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Introduction to Quantum Biosensing: A New Frontier in Diagnostics

Jyotirmayee Sahoo[1,2], Muneshwar Harsha Vardhan[1,2], Nireekshana Nandigam[1], and Sonu Gandhi[1,2]

[1]BRIC-National Institute of Animal Biotechnology (NIAB), Hyderabad, Telangana, India
[2]BRIC-Regional Centre for Biotechnology (RCB), Faridabad, Haryana (NCR Delhi), India

1.1 Introduction

Biosensing technology has undergone significant evolution since its outset in the mid-twentieth century, driven by advancements in biochemistry, engineering, and nanotechnology, leading to transformative impacts across various domains, including clinical treatment, pharmacy, healthcare sectors, environmental monitoring, and food safety [1]. The earliest biosensor, innovated by Clark and Lyons in 1962 for glucose detection, employed enzyme-based recognition systems to selectively identify target analytes, integrating biological recognition elements with electrochemical transducers [2, 3] to yield measurable signals as shown in Figure 1.1 [5]. This groundbreaking discovery set the stage for the advancement of complex biochemical sensing systems, paving the way for the evolution of modern biosensing technologies. Advancing further, second-generation biosensors incorporated mediated interactions, improving sensitivity and specificity by employing redox mediators to enhance electron transfer at electrode surfaces [6]. Furthermore, third-generation biosensors have greatly benefited from advancements in nanotechnology, where nanoscale materials and advanced fabrication methods have led to the creation of highly sensitive biosensors [7]. These innovations enable the detection of single molecules, expanding their use in clinical diagnostics and personalized medicine. Various sensing technologies, including optical, electrochemical, and piezoelectric detection, have expanded biosensing capabilities. Each method provides distinct advantages in sensitivity, portability, and speed of analysis, making biosensors more versatile and efficient. The following timeline map illustrates the evolution of biosensors and shows the key advancements from their inception to modern innovations, as shown in Figure 1.1.

Moving forward, in the early twenty-first century (around 2010–2011), a new sensing approach emerged—quantum biosensing [8]. This pioneering advancement in diagnostic technology uses the principles of quantum mechanics (QMs). This plays a vital role in

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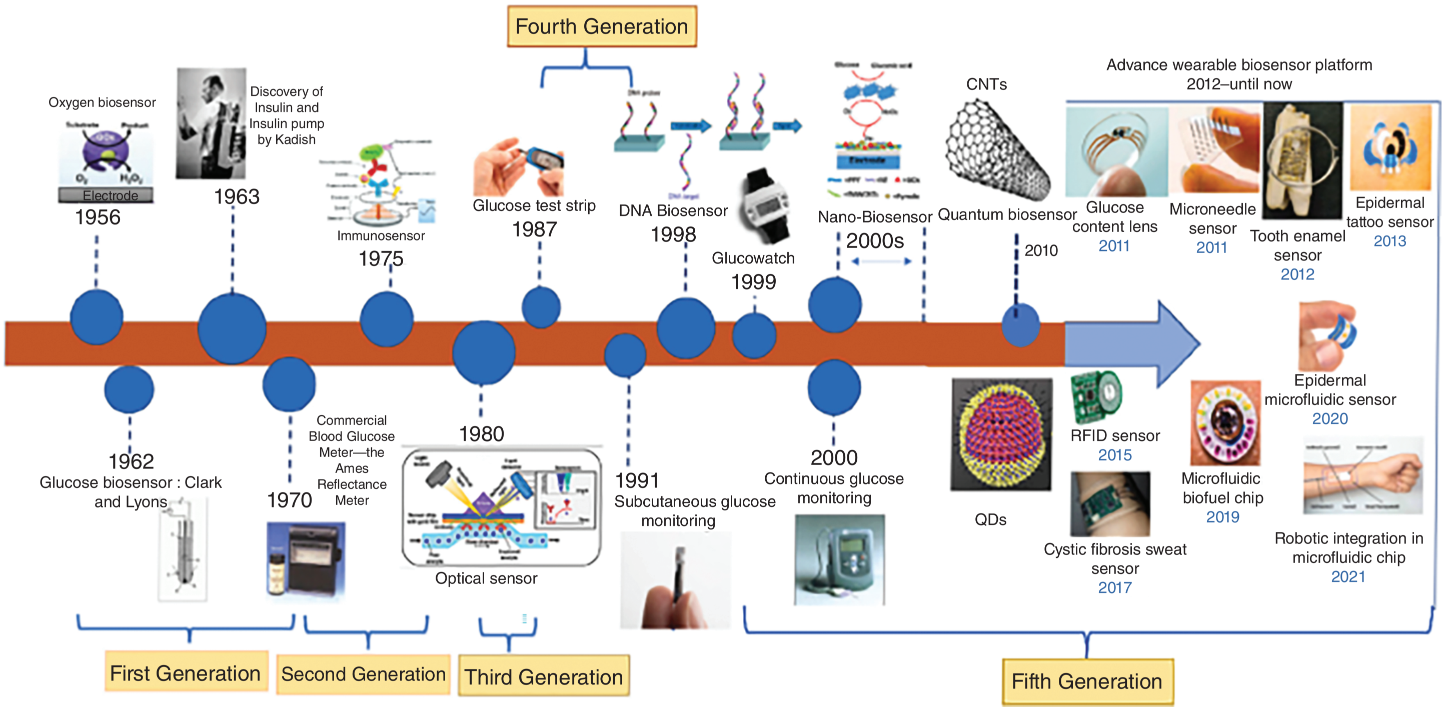

Figure 1.1 Evolution of biosensor technology, progressing from first-generation glucose biosensors to fifth-generation advanced wearable and microfluidic-integrated biosensors. Malik et al. [4] / with permission of Elsevier / CC BY 4.0.

Figure 1.2 The role of quantum biosensing across various fields of biology and its contribution to the advancement of biosensor technology. [10] / with permission of Twishmay.

biological systems, influencing phenomena like superposition, entanglement, coherence, and tunneling in biomolecular interactions and energy transfer. Furthermore, its applications span quantum photonics, information science, and complexity in biology, driving innovations in biosensing, neurobiology, and enzymatic regulation as detailed in Figure 1.2. By integrating QMs with biomedicine, quantum biosensors (QBs) enable the precise detection and characterization of subtle biological changes that conventional sensors often fail to identify, thereby transforming the landscape of biosensing and diagnostics. Furthermore, QBs exhibit a significant reduction in background noise compared to classical sensors, enhancing their ability to differentiate biophysical signals from background interference with exceptional sensitivity and specificity. Numerous QBs have been developed for diagnosing various diseases, yet their incorporation with next-generation sensing technologies may represent a groundbreaking advancement, offering exciting possibilities for future applications.

QB has come up as a transformative means in medical diagnostics, taking advantage of the principles of QMs to achieve unequaled precision and sensitivity in detecting biological analytes such as DNA, RNA proteins, and small biomolecules. These biosensors show quantum confinement effects, size-based optical properties, and exceptional electronic conductivity, making them highly responsive to micro-environmental changes induced by biomolecular interactions [11–13]. Upon interaction with target biomolecules, quantum materials exhibit measurable alterations in surface plasmon resonance (SPR), fluorescence intensity, electrical conductivity, etc., facilitating the transduction of biological signals into quantifiable outputs. Based on the transduction mechanism, various detection techniques are employed to interpret and generate the response, which is further explained in the subsequent section.

QBs serve as highly sensitive and precise tools with applications extending beyond medicine to agriculture and environmental monitoring. For instance, Chen et al. [14] explored the surface modifications and optical attributes of quantum dots (QDs) for detecting pollutants in aquaculture, focusing on their distinctive optical properties, including narrow emission bandwidths, broad excitation spectra, adjustable emission wavelengths, and resistance to photobleaching. Similarly, Safarpour et al. [15] developed a nanobiosensor for detecting plant pathogenic fungi by biofunctionalizing cadmium telluride QDs (CdTe-QDs) with a specific antibody against *Protostrongylus betae*, attaching the Glutathione-S-transferase (GST) antibody to thioglycolic acid-modified QDs. The formation of donor-acceptor complexes using rhodamine dye enabled the immunosensor to achieve 100% sensitivity and specificity with excellent stability and reproducibility. QDs have also proven to be an exceptional material for constructing biosensors with remarkable specificity and sensitivity for antibiotic detection. Additionally, their widespread integration into the detection of veterinary drug residues and pesticides underscores their significant impact on nanoscience-driven analytical advancements. The transition of quantum sensors from laboratory research to real-world applications is evident in the emergence of innovative commercial ventures in this domain. QBs, operating at atomic-scale dimensions with exceptional coherence properties, provide unprecedented spatial sensitivity and accuracy. Although assessing their full potential remains challenging, these quantum technologies hold immense promise for advancing biological research and diagnostics.

This introductory chapter provides a foundational understanding of biosensors by explaining their fundamental principles and working mechanisms. It then explores the concepts of QMs and the technological components integral to QB. This chapter also provides an overview of the diverse applications of QMs in medical diagnostics, showing their potential to revolutionize disease detection and monitoring with unparalleled precision. However, the scope of QMs extends far beyond medical diagnosis, playing a crucial role in various scientific and industrial fields, including environmental monitoring, food safety, and advanced material science. The subsequent chapters of this book will delve deeper into these applications in detail and their real-world implications.

1.2 Foundations of Quantum Mechanics in Biosensing

1.2.1 Basics of Biosensing Technologies

Biosensing technology combines biological recognition elements with physicochemical transducers to detect and quantify target analytes with high specificity and sensitivity.

A biosensor consists of three key components: a bioreceptor, a transducer, and a signal processor [16–18]. The bioreceptor, such as an aptamer, nucleic acid, antibody, or enzyme, selectively interacts with the target molecule, triggering a measurable biochemical or chemical event. The transducer then converts this event into a quantifiable signal, which may be optical, electrochemical [19], piezoelectric, or thermal. Finally, the signal processor amplifies and interprets the signal, providing a readable output corresponding to the analyte concentration. Moreover, biosensors employ various detection mechanisms tailored for specific applications, leading to different types of biosensors (Figure 1.3). Electrochemical biosensors detect biochemical reactions by measuring changes in current, voltage, or impedance at an electrode surface [20–22]. Optical biosensors utilize fluorescence, absorbance, or SPR to enable highly sensitive, real-time biomolecular detection without requiring labels or chemical modifications [23]. Piezoelectric biosensors, based on quartz crystal microbalance (QCM) technology, detect mass or mechanical changes upon analyte binding, providing high sensitivity [24, 25].

Recent advancements in nanotechnology have significantly enhanced the performance of biosensors. The incorporation of nanomaterials such as graphene, gold nanoparticles (AuNPs), and QDs has improved sensitivity, miniaturization, and real-time detection capabilities. For example, graphene-based biosensors exhibit excellent electrical conductivity and high surface area, which makes them ideal for electrochemical sensing applications [23]. Similarly, QDs, due to their size-dependent photoluminescence, enable multiplexed detection of multiple analytes in a single assay. The following sections provide an in-depth exploration of the fundamental principles of QMs that govern the optical and electronic properties of QDs, elucidating their role in biosensing applications.

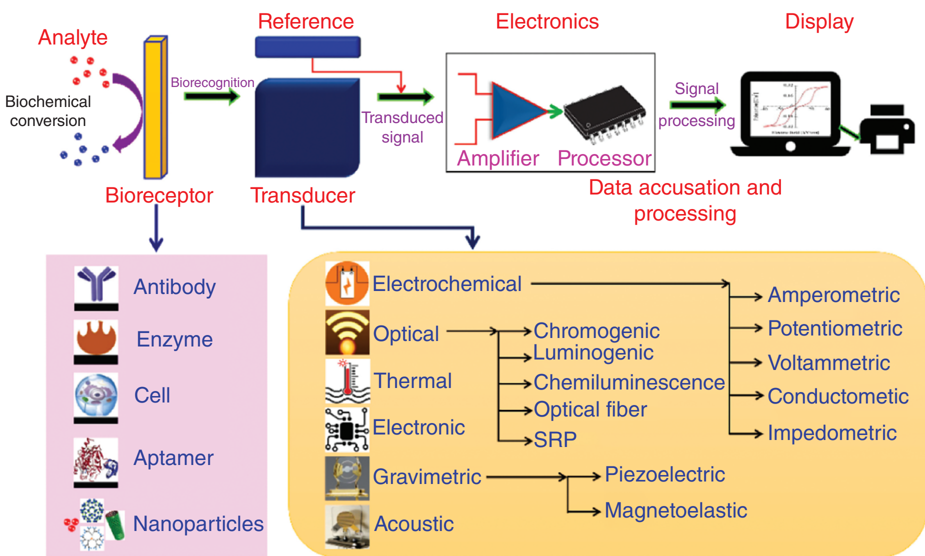

Figure 1.3 Overview of biosensor principle, where analyte undergoes biochemical recognition via bioreceptor, generating a signal transduced into electrical, optical, thermal, electronic, gravimetric, or acoustic responses. Mokhtari et al. [9]/ with permission of Elsevier / CC BY 4.0.

1.2.2 Principles of Quantum Mechanics

QMs is a fundamental theory in physics that governs the behavior of matter and energy at atomic and subatomic scales, where particles exhibit both particle-like and wave-like properties depending on how they are observed [26]. The foundation of QMs is built upon several key principles, including wave-particle duality, superposition, entanglement, and quantum tunneling. Wave-particle duality states that elementary particles, such as photons and electrons, can behave as discrete particles and continuous waves. Superposition is another fundamental concept, which asserts that a quantum system, until measured, can simultaneously exist in multiple states. Quantum entanglement is a phenomenon where two or more particles become correlated such that the state of one instantly influences the other, regardless of the distance between them [27]. Each of these principles plays an essential role in modern quantum technologies, including quantum biosensing, quantum computing, and cryptography. Quantum biosensing refers to the application of these quantum phenomena in biological detection and diagnostic systems [28]. By leveraging quantum properties, quantum biosensing enables highly sensitive, selective, and rapid detection of biomolecules, pathogens, and disease markers at ultralow concentrations. The integration of QDs, spin-based sensors, and quantum interference techniques has revolutionized biosensor technology, pushing the boundaries of detection limits and analytical performance [29]. In the following sections, the fundamental principles of QMs relevant to biosensor development will be explored in detail, highlighting their impact on emerging diagnostic technologies and next-generation biosensing platforms.

1.2.2.1 Quantum Superpositions

Quantum superposition, a basic principle of QMs, states that a quantum system, such as an electron, photon, or atom, can exist simultaneously in a combination of multiple states [30]. Unlike classical systems, which exist in well-defined states at any given time, quantum superposition allows particles to occupy a probabilistic distribution of states, described mathematically by a wave function. The mathematical foundation of superposition is rooted in the Schrodinger equation, which governs the evolution of a quantum system. A quantum state (Ψ) can be expressed as a linear combination of basis states: $|\psi\rangle = c1|\psi1\rangle + c2|\psi2\rangle + \cdots + cn|\psi n\rangle$, where c1, c2, … , c_n are probability amplitudes associated with each possible state [31]. The square of these amplitudes represents the probability of observing the system in a particular state upon measurement.

In quantum biosensing, superposition is used to enhance the sensitivity and resolution of measurements. Quantum states of QDs and superconducting qubits can be manipulated to detect minute changes in biological environments. For instance, in quantum coherence-based sensing, superposition states allow for interference effects that improve the precision of detecting biomolecular interactions. In addition to this, quantum-enhanced spectroscopy employs superposition to improve signal-to-noise ratios, enabling ultrasensitive detection of disease biomarkers at single-molecule levels. Furthermore, the concept of quantum decoherence, where environmental interactions cause a quantum system to lose its superposition state, poses a major challenge in practical applications. Understanding and controlling decoherence is essential for maintaining the integrity of quantum superposition in biosensing applications, ensuring accurate and reliable detection of biological targets.

1.2.2.2 Entanglement

The phenomenon of quantum entanglement takes place when two or more particles become intrinsically correlated, such that the state of one particle instantaneously influences the state of the other, regardless of the physical distance between them [32]. This unique property, which defines classical intuitions, has profound implications in biosensing and medical imaging, particularly enhancing the sensitivity and accuracy of techniques such as positron emission tomography (PET) [33]. Traditional PET imaging relies on detecting gamma-ray photons emitted during positron-electron annihilation but suffers from resolution limitations and background noise. By utilizing entangled photon pairs, PET imaging can achieve superior spatial and temporal resolution, reducing noise and significantly improving signal fidelity. This advancement enables the detection of early-stage disease biomarkers, which is crucial for conditions like cancer [34, 35], neurodegenerative disorders [36], and metabolic syndromes. Beyond imaging, quantum entanglement is also being explored in biosensors for real-time molecular detection. Quantum-enhanced fluorescence imaging, entanglement-assisted spectroscopy, and spin-based magnetic field sensing have demonstrated exceptional sensitivity in tracking biomolecular interactions at the single-molecule level. However, practical implementation faces challenges such as quantum decoherence in biological environments, which can rapidly degrade entangled states. Currently, research is focused on developing quantum error correction techniques, noise-resistant entangled states, and cryogenic quantum sensing platforms to overcome these limitations.

1.2.2.3 Quantum Tunneling

Another pivotal principle of QMs is quantum tunneling, which allows particles to pass through energy barriers [37]. This phenomenon arises due to the wave-like nature of quantum particles, described by the Schrodinger equation, which allows for nonzero probability amplitudes extending beyond an energy barrier. Mathematically, the probability of tunneling is governed by the transmission coefficient in the time-independent Schrodinger equation, which is exponentially dependent on the barrier width and height [27]. Electron tunneling sensors work by measuring minute variations in electrical conductance when a target biomolecule interacts with the sensor surface. These sensors utilize nanoscale junctions, such as metal-insulator-metal (MIM) and single-molecule transistor structures, where electron flow across an insulating barrier is modulated by molecular interactions [38]. Changes in tunneling current can indicate the presence of specific biomolecules, allowing for highly sensitive detection. Furthermore, quantum tunneling-based biosensors can detect viral RNA or antigenic proteins at femtomolar concentrations, significantly surpassing the sensitivity of conventional polymerase chain reaction (PCR) or enzyme-linked immunosorbent assay (ELISA) techniques. In addition to this, in label-free biosensing, tunneling-based field-effect transistors (FETs) and molecular break-junction sensors allow real-time monitoring of biomolecular interactions, eliminating the need for fluorescent or enzymatic labeling, which can introduce artifacts and lower detection fidelity [39].

1.2.3 Technological Components of Quantum Biosensing

QBs use the principles of QMs to achieve precise and highly sensitive detection of biomolecules. Their functionality is based on the ability to transduce biomolecular interactions into quantifiable signals, including variations in electrical conductivity, shifts in SPR, and fluorescence modulation. Such signal transduction mechanisms significantly enhance sensitivity and specificity, making QBs highly advantageous for medical diagnostics and early disease detection. A diverse range of quantum-engineered platforms contributes to the development of these biosensors, including QDs, nitrogen-vacancy (NV) centers in diamonds, quantum photonics, and light-matter interactions [28]. These technologies play a crucial role in advancing biosensing applications by enabling fast detection, multiplexed analysis, and single-molecule resolution. The subsequent sections will explore these key technological components in detail, elucidating their underlying mechanisms, practical applications, advantages, and the challenges associated with their implementation in real-world biosensing systems.

1.2.3.1 Quantum Dots

QDs are semiconductor nanocrystals that exhibit unique optical and electronic properties [40] due to their nanoscale dimensions, ranging from 2 to 10 nm. These properties arise from the quantum confinement effect, where the electronic characteristics of the material are influenced by its size and shape, allowing for diverse photoluminescence and high stability against photobleaching. The applications of QDs extend to bioimaging and medicine, where they serve as fluorescent biolabels, sensors, and drug delivery agents; quantum information, facilitated by their bright, narrowband emission and potential use in lasing and heterostructures; communications, where QDs contribute to advanced optical and electronic signaling; machine vision, aiding in enhanced imaging and recognition technologies; augmented reality, enabling improved interactive displays; cameras and displays, where their size-dependent absorption and emission properties enhance imaging quality; illumination, improving light sources due to their efficient luminescence; and energy harvesting, where they contribute to photovoltaic cells and solar concentrators. These wide-ranging applications stem from the unique quantum confinement effects and tunable electronic properties of QDs, as shown in Figure 1.4. It possesses a high surface area-to-volume ratio, making it suitable for bioconjugation with various biomolecules, including antibodies, nucleic acids, and peptides, thereby enhancing sensitivity and specificity in biosensing applications [42].

Although a universally accepted classification framework for QDs has yet to be established, the scientific community has recently categorized them into two broad classes: semiconductor quantum dots (SQDs) and carbon-based nanomaterials [43, 44], especially carbon quantum dots (CQDs). SQDs are primarily composed of metallic and other inorganic elements, exhibiting size-dependent electronic and optical properties due to quantum confinement effects. These materials, often synthesized from compounds such as cadmium selenide (CdSe), indium phosphide (InP), and lead sulfide (PbS) [45], demonstrate high quantum yield and tunable emission spectra, making them highly effective in optoelectronic and biosensing applications. In contrast, CQDs encompass a diverse range of carbon-based nanomaterials, including graphene quantum dots (GQDs) [46], carbon nanodots (CNDs) [47], and polymer dots (PDs). The following flowchart outlines the classification of QDs. Apart from their semiconductor counterparts, CQDs offer inherent biocompatibility, reduced cytotoxicity, and strong photostability, making them particularly suitable for biomedical applications like drug delivery, bioimaging, and fluorescence-based

