

Integration of Molecular Imaging and Biosensors for Disease Diagnosis

Xiaoya Liu

1Department of North Sichuan Medical College, Medical Imaging University, Sichuan, 634700, China

nanamiu084@gmail.com

Abstract. Molecular imaging and biosensors are two complementary ways in modern biomedical diagnostics. Molecular imaging enables real-time visualization of molecular and cellular processes in vivo with spatial resolution, while biosensors provide rapid and highly sensitive quantitative detection of biomarkers in body fluids and tissues. The combined application of these two technologies has great potential in disease detection, particularly in early cancer screening, neurological disorders, and infectious disease diagnosis. Clinicians can achieve a more comprehensive understanding of disease progression by combining the spatial distribution information obtained from imaging with the temporal and quantitative signals obtained from biosensors. This integration enables the early prevention of disease deterioration. This review summarizes the fundamental principles of molecular imaging and biosensors, and their advantages and disadvantages are comparatively analyzed, explores their clinical applications and integration strategies, emphasizes the approaches of system integration and the methods of data and signal fusion, and discusses the challenges and future perspectives in clinical translation.

Keywords: Biosensor, molecular Imaging, biosensor-molecular Imaging Interaction.

1. Introduction

Early and accurate diagnosis is essential for effective disease management. Conventional imaging techniques and laboratory testing methods are widely applied, yet they often provide only macroscopic structural information or isolated molecular data, falling short of fully capturing the dynamic complexity of disease processes [1]. In contrast, biosensors excel in high sensitivity and rapid responsiveness, making them particularly suitable for point-of-care testing and minimally invasive diagnostics.

Nevertheless, both methods face inherent limitations. Imaging techniques are often constrained by challenges in sensitivity and the complexity of instrumentation, while biosensors are limited by sample availability and the absence of spatial localization capacity. Combining these two approaches represents a rational solution: molecular imaging provides insights into disease localization and progression, while biosensors deliver precise and real-time quantitative data. Together, they establish a multidimensional diagnostic framework that integrates spatial, temporal, and molecular information. This synergistic integration not only enhances diagnostic accuracy but also opens new opportunities for early disease screening, personalized monitoring, and predictive medicine.

Therefore, this review is organized into four sections. Section 1 introduces the fundamental principles and representative modalities of molecular imaging. Section 2 summarizes the design, classification, and clinical applications of biosensors, with particular emphasis on their use in different sample types. Section 3 explores the integration strategies and application scenarios of combining molecular imaging and biosensors. Section 4 highlights the major challenges in clinical translation and outlines the future opportunities for this interdisciplinary field.

2. Overview of Molecular Imaging

2.1. Definition and Basic Principles

Molecular imaging is a biomedical technology that enables noninvasive and highly sensitive detection of biochemical and physiological processes in living systems, including cancer cells. It is primarily applied to the study of disease initiation and progression, as well as drug development. The principle involves the use of specific imaging instruments, alone or in combination with molecular probes, to characterize or quantify tissue features or biochemical biomarkers at the cellular and molecular levels in vivo [2].

2.2. Common Imaging Modalities

Currently, widely used imaging techniques include optical imaging, magnetic resonance imaging (MRI), single-photon emission computed tomography (SPECT), positron emission tomography (PET), and ultrasound [2].

2.2.1 Optical imaging

Optical imaging is one of the most extensively applied modalities in molecular imaging. It is based on the interaction between light and biological tissues, which generates optical phenomena such as absorption, scattering, reflection, and interference. When light interacts with tissues or probe molecules, these processes can alter the intensity, phase, or wavelength of light, thereby transforming structural or molecular information into visualized images [3].

2.2.2 MRI

When nuclei with spin are placed in an external static magnetic field, they occupy different spin states with distinct energy levels [4]. The energy difference is proportional to the magnetic field strength. MRI employs magnetic field gradients to achieve frequency, phase, and slice selection encoding, thereby acquiring two- or three-dimensional images of the body with spatial localization.

2.2.3 SPECT

SPECT is a nuclear medicine functional imaging technique based on the detection of γ -rays. By visualizing the in vivo distribution of radiopharmaceuticals, SPECT provides three-dimensional functional and metabolic information.

2.2.4 PET

PET is a molecular imaging technique based on the positron decay of radionuclides. It enables quantitative three-dimensional imaging of metabolic and functional processes in vivo.

2.2.5 Ultrasound imaging

Ultrasound imaging is a clinical imaging technique based on the propagation properties of high-frequency sound waves (typically 2–15 MHz). By emitting and receiving ultrasound waves, this method provides structural and functional information of tissues and blood flow in vivo [5].

2.3. Imaging Probes and Signal Mechanisms

In molecular imaging, imaging probes are the core tools enabling specific visualization. By selectively binding to target molecules, receptors, or biological processes, these probes convert otherwise invisible molecular events into detectable signals. Different imaging modalities (MRI, PET, SPECT, optical imaging, ultrasound, etc.) rely on specific types of probes and corresponding signal mechanisms [6].

2.4. Clinical Applications and Advantages

Molecular imaging enables in vivo visualization of metabolism, receptor expression, gene regