AUTHOR QUERIES

[AQ01]	As per publication guidelines, the first section of the chapter has been renamed to "Introduction". Please review and acknowledge if OK.	it's ok
[AQ02]	Please check the hierarchy of section titles, and amend if necessary.	it's ok
[AQ03]	As per style, all the display equations should be numbered. But few display equations are in unnumbered format. Please check and correct accordingly.	Fixed
[AQ04]	Please provide the publisher location for Refs. [4, 23, 25, 33, 35, 46, 73, 77, 90, 92, 93, 94, 100, 102, 114, 129].	Fixed
[AQ05]	Please provide the page range for Refs. [18, 71, 75, 87, 97, 115, 118].	Fixed
[AQ06]	Please provide the publisher name and the publisher location for Refs. [27, 32, 39, 49].	Fixed
[AQ07]	Please provide the volume for Refs. [30, 38, 55, 95].	Fixed
[AQ08]	Please provide the volume, page range for Ref. [88].	Fixed

Chapter

Recent Advances in Quantum Biosensing Technologies

Kelvin Tafadzwa Mpofu and Patience Mthunzi-Kufa

Abstract

Recent advances in biosensing technologies have revolutionized the field of biomedical diagnostics and environmental monitoring. This chapter reviews cutting-edge developments in quantum sensing and quantum biosensing, with examples including diamond defect sensing and quantum plasmonic biosensing, among other novel methodologies. Diamond defect sensing, leveraging nitrogen-vacancy centers in diamond, offers unparalleled sensitivity and precision in detecting magnetic and electric fields at the nanoscale. Quantum plasmonic biosensing, combining the unique properties of plasmons and quantum mechanics, enhances sensitivity and specificity, enabling the detection of biomolecules at ultra-low concentrations. Additionally, advancements in other quantum biosensing technologies, such as quantum dot-based sensors and single-photon detection, will be discussed, highlighting their potential applications in real-time, high-resolution biosensing. These innovative approaches promise to significantly improve the accuracy, speed, and versatility of biosensing, paving the way for new diagnostic tools and environmental monitoring solutions. The chapter will delve into the principles behind these technologies, their current applications, and the future directions they may take, providing a comprehensive overview of the transformative impact of quantum biosensing on medical diagnostics and beyond.

Keywords: quantum sensing, biosensing, precision, technologies, nitrogen vacancy, SQUIDs

1. Introduction

The continual rise in pandemics and epidemics has necessitated the development of more sensitive and precise biosensing technologies [1–3]. Biosensing, a field that has its roots in the mid-twentieth century, originally emerged with the development of the first enzyme-based sensors in the 1960s, such as the glucose biosensor [4]. These early devices were based on classical principles of chemistry and physics, and they laid the groundwork for a wide range of applications in medical diagnostics, environmental monitoring, and food safety. As the demand for more sensitive, accurate, and real-time detection methods grew, biosensing technologies evolved rapidly. The introduction of optical, electrochemical, and piezoelectric sensors marked significant milestones in the field [5]. By the late twentieth century, advances in nanotechnology and materials science further propelled biosensing capabilities, enabling the detection of analytes at increasingly lower concentrations and with greater specificity [6].

However, despite these advances, which have significantly improved sensitivity in biosensors, classical biosensors are inherently limited by the principles of classical physics (shot-noise limit [7–12]), limiting the sensitivity and precision that can be achieved. This is where quantum biosensing enters the scene, representing a paradigm shift in the way we approach biosensing challenges [13–16]. Quantum biosensing takes advantage of the unique properties of quantum mechanics, such as superposition, entanglement, and quantum coherence, to overcome the limitations of classical sensors [13, 17]. These quantum effects allow for the detection of small changes in biological systems with unparalleled sensitivity, even at the single-molecule level. Quantum biosensing not only builds on the foundation laid by classical biosensors but also extends the capabilities of biosensing to a level that was previously unattainable. This chapter explores recent advances in quantum biosensing technologies, highlighting key developments such as diamond defect sensing [18–22], quantum plasmonic biosensing, and other novel methodologies. By examining these cutting-edge technologies, we aim to provide a comprehensive overview of how quantum biosensing is revolutionizing the field of biomedical diagnostics and environmental monitoring, offering new tools and techniques that promise to transform how we detect and analyze biological systems.

Harnessing of quantum mechanics properties for practical applications has captivated physicists since the early twentieth century [23]. Finding a real-world application of quantum mechanics that exploits its unique principles has driven groundbreaking research in various fields, including quantum computing [24–28] and quantum cryptography [29–33]. These areas have long been considered the leading candidates for the most impactful quantum technologies. However, recent developments suggest that the potential of quantum mechanics extends beyond computation and encryption. A new frontier has emerged, known as quantum sensing [13, 34–39], which utilizes quantum mechanical systems to measure physical quantities with unprecedented sensitivity and precision.

Quantum sensing has the capability to reach measurement precision levels below the shot noise limit and potentially reaching the Heisenberg limit [13, 34]. This sensitivity, while a challenge in other quantum technologies, becomes a powerful asset in sensing applications. Quantum sensors can detect small changes in magnetic and electric fields, time, frequency, rotations, temperature, and pressure with precision below the shot noise limit [39–42]. This new trend in quantum technology mirrors the historical evolution of semiconductor technology, where sensors such as light meters based on selenium photocells found practical use long before the advent of semiconductor-based computers. An effective sensing tool should have high sensitivity, low precision, and high specificity [13]. For example, in biosensor devices, two commonly evaluated metrics are sensitivity and the detection limit, with the latter serving as an indicator of precision. Sensitivity can be mathematically represented as:

$$S_p = \frac{\partial O}{\partial p}, \tag{1}$$

where "p" represents an independent parameter that indicates the presence or absence of the target agent in the biosensor, and "O" is an observable that depends on "p". Sensitivity quantifies the rate at which changes are observed in response to variations in the independent parameter "p".

Although the formal recognition of quantum sensing as a distinct research field is relatively recent, its foundational concepts have deep roots in physics. High-resolution spectroscopy, particularly in atomic physics and magnetic resonance, has laid much of the groundwork for quantum sensing technologies. Established examples include atomic clocks, atomic vapor magnetometers, and superconducting quantum interference devices (SQUIDs) [42–46]. The novel aspects of contemporary quantum sensing arise from advancements such as the manipulation of quantum systems at the single-atom level, the use of entanglement to enhance sensitivity, and the deliberate design and engineering of quantum systems specifically for sensing purposes.

The development of quantum sensors represents a significant leap in measurement science, offering several advantages over classical sensors. Quantum sensors can operate at the nanoscale, detecting signals that classical sensors cannot access. They also promise enhanced precision and sensitivity, particularly when quantum entanglement is employed. This is especially relevant in applications where the ultimate goal is to achieve Heisenberg-limited measurements, where the precision of a measurement is pushed to the quantum mechanical limit. The motivation behind developing quantum sensing technologies extends beyond the pursuit of scientific knowledge. Quantum sensors hold the potential to revolutionize various fields, including medicine, environmental monitoring, and defense, by enabling measurements that were previously impossible. For instance, in biosensing, quantum technologies could lead to the development of ultra-sensitive diagnostic tools capable of detecting diseases at their earliest stages or monitoring biological processes at the molecular level. Quantum biosensing is a subset of quantum sensing. This chapter will explore the key concepts, developments, and methods of quantum sensing, with a particular focus on practical applications in biosensing. The discussion will cover the historical context of quantum sensing, its current state of development, and the future directions of this rapidly evolving field. By examining the fundamental principles that underlie quantum sensors and their real-world implementations, this chapter aims to provide a comprehensive introduction to students and researchers new to the field, as well as a valuable reference for those already engaged in quantum sensing research.

2. Examples of quantum sensors

Quantum sensors are advanced systems that utilize quantum coherence, interference, and entanglement to measure physical quantities with exceptional precision (**Figure 1**) [80]. These sensors are designed to exploit quantum mechanical effects to enhance sensitivity and accuracy to detect various physical parameters such as magnetic fields, temperature, and pressure. Unlike classical sensors, quantum sensors offer the potential for unprecedented sensitivity, allowing them to detect extremely weak signals that would otherwise be imperceptible. In this section, the authors describe different types of quantum sensors (**Table 1**).

