidly. Research teams have mainly focused on improving existing material systems or detection methods, altering the structure, composition, and mechanism of action of nanomaterials through various approaches to enhance the detection limits of sensors. At the same time, to meet the specific needs of different application scenarios such as clinical diagnostics, food safety, and environmental monitoring, various new nanodetection platforms have continuously been developed. Looking ahead, with the continuous advancement of nanotechnology and the deep integration of artificial intelligence, nanobiosensing technology is bound to achieve broader applications in fields such as precision medicine, smart wearable devices, and online monitoring of environmental pollutants, making even more outstanding contributions to improving human health and protecting the ecological environment.

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