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โรงเรียนเตรียมวิทย์พัฒนา

โรงเรียนเตรียมอุดมศึกษา

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บทคัดย่อ

ไบโอเซนเซอร์ (Biosensor) เป็นเครื่องมือวิเคราะห์ที่มีความสำคัญอย่างยิ่งในด้านการวินิจฉัยทางการแพทย์ การตรวจสอบสิ่งแวดล้อมและความปลอดภัยทางอาหาร เนื่องจากมีความไวสูงและสามารถตรวจวัดได้อย่างรวดเร็ว อย่างไรก็ตามไบโอเซนเซอร์แบบดั้งเดิมยังมีข้อจำกัดด้านความเสถียร ความสามารถในการทำซ้ำ และระยะเวลาการตรวจวัดที่ยาวนาน การเกิดขึ้นของชีววิทยาสังเคราะห์ (Synthetic Biology) ได้ปฏิวัติการพัฒนาไบโอเซนเซอร์ โดยทำให้สามารถออกแบบวงจรพันธุกรรมและระบบชีวภาพเชิงโปรแกรมได้อย่างแม่นยำ และคาดการณ์ได้ งานทบทวนอย่างเป็นระบบนี้มีวัตถุประสงค์เพื่อสังเคราะห์และประเมินความก้าวหน้าของไบโอเซนเซอร์ที่พัฒนาจากชีววิทยาสังเคราะห์เพื่อเพิ่มประสิทธิภาพการตรวจหาการปนเปื้อนของเชื้อแบคทีเรีย พร้อมเปรียบเทียบกับวิธีการวินิจฉัยแบบดั้งเดิม การสืบค้นข้อมูลครอบคลุมงานวิจัยระหว่างปี ค.ศ. 2010-2024 ตามแนวทาง PRISMA โดยมุ่งเน้นไบโอเซนเซอร์ชนิดเซลล์ทั้งหมด (Whole-cell) ชนิดไร้เซลล์ (Cell-free) ระบบ CRISPR/Cas และระบบที่ผสานวัสดุนาโนผลการทบทวนพบว่า ชีววิทยาสังเคราะห์ช่วยเพิ่มความไว ความจำเพาะ และความเสถียรในการใช้งานของไบโอเซนเซอร์ โดยระบบที่ผสานเทคโนโลยี CRISPR และวัสดุนาโนสามารถตรวจเชื้อได้ในระดับ 10 CFU/mL ภายในเวลาไม่เกิน 60 นาที อย่างไรก็ตามยังมีความท้าทายด้านการกำหนดมาตรฐานการทดสอบภาคสนาม ความปลอดภัยทางชีวภาพ และการบูรณาการกับเทคโนโลยีดิจิทัล เช่น ปัญญาประดิษฐ์ (AI) และอินเทอร์เน็ตในทุกสิ่ง (IoT) โดยสรุปชีววิทยาสังเคราะห์ได้พลิกโฉมเทคโนโลยีไบโอเซนเซอร์ให้ก้าวสู่ยุคใหม่ของระบบการตรวจวินิจฉัยที่รวดเร็ว แม่นยำ และชาญฉลาด ซึ่งสามารถประยุกต์ใช้ได้ทั้งในทางการแพทย์ สิ่งแวดล้อมและความปลอดภัยทางอาหาร

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Synthetic Biology Advances in Biosensors for Effective Bacterial Detection: A Systematic Review

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Abstract

Biosensors have emerged as vital tools in medical diagnostics, environmental monitoring, and food safety due to their high sensitivity and rapid response. However, conventional biosensors remain limited by stability, reproducibility, and slow detection times. The rise of synthetic biology has transformed this field by enabling programmable genetic circuits and modular biological systems that enhance sensor performance and adaptability. This systematic review synthesizes current advancements in synthetic biology-based biosensors for bacterial detection and compares their performance with conventional diagnostic methods. Literature published between 2010 and 2024 was systematically analyzed following PRISMA guidelines, focusing on biosensors integrating whole-cell, cell-free, CRISPR/Cas, and nanomaterial-based designs. Findings reveal that synthetic biology has significantly improved biosensor sensitivity, specificity, and portability, with CRISPR and nanomaterial-integrated platforms achieving detection limits as low as 10 CFU/mL and providing results within 60 minutes. Despite these advances, challenges remain in standardization, large-scale validation, biosafety, and integration with digital technologies such as artificial intelligence (AI) and the Internet of Things (IoT). Overall, synthetic biology has revolutionized bacterial biosensing, offering a foundation for next-generation, rapid, and intelligent diagnostic platforms applicable to clinical, environmental, and food safety contexts.

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Keywords: Synthetic Biology, Biosensors, Bacterial Detection, Nanobiosensors, PCR

Introduction

Biosensors are integrated receptor-transducer devices that convert biological responses into quantifiable electrical signals, providing a powerful platform for rapid, accurate, and real-time biological detection⁽¹⁾. They have become increasingly important across diverse fields, including healthcare, environmental monitoring, food safety, and biotechnology, due to their high sensitivity, specificity, and adaptability⁽²⁾. Among the available biosensing techniques, surface plasmon resonance (SPR) and electrochemical biosensors are particularly noteworthy for their precision and reproducibility, with continuous innovations further enhancing their performance over recent decades⁽³⁾.

Traditional biosensors, such as enzyme-based glucose monitors, have primarily focused on optimizing analytical performance, particularly in terms of stability, sensitivity, and reproducibility. However, recent advancements have shifted attention toward more complex affinity-based biosensors capable of detecting nucleic acids, peptides, and whole microorganisms⁽⁴⁾. These nucleic acid biosensors rely on DNA or RNA hybridization and amplification techniques such as Polymerase Chain Reaction (PCR) or isothermal amplification to identify bacterial genetic materials with high accuracy. Another emerging class of biosensors involves transmembrane and whole-cell systems that interact directly with bacterial membranes or employ genetically modified cells to detect pathogens in real time, including *Escherichia coli*, *Listeria monocytogenes*, *Salmonella* species, and antimicrobial-resistant strains⁽⁵⁾.

Rapid and accurate bacterial detection is essential for addressing persistent global health challenges such as infectious diseases, foodborne illnesses, and environmental contamination. Conventional diagnostic approaches including culture-based assays, microscopy, and biochemical tests are often time-consuming, labor-intensive, and costly, frequently resulting in delayed or incomplete diagnoses that compromise clinical and public health outcomes⁽⁶⁻⁸⁾. In contrast, biosensor technologies offer faster, more accurate, and cost-effective alternatives by providing near-real-time detection of bacterial pathogens, thereby supporting prompt therapeutic decision-making and improving patient care⁽⁹⁾. Nevertheless, most traditional biosensors continue to face inherent limitations in sensitivity, selectivity, and adaptability, particularly when used with complex or unprocessed biological samples.

In recent years, synthetic biology has emerged as a transformative discipline that integrates principles of biology and engineering to design programmable biological systems with defined functions. When applied to biosensor development, synthetic biology enables the creation of genetically engineered circuits, cell-free diagnostic platforms, and CRISPR-based detectors that significantly enhance detection speed, precision, and flexibility⁽⁶⁾. Synthetic biology also allows the modular assembly of biological components such as promoters, riboregulators, and enzymes into predictable sensing networks capable of detecting bacterial signals and generating measurable outputs through fluorescence, colorimetric, or electrochemical responses. When combined with nanotechnology, synthetic biology further expands the detection frontier by incorporating nanomaterials such as gold nanoparticles and graphene, which amplify sensor signals and lower detection limits to levels unattainable with conventional systems⁽¹⁰⁻¹²⁾.

Given these advancements, biosensors powered by synthetic biology represent a new generation of diagnostic platforms capable of overcoming many limitations of traditional bacterial detection methods. However, despite the increasing number of innovative designs, the literature remains fragmented, and comparative performance data are often inconsistent across different biosensor types. A comprehensive evaluation is therefore needed to consolidate current knowledge and identify opportunities for practical translation.

Literature Review

Biosensors have become essential analytical tools in healthcare, environmental monitoring, and food safety because they enable rapid, selective, and sensitive detection of biological analytes. Conventional biosensors combine biological recognition elements such as enzymes, antibodies, or nucleic acids with physicochemical transducers that convert biochemical interactions into measurable signals^(1,3). Although early biosensors, including enzyme-based glucose sensors, achieved significant clinical success, they were limited by factors such as stability, dynamic range, and dependence on laboratory infrastructure⁽¹³⁾. These limitations have accelerated innovation toward more integrated and programmable systems, increasingly driven by synthetic biology⁽⁶⁾.

Synthetic biology introduces a new design paradigm, enabling biological systems to be engineered with predictable and programmable functions. Using modular genetic circuits, whole-cell biosensors such as *Escherichia coli* or *Bacillus subtilis* can detect bacterial metabolites, toxins, or quorum-sensing molecules and generate optical or electrochemical outputs^(4,6). Recent advances in cell-free systems which utilize lyophilized transcription-translation machinery and programmable elements such as toehold switches or CRISPR/Cas modules allow safe, portable, and low-cost detection of bacterial DNA or RNA at the point of care^(6,7). These platforms provide high specificity and stability without the need for living cells, representing a significant advancement in the miniaturization and accessibility of molecular diagnostics.

Parallel advances in nanotechnology have enhanced biosensor performance. Nanomaterials such as gold nanoparticles (AuNPs), graphene, and carbon nanotubes provide high surface area and excellent conductivity, enabling lower detection limits and stronger signal amplification⁽¹⁰⁻¹²⁾. AuNP-based sensors exploit localized surface plasmon resonance (LSPR) for colorimetric bacterial detection within minutes, whereas graphene-based field-effect transistors (GFETs) can achieve femtomolar sensitivity⁽¹⁴⁾. Synthetic biology complements these innovations by incorporating engineered recognition molecules such as aptamers, peptide nucleic acids (PNAs), and nanobodies, which improve selectivity and reproducibility compared with traditional antibodies^(10,15). Despite these advances, fabrication cost, batch variability, and scalability remain key challenges to commercialization^(12,16).

Among the most significant breakthroughs are CRISPR/Cas-integrated biosensors, which utilize programmable nucleases such as Cas12 and Cas13 for sequence-specific bacterial detection. When coupled with isothermal amplification (RPA or LAMP), these platforms can achieve attomolar sensitivity and single-nucleotide resolution without the need for thermocyclers, delivering results within 30-60 minutes^(10,12). Such systems are particularly valuable for detecting multidrug-resistant pathogens and supporting antimicrobial resistance (AMR) surveillance. However, reagent instability, limited multiplexing, and dependence on controlled conditions continue to hinder their large-scale deployment^(10,12).

Emerging research is also exploring wearable and portable biosensors, that integrate synthetic biological components with flexible polymers or graphene substrates to enable continuous, non-invasive monitoring of bacterial toxins or metabolic biomarkers in sweat, saliva, or interstitial fluid^(17,18). These devices can transmit real-time data via wireless interfaces, linking biosensing capabilities with mobile health systems^(17,19). Nonetheless, long-term stability, biosafety, and data calibration remain significant challenges^(16,17).

Overall, current evidence demonstrates that the integration of synthetic biology with nanotechnology has transformed biosensors into programmable and intelligent systems capable of rapid, multiplexed bacterial detection across clinical, environmental, and food safety applications^(1,4,6,10,12). However, critical knowledge gaps persist: (1) the absence of standardized evaluation metrics for sensitivity and response time; (2) limited large-scale validation and slow regulatory approval; (3) insufficient data on long-term stability and biosafety; and (4) minimal empirical integration with artificial intelligence (AI) or Internet of Things (IoT) frameworks^(16,19,20).

While synthetic biology has greatly expanded the capabilities of biosensors, further systematic evaluation is required to consolidate current findings, compare platform performance, and identify viable pathways for clinical and industrial translation of next-generation bacterial detection technologies.

Findings

This systematic review was conducted in accordance with the PRISMA guidelines to evaluate recent applications of synthetic biology in biosensors for bacterial detection. Relevant studies published between January 2010 and March 2024 were identified from PubMed, Web of Science, ScienceDirect, and Google Scholar using the keywords “synthetic biology,” “biosensors,” “bacterial detection,” “PCR,” and “nanobiosensors.” Eligible studies were peer-reviewed, English-language articles that focused on synthetic biology-based biosensors and reported measurable performance data such as detection limit, sensitivity, and specificity. Conference abstracts, reviews, and unrelated studies were excluded. Titles, abstracts, and full texts were screened, and two reviewers independently extracted data on biosensor type, bacterial target, detection mechanism, and reported advantages or limitations. Study quality was assessed for methodological rigor, reproducibility, and data reliability. Extracted information was synthesized narratively and summarized in comparative tables, highlighting biosensor classification, detection mechanisms, performance outcomes, and research gaps between traditional and synthetic biology-driven approaches.

Biosensor

Biosensors are analytical devices that detect biological molecules by integrating of biological recognition elements with physicochemical transducers, which convert biological interactions into measurable signals⁽¹⁾. These sensors have become essential in clinical diagnostics, environmental surveillance, and food safety due to their sensitivity, selectivity,

and rapid response^(1,2). The fundamental architecture of a biosensor includes three primary components: a biological recognition element, a transducer, and a signal processor. The biological recognition element specifically interacts with the target analyte, which may include bacterial antigens, nucleic acids, or metabolites⁽²⁾. Common recognition elements include antibodies for immunosensors, oligonucleotide probes for DNA biosensors, and enzymes for enzyme-based sensors. DNA and RNA probes typically hybridize with complementary bacterial genetic sequences, with binding events converted into detectable outputs via fluorescent, electrochemical, or optical transducers⁽²¹⁾. The transducer then translates this biochemical interaction into a quantifiable electrical or optical signal, while the signal processor interprets and refines the data for diagnostic readout⁽³⁾.

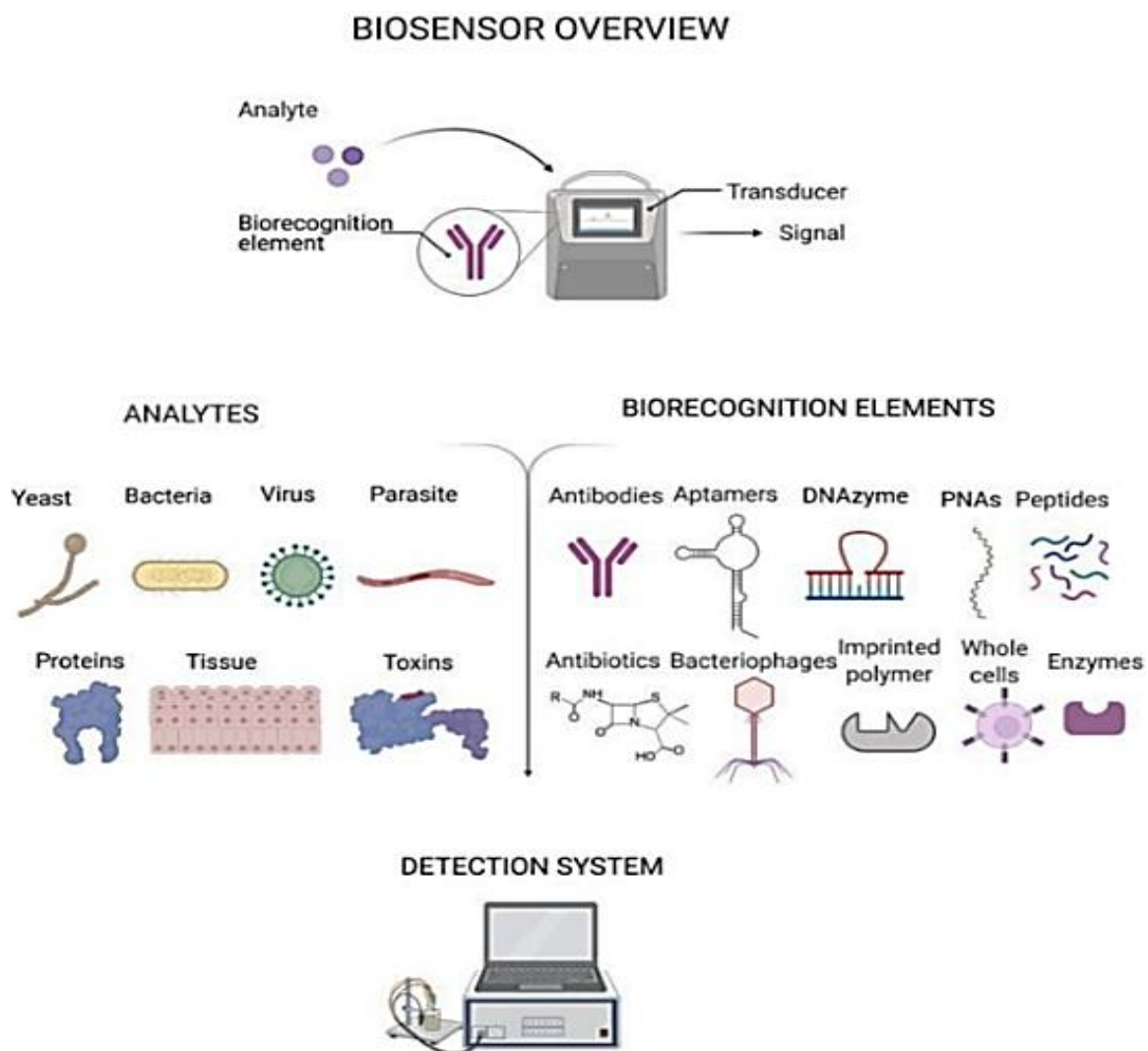


Figure 1 A biosensor has three main components: an analyte, a biorecognition element, and a transducer that generates a detectable signal. The major types of biorecognition elements and analytes used to detect clinical pathogens are included. PNAs are peptide nucleic acids⁽¹⁵⁾.