One of the earliest and most well-known quantum sensors is the superconducting quantum interference device (SQUID) [71, 82]. SQUIDs are based on superconducting Josephson junctions and are capable of measuring minute magnetic fields with sensitivities as high as 10 aT $Hz^{-\frac{1}{2}}$ in controlled laboratory settings (**Figure 2**). These sensors have found commercial applications, particularly in

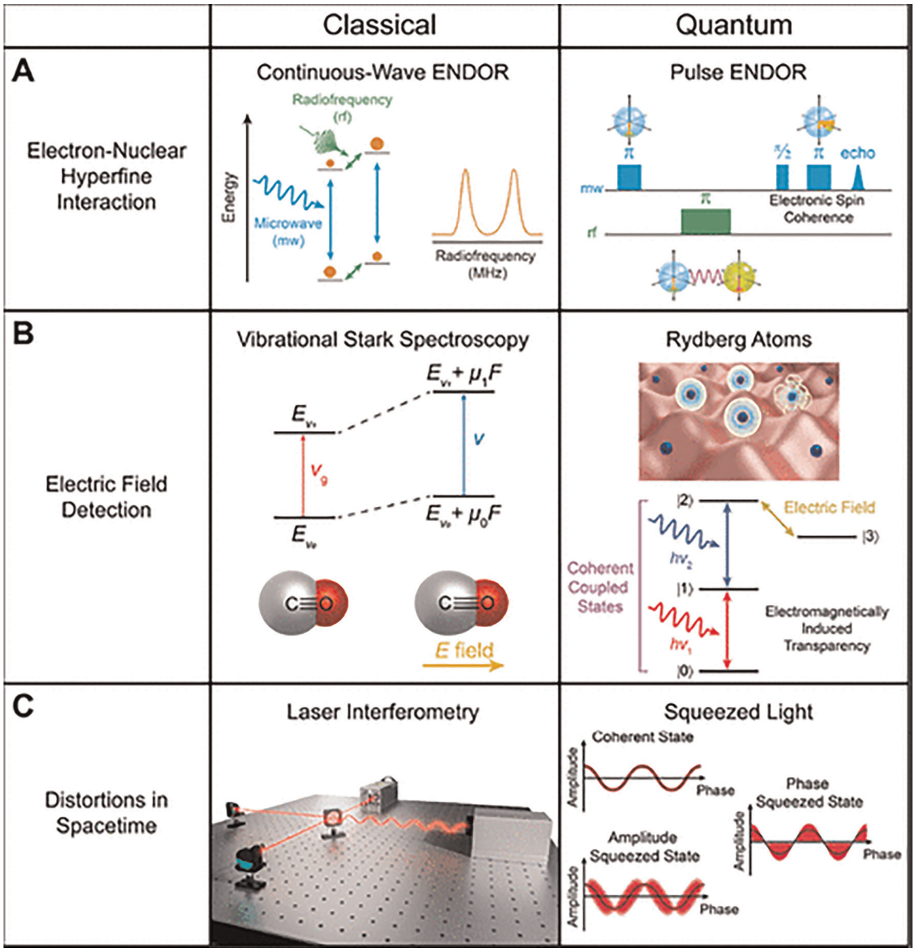


Figure 1.
Examples of classical versus quantum sensing techniques for (A) electron-nuclear hyperfine interactions, (B) electric field detection, and (C) spacetime distortions, highlighting quantum advancements such as coherence and entanglement [80].

magnetoencephalography (MEG), where they detect magnetic signals from the brain. However, the need for cryogenic operation imposes limitations on their use, requiring bulky setups and reducing the achievable spatial resolution in real-world applications.

Atomic ensemble-based quantum sensors, particularly those using alkali atoms like rubidium, have also been developed for magnetic field detection [83]. These sensors operate by spin-polarizing atomic vapors and probing their magnetic field coupling optically. This technique allows for high sensitivity, with coherence times reaching up to several minutes and magnetic field sensitivities of 100 aT $Hz^{-\frac{1}{2}}$ in laboratory conditions. Optically pumped magnetometers (OPMs), a type of atomic ensemble sensor (**Figure 3**), have been miniaturized for various applications, including nuclear magnetic resonance (NMR), magnetocardiography (MCG), and magnetic induction tomography. Despite their high sensitivity, these sensors require elevated operating temperatures and near-zero magnetic field environments, necessitating additional insulation and environmental control.

Type of quantum sensor	Introduction	Principles/techniques/types
Atomic clocks [47, 48]	Atomic clocks utilize the precise transition frequencies of atoms to keep time with exceptional precision.	Discuss the Hamiltonian describing the transition between two energy levels in an atom and techniques like Ramsey interferometry used in these clocks.
Quantum magnetometers [39, 49–54]	Magnetometers that measure magnetic fields with high sensitivity, leveraging quantum effects in systems like NV centers in diamond and superconducting qubits.	Explore the principles of the Zeeman effect and spin precession, central to quantum magnetometers.
Quantum interferometers [55]	Devices that measure phase differences between coherent waves, using quantum mechanical effects to enhance precision.	Discuss various interferometers like Mach-Zehnder, Michelson, and Sagnac and their applications in quantum sensing.
Optomechanical sensors [51–61]	Sensors that harness the interaction between light and mechanical systems, with applications in measuring minute displacements, forces, and fields.	To reach the quantum regime of sensitivity, optomechanical systems often use techniques like backaction evasion, where the measurement noise caused by quantum fluctuations in light is minimized.
Spin-based quantum sensors [62–65]	These sensors utilize the quantum properties of nitrogen-vacancy (NV) centers in diamond to detect magnetic fields with high sensitivity.	These sensors are used in nanoscale magnetic resonance imaging and in studying quantum effects in biological systems.
Photon-based quantum sensors [66–69]	These sensors utilize the quantum nature of photons to detect extremely low light levels.	Applications include quantum key distribution, astrophysics, and optical communication.
Superconducting quantum interference devices [70, 71]	SQUIDs exploit quantum interference in superconducting loops to measure extremely small magnetic fields, useful in fields ranging from medicine to material science.	SQUIDs are built around Josephson junctions, which allow for the flow of supercurrents across a thin insulating barrier between two superconductors. The phase difference of the superconducting wavefunction across the junction governs the current through the device.
Trapped ion quantum sensors [72–74]	Use trapped ions to achieve ultra-high precision in timekeeping and detecting minute forces.	• Ion clocks: Used in GPS and deep space navigation. • Force sensors: Used in fundamental physics experiments and tests of quantum mechanics.
Cold atom sensors [75–77]	Measure magnetic fields by detecting the precession of atomic spins in vapor cells.	Used in fundamental physics research and applications like mineral exploration.
Optomechanical crystals [78, 79]	Confine both optical and mechanical modes, enabling strong coupling and high sensitivity.	Used in detecting minute forces and displacements, with applications in precision measurement and quantum information processing.

Table 1.
Types of quantum sensors.

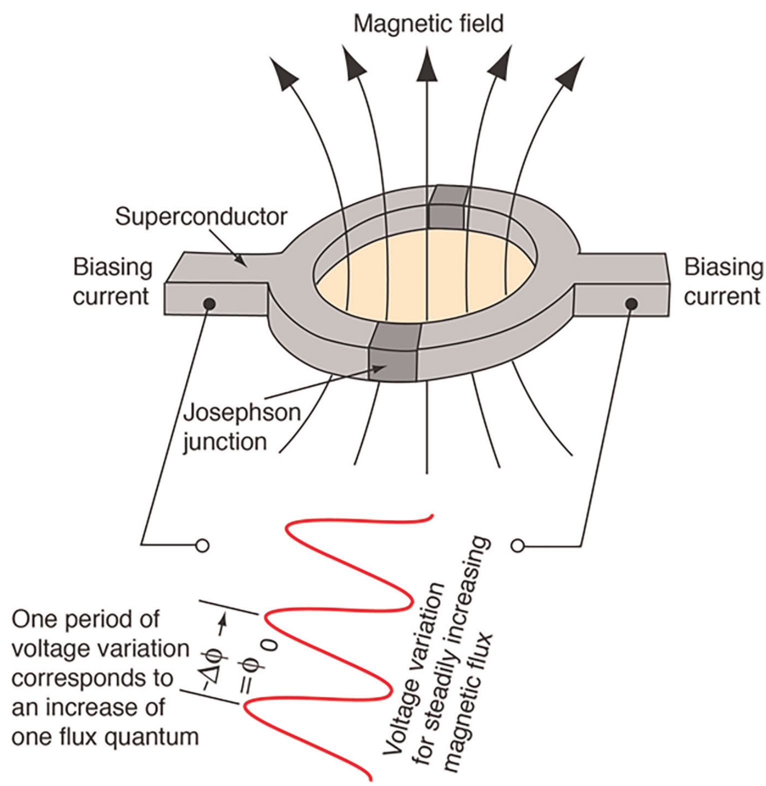
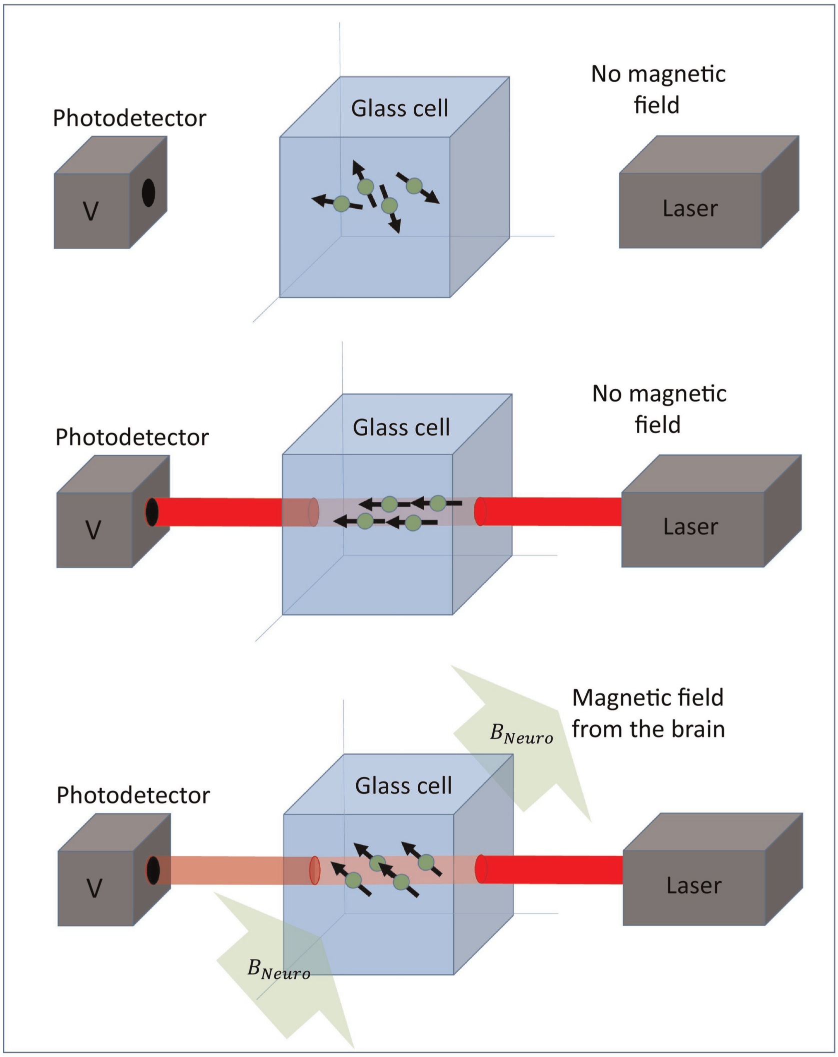


Figure 2.
Illustration of a superconducting quantum interference device (SQUID). The SQUID consists of a superconducting loop containing one or more Josephson junctions. It is highly sensitive to magnetic fields, making it a powerful tool in quantum sensing and metrology [81].