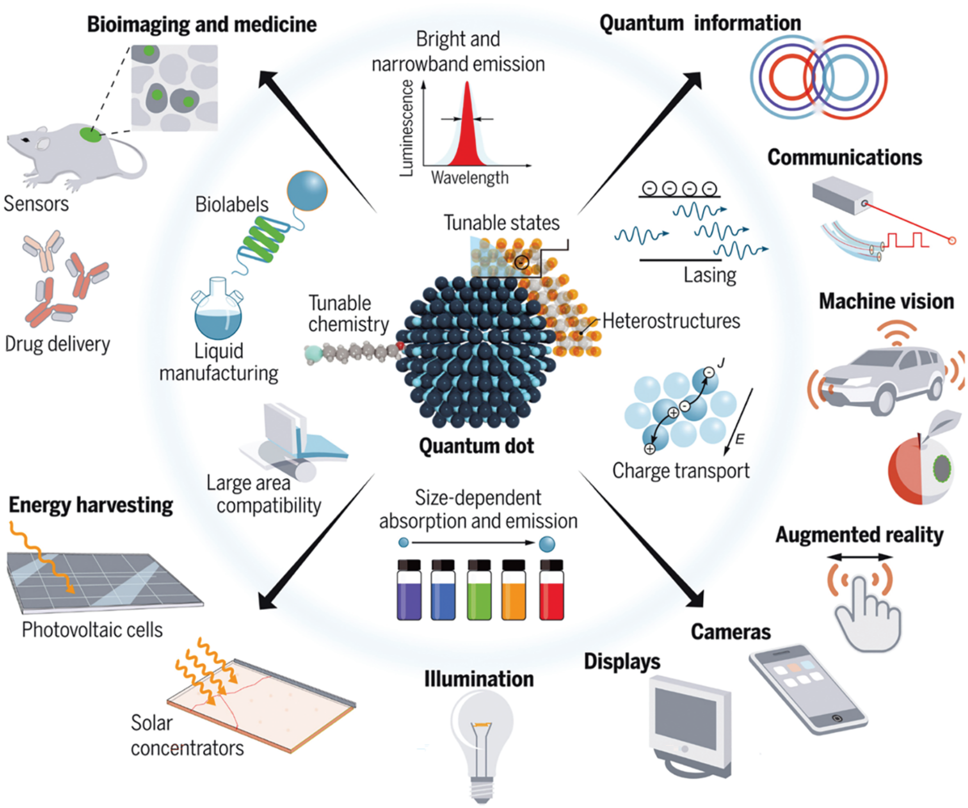

Figure 1.4 Diverse applications of semiconductor quantum dots, which extend up to bioimaging and medicine (fluorescent biolabels, sensors, drug delivery), quantum information (narrowband emission, lasing, heterostructures), biosensing (optical and electronic signaling), machine vision (enhanced imaging, recognition), augmented reality (interactive displays), cameras and displays, and energy harvesting (photovoltaics, solar concentrators). García de Arquer et al. [41] / American Association for the Advancement of Science / CC BY 4.0.

biosensing [48]. The distinct physicochemical properties of both categories have paved the way for their integration into advanced quantum biosensing technologies, enabling highly sensitive and selective detection of biomolecules at the molecular level.

1.2.3.2 Nitrogen-Vacancy (NV) Centers in Diamonds

The nitrogen-vacancy (NV), an intriguing defect in diamond crystal structures, has gained notable attention in recent years due to its exceptional properties and potential applications in quantum technologies, particularly in biosensor development [49, 50]. An NV center is formed when a nitrogen atom replaces a carbon atom in the diamond lattice and an adjacent carbon atom is missing, leading to a vacancy [51]. This defect gives the diamond unique quantum properties, such as the ability to exhibit optically detected electron spin resonance at room temperature [52]. NV centers utilize superposition in electron spin states to detect minute variations in magnetic fields, enabling highly precise mapping of biomolecular interactions and intracellular dynamics [77]. The highly sensitive nature of the electron spin in NV centers allows these diamonds to function as effective quantum bits (qubits) for quantum information processing and versatile nanoscale sensors. Furthermore, the NV centers in diamonds possess remarkable magnetic sensitivity, which stems from their spin states that can be manipulated and read optically [53]. These characteristics enable NV centers to detect minute changes in their environment, making them ideal for various applications in biosensing technologies. The emitted fluorescence from the NV center when excited by light serves as a powerful tool for quantitative measurement, further enriching their utility in biological sensing applications.

1.2.3.3 Quantum Photonics and Light-Matter Interaction

The principles of quantum photonics and light–matter interactions play a pivotal role in advancing biosensor technologies by enabling highly sensitive and precise detection mechanisms [54]. Quantum photonics involves the generation, control, and manipulation of photons exhibiting quantum phenomena such as superposition and entanglement, allowing for enhanced optical sensing and quantum-level interrogation of biological systems [55]. On the other hand, light-matter interaction encompasses the fundamental processes that occur when photons interact with matter, ranging from atoms and molecules to complex biomolecular structures. These interactions give rise to various optical phenomena, including absorption, scattering, and emission, which are governed by quantum mechanical principles dictating energy exchange and electronic state transitions within the interacting material [56]. One of the most widely employed techniques showing light-matter interaction in biosensing is fluorescence spectroscopy, which enables molecular-level investigations by measuring the emission spectra of biomolecules upon excitation by incident photons. This technique provides critical insights into cellular dynamics, protein interactions, and nucleic acid hybridization, making it vitally important in biomedical research and diagnostics. Another easy-advanced biosensing approach, SPR sensing, exploits the resonant oscillations of conduction electrons at the interface between a metal and a dielectric material. The resonance condition is highly sensitive to refractive index changes caused by the binding of biomolecules, making SPR a powerful tool for real-time, label-free detection of biomolecular interactions. This technology has been extensively utilized in diverse biomedical applications, including blood glucose monitoring, early-stage cancer biomarker detection, and pathogen identification. As quantum photonics and light-matter interactions continue to be refined, their integration into biosensors is expected to further revolutionize diagnostic platforms, enabling ultra-sensitive, high-resolution, and multiplexed detection systems. Future advancements may include the incorporation of entangled photon pairs for enhanced signal-to-noise ratio, quantum-enhanced Raman spectroscopy for single-molecule analysis, and nanoplasmonic structures for adjustable biosensing platforms, thereby crossing the boundaries of precision in real-time disease diagnostics.

1.3 Applications of Quantum Biosensing in Diagnostics

The efficacy of disease management is based on early and precise diagnosis, which necessitates a comprehensive understanding of its pathophysiology and progression. At the onset of the twenty-first century, the emergence of quantum biosensing has revolutionized medical diagnostics, enabling ultrasensitive, high-specificity, and real-time detection of biomarkers at the molecular level. By integrating quantum-enhanced sensing technologies with traditional diagnostic methodologies, researchers have unlocked unparalleled capabilities in oncology, neurology, cardiovascular disease diagnostics, infectious disease surveillance, and pharmaceutical research. These advancements leverage quantum phenomena such as quantum confinement, entanglement, and superposition, offering miniaturized, non-invasive, and highly efficient biosensing platforms. The following sections delve into the multifaceted applications of QBs, examining their technological foundations, diagnostic advantages, and future potential in reshaping the landscape of precision medicine and biomedical research.

1.3.1 Fluorescent Probes in Medical Diagnostics

One of the most significant contributions of quantum biosensing in diagnostics is the use of fluorescent quantum probes, which surpass conventional fluorescent dyes and organic fluorophores in terms of brightness, photostability, and tunability. A fluorescent probe fundamentally consists of three key components: a recognition unit that selectively binds to the target analyte, a fluorophore responsible for light emission, and a connector or linker that facilitates interaction between the recognition unit and the fluorophore, as illustrated in Figure 1.5a [57]. A diverse array of fluorescent probes has been engineered for the diagnosis of complex neurological disorders, including Alzheimer's disease (AD), stroke, depression, Wilson's disease, epilepsy, and Parkinson's disease (PD).

For instance, in 2022, Kim and colleagues designed Probe 5, an NIR fluorescent probe specifically tailored for detecting peroxynitrite ($ONOO^-$) [60], a reactive nitrogen species implicated in oxidative stress and neurodegeneration. Probe 5 is made up of diamino-substituted rhodol dye as the fluorophore, while the 4-aminophenol moiety serves as the selective $ONOO^-$ recognition unit. This molecular design enabled *in situ* imaging of $ONOO^-$ in AD mouse models, allowing Kim et al. to establish that $ONOO^-$ functions as a potential biomarker for AD, as shown in Figure 1.5b. The ability to visualize and quantify such reactive species in living biological systems underscores the significance of fluorescent quantum probes in advancing biomedical imaging, early disease diagnostics, and precision medicine applications.