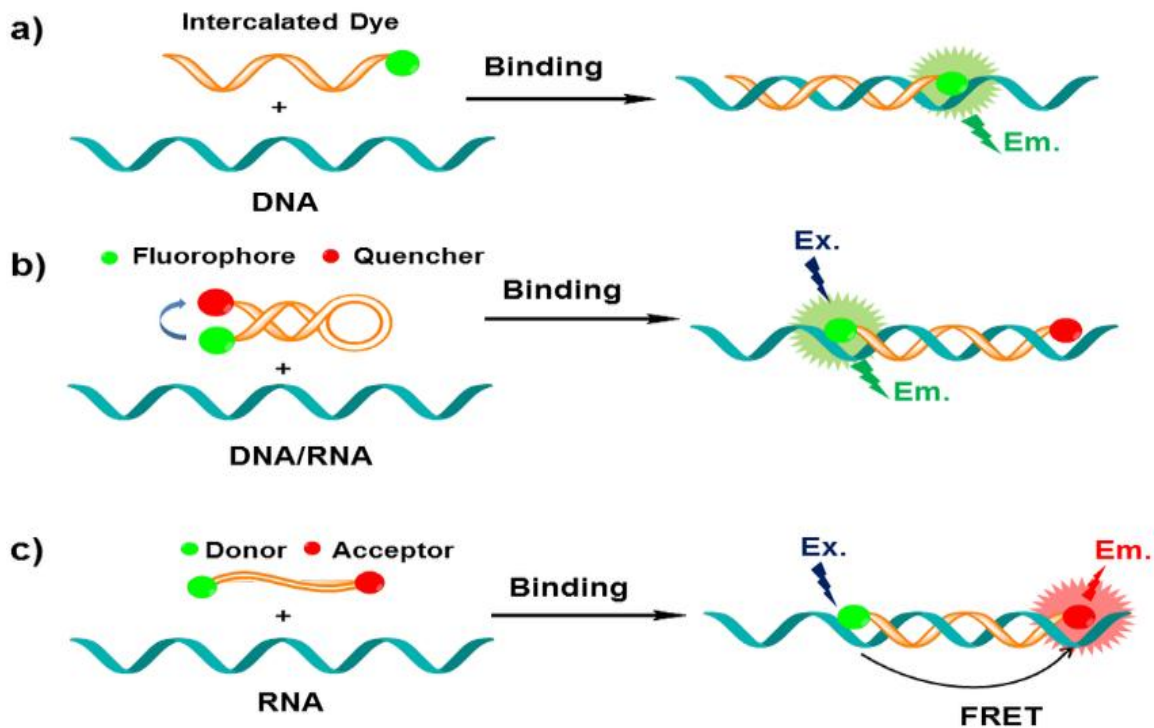


Figure 2 MBs are used to detect DNA/RNA sequences in samples. The probe's dye can integrate between Watson-Crick base pairs or act as a base surrogate. When combined with complementary sequences, the MB's stem-loop hairpin structure opens, increasing fluorescence intensity. When interacting with target RNA, the MB undergoes conformational restructuring⁽²²⁾.

Biosensors can be classified based on their biorecognition mechanism, transduction principle, or operational mode⁽⁴⁾. Immunosensors utilize antibodies for high-affinity detection of bacterial antigens, whereas DNAbiosensors rely on nucleic acid hybridization to identify pathogen-specific genetic markers. Enzyme-based biosensors exploit catalytic reactions to generate measurable signals⁽²¹⁾. In terms of transduction, electrochemical biosensors detect changes in current or potential; optical biosensors utilize fluorescence, absorbance, or resonance; and mass-based sensors, such as piezoelectric devices, detect changes in acoustic waves or mass upon bacterial attachment⁽⁵⁾. Furthermore, whole-cell biosensors employ genetically modified living cells as active components capable of responding to bacterial signals with measurable luminescent or electrochemical outputs, whereas label-free biosensors rely on impedance or resonance changes without the need for labeling reagents⁽⁴⁾.

Table 1 Classification of biosensors for bacterial detection

Classification	Image	Type of biosensors	Description
Biological Recognition Element		Immunosensors	Use antibodies to detect specific bacterial antigens ⁽¹⁾ .
		DNA Biosensors	Use nucleic acid hybridization to detect bacterial genetic sequences ⁽²⁾ .
		Enzyme-Based Sensors	Use enzymes to interact with bacterial substrates, producing detectable signals ⁽²¹⁾ .
Transduction Mechanism		Electrochemical Biosensors	Measure electrical changes such as amperometric or potentiometric signals ⁽¹⁵⁾ .
		Optical Biosensors	Use light-based detection methods. (e.g., fluorescence or label-free sensors) ⁽⁵⁾ .
		Mass-Based Sensors	Measure changes in mass or acoustic waves due to bacterial binding. (e.g., piezoelectric devices) ⁽⁴⁾ .

Table 1 Classification of biosensors for bacterial detection (continued)[illegible]

Although biosensors offer significant advantages in speed, portability, and sensitivity, several limitations persist. These include a narrow dynamic range, potential interference from complex biological matrices, and difficulties in detecting low analyte concentrations, particularly during early stages of infection^(7,8,13). Variability in sample composition, temperature, and pH can further affect biosensor reproducibility^(23,24). Consequently, improving biosensor robustness and standardization remains a central challenge for translating these systems from laboratory prototypes into field-ready diagnostic tools.

Feature biosensor: Nanotechnological

The integration of nanotechnology into biosensor design has revolutionized the field by significantly enhancing sensitivity, selectivity, and miniaturization. Nanobiosensors merge nanomaterials such as gold nanoparticles (AuNPs), graphene, and carbon nanotubes with biological recognition elements, enabling efficient signal amplification and ultra-sensitive detection^(10,11). The nanoscale dimensions of these materials provide an exceptionally high surface-to-volume ratio, increasing the density of binding sites and accelerating reaction kinetics between biological receptors and target analytes⁽²⁵⁾.

Nanoparticle-based biosensors exploit the unique optical, electrical, and catalytic properties of metallic nanoparticles. Gold nanoparticles, in particular, exhibit localized surface plasmon resonance (LSPR), producing distinct optical shifts upon interaction with bacterial targets. This property enables direct visual detection and quantitative analysis through colorimetric or spectrophotometric methods⁽¹⁷⁾. Platinum and silver nanoparticles have also been employed to enhance electron transfer and catalytic activity in electrochemical biosensors, increasing sensitivity and reducing detection time⁽²⁶⁾. Additionally, magnetic nanoparticles functionalized with antibodies or oligonucleotide probes facilitate rapid bacterial isolation from complex biological samples, thereby improving detection specificity⁽²⁷⁾.

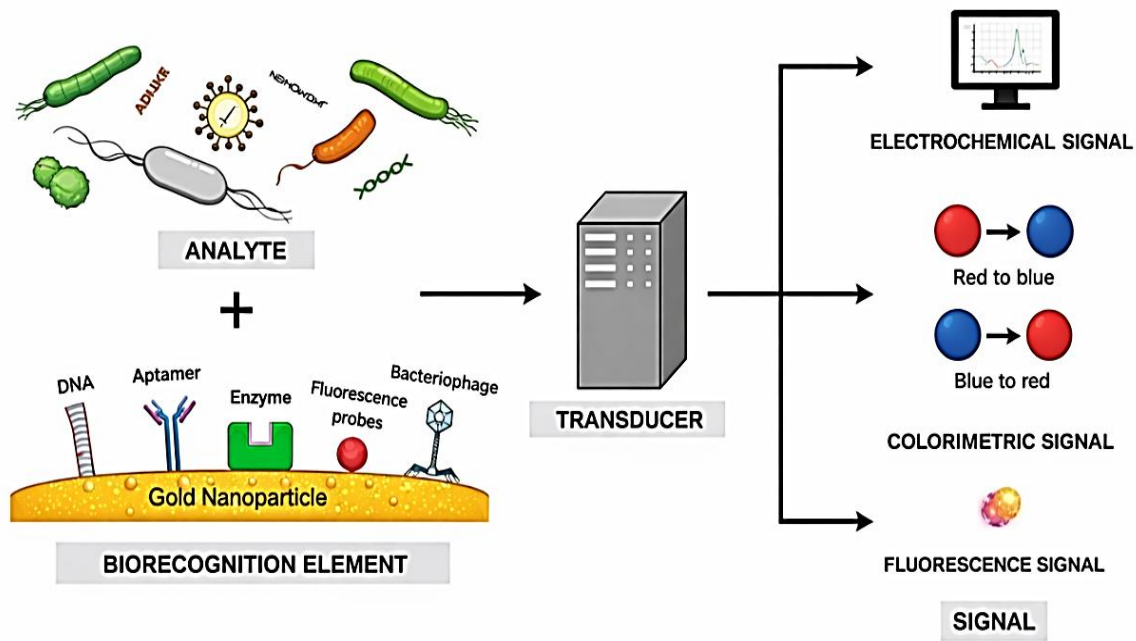


Figure 3 Overview of nanoparticle-based biosensors⁽¹²⁾

Graphene-based biosensors represent another major advancement due to graphene's outstanding electrical conductivity, large surface area, and chemical stability⁽¹⁴⁾. Graphene field-effect transistors (GFETs) can detect minute changes in conductivity upon analyte binding, achieving detection limits in the femtomolar range. Their compatibility with both optical and electrochemical sensing modes further supports multifunctional operation for environmental and biomedical applications^(25,28). However, despite their superior sensitivity, graphene-based biosensors face fabrication challenges and potential toxicity concerns that may hinder large-scale implementation⁽¹⁴⁾.