Another class of quantum sensors are those based on solid-state spins, such as nitrogen-vacancy (NV) centers in diamond, which have garnered significant attention due to their unique properties (**Figure 4**). Diamond is a crystal composed of carbon atoms. When a carbon atom in the diamond's lattice is substituted with a nitrogen atom, it creates electron vacancies, leading to the formation of nitrogen-vacancy centers. These NV centers are highly sensitive to environmental changes and alterations in their quantum state, making them useful as sensors. Consequently, diamonds containing NV centers are recognized as quantum sensors and are gaining attention as cutting-edge, ultra-sensitive sensors. Additionally, nitrogen-vacancy centers are promising candidates for qubits in quantum computing and quantum simulation due to their capability to function at room temperature. NV centers are defects in the diamond lattice that can be optically initialized and read out, offering high sensitivity to magnetic fields, temperature, electric fields, and pressure. These centers can operate over a broad range of conditions, including temperatures from 4 K to 625 K, magnetic fields up to 8.3 T, and pressures up to 13.6 GPa. The sensitivity of NV-based magnetometers can be enhanced using an ensemble of NV centers, achieving sensitivities around 1 pT $Hz^{-\frac{1}{2}}$. Furthermore, NV centers can be integrated into nanodiamonds for localized sensing, making them highly versatile for applications ranging from wide-field imaging to nanoscale diagnostics.

DOI: http://dx.doi.org/10.5772/intechopen.1007858



Trends in Neurosciences

Figure 3.
Schematic operation of an optically pumped magnetometer (OPM): top panel shows a glass cell without an applied magnetic field, with randomly oriented atomic spins. The middle panel illustrates the effect of laser light passing through the glass cell, aligning atomic spins along the laser axis in the absence of a magnetic field. In the bottom panel, a magnetic field from the brain (BNeuro) causes a rotation in the atomic spins, altering the polarization of the laser light as it exits the cell, which is then detected by a photodetector [84].

Quantum sensors like OPMs and NV centers have complementary strengths that make them suitable for different applications. OPMs, with their high sensitivity, are ideal for macroscopic detection of weak magnetic fields generated by organs such as the brain and heart. In contrast, NV centers excel in high spatial resolution due to their proximity to the sample, making them suitable for detecting microscopic signals at the cellular level. Additionally, the multifunctionality of NV centers, capable of detecting magnetic fields, temperature, and other parameters, makes them valuable tools for spectroscopy and diagnostics in biomedical applications.

Overall, quantum sensors represent a rapidly advancing field with the potential to revolutionize various industries by providing tools for precise and sensitive

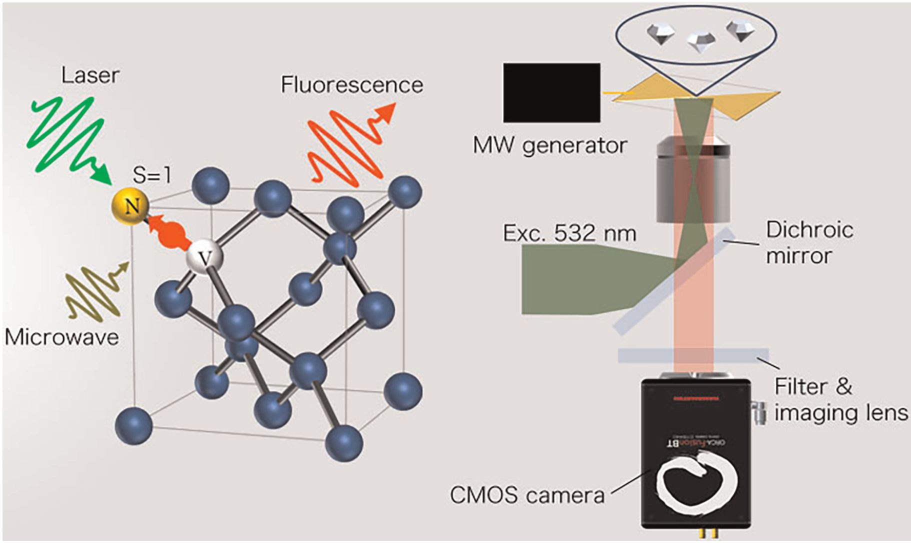


Figure 4.
The image illustrates a quantum sensing setup utilizing nitrogen-vacancy (NV) centers in diamond. A laser with a wavelength of 532 nm excites the NV centers, while microwaves are applied to manipulate their spin state (S = 1). The resulting fluorescence, modulated by the spin state, is detected by a CMOS camera through a dichroic mirror and an imaging lens. The NV centers' fluorescence provides information about magnetic fields, temperature, or other quantum properties, making it a powerful tool for precision sensing in various applications [85].

measurements at both macroscopic and microscopic scales. Single-photon sensing is also a critical phenomenon, which is studied frequently [86].

2.1 Atomic clocks

Atomic clocks use the highly precise transition frequencies of atoms to maintain time with extraordinary accuracy, outperforming traditional timekeeping devices by orders of magnitude. These clocks typically measure the energy difference between two states of an atom, such as the hyperfine levels in cesium or rubidium, where the Hamiltonian describing the transition between these states is key to their operation. The time evolution of these energy states can be modeled using a Hamiltonian of the form:

$$\hat{H} = \hbar\omega_0\hat{\sigma}_z$$

where ω_0 is the resonant frequency of the transition, and $\hat{\sigma}_z$ is the Pauli matrix for the energy levels. Techniques like Ramsey interferometry, which involves a sequence of microwave pulses separated by a free evolution period, are utilized to increase the precision of atomic clocks. These interferometric techniques allow for measuring the phase difference between atomic states, offering a robust method to track time with exceptional precision.

2.2 Quantum magnetometers

Quantum magnetometers measure magnetic fields with extreme sensitivity by harnessing quantum effects in specific materials such as NV centers in diamond or superconducting qubits. These devices exploit the Zeeman effect, where the energy

DOI: http://dx.doi.org/10.5772/intechopen.1007858

levels of particles split in response to an external magnetic field, and the principles of spin precession. The Hamiltonian governing the NV centers in the presence of a magnetic field can be expressed as:

$$\hat{H} = D\hat{S}_z^2 + \gamma B_z \hat{S}_z$$

where D is the zero-field splitting parameter, γ is the gyromagnetic ratio, and B_z is the external magnetic field. By measuring the precession of the spins, quantum magnetometers can detect even minute changes in the magnetic field, with applications in both fundamental physics and biological systems.

2.3 Quantum interferometers

Quantum interferometers are devices that measure phase differences between coherent waves, often utilizing quantum mechanical principles to enhance precision. Common interferometers such as the Mach-Zehnder, Michelson, and Sagnac interferometers are designed to split a beam of light into two paths, later recombining them to detect phase shifts caused by the environment. The Mach-Zehnder interferometer, for instance, can be described by unitary operations corresponding to beam splitters and phase shifters, and it is widely used in quantum sensing and gravitational wave detection. Quantum mechanical effects like superposition allow interferometers to measure these phase shifts with remarkable sensitivity, making them essential in precision measurement tasks.

2.4 Optomechanical sensors

Optomechanical sensors exploit the interaction between light and mechanical systems to detect tiny displacements, forces, and fields. These systems operate in the quantum regime by coupling the mechanical motion of mirrors or membranes to the light field within an optical cavity. A common challenge in these systems is the quantum backaction, where the quantum fluctuations in the light field induce measurement noise in the mechanical system. Techniques like backaction evasion are employed to mitigate this noise, using cleverly designed measurement schemes to push the sensitivity of these sensors to their quantum limits. Optomechanical sensors are pivotal in detecting weak forces and are widely used in gravitational wave detection and fundamental tests of quantum mechanics.

2.5 Spin-based quantum sensors

Spin-based quantum sensors make use of NV centers in diamond or other spintronic materials to detect magnetic fields at the nanoscale. The quantum properties of these spins allow them to act as highly sensitive detectors of magnetic fields, especially useful in nanoscale magnetic resonance imaging (MRI) and biological systems. The interaction between the NV center's spin state and external magnetic fields causes shifts in energy levels, which can be detected via fluorescence. These sensors are invaluable in biological imaging, quantum control experiments, and material science applications.

2.6 Photon-based quantum sensors

Photon-based quantum sensors utilize the quantum properties of light, particularly single-photon detection, to achieve exceptional sensitivity in low-light environments.

These sensors are widely used in quantum key distribution (QKD), where the secure transmission of information is guaranteed by the fundamental principles of quantum mechanics. Moreover, they find applications in optical communications, astrophysics, and precision measurement systems. Photon-based quantum sensors push the boundaries of sensitivity and precision, opening up new possibilities in secure communication and scientific research.

2.7 Superconducting quantum interference devices (SQUIDs)

SQUIDs operate by exploiting quantum interference in superconducting loops, enabling them to measure extremely small magnetic fields. The core component of a SQUID is the Josephson junction, which allows for supercurrents to flow across an insulating barrier between two superconductors. The current through the device is controlled by the phase difference of the superconducting wavefunctions on either side of the junction, which in turn depends on the external magnetic field. SQUIDs are crucial in various fields ranging from medicine, where they are used in magnetoencephalography (MEG), to material science and fundamental physics experiments.

2.8 Trapped ion quantum sensors

Trapped ion quantum sensors achieve ultra-high precision in measuring time and detecting minute forces by trapping single ions in electromagnetic fields. These sensors are often used in atomic clocks and force detection experiments. In atomic ion clocks, trapped ions such as aluminum or mercury are used to measure time with incredible precision, while in force sensors, trapped ions can detect tiny displacements and forces, contributing to advancements in fundamental physics and quantum mechanics tests.

2.9 Cold atom sensors

Cold atom sensors measure magnetic fields by detecting the precession of atomic spins in vapor cells. These sensors are highly sensitive to magnetic fields and are used in a variety of applications, from fundamental physics research to mineral exploration. By cooling the atoms to near absolute zero, the sensor increases its precision and sensitivity, allowing for better measurements of weak magnetic fields.

2.10 Optomechanical crystals

Optomechanical crystals are engineered to confine both optical and mechanical modes, enabling strong coupling between light and mechanical vibrations. This strong coupling enhances the sensitivity of these systems to detect minute forces and displacements. Optomechanical crystals are integral to precision measurement applications, where detecting small changes in position or force with high sensitivity is critical, and they also play a role in quantum information processing.

3. Examples of quantum biosensors

Quantum biosensing is an emerging field at the intersection of quantum physics and biological sensing, offering unprecedented sensitivity and precision in detecting biological molecules. This innovative technology leverages the unique properties of quantum systems, such as superposition, entanglement, and quantum coherence, to measure extremely low concentrations of biological analytes, even at the single-molecule level. One of the key advantages of quantum biosensors is their ability to detect subtle changes in biological systems with a level of sensitivity that surpasses traditional biosensors. This is achieved through the integration of quantum phenomena into the sensing mechanisms, enabling the detection of minute variations in environmental factors such as temperature, magnetic fields, and chemical concentrations.

3.1 Quantum plasmonic biosensors

Quantum plasmonic biosensors are a notable category within quantum biosensing, utilizing the interaction between quantum light and plasmons—coherent oscillations of free electrons at the surface of a metal—to achieve enhanced detection capabilities. An example of these biosensors is that which operates based on surface plasmon resonance (SPR) (**Figure 5**), a technique that allows for label-free detection of biomolecules with high sensitivity [88–90]. Quantum enhancements in plasmonic biosensing have shown potential to achieve sensitivities below the shot-noise limit, enabling the detection of single molecules or even smaller biological entities. Recent advancements have demonstrated the use of quantum light sources, such as squeezed light and entangled photons, in plasmonic biosensing, leading to significant improvements in the SNR and detection accuracy. For example, quantum plasmonic biosensors have been employed in various applications, including the detection of cancer biomarkers and real-time monitoring of molecular interactions.

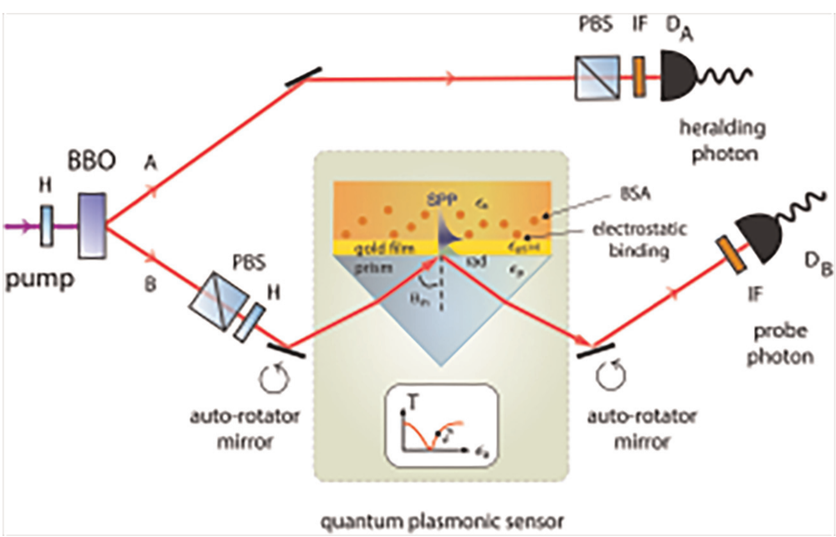


Figure 5.
A schematic representation of a quantum plasmonic sensor setup. The system utilizes a pump source to generate photon pairs through a beta barium borate (BBO) crystal. The heralding photon (path A) is directed toward detector D_A, while the probe photon (path B) interacts with a surface plasmon polariton (SPP) mode on a gold film prism, where biotin-streptavidin (BSA) binding is used for sensing. Polarizing beam splitters (PBS) and interference filters (IF) are used to manage the photonic paths, with auto-rotator mirrors adjusting the polarization states of the probe photon. The transmitted signal is detected by D_B, providing information about the target analyte's presence and concentration. This image is taken from [87].

3.2 Quantum Raman spectroscopy

Raman scattering is a phenomenon in which light interacts with the molecular vibrations of a material, causing the light to scatter and shift in wavelength [91–93]. This shift provides information about the molecular structure, chemical composition, and physical properties of the material being studied. Raman scattering is a relatively rare event, occurring in only about 1 out of every 1 million photons that interact with a sample (**Figure 6**), which usually necessitates the use of a high-power light source to excite the sample [94, 95]. Recent advancements in quantum biosensing and sensing technologies have yielded several notable breakthroughs. One example is coherent Raman microscopy, where a bright squeezed state was employed to reduce imaging noise below the shot-noise limit [96]. Additionally, stimulated emission microscopy has seen improvements through the use of intensity-squeezed light, enabling sub-shot-noise limited microscopy [97]. Further research in quantum-enhanced continuous-wave stimulated Raman scattering spectroscopy utilized squeezed bright light to reduce the SNR ratio by 3.60 dB relative to the shot-noise limit [98]. Surface-enhanced Raman scattering (SERS) is a technique that amplifies Raman scattering by utilizing a metal surface as the sample substrate. This enhancement occurs through two main mechanisms, the first being electric field enhancement, generated by the excitation of localized surface plasmons. When molecules are within this enhanced electric field, the likelihood of Raman scattering increases significantly. The second mechanism involves chemical enhancement, which arises from inter- and intra-molecular charge transfer between the metal and the target molecule. As a result, SERS is a non-destructive, highly sensitive technique that can detect extremely low concentrations of a sample using much lower laser power than what classical Raman measurements require.

Classical optical detection techniques are inherently limited by shot noise, which imposes a fundamental restriction on the accuracy of spectroscopic measurements. In the pursuit of overcoming these classical limits, quantum Raman (qRaman) spectroscopy emerges as a novel approach that leverages non-classical light to achieve high-precision spectroscopic fingerprinting. This advancement opens new avenues for high-accuracy medical diagnostics, particularly in the context of biomarker identification at the single cellular level, which is crucial for understanding disease status and progression. Raman spectroscopy is a powerful analytical tool for identifying biomarkers that correlate with disease, especially at the single-cell level. However, inherently weak Raman signals obtained from small biological samples present a significant challenge. To

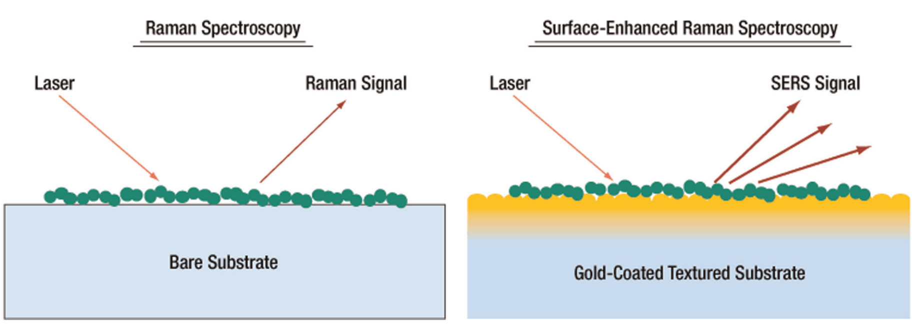


Figure 6.
Comparison of Raman Spectroscopy and Surface-Enhanced Raman Spectroscopy (SERS): the left panel illustrates Raman spectroscopy using a bare substrate, where a laser excites the sample, resulting in a weak Raman signal. The right panel shows SERS using a gold-coated textured substrate, which significantly enhances the Raman signal through the excitation of localized surface plasmons, allowing for a much stronger SERS signal with lower laser power [99].

achieve satisfactory signal-to-noise ratios (SNR), classical Raman spectroscopy often requires the use of high optical powers. This requirement poses a dilemma in biological systems, where maintaining optical intensity below certain thresholds is essential to avoid damaging the specimens or altering their biological dynamics. Such damage could lead to erroneous results, compromising the integrity of the diagnostic process. In response to these challenges, the qRaman project aims to revolutionize the field of optical microscopy for biomedical and bio-imaging applications by developing a novel quantum Raman microscope. This cutting-edge system introduces a new paradigm in quantum bio-optical measurements by integrating pulsed non-classical squeezed light with stimulated Raman scattering (SRS). SRS is a highly effective technique for studying the spatio-temporal dynamics of molecular bonds within biological specimens, offering high sensitivity and speed. The utilization of an amplitude-squeezed probe beam in this context allows for a significant improvement in the achievable SNR at lower optical intensity levels, thereby mitigating the risk of optical damage to the sample. This approach not only preserves the integrity of the biological specimens but also enhances the accuracy and reliability of the measurements.

An example of a qRaman project is the QuRAMAN system, which is specifically designed to support intraoperative decision-making in cancer screening, with a focus on lung cancer diagnostics [100]. Currently, the assessment of cancerous tissues relies heavily on the subjective judgment of trained pathologists during intraoperative examination of frozen sections. This process is both costly and time-consuming, requiring years of specialized training and experience. The QuRAMAN microscope seeks to address these limitations by providing a fast, objective, and reliable diagnostic tool that could significantly reduce the reliance on subjective assessments [100]. The QuRAMAN project is working on three main things: making the quantum Raman microscope better at finding lung cancer in human tissue, testing the quantum Raman microscope on human tissue, and giving manufacturers an OEM light source and a small microscope that they can just plug in and use [100]. These components are intended to support bioimaging and quantum technologies across various sectors, including education, science, and industry. By addressing the intersection of quantum optics, bio-optics, and Raman spectroscopy, the QuRAMAN device is poised to push the boundaries of current medical diagnostic tools [100]. Its applications in quantum metrology and quantum sensing are expected to have significant implications for the biomedical sciences, particularly in the early and accurate detection of cancer. The interdisciplinary nature of the QuRAMAN project holds the promise of fostering innovation and collaboration across traditionally distinct fields, ultimately leading to more effective and efficient diagnostic solutions in medical practice.

3.3 Nitrogen vacancy (NV) center biosensors

Another prominent quantum biosensing technology is based on NV centers in diamonds [101]. NV centers are defects in the diamond lattice that possess unique quantum properties, making them highly sensitive to magnetic fields, temperature, and other environmental parameters. NV center biosensors are particularly advantageous for their ability to operate at room temperature and provide non-invasive, real-time monitoring of biological processes. The application of NV centers in biosensing includes MRI at the nanoscale, detection of single molecules, and the measurement of intracellular processes. These sensors are capable of detecting variations in magnetic fields with exceptional spatial resolution, which is crucial for applications such as tracking the movement of molecules within cells or detecting minute changes in the local environment of biomolecules.

3.4 Quantum dot-based quantum biosensors

Quantum dot-based quantum biosensors represent an advanced class of biosensing devices that combine the unique properties of QDs with quantum principles to enhance the detection and analysis of biological molecules [102]. Quantum dots, which are semiconductor nanocrystals, are prized for their size-tunable fluorescence, high photostability, and narrow emission spectra, making them ideal for sensitive and multiplexed detection. When integrated with quantum techniques, these biosensors can exploit quantum coherence, entanglement, and other quantum phenomena to achieve even greater sensitivity and specificity in detecting biomolecules. Quantum dot-based quantum biosensors are particularly promising in applications requiring ultra-sensitive detection, such as in medical diagnostics, where they can identify trace amounts of biomarkers for diseases like cancer, neurodegenerative disorders, and infectious diseases. Additionally, these biosensors have potential in environmental monitoring, detecting low concentrations of pollutants or pathogens with unprecedented accuracy. The ability to use quantum dots of different sizes enables multiplexing, allowing simultaneous detection of multiple targets within a single sample. Moreover, the integration of quantum dots with quantum technologies opens new avenues in quantum imaging and sensing, where quantum effects can improve resolution and signal-to-noise ratios. However, challenges remain, particularly regarding the biocompatibility and potential toxicity of quantum dot materials, as well as the complexity of integrating quantum principles into practical biosensor designs. Despite these hurdles, quantum dot-based quantum biosensors are at the forefront of biosensing technology, offering the potential for breakthroughs in both diagnostic and environmental applications by harnessing the power of quantum mechanics.

4. Solid-state quantum biosensors

Solid-state quantum biosensors, which include systems like NV centers and quantum dots, represent a robust platform for integrating quantum technology into practical sensing devices [103–105]. These biosensors are characterized by their solid-state nature, which offers advantages in terms of stability, miniaturization, and integration into existing technologies. Solid-state quantum biosensors have been employed in a range of applications, from environmental monitoring to medical diagnostics, because of their ability to operate in diverse conditions and compatibility with various sensing modalities. Quantum biosensing represents a transformative approach in the field of biosensors with the potential to revolutionize medical diagnostics, environmental monitoring, and many other fields. More work on quantum plasmonic biosensors, NV center-based sensors, and solid-state quantum biosensors is likely to make biosensors more sensitive, accurate, and useful, which will make it easier for them to be used in many clinical and research settings. The integration of quantum technologies into biosensing platforms not only enhances detection capabilities but also opens new avenues for exploring complex biological processes with unprecedented detail.

5. Single-photon sensing

Single-photon sensing plays a pivotal role in quantum sensing technologies [106–109]. This capability allows for the detection of individual photons, which is essential in various quantum systems, from quantum communication to quantum imaging. Single-photon detectors are vital for measuring weak signals with high precision, enabling enhanced sensitivity in experiments that operate at the quantum limit. For instance, in quantum key distribution (QKD) and other quantum cryptographic protocols, the ability to detect individual photons ensures the security of information transmission. Moreover, single-photon sensing is critical in developing ultra-sensitive biosensors and imaging systems, where the detection of single-photon events can provide deeper insights into molecular-level interactions. By leveraging quantum properties such as superposition and entanglement, single-photon detection opens the door to unprecedented levels of precision and accuracy, which is crucial for advancing quantum sensing applications [110]. Single-photon sensing is critical in enhancing the sensitivity and precision of quantum biosensing technologies, particularly in detecting low-concentration biomarkers. In biosensor applications, biomarkers are biological molecules that indicate a particular disease state, infection, or other physiological conditions. Examples of biomarkers commonly detected in sensor applications include:

- *Prostate-specific antigen* (*PSA*): PSA is a protein biomarker used to detect prostate cancer [111]. Quantum-based biosensors, including those using single-photon detection, have shown potential in improving sensitivity for early detection, especially at low PSA concentrations in blood samples.

- *C-reactive protein* (*CRP*): CRP is a biomarker associated with inflammation and cardiovascular diseases [112]. Quantum biosensors utilizing single-photon technologies have demonstrated enhanced detection of CRP levels, allowing for earlier diagnosis of inflammatory conditions.

- *Cardiac troponins*: Cardiac troponins are essential biomarkers for detecting myocardial infarctions (heart attacks) [113]. Single-photon sensing in optical biosensors have the capacity for enabled rapid and highly sensitive detection of cardiac troponins, improving response times in critical care settings.

- *DNA sequences*: Quantum sensing can also be applied to detect specific DNA sequences used as biomarkers for various genetic disorders and infectious diseases. The ability to detect single-photon events enhances the sensitivity required for identifying low concentrations of target DNA, enabling early-stage diagnostics for diseases such as cancer and viral infections.

In each of these cases, the ability to detect individual photons enhances the biosensor's performance by allowing for detection at ultra-low concentrations, reducing false negatives, and increasing the dynamic range. This makes single-photon sensing an indispensable tool in biosensing technologies aimed at biomarker detection, pushing the boundaries of medical diagnostics.

6. Examples of quantum states in optical sensing

Quantum metrology studies the potential of different quantum states to enhance the precision of quantum systems [114–117]. Examples of quantum states used in optical sensors are squeezed states, entangled states such as NOON states, Fock states, and coherent states [88]. In optical sensing, quantum states can be harnessed to

Method	Description	Reference
Spontaneous parametric down-conversion	A nonlinear crystal is pumped by a laser to generate pairs of correlated photons at half the pump frequency.	[121–124]
Four-wave mixing (FWM)	Involves the interaction of several light fields in a nonlinear medium, leading to the generation of new fields.	[125]
Optomechanical squeezing	The motion of a mechanical oscillator is coupled to the amplitude or phase of a light field. Properly driving these systems can lead to the generation of squeezed light.	[126, 127]
Squeezing via Feedback	Involves detecting the noise in a system and then feeding back a signal to reduce that noise, effectively squeezing the state.	[128, 129]
Quantum dots	Can be used to produce single photons, and under certain conditions, they can be used to produce squeezed light.	[130]

Table 2.
Methods of squeezed light generation.

achieve ultra-sensitive detection. By manipulating light at the quantum level, we can enhance signal-to-noise ratios, reduce uncertainty in measurements, and even enable new sensing modalities that were previously unattainable. For instance, techniques that generate non-classical light, such as squeezed states (**Table 2**) or entangled photons, can dramatically improve the precision of measurements in optical systems. These quantum states enable sensors to operate below the classical shot-noise limit, pushing the boundaries of precision. An exemplary development is the use of entangled photons, specifically a two-photon NOON state, for protein concentration measurements; this work provided proof of concept for the application of quantum states to a biosensing experiment and displayed the potential of quantum biosensors [118]. In quantum magnetometry, a quantum-enhanced optomechanical magnetometer was developed using squeezed light, resulting in a 20% improvement in magnetic field sensitivity [119]. Single-molecule detection at the quantum noise limit was achieved using a coherent state for biosensing, and particle tracking in living cells was enhanced by 42% using a squeezed local oscillator [120]. Additional advancements include the use of a squeezed local oscillator for particle tracking with sub-diffraction limit spatial resolution and quantum-enhanced microcantilever displacement measurement with squeezed light [120]. There are several key methods for generating and manipulating quantum states in optical systems, each with distinct advantages for different sensing applications. **Table 2** shows some of the most widely used methods for generating squeezed quantum states in optical sensors.

7. Recent advances and challenges with quantum biosensors

7.1 Limitations

Despite the promising potential of quantum biosensing technologies, several challenges remain. One significant limitation is the complexity of integrating quantum sensors into practical, user-friendly devices suitable for widespread clinical use. The cost and technical expertise required to operate quantum sensors may also hinder their adoption in low-resource settings. Furthermore, many quantum biosensing platforms, such as those utilizing NV centers or quantum dots, require precise environmental

DOI: http://dx.doi.org/10.5772/intechopen.1007858

controls to maintain their sensitivity, which may limit their applicability in real-world settings. Another limitation is the scalability of quantum biosensing technologies. While proof-of-concept experiments have shown remarkable results, transitioning these technologies from laboratory-scale experiments to mass production remains a challenge. Additionally, ensuring the biocompatibility of quantum sensors, particularly those using materials such as quantum dots, is critical to avoid toxicity in biological applications. Addressing these limitations will require interdisciplinary collaboration across fields such as quantum physics, materials science, and biomedical engineering, along with continued investment in research and development. As these challenges are overcome, quantum biosensing technologies will likely become a transformative force in diagnostics and environmental monitoring.

7.2 Future directions

The future of quantum biosensing holds numerous exciting possibilities. Continued research into quantum-enhanced detection methods, such as quantum plasmonics, quantum dot biosensors, and NV centers, could lead to even greater improvements in sensitivity and specificity. Future developments may focus on miniaturizing quantum biosensing platforms, making them more accessible for point-of-care diagnostics and personalized medicine. Moreover, the integration of artificial intelligence and machine learning algorithms with quantum sensors could allow for the analysis of large-scale biosensing data in real time, providing more accurate and faster results. Quantum biosensing is also expected to expand its applications beyond biomedical diagnostics into areas such as food safety, environmental monitoring, and industrial quality control. By leveraging the capabilities of quantum mechanics, future biosensors may be able to detect a wider range of chemical and biological agents with unprecedented precision. Furthermore, advances in quantum metrology could improve the accuracy of biosensing devices, making them invaluable tools for research in molecular biology and biochemistry.

8. Conclusions

Recent advances in quantum biosensing technologies have revolutionized the field of biomedical diagnostics and environmental monitoring. The integration of quantum principles such as superposition, entanglement, and quantum coherence into biosensing platforms has enabled unprecedented levels of sensitivity and specificity in detecting biomolecules at ultra-low concentrations. Key innovations, including diamond defect sensing and quantum plasmonic biosensing, have demonstrated their potential in real-time, high-resolution biosensing applications. These technologies, in conjunction with quantum dot-based biosensors and single-photon detection, hold the promise of transforming the precision and speed of diagnostics, offering new opportunities for early disease detection and environmental monitoring. As this chapter has explored, the unique properties of quantum sensors have the potential to overcome the limitations of classical biosensing approaches. This shift marks a new era in biosensing capabilities, opening the door for future research and clinical applications that will continue to push the boundaries of what can be achieved in detecting and analyzing biological systems. The ongoing development of quantum biosensing technologies is expected to play a crucial role in addressing global health challenges, environmental sustainability, and the development of next-generation diagnostic tools.

Acknowledgements

The authors acknowledge the Council for Scientific and Industrial Research (CSIR) and the Department of Science and Innovation (DSI) for the grant of funding for this research. K.M. was also supported by the South African Quantum Technology Initiative (SAQuTi) and South African Medical Research Council (SAMRC).

Conflict of interest

The authors declare no conflict of interest.

Nomenclature

SPR	surface plasmon resonance
LSPR	localized surface plasmon resonance
NV	nitrogen vacancy
VQE	variational quantum eigensolver
OAQA	optimization algorithm for quantum annealers
SERS	surface-enhanced Raman spectroscopy
MEG	magnetoencephalography
SNR	signal-to-noise ratio
MRI	magnetic resonance imaging
NMR	nuclear magnetic resonance
SQUID	superconducting quantum interference device

DOI: http://dx.doi.org/10.5772/intechopen.1007858

Author details

Kelvin Tafadzwa Mpofu[1*†] and Patience Mthunzi-Kufa[1,2,3†]

1 Biophotonics, Photonic Centre, Manufacturing, Council of Scientific and Industrial Research (CSIR), Pretoria, South Africa

2 Molecular and Cell Biology Department, University of Cape Town, Cape Town, South Africa

3 School of Interdisciplinary Research and Graduate Studies (UNESCO), College of Graduate Studies, University of South Africa, Pretoria, South Africa

*Address all correspondence to: kmpofu@csir.co.za

† These authors contributed equally.

References

[1] Erdem O, Eş I, Saylan Y, Inci F. Unifying the efforts of medicine, chemistry, and engineering in biosensing technologies to tackle the challenges of the covid-19 pandemic. Analytical Chemistry. 2021;**94**(1):3-25

[2] de Araujo WR, Lukas H, Torres MD, Gao W, de la Fuente-Nunez C. Low-cost biosensor technologies for rapid detection of covid-19 and future pandemics. ACS Nano. 2024;**18**(3):1757-1777

[3] Kabay G, DeCastro J, Altay A, Smith K, Lu H-W, Capossela AM, et al. Emerging biosensing technologies for the diagnostics of viral infectious diseases. Advanced Materials. 2022;**34**(30):2201085

AQ04 [4] Franklin RK. In vivo electrochemical sensors. University of Michigan; 2010

[5] Feyziazar M, Amini M, Jahanban-Esfahlan A, Baradaran B, Oroojalian F, Kamrani A, et al. Recent advances on the piezoelectric, electrochemical, and optical biosensors for the detection of protozoan pathogens. TrAC Trends in Analytical Chemistry. 2022;**157**:116803

[6] Ramesh M, Janani R, Deepa C, Rajeshkumar L. Nanotechnology-enabled biosensors: A review of fundamentals, design principles, materials, and applications. Biosensors. 2022;**13**(1):40

[7] Xiao M, Wu L-A, Kimble HJ. Precision measurement beyond the shot-noise limit. Physical Review Letters. 1987;**59**(3):278

[8] Gover A, Nause A, Dyunin E, Fedurin M. Beating the shot-noise limit. Nature Physics. 2012;**8**(12):877-880

[9] T. L. S. Collaboration. A gravitational wave observatory operating beyond the quantum shot-noise limit. Nature Physics. 2011;**7**(12):962-965

[10] Slussarenko S, Weston MM, Chrzanowski HM, Shalm LK, Verma VB, Nam SW, et al. Unconditional violation of the shot-noise limit in photonic quantum metrology. Nature Photonics. 2017;**11**(11):700-703

[11] Beenakker C, Patra M. Photon shot noise. Modern Physics Letters B. 1999;**13**(11):337-347

[12] Pooser RC, Lawrie B. Plasmonic trace sensing below the photon shot noise limit. ACS Photonics. 2016;**3**(1):8-13

[13] Dowling JP. Quantum optical metrology–the lowdown on high-n00n states. Contemporary Physics. 2008;**49**(2):125-143

[14] Dür W, Skotiniotis M, Froewis F, Kraus B. Improved quantum metrology using quantum error correction. Physical Review Letters. 2014;**112**(8):080801

[15] Szczykulska M, Baumgratz T, Datta A. Multi-parameter quantum metrology. Advances in Physics: X. 2016;**1**(4):621-639

[16] Taylor MA, Bowen WP. Quantum metrology and its application in biology. Physics Reports. 2016;**615**:1-59

[17] Joo J, Munro WJ, Spiller TP. Quantum metrology with entangled coherent states. Physical Review Letters. 2011;**107**(8):083601

[18] Wang X, Xu J, Ge S, Zou L, Sang D, Fan J, et al. Recent applications of AQ05

nanodiamond quantum biosensors: A review. APL Materials. 2023;**11**(9)

[19] Balasubramanian G, Lazariev A, Arumugam SR, Duan D-W. Nitrogen-vacancy color center in diamond—emerging nanoscale applications in bioimaging and biosensing. Current Opinion in Chemical Biology. 2014;**20**: 69-77

[20] Petrini G, Moreva E, Bernardi E, Traina P, Tomagra G, Carabelli V, et al. Is a quantum biosensing revolution approaching? Perspectives in nv-assisted current and thermal biosensing in living cells. Advanced Quantum Technologies. 2020;**3**(12):2000066

[21] Savage N. Quantum diamond sensors. Nature. 2021;**591**(7851):S37

[22] Wu Y, Jelezko F, Plenio MB, Weil T. Diamond quantum devices in biology. Angewandte Chemie International Edition. 2016;**55**(23):6586-6598

[23] Singh J. Quantum Mechanics: Fundamentals and Applications to Technology. John Wiley & Sons; 2008

[24] Rieffel E, Polak W. An introduction to quantum computing for non-physicists. ACM Computing Surveys (CSUR). 2000;**32**(3):300-335

[25] Gruska J et al. Quantum Computing. Vol. 2005. McGraw-Hill London; 1999

[26] Nielsen MA, Chuang IL. Quantum Computation and Quantum Information. Vol. 2. Cambridge: Cambridge University Press; 2001

AQ06 [27] Mpofu KT, Mthunzi-Kufa P. Application of quantum computers to phase-based quantum biosensing experiments. In: Proceedings of the 9th Military Information and Communication Symposium of South Africa (MICSSA 2023). 2023. pp. 29-36. Available from: https://researchspace.csir.co.za/dspace/handle/10204/13451