1.3.2 Applications of Quantum Biosensing in Oncology

Cancer remains one of the leading causes of mortality worldwide, with an alarming 19.3 million new cases and nearly 10 million cancer-related deaths reported in the twenty-first century. A major contributing factor to high cancer mortality is late-stage diagnosis, which significantly limits therapeutic efficacy and survival rates. Consequently, early and accurate detection of cancer-specific biomarkers is crucial for improving patient prognosis. In this context, QBs have emerged as highly sensitive diagnostic tools, offering exceptional precision in detecting circulating tumor cells (CTCs), extracellular vesicles, tumor-specific genetic mutations, and oncogenic biomarkers [61]. Recent advancements in nanomaterial-based QB have demonstrated the potential of GQDs in electrochemical biosensing for early cancer detection. Notably, Ganganboina et al. (2019) leveraged

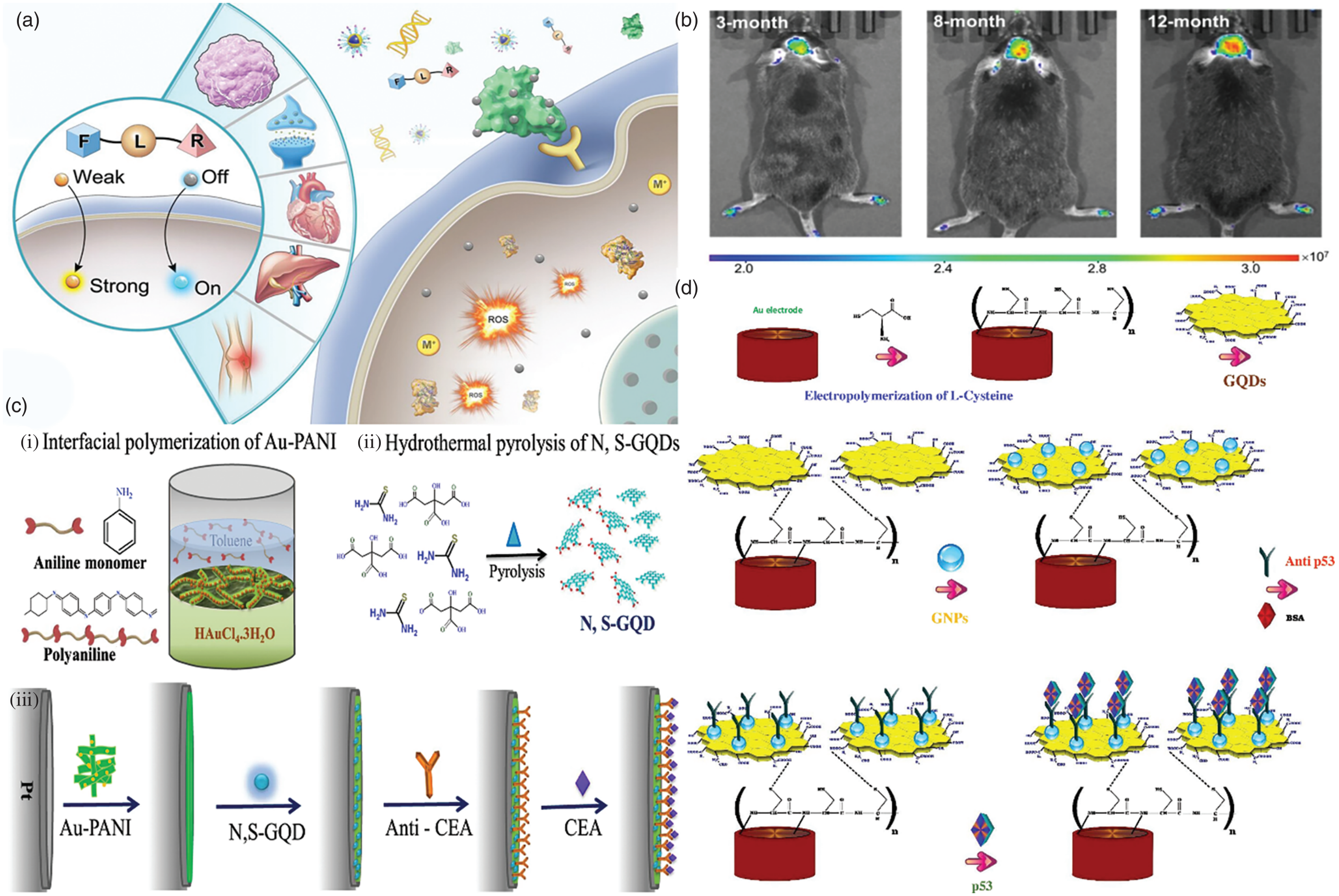

Figure 1.5 (a) Overview of fluorescent probes for medical diagnostics. (b) *in vivo* fluorescence imaging of AD mice at 3, 8, and 12 months via tail injection of Probe 5, indicating age-related elevation of $ONOO^-$ in the brain. Wang et al. [57] / with permission of American Chemical Society / CC BY 4.0. (c) (i) Synthesis of Au-PANI through polymerization, (ii) hydrothermal pyrolysis of N, S-GQD, and (iii) development of a label-free CEA electrochemical impedimetric immunosensor. Ganganboina and Doong [58] / Springer Nature / CC BY 4.0. (d) Label-free electrochemical immunosensor for detecting the p53, incorporating ternary signal amplification through P-Cys, GQDs, and GNPs to enhance sensitivity and performance. Hasanzadeh et al. [59] / with permission of Elsevier.

the inherent synergy between GQDs and electrochemical biosensors to develop an ultrasensitive detection platform. They employed N, S-doped GQDs@Au-polyaniline (N, S-GQDs@Au-PANI) nanowires as depicted in Figure 1.5c to detect carcinoembryonic antigen (CEA), a well-established biomarker, achieving an exceptionally low limit of detection (LoD) of 0.01 ng/mL. This approach underscores the potential of quantum-enhanced biosensing platforms in real-time cancer biomarker detection [58]. Similarly, Hasanzadeh et al. developed a P-Cys/GQDs/GNPs nanocomposite-based biosensor for the electrochemical detection of suppressor protein p53, as shown in Figure 1.5d, a key regulator of genomic stability. The integration of QDs and AuNPs enhanced the electrochemical response, enabling ultra-sensitive p53 quantification [59].

1.3.3 Quantum Biosensors for Cardiovascular Disease Detection

Cardiovascular diseases (CVDs) constitute a broad spectrum of disorders affecting the heart and vascular system, including coronary artery disease, heart failure, stroke, and hypertension. A primary underlying cause of these conditions is atherosclerosis, characterized by the progressive accumulation of lipid plaques within arterial walls, leading to vascular occlusion, impaired blood circulation, and an elevated risk of myocardial infarction and stroke [62]. Because of the asymptomatic nature of early-stage CVDs, their timely diagnosis is crucial for effective intervention and disease management. QBs have revolutionized cardiovascular diagnostics by enabling the ultrasensitive detection of key cardiac biomarkers, such as troponins, C-reactive protein (CRP), and procalcitonin (PCT), at exceptionally low concentrations. Among their most significant applications is the detection of cardiac troponin I (cTnI), a highly specific biomarker for myocardial infarction. To achieve this, photoelectrochemical biosensors incorporating CdSe/CdS/ZnS core-shell QDs in conjunction with TiO_2 heterostructures have been synthesized (Figure 1.6a), demonstrating enhanced photocurrent responsiveness, a broad dynamic detection range (10 pg/mL to 0.2 ng/mL), and remarkable chemical stability. Furthermore, QD-based immunochromatographic strips have been designed for the rapid and precise detection of CRP and PCT, both of which serve as critical indicators of myocardial inflammation and cardiovascular disease risk. These label-free, high-sensitivity diagnostic platforms not only facilitate early disease detection but also offer a non-invasive, portable, and cost-effective alternative to conventional biochemical assays [66]. As advancements in quantum biosensing technology continue to evolve, its integration into clinical cardiology holds immense potential for transforming point-of-care diagnostics, real-time monitoring, and personalized treatment strategies in CVD management.

1.3.4 Quantum Biosensing in Infectious Disease Diagnostics

Infectious diseases driven by highly adaptive pathogens account for nearly 15% of global mortality [67]. The transmission routes could be direct contact, contaminated substrates, vector mediation, and aerosolized dispersal. The increasing threat of antimicrobial resistance necessitates the development of advanced biosensing technologies that are crucial for early diagnosis, outbreak control, and therapeutics. Quantum-enabled biosensors can

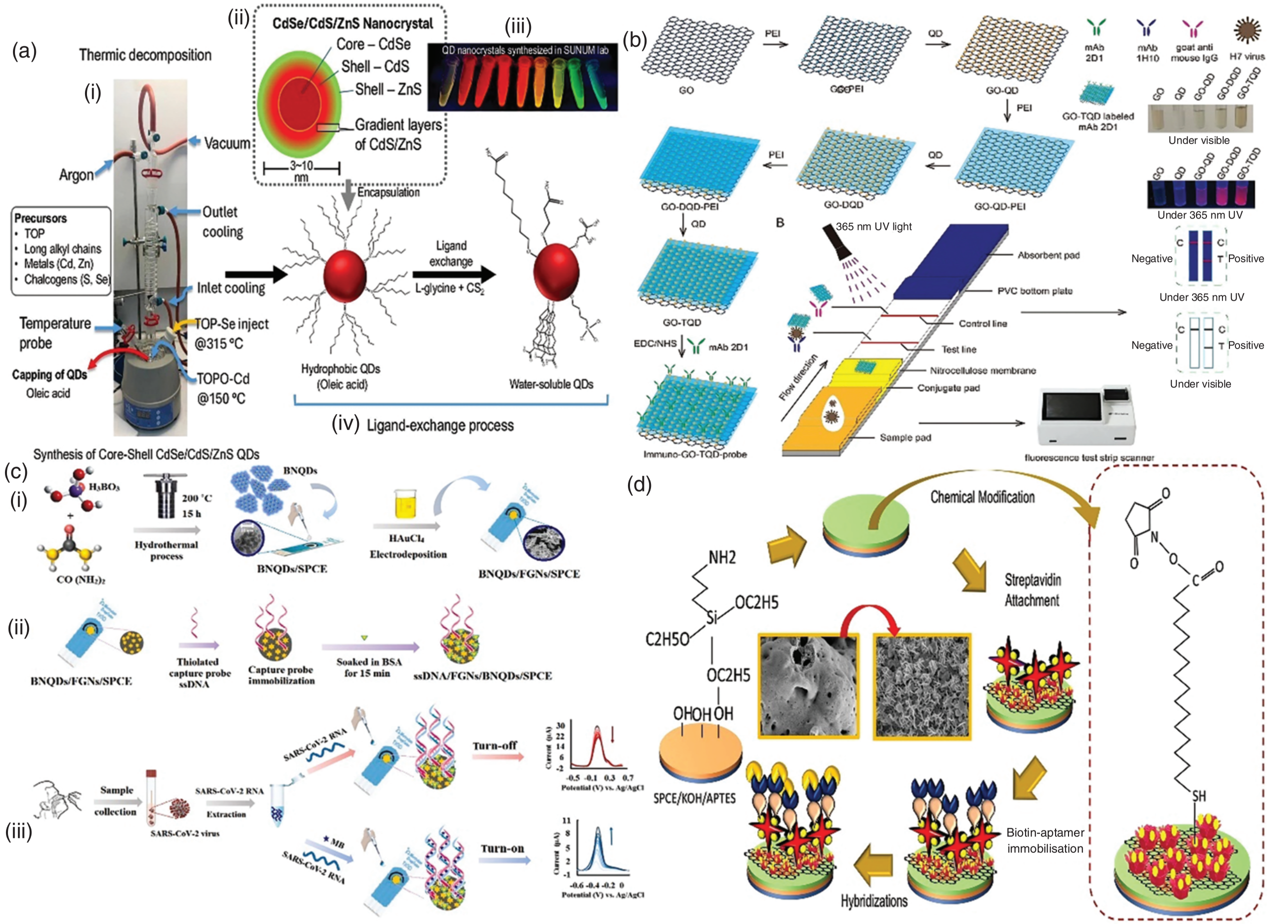

Figure 1.6 (a) Synthesis of core-shell CdSe/CdS/ZnS quantum dots (QDs) for cardiac troponin detection of cardiovascular disease monitoring. Memon et al. [62] / with permission of Elsevier. (b) GO-TQD nanoprobe and GO-TQD LFA were designed for the direct detection of H_7AIVs, enabling sensitive and specific analysis of avian influenza virus. Fu et al. [63] / with permission of Elsevier / CC BY 4.0. (c) Electrochemical biosensor was developed for the sensitive and specific detection of SARS-CoV-2. Hatamluyi et al. [64] / with permission of Elsevier. (d) An LSG/MoS_2/N-GQDs/L-Ag NPs hybrid was synthesized on a modified surface to facilitate aptamer–troponin I interaction, enhancing detection sensitivity and specificity. Vasudevan et al. [65] / with permission of Elsevier.

detect viral RNA [68–70], bacterial antigens, and inflammatory cytokines with ultrafast response times and minimal sample volumes. These technologies are being applied to pandemic preparedness, point-of-care testing, and antimicrobial resistance monitoring, ensuring early and accurate detection of infectious agents. Notable breakthroughs include graphene oxide multilayer quantum dot-based immunochromatographic strips (Figure 1.6b), which detect the H7N9 avian influenza virus with an exceptionally low detection limit of 0.016 ng/mL for hemagglutinin protein [63]. Similarly, a boron nitride quantum dot-based biosensor, integrated with gold nanostructures, has shown 100% specificity and sensitivity for SARS-CoV-2 detection, eliminating the need for nucleic acid amplification and significantly outperforming conventional RT-PCR methods [64]. Additionally, fluorescent biosensors leveraging Förster resonance energy transfer (FRET) between QDs and two-dimensional metal-organic frameworks, as shown in Figure 1.6c, have been successfully employed to detect the *Mycobacterium tuberculosis* IS6110 gene fragment, achieving a detection limit as low as 35 pM [71].

1.3.5 Nanoparticles in Quantum Biosensing

Nanoparticles are revolutionizing quantum biosensing by enabling highly sensitive and precise biomolecular detection. The integration of nanoparticles in quantum biosensing has further enhanced detection efficiency, with AuNPs, GQDs, and plasmonic nanostructures enabling highly sensitive, multiplexed, and miniaturized biosensors. Materials like QDs and AuNPs stand out due to their unique optical and electronic properties, such as fluorescence and SPR, which significantly enhance signal transduction in biosensors. These nanoparticles amplify sensor signals, allowing for real-time, high-resolution monitoring in medical diagnostics and environmental analysis, paving the way for more accurate and efficient detection methods [18]. In a recent study, Vasudevan et al. developed a biosensor using a quadruplet hybrid of 3D laser-scribed graphene (LSG), molybdenum disulfide (MoS_2), nitrogen-doped graphene quantum dots (N-GQDs), and lignin-based silver nanoparticles (L-AgNPs) to detect troponin I, as depicted in Figure 1.6d, a critical biomarker for myocardial injury. The integration of L-AgNPs improved biomarker recognition and binding stability, offering a cost-effective and environmentally friendly alternative to traditional gold nanoparticles [65]. Similarly, Gharehaghaji et al. designed a biosensor incorporating self-assembled Prussian blue (PB) nanoparticles on MXene quantum dots, supported by AuNPs, for the detection of ovarian cancer antigen (CA-125). The AuNPs in this system enhanced conductivity and facilitated the immobilization of CA-125 antibodies, ensuring highly specific and efficient biomarker capture. These cutting-edge nanoparticle-based biosensors demonstrate remarkable sensitivity, stability, and real-time detection capabilities, making them promising tools for early disease diagnosis and clinical applications [72].