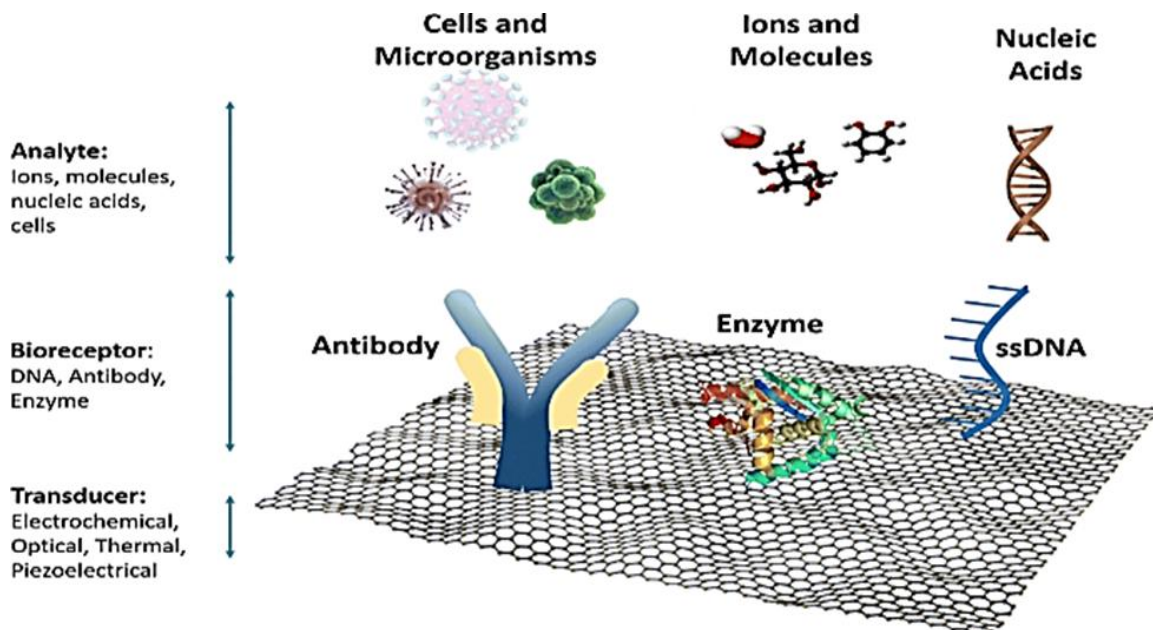


Figure 4 Examples of biosensors and components on a graphene platform⁽¹⁴⁾

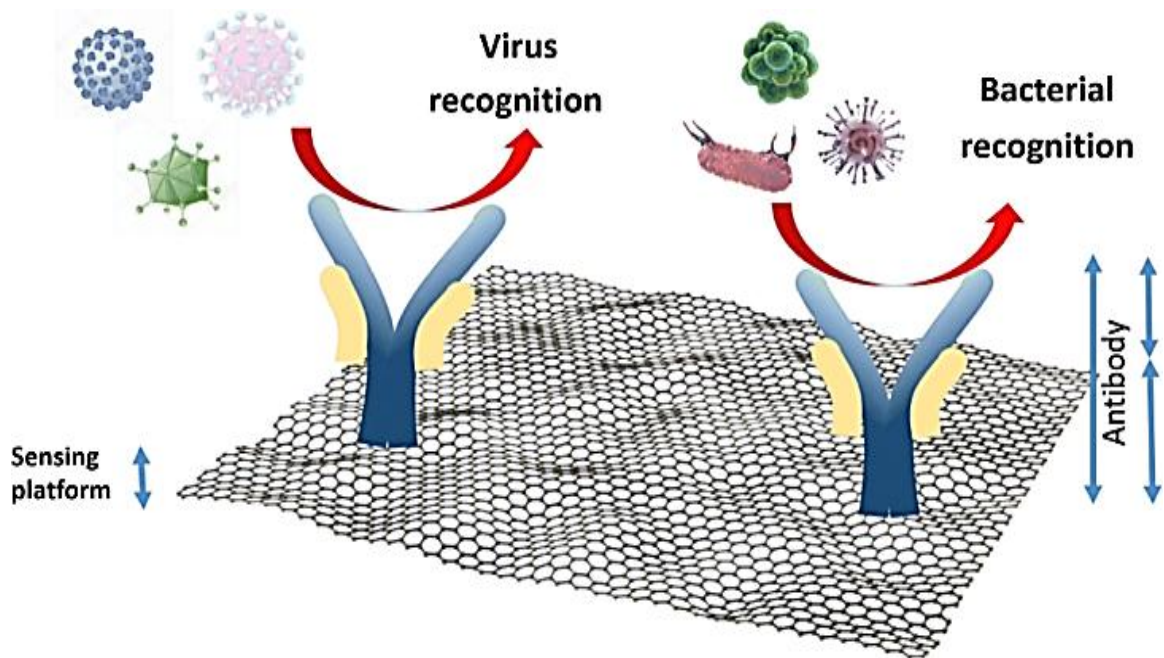


Figure 5 Scheme of graphene modified with antibodies for the recognition of pathogens⁽¹⁴⁾

Wearable nanobiosensors extend biosensing capabilities into continuous, non-invasive health monitoring. Constructed using flexible polymeric or graphene-based substrates, these devices can detect biomarkers such as glucose, lactate, electrolytes, or bacterial toxins in sweat, saliva, or interstitial fluids^(17,18). They utilize electrochemical or optical detection mechanisms integrated with wireless data transmission for real-time analysis⁽¹⁰⁾. While wearable sensors show strong potential for managing chronic diseases and enabling early infection detection, challenges remain regarding battery life, durability, and biosafety, particularly when synthetic or nanobiological components are involved⁽¹⁰⁾.



Figure 6 Example of Non-invasive Epidermal Glucose Sensors⁽¹⁸⁾

Table 2 Comparison of the Three Types of Nanobiosensors

Type of Biosensor	Nanomaterials Used	Detection Mechanism	Applications	Advantages	Limitations
Nanoparticle-Based	Gold nanoparticles, silver nanoparticles, platinum nanoparticles	Optical detection (LSPR), enzymatic enhancement, electrochemical sensing	Cancer diagnostics, glucose monitoring, pathogen detection	High sensitivity, signal amplification, versatile for optical/electrochemical sensing	High cost of nanoparticles, potential aggregation issues
Graphene-based	Graphene, graphene oxide, reduced graphene oxide	Electrical conductivity (GFETs), fluorescence quenching, electrochemical sensing	Early disease detection (e.g., Alzheimer's cardiovascular diseases), environmental pollutant monitoring	High conductivity, low noise, large surface area, versatile detection	Fabrication complexity, potential toxicity concerns
Wearable Biosensors	Flexible polymers, graphene-based composites	Electrochemical sensing, optical sensing	Continuous glucose monitoring, fitness tracking (lactate, hydration), stress monitoring (cortisol)	Real-time monitoring, non-invasive, integration with mobile devices	Limited battery life, durability under long-term use

Overall, nanotechnology has markedly advanced biosensor performance, lowering detection limits to as low as 10 colony-forming units (CFU)/mL for certain pathogens while maintaining rapid response times of under 15 minutes. Nevertheless, challenges related to cost, fabrication reproducibility, and potential environmental risks associated with nanomaterials remain critical areas for further research.

Application

Bacterial detection: detailing

Biosensors have significantly improved the detection and monitoring of bacterial pathogens, providing faster, more reliable, and cost-effective alternatives to conventional microbiological methods such as culturing, microscopy, and biochemical assays⁽⁴⁾. Although traditional laboratory diagnostics remain highly accurate, they often require several hours to days, skilled technicians, and specialized equipment, limiting their suitability for real-time monitoring and rapid decision-making in clinical or environmental contexts⁽²⁹⁾.