[28] Mpofu KT. Quantum analogues of classical optimization algorithms [Ph.D. dissertation]. Westville: University of KwaZulu-Natal; 2017. Available from: https://www.academia.edu

[29] Sonko S, Ibekwe KI, Ilojianya VI, Etukudoh EA, Fabuyide A. Quantum cryptography and us digital security: A comprehensive review: Investigating the potential of quantum technologies in creating unbreakable encryption and their future in national security. Computer Science & IT Research Journal. 2024;**5**(2):390-414

[30] Rawal BS, Biswas A. A comprehensive survey of post-quantum cryptography and its implications. Engineering Science & Technology. 2024:256-269 AQ07

[31] Radanliev P. Artificial intelligence and quantum cryptography. Journal of Analytical Science and Technology. 2024;**15**(1):4

[32] Allgyer W, White T, Youssef TA. Securing the future: A comprehensive review of post-quantum cryptography and emerging algorithms. In: SoutheastCon. Vol. 2024. 2024. pp. 1282-1287

[33] Ageed ZS, Zeebaree SR, Ibrahim RK. A comprehensive survey for cryptography implementation using quantum computing. In: AIP Conference Proceedings. Vol. 2944(1). AIP Publishing; 2024

[34] Dowling JP, Seshadreesan KP. Quantum optical technologies for metrology, sensing, and imaging. Journal of Lightwave Technology. 2015;**33**(12): 2359-2370

[35] Didomenico LD, Lee H, Kok P, Dowling JP. Quantum interferometric sensors. In: Quantum Sensing and Nanophotonic Devices. Vol. 5359. SPIE; 2004. pp. 169-176

[36] Lawrie BJ, Lett PD, Marino AM, Pooser RC. Quantum sensing with squeezed light. ACS Photonics. 2019; **6**(6):1307-1318

[37] Gefen T, Rotem A, Retzker A. Overcoming resolution limits with quantum sensing. Nature Communications. 2019;**10**(1):4992

[38] DeMille D, Hutzler NR, Rey AM, Zelevinsky T. Quantum sensing and metrology for fundamental physics with molecules. Nature Physics. 2024:1-9

[39] Kantsepolsky B, Aviv I, Weitzfeld R, Bordo E. Exploring quantum sensing potential for systems applications. In: IEEE Access. Vol. 11. 2023. pp. 31569-31582

[40] Oh E, Gregoire MD, Black AT, Hughes KJ, Kunz PD, Larsen M et al. A perspective on quantum sensors from basic research to commercial applications. arXiv preprint arXiv: 2407.00689. 2024

[41] Murzin D, Mapps DJ, Levada K, Belyaev V, Omelyanchik A, Panina L, et al. Ultrasensitive magnetic field sensors for biomedical applications. Sensors. 2020;**20**(6):1569

[42] Lenz J, Edelstein S. Magnetic sensors and their applications. IEEE Sensors Journal. 2006;**6**(3):631-649

[43] Fabricant A, Novikova I, Bison G. How to build a magnetometer with thermal atomic vapor: A tutorial. New Journal of Physics. 2023;**25**(2):025001

[44] Stolz R, Schiffler M, Becken M, Thiede A, Schneider M, Chubak G, et al. Squids for magnetic and electromagnetic methods in mineral exploration. Mineral Economics. 2022;**35**(3):467-494

[45] Trahms L. Ultrasensitive magnetometry using quantum-based sensor technology. PTB Mitteilungen. 2020;**130**(3):63-68

[46] Kitching J, Knappe S, Shah V, Schwindt P, Griffith C, Jimenez R, et al. Microfabricated atomic magnetometers and applications. In: 2008 IEEE International Frequency Control Symposium. Vol. 2008. IEEE. pp. 789-794

[47] Bandi TN. A comprehensive overview of atomic clocks and their applications. Demo Journal. 2024;**1**(1): 40-50

[48] Ludlow AD, Boyd MM, Ye J, Peik E, Schmidt PO. Optical atomic clocks. Reviews of Modern Physics. 2015;**87**(2): 637-701

[49] Hrvoic I, Hollyer GM, Eng P. Brief review of quantum magnetometers. In: GEM Systems Technical Papers. 2005

[50] Robbes D. Highly sensitive magnetometers—A review. Sensors and Actuators A: Physical. 2006;**129**(1–2): 86-93

[51] Aleksandrov EB, Vershovskii AK. Modern radio-optical methods in quantum magnetometry. Physics-Uspekhi. 2009;**52**(6):573

[52] Bennett JS, Vyhnalek BE, Greenall H, Bridge EM, Gotardo F, Forstner S, et al. Precision magnetometers for aerospace applications: A review. Sensors. 2021; **21**(16):5568

[53] Moreno-Pineda E, Wernsdorfer W. Measuring molecular magnets for

quantum technologies. Nature Reviews Physics. 2021;**3**(9):645-659

[54] Budker D, Romalis M. Optical magnetometry. Nature Physics. 2007; **3**(4):227-234

[55] Jin R-B, Zeng Z-Q, You C, Yuan C. Quantum interferometers: Principles and applications. Progress in Quantum Electronics. 2024:100519

[56] Barzanjeh S, Xuereb A, Gröblacher S, Paternostro M, Regal CA, Weig EM. Optomechanics for quantum technologies. Nature Physics. 2022;**18**(1): 15-24

[57] Khalili FY, Danilishin SL. Quantum optomechanics. Progress in Optics. 2016; **61**:113-236

[58] Liu X, Liu W, Ren Z, Ma Y, Dong B, Zhou G, et al. Progress of optomechanical micro/nano sensors: A review. International Journal of Optomechatronics. 2021;**15**(1):120-159

[59] Milburn G, Woolley M. An introduction to quantum optomechanics. Acta Physica Slovaca. 2011;**61**(5): 483-601

[60] Arcizet O, Briant T, Heidmann A, Pinard M. Beating quantum limits in an optomechanical sensor by cavity detuning. Physical Review A—Atomic, Molecular, and Optical Physics. 2006; **73**(3):033819

[61] Xia Y, Agrawal AR, Pluchar CM, Brady AJ, Liu Z, Zhuang Q, et al. Entanglement-enhanced optomechanical sensing. Nature Photonics. 2023;**17**(6): 470-477

[62] Jackson Kimball DF, Budker D, Chupp TE, Geraci AA, Kolkowitz S, Singh JT, et al. Probing fundamental physics with spin-based quantum sensors. Physical Review A. 2023;**108**(1): 010101

[63] Budker D, Cecil T, Chupp TE, Geraci AA, Kimball DFJ, Kolkowitz S, et al. Quantum sensors for high precision measurements of spin-dependent interactions. arXiv preprint arXiv: 2203.09488. 2022

[64] Atatüre M, Englund D, Vamivakas N, Lee S-Y, Wrachtrup J. Material platforms for spin-based photonic quantum technologies. Nature Reviews Materials. 2018;**3**(5):38-51

[65] Jaskula J-C, Shields BJ, Bauch E, Lukin MD, Trifonov AS, Walsworth RL. Improved quantum sensing with a single solid-state spin via spin-to-charge conversion. Physical Review Applied. 2019;**11**(6):064003

[66] Basiri-Esfahani S, Myers CR, Armin A, Combes J, Milburn GJ. Integrated quantum photonic sensor based on hong-ou-mandel interference. Optics Express. 2015;**23**(12): 16008-16023

[67] Berchera IR, Degiovanni IP. Quantum imaging with sub-poissonian light: Challenges and perspectives in optical metrology. Metrologia. 2019;**56**(2):024001

[68] Liu J, Shi M, Chen Z, Wang S, Wang Z, Zhu S. Quantum photonics based on metasurfaces. Opto-Electronic Advances. 2021;**4**(9):200092

[69] Bhusal N. Smart quantum technologies using photons. arXiv preprint arXiv:2103.07081. 2021

[70] Kleiner R, Koelle D, Ludwig F, Clarke J. Superconducting quantum interference devices: State of the art and applications. Proceedings of the IEEE. 2004;**92**(10):1534-1548

[71] Fagaly R. Superconducting quantum interference device instruments and applications. Review of Scientific Instruments. 2006;**77**(10)

[72] Katori H. Optical lattice clocks and quantum metrology. Nature Photonics. 2011;**5**(4):203-210

[73] Sinclair A. An introduction to trapped ions, scalability and quantum metrology. In: Quantum Information and Coherence. Springer; 2014. pp. 211-245

[74] Wineland DJ, Leibfried D. Quantum information processing and metrology with trapped ions. Laser Physics Letters. 2011;**8**(3):175-188

[75] Szigeti SS, Hosten O, Haine SA. Improving cold-atom sensors with quantum entanglement: Prospects and challenges. Applied Physics Letters. 2021;**118**(14)

[76] Wright MJ, Anastassiou L, Mishra C, Davies JM, Phillips AM, Maskell S, et al. Cold atom inertial sensors for navigation applications. Frontiers in Physics. 2022; **10**:994459

[77] Bochkati M, Schön S, Schlippert D, Schubert C, Rasel E. Could cold atom interferometry sensors be the future inertial sensors?—First simulation results. In: 2017 DGON Inertial Sensors and Systems (ISS). Vol. 2017. IEEE. pp. 1-20

[78] Eichenfield M, Chan J, Camacho RM, Vahala KJ, Painter O. Optomechanical crystals. Nature. 2009; **462**(7269):78-82

[79] Burek MJ, Cohen JD, Meenehan SM, El-Sawah N, Chia C, Ruelle T, et al. Diamond optomechanical crystals. Optica. 2016;**3**(12): 1404-1411