1.3.6 Quantum Optical Sensors for Biomedical Applications

Finally, quantum optical sensors are also gaining prominence in biomedical applications, utilizing quantum-enhanced light-matter interactions to achieve superior detection limits in biospectroscopy, biophotonics, and precision diagnostics. Quantum optical sensors are transforming biomedical applications by offering high precision and real-time detection of biological molecules. By utilizing quantum principles like fluorescence enhancement and SPR [73, 74], these sensors significantly improve sensitivity in disease diagnostics. With advancements in microfluidics and artificial intelligence (AI) integration, they are proving to be valuable tools for personalized medicine, continuous health monitoring, and early disease detection [23]. Zhang et al. developed an optical fiber biosensor to detect acetylcholine, a crucial neurotransmitter, using pH-sensitive nitrogen-doped carbon QDs (N-CQDs) [75]. The sensor works by measuring changes in fluorescence—when acetylcholine is broken down by acetylcholinesterase, it causes a drop in pH, which in turn reduces the fluorescence intensity (Figure 1.7c). This simple yet highly sensitive approach makes it a valuable tool for monitoring neurotransmitter activity [78]. Similarly, Loyez et al. designed an optical fiber-based SPR (OF-SPR) sensor for detecting HER2, a key biomarker for breast cancer (Figure 1.7a,b). Their sensor uses a sandwich assay with aptamers and antibodies, which significantly boosts the signal, making detection much

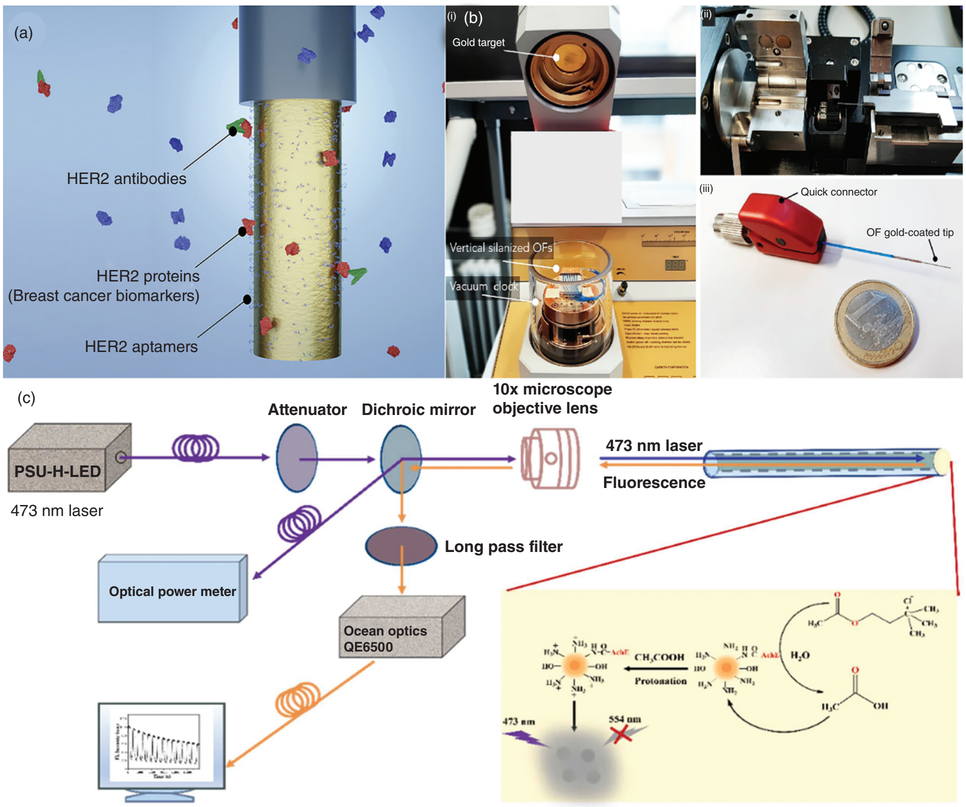

Figure 1.7 (a,b) Detection of the breast cancer biomarker HER2 using a sandwich-type surface plasmon resonance optical biosensor. Loyez et al. [76] / with permission of Elsevier. (c) Optical fiber biosensor for acetylcholine detection based on pH-sensitive fluorescent carbon quantum dots. Zhang et al. [78] / with permission of Elsevier.

more precise. By carefully optimizing the thickness of the gold coating on the optical fiber, they achieved ultra-sensitive detection, making this technology a promising candidate for early cancer diagnosis and improved patient care [76].

Furthermore, various types of materials have been utilized to enhance detection range and sensitivity, as summarized in Table 1.1. Beyond biomedical applications, QB is emerging as a powerful tool in environmental monitoring and public health surveillance. Quantum sensors can detect airborne pathogens, waterborne contaminants, and toxic heavy metals at extremely low concentrations, playing a crucial role in epidemiological studies and pollution monitoring. The integration of nanoparticles in QB has further enhanced detection efficiency, with gold nanoparticles, GQDs, and plasmonic nanostructures enabling highly sensitive, multiplexed, and miniaturized biosensors. However, the scope of QMs in diagnostics extends far beyond these applications. The subsequent

Table 1.1 Various types of quantum materials used in medical diagnosis.

S. No.	Material	Analyte	LOD	References
1	NV Centers in Diamonds	mi-RNA	2.6 aM	[78]
2	Quantum Dots	Serum albumin	0.2129 μM	[79]
3	Carbon Nanotubes	Paraoxon-ethyl	10 nM	[80]
4	Quantum Photonics	Glucose	1 mM	[81]
5	Single Electron Transistors	Dibutyl phthalate	0.08 fM	[82]
6	Copper Nanoclusters	Kanamycin	1.07 nM	[83]
7	Graphene Quantum Dots	Peroxide	20 nM	[84]
8	Silicon Quantum Dots	Virus	0.08 nM	[85]
9	Carbon Quantum Dots	Pyocyanin	37 nM	[86]
10	Gold Nanoclusters	micro-RNA 21	0.7 pM	[87]
11	Platinum Nanoclusters	Glutathione	0.37 μM	[88]
12	Copper Indium Sulfide Quantum Dots	Cholesterol	0.222 mM	[89]
13	Zinc Sulfide Quantum Dots	Bilirubin	1.8 μM	[90]
14	Cadmium Quantum Dots	DNA	1 fM	[91]
15	Silicon Nanowires	Prostate-specific antigen	0.01 pM	[92]
16	Gold Polyaniline Nanowires	Carcinoembryonic antigen	0.01 nM	[58]
17	Zinc Oxide Nanowires	Glycosylated hemoglobin A1c	61.8 nM	[93]
18	Boron Nitride Quantum Dots	Cardiac troponin	0.0005 nM	[94]
19	Molybdenum Disulfide Quantum Dots	Prostate-specific antigen	0.01 pM	[95]
20	Quantum Raman Spectroscopy	Folic acid	9 nM	[96]

chapters will provide an in-depth exploration of its broader potential and emerging innovations in the field.

1.4 Role of Artificial Intelligence in Quantum Biosensing

Recently, AI, 3D bioprinting [97], and the Internet of Things (IoT) have emerged as cutting-edge technologies that have been integrated to enhance conventional methodologies. These advancements have significantly transformed modern healthcare, facilitating the implementation of digital prescriptions, point-of-care diagnostics, and personalized drug monitoring systems, thereby improving efficiency, accessibility, and patient outcomes [98]. This convergence fosters a decentralized healthcare model, which is connected to IoT and has reduced the burden on medical professionals [99]. AI plays a pivotal role in precision medicine, offering breakthroughs in disease prevention, early diagnosis, and targeted treatment [28]. The success of AI-driven healthcare depends on its equitable, robust, and ethically responsible deployment, particularly in domains such as AI-assisted diagnostics, treatment optimization, wearable and implantable biosensors, clinical decision support, and bioinformatics [100]. Future IoT-based medical systems are expected to incorporate Green IoT, emphasizing energy efficiency, waste reduction, and minimal environmental impact. The emergence of the Internet of Medical Things (IoMTs) further revolutionizes healthcare by integrating software-driven, network-connected biomedical devices for real-time health monitoring [101]. Electrochemical biosensors, with their rapid analysis times, cost-effectiveness, and adaptability, are poised to play a crucial role in precision medicine and improving patient outcomes.