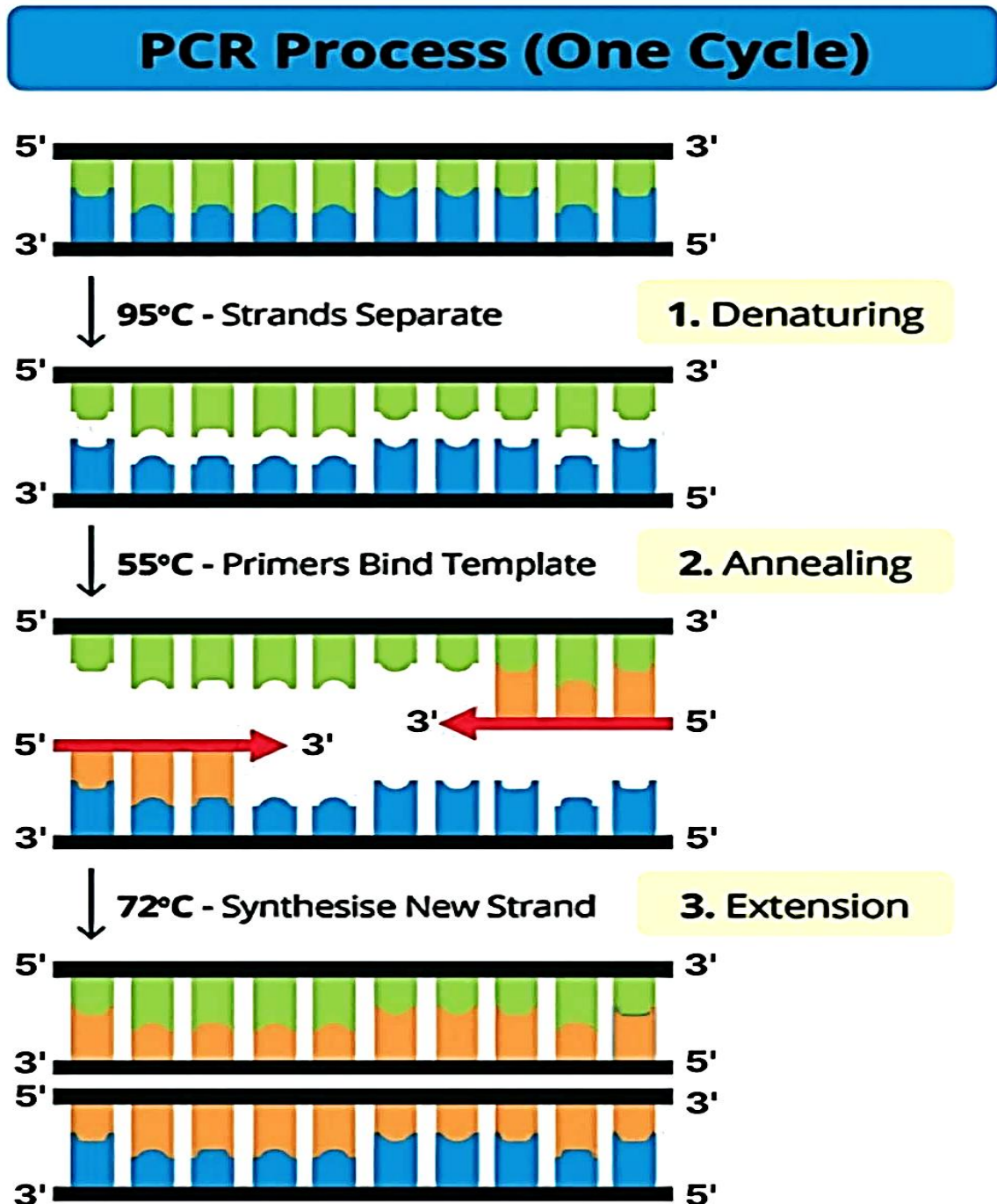


Figure 7 Flowchart of the three main steps of PCR⁽²⁹⁾

Polymerase Chain Reaction (PCR) and its derivatives remain among the most widely used nucleic acid-based detection methods. Biosensors integrated with PCR amplification or isothermal techniques such as loop-mediated isothermal amplification (LAMP) provide rapid, high-sensitivity detection of bacterial DNA without the need for culturing⁽²⁹⁾. For instance, CRISPR-Cas12a and Cas13a biosensors integrated with recombinase polymerase amplification (RPA) have achieved single-molecule-level sensitivity, detecting bacterial pathogens such as *E. coli*, *Salmonella*, and *Mycobacterium tuberculosis* within 30-60 minutes.

Recent advances also demonstrate biosensor applications for specific infectious diseases. Lower respiratory tract infections caused by *Streptococcus pneumoniae* and *Haemophilus influenzae* remain leading causes of morbidity, where biosensor-based diagnostics can facilitate early, targeted antibiotic therapy (Table 3). Similarly, diarrheal diseases caused by *Shigella*, *Campylobacter*, and *E. coli* O157:H7 require rapid detection to prevent outbreaks. For tuberculosis, *Mycobacterium tuberculosis*-specific DNA biosensors and CRISPR-based assays have shown potential to replace conventional staining and culture methods, substantially reducing diagnostic turnaround time.

Table 3 The table below identifies diseases and each method of biosensors.

Disease(s)	Causative bacterial agent(s)	Burden of disease (DALY), millions	Annual death, millions	Annual cases, millions	Conventional methods of diagnosis	Diagnosis time critical?	Spread prevention critical?
Lower respiratory tract infections (e.g., pneumonia) ⁽¹⁾	<i>Streptococcus pneumoniae</i> , <i>Haemophilus influenzae</i>	94.5	4.2	430	Physical examination, chest X-ray, sputum and blood cultures, PCR	No	No
Diarrheal diseases ^(2,3)	<i>Shigella</i> spp., <i>Campylobacter</i> spp., <i>Salmonella</i> spp., <i>Escherichia coli</i> O157:H7	72.8	2.1	4,620	Microbiology (culture on Gram-negative-selective media), PCR, ELISA, particle agglutination assay	Can be	Yes

Table 3 The table below identifies diseases and each method of biosensors. (continued)

Disease(s)	Causative bacterial agent(s)	Burden of disease (DALY), millions	Annual death, millions	Annual cases, millions	Conventional methods of diagnosis	Diagnosis time critical?	Spread prevention critical?
TB ⁽⁴⁾	<i>Mycobacterium tuberculosis</i>	34.2	1.5	7.8	Chest X-ray, blood test, Mantoux TST, sputum smear and culture, staining and microscopy	No	Yes
Meningitis ⁽⁵⁾	<i>Neisseria meningitidis</i> , <i>Streptococcus pneumoniae</i> , <i>Escherichia coli</i>	11.4	0.34	0.7	Lumbar puncture, blood cultures, PCR	Yes	No
Sexually transmitted infections (excluding HIV) ^(6,7)	<i>Treponema pallidum</i> (syphilis), <i>Chlamydia trachomatis</i> (chlamydia), <i>Neisseria gonorrhoeae</i> (gonorrhea)	10.4	0.13	222	Urethral/vaginal swab and culture, Gram staining and microscopy, immunoassay, particle agglutination assay	No	Yes

Beyond clinical applications, biosensors are increasingly employed for environmental and food safety surveillance. Portable biosensors can monitor water and soil contamination by detecting *Vibrio cholerae*, *Salmonella*, or *Listeria* species, while wearable or IoT-linked biosensors facilitate real-time monitoring of bacterial exposure in healthcare and industrial settings.

While biosensors have successfully overcome many limitations of conventional diagnostics, challenges remain in scalability, reproducibility, and regulatory approval. The diversity of materials and detection mechanisms complicates standardization across platforms. Future innovations are likely to focus on AI- and IoT-assisted biosensing, enabling autonomous data analysis, improved accuracy, and cloud-based outbreak surveillance systems. The integration of synthetic biology with nanotechnology and computational analytics thus represents the next phase in achieving rapid, field-deployable, and intelligent bacterial detection systems.