[80] Yu C-J, Von Kugelgen S, Laorenza DW, Freedman DE. A molecular approach to quantum sensing. ACS Central Science. 2021;**7**(5):712-723

[81] GS University. Superconducting quantum interference devices (squid). n. d. Available from: http://230nsc1.phy-astr.gsu.edu/hbase/Solids/Squid.html [Accessed: August 26, 2024]

[82] Degen CL, Reinhard F, Cappellaro P. Quantum sensing. Reviews of Modern Physics. 2017;**89**(3):035002

[83] Schaffry M, Gauger EM, Morton JJ, Fitzsimons J, Benjamin SC, Lovett BW. Ensemble based quantum metrology. arXiv preprint arXiv:1007.2491. 2010

[84] Brookes MJ, Leggett J, Rea M, Hill RM, Holmes N, Boto E, et al. Magnetoencephalography with optically pumped magnetometers (opm-meg): The next generation of functional neuroimaging. Trends in Neurosciences. 2022;**45**(8):621-634

[85] Photonics H. Nitrogen-vacancy (nv) centers in diamond for quantum sensing. Available from: https://www.hamamatsu.com/eu/en/applications/quantum-technologies/nitrogen-vacancy-nv.html [Accessed: August 30, 2024]

[86] Nutshell KI. The last human – A glimpse into the far future [Online]. YouTube video. 2020. Available from: https://www.youtube.com/watch?v=lD3eNstS6ZE [Accessed: August 26, 2024]

[87] Mpofu K, Lee C, Maguire G, Kruger H, Tame M. Experimental measurement of kinetic parameters using quantum plasmonic sensing. Journal of Applied Physics. 2022;**131**(8)

AQ08

[88] Mpofu K, Mthunzi-Kufa P. Enhanced signal-to-noise ratio in quantum plasmonic image sensing including loss and varying photon number. Physica Scripta. 2023

[89] Mpofu K, Lee C, Maguire G, Kruger H, Tame M. Measuring kinetic parameters using quantum plasmonic sensing. Physical Review A. 2022;**105**(3): 032619

[90] Mpofu KT. Quantum plasmonic sensing with application to hiv research [Ph.D. dissertation]. University of KwaZulu-Natal; 2020

[91] Langer J, Jimenez de Aberasturi D, Aizpurua J, Alvarez-Puebla RA, Auguié B, Baumberg JJ, et al. Present and future of surface-enhanced Raman scattering. ACS Nano. 2019;**14**(1):28-117

[92] Chang R. Surface enhanced Raman scattering. Springer Science & Business Media; 2013

[93] Gardiner DJ. Introduction to Raman scattering. In: Practical Raman Spectroscopy. Springer; 1989. pp. 1-12

[94] Zoubir A. Raman Imaging: Techniques and Applications. Vol. 168. Springer; 2012

[95] Procházka M. Surface-enhanced raman spectroscopy. Biological and Medical Physics, Biomedical Engineering. 2016:1-221

[96] Casacio CA, Madsen LS, Terrasson A, Waleed M, Barnscheidt K, Hage B, et al. Quantum-enhanced nonlinear microscopy. Nature. 2021; **594**(7862):201-206

[97] Triginer Garces G, Chrzanowski HM, Daryanoosh S, Thiel V, Marchant AL, Patel RB, et al. Quantum-enhanced stimulated emission detection for label-free microscopy. Applied Physics Letters. 2020;**117**(2)

[98] de Andrade RB, Kerdoncuff H, Berg-Sørensen K, Gehring T, Lassen M, Andersen UL. Quantum-enhanced continuous-wave stimulated raman scattering spectroscopy. Optica. 2020; **7**(5):470-475

[99] Thorlabs, "Surface-enhanced raman spectroscopy (sers)," 2024, accessed: August 27, 2024. [Online]. Available: https://www.thorlabs.com/newgrouppage9.cfm?objectgroup_id=16610

[100] Lassen M, Ilchenko O, Andersen U, Fritzsche M, Chekhova M, Kriegsmann M, et al. Towards quantum-enhanced Raman spectroscopy for bioimaging applications. In: Quantum Sensing, Imaging, and Precision Metrology. Vol. 12447. SPIE; 2023. pp. 285-289

[101] Zhang T, Pramanik G, Zhang K, Gulka M, Wang L, Jing J, et al. Toward quantitative bio-sensing with nitrogen–vacancy center in diamond. ACS Sensors. 2021;**6**(6):2077-2107

[102] Ulag S, Gunduz O. Quantum dot-based nanomaterials for diagnostic and therapeutic applications. In: Pharmaceutical Nanobiotechnology for Targeted Therapy. Springer; 2022. pp. 429-453

[103] Sánchez Toural J, Marzoa V, Bernardo-Gavito R, Pau J, Granados D. Hands-on quantum sensing with nv-centers in diamonds. C. 2023;**9**(1):16

[104] Das S, Mazumdar H, Khondakar KR, Mishra YK, Kaushik A. Quantum biosensors: Principles and applications in medical diagnostics. ECS Sensors Plus. 2024;**3**(2):025001

[105] Frasco MF, Chaniotakis N. Semiconductor quantum dots in chemical sensors and biosensors. Sensors. 2009;**9**(9):7266-7286

[106] Toropov NA, Houghton MC, Yu D, Vollmer F. Thermo-optoplasmonic single-molecule sensing on optical microcavities. ACS Nano. 2024;**18**(27): 17534-17546

[107] Tobar G, Manikandan SK, Beitel T, Pikovski I. Detecting single gravitons with quantum sensing. Nature Communications. 2024;**15**(1):7229

[108] Fröjdh E, Bergamaschi A, Schmitt B. Single-photon counting detectors for diffraction-limited light sources. Frontiers in Physics. 2024;**12**: 1304896

[109] Kim D-H, Hong S, Kim Y-S, Kim Y, Lee S-W, Pooser RC, et al. Distributed quantum sensing of multiple phases with fewer photons. Nature Communications. 2024;**15**(1):266

[110] Vernekar S, Xavier J. Quantum correlation enhanced optical imaging. Quantum Beam Science. 2024;**8**(3):19

[111] Ray S, Reddy PJ, Choudhary S, Raghu D, Srivastava S. Emerging nanoproteomics approaches for disease biomarker detection: A current perspective. Journal of Proteomics. 2011; **74**(12):2660-2681

[112] Letchumanan I, Arshad MM, Gopinath SC. Nanodiagnostic attainments and clinical perspectives on c-reactive protein: Cardiovascular disease risks assessment. Current Medicinal Chemistry. 2021;**28**(5): 986-1002

[113] Fathil M, Arshad MM, Gopinath SC, Hashim U, Adzhri R, Ayub R, et al. Diagnostics on acute myocardial infarction: Cardiac troponin biomarkers. Biosensors and Bioelectronics. 2015;**70**: 209-220

[114] Simon DS, Jaeger G, Sergienko AV, Simon DS, Jaeger G, Sergienko AV. Quantum Metrology. Springer; 2017

[115] Polino E, Valeri M, Spagnolo N, Sciarrino F. Photonic quantum metrology. AVS Quantum Science. 2020; **2**(2)

[116] Xiang G-Y, Guo G-C. Quantum metrology. Chinese Physics B. 2013; **22**(11):110601

[117] Giovannetti V, Lloyd S, Maccone L. Advances in quantum metrology. Nature Photonics. 2011;**5**(4):222-229

[118] Crespi A, Lobino M, Matthews JC, Politi A, Neal CR, Ramponi R, et al. Measuring protein concentration with entangled photons. Applied Physics Letters. 2012;**100**(23)

[119] Li B-B, Bílek J, Hoff UB, Madsen LS, Forstner S, Prakash V, et al. Quantum enhanced optomechanical magnetometry. Optica. 2018;**5**(7): 850-856

[120] Mauranyapin NP, Madsen L, Taylor M, Waleed M, Bowen W. Evanescent single-molecule biosensing with quantum-limited precision. Nature Photonics. 2017;**11**(8):477-481

[121] Kitaeva GK, Penin AN. Spontaneous parametric down-conversion. Journal of Experimental and Theoretical Physics Letters. 2005;**82**:350-355

[122] Couteau C. Spontaneous parametric down-conversion. Contemporary Physics. 2018;**59**(3):291-304

[123] Kulkarni G, Rioux J, Braverman B, Chekhova MV, Boyd RW. Classical

model of spontaneous parametric down-conversion. Physical Review Research. 2022;**4**(3):033098

[124] Schneeloch J, Knarr SH, Bogorin DF, Levangie ML, Tison CC, Frank R, et al. Introduction to the absolute brightness and number statistics in spontaneous parametric down-conversion. Journal of Optics. 2019;**21**(4):043501

[125] Thiel C. Four-wave Mixing and Its Applications. Washington DC: Faculty of Washington; 2008

[126] Zhang Z-C, Wang Y-P, Yu Y-F, Zhang Z-M. Quantum squeezing in a modulated optomechanical system. Optics Express. 2018;**26**(9):11915-11927

[127] Purdy TP, Yu P-L, Peterson RW, Kampel NS, Regal CA. Strong optomechanical squeezing of light. Physical Review X. 2013;**3**(3):031012

[128] Wiseman H, Milburn G. Squeezing via feedback. Physical Review A. 1994; **49**(2):1350

[129] Wiseman H. Squeezing and feedback. In: Quantum Squeezing. Springer; 2004. pp. 171-223

[130] Zwiller V, Blom H, Jonsson P, Panev N, Jeppesen S, Tsegaye T, et al. Single quantum dots emit single photons at a time: Antibunching experiments. Applied Physics Letters. 2001;**78**(17): 2476-2478