The rapid expansion of biomedical data demands high-performance computing tools such as cloud-based computing, GPUs, and TPUs to efficiently process complex QB datasets [102]. High-performance computing (HPC) clusters and distributed computing enable real-time data interpretation, feature extraction, and pattern recognition, accelerating diagnostics. GPU acceleration enhances DL models for image analysis and signal processing, while TPUs optimize large-scale AI-driven medical applications with improved energy efficiency [103]. machine learning (ML) techniques, including regression analysis and classification, play a crucial role in biosensor data analysis, enabling nanobiosensors to extract meaningful insights through advanced pattern recognition. ML reduces background noise, false positives, and cross-sensitivity, improving biosensor accuracy and detection limits [104]. Additionally, ML-driven advancements in fluorescent nanodiamonds (FNDs) for intracellular magnetic microscopy have led to 20-fold enhancements in imaging contrast and resolution. DL techniques further refine magnetic image reconstruction, boosting biosensor imaging precision. Fluorescence-based biosensors benefit from on-chip data processing, noise suppression, and segmentation, enabling real-time detection of specific cells or tissues.

Furthermore, the integration of AI-driven processors with medical test strips enhances real-time biosensor monitoring, mitigating inaccuracies caused by environmental fluctuations or sample contamination. Advancements in biomedical engineering, biosensor miniaturization, and long-term implantable sensing technologies will be instrumental in the development of next-generation high-performance biosensor systems.

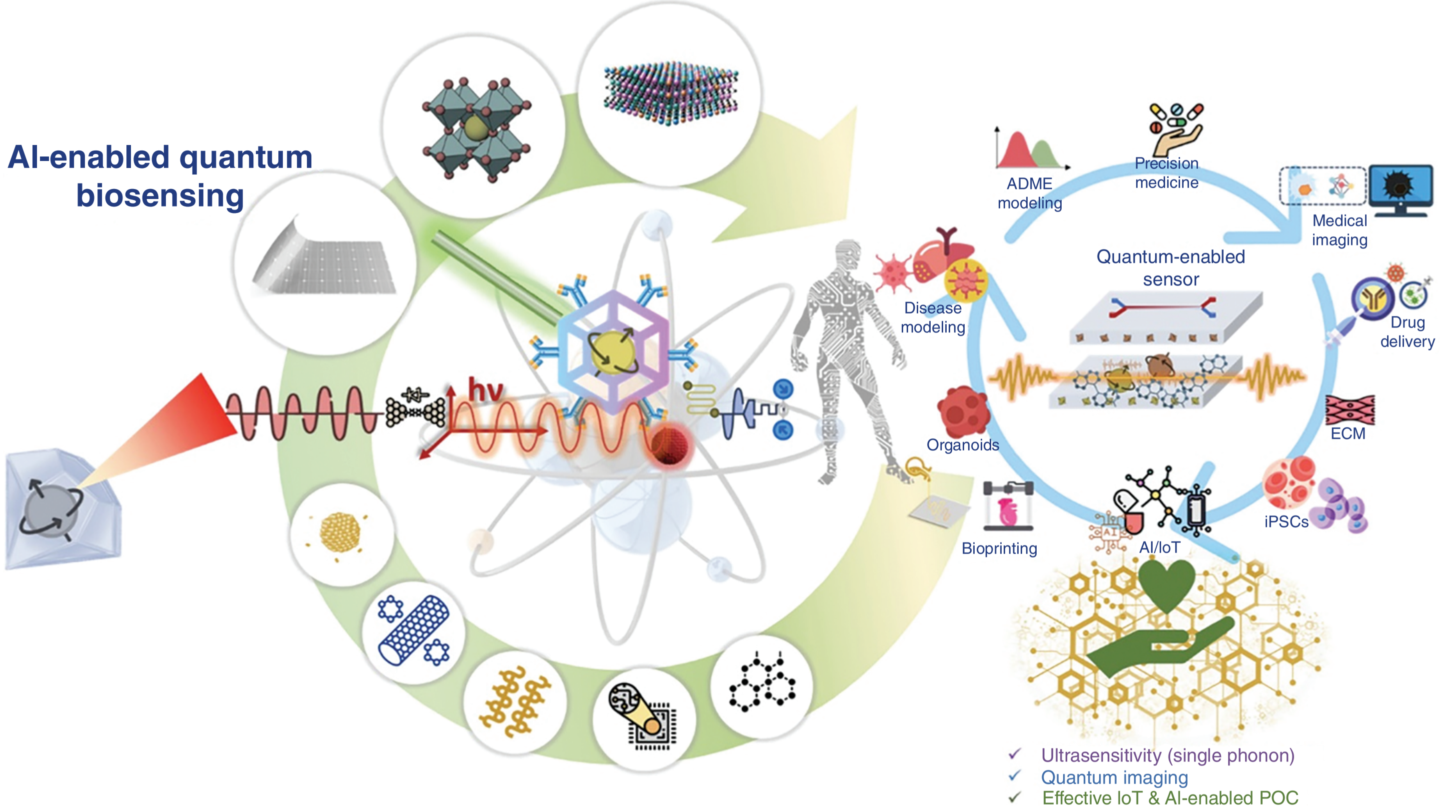

Figure 1.8 Futuristic plan of integration of AI into quantum biosensing to revolutionize medical diagnostics. Das et al. [28] / IOP Publishing / CC BY 4.0.

1.5 Conclusion

Quantum biosensing is revolutionizing modern diagnostics by offering incomparable sensitivity, specificity, and real-time biomolecular detection through fundamental QMs principles, including superposition, entanglement, and tunneling. These biosensors enable single-molecule detection, overcoming the limitations of conventional methods. The integration of QDs, NV centers in diamonds, and quantum photonics has further enhanced their performance, facilitating early precision medicine, disease detection, and continuous health monitoring. Beyond healthcare, QB demonstrates significant potential in environmental monitoring, food safety, and agriculture, highlighting its versatility across scientific disciplines. The convergence of AI, ML, and high-performance computing with QBs has expanded their diagnostic capabilities, enabling faster data analysis, noise reduction, and advanced pattern recognition in complex biological systems, as shown in Figure 1.8. These advancements support critical applications such as cancer biomarker identification, infectious disease detection, and therapeutic monitoring. Despite their transformative potential, challenges such as scalability, coherence preservation, specificity, and cost-efficiency remain, necessitating continuous research and innovation. Collaborative efforts among scientists, engineers, and medical professionals will be crucial in translating QBs into practical clinical applications.

As the field progresses, QBs are expected to redefine early disease detection, personalized treatment, and global healthcare outcomes. Their multiplexing capabilities, real-time monitoring, and precise biomarker detection enable rapid, non-invasive diagnostics, with significant applications in quantum-enhanced medical imaging, pathogen detection, and targeted therapy. The integration of AI and data analytics further improves diagnostic precision, while point-of-care biosensors optimize treatment regimens, reducing medication resistance risks. However, ethical, legal, and societal considerations-including privacy concerns, potential biases, and healthcare accessibility disparities-must be addressed to ensure equitable distribution and seamless clinical implementation. With continuous advancements, the synergy between nanotechnology, quantum computing, and biosensor miniaturization will drive the development of efficient, portable, and ultra-sensitive diagnostic platforms. Quantum biosensing is poised to redefine biomedical research and diagnostics, unlocking new possibilities for early disease intervention, precision medicine, and global healthcare improvements.

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