Discussion

This systematic review demonstrates that integrating of synthetic biology with biosensor technologies has greatly advanced bacterial detection by improving analytical performance, design versatility, and real-world applicability. Across the reviewed literature, synthetic biology-enabled biosensors ranging from whole-cell systems to CRISPR- and nanomaterial-based platforms consistently outperform traditional diagnostic methods in sensitivity, specificity, and response time^(6,10,12,19). These innovations reflect a paradigm shift from passive detection toward programmable, intelligent sensing systems capable of real-time monitoring in clinical, environmental, and food safety contexts.

The first major advancement is the programmability and modularity of synthetic biological components. By employing engineered genetic circuits, promoters, and regulatory elements, biosensors can now be tailored to detect specific bacterial metabolites, toxins, or nucleic acid sequences^(6,7). This flexibility allows for multiplexed detection, enabling one biosensor platform to simultaneously identify multiple pathogens. For example, whole-cell biosensors, convert bacterial recognition into luminescent or electrochemical signals, whereas cell-free synthetic systems using lyophilized transcription-translation (TX-TL) machinery eliminate biosafety concerns associated with live organisms. These developments have significantly enhanced portability and safety for point-of-care diagnostics, particularly in low-resource or field settings^(4,6,7).

The second critical trend is the integration of nanotechnology with synthetic biology, which has substantially enhanced biosensor performance. Nanomaterials such as gold nanoparticles (AuNPs), graphene, and carbon nanotubes improve signal amplification and reduce detection limits to as low as 10 CFU/mL for pathogens such as *E. coli* and *Salmonella*^(10,12). Graphene-based field-effect transistors (GFETs) further extend biosensor sensitivity into the femtomolar range, providing ultra-fast, label-free bacterial detection. Meanwhile, wearable nanobiosensors exemplify the translation of these technologies into continuous, non-invasive health monitoring, with the capacity to detect infection biomarkers in sweat or interstitial fluid^(17,18). The convergence of synthetic biology and nanomaterials thus represents a synergistic innovation that enhances both analytical precision and device adaptability.

Another significant breakthrough lies in CRISPR/Cas-based biosensors, which leverage the programmable nuclease activity of Cas enzymes for sequence-specific nucleic acid recognition. When coupled with isothermal amplification techniques such as recombinase polymerase amplification (RPA) or loop-mediated isothermal amplification (LAMP), these systems achieve single-nucleotide resolution and enable rapid detection within 30-60 minutes^(10,12). CRISPR-based biosensors hold particular promise for antimicrobial resistance (AMR) surveillance and outbreak detection, as they combine genetic-level precision with field deployability. Nonetheless, their translation into standardized clinical diagnostics remains limited by reagent instability, temperature sensitivity, and lack of multiplexing capacity.

While these findings underscore substantial progress, several critical limitations and knowledge gaps persist. A recurring challenge across studies is the absence of standardized performance evaluation frameworks. Reported detection limits, sensitivities, and specificities vary widely, often depending on experimental design, sample type, or detection medium. This heterogeneity complicates cross-comparison between biosensor platforms and hinders regulatory validation^(12,16). Furthermore, although many studies highlight laboratory success, real-world clinical and environmental validations remain limited. Most synthetic biology-driven biosensors have not yet undergone large-scale field trials or regulatory approval processes, limiting their adoption in public health and industrial monitoring systems^(16,17).

Another major challenge concerns scalability and cost-effectiveness. Nanomaterial fabrication, sensor miniaturization, and biocomponent stability often require high production costs and specialized infrastructure. These factors restrict large-scale manufacturing and commercialization, particularly in low- and middle-income countries where bacterial outbreaks pose significant health risks^(12,19). Similarly, long-term stability under fluctuating environmental conditions, including temperature, humidity, and pH remains insufficiently characterized for many prototype biosensors^(23,24). Biosafety concerns associated with live-cell systems and environmental release of genetically modified microorganisms also necessitate further research and policy attention^(4,18).

Looking forward, the literature indicates that multidisciplinary convergence will be key to overcoming these challenges. Future research should focus on integrating synthetic biology-based biosensors with artificial intelligence (AI) and Internet of Things (IoT) platforms to enable real-time data processing, predictive analytics, and remote monitoring. AI-driven algorithms could standardize data interpretation, enhance signal-to-noise discrimination, and enable autonomous calibration, thereby improving diagnostic accuracy and reliability. Similarly, cloud-connected biosensors could facilitate epidemiological surveillance, providing early warning systems for infectious disease outbreaks and contamination events.

In addition, greater emphasis is needed on standardizing and benchmarking of biosensor performance across laboratories. Establishing unified criteria for evaluating detection limits, stability, and reproducibility would accelerate regulatory approval and commercialization. The development of cost-effective, biodegradable, and environmentally safe materials could further address sustainability concerns and promote scalable production. Collaborative efforts among biologists, engineers, data scientists, and policymakers are essential to translate these technological advances into tangible public health benefits.

In summary, this review demonstrates that synthetic biology has transformed biosensing from static detection tools into dynamic, programmable systems capable of high-precision bacterial monitoring. By integrating nanotechnology, CRISPR diagnostics, and AI-enabled analytics, next-generation biosensors can overcome the limitations of conventional assays. However, successful clinical and industrial translation will require concerted efforts to address standardization, scalability, and biosafety. Strengthening interdisciplinary collaboration and fostering innovation-

driven regulation will be essential to fully realize the potential of synthetic biology-based biosensors for global health and environmental sustainability.

Conclusion

This review highlights how synthetic biology has revolutionized biosensor technology for bacterial detection. Advances in genetic circuit design, cell-free systems, CRISPR-based diagnostics, and nanomaterial integration have enabled faster, more sensitive, and programmable biosensors compared with traditional assays. Among these, CRISPR and nanobiosensors demonstrate exceptional precision and portability, while whole-cell and cell-free systems provide cost-effective solutions for point-of-care use.

Despite these advances, challenges remain in standardization, large-scale validation, and biosafety, which limit clinical and industrial translation. Future research should prioritize the development of unified evaluation frameworks, the enhancement of stability and scalability, and the integration of biosensors with artificial intelligence (AI) and Internet of Things (IoT) systems for real-time monitoring.

Overall, synthetic biology-driven biosensors represent a transformative platform for rapid, accurate, and accessible bacterial detection, with significant potential to improve global health, food safety, and environmental monitoring.

Recommendation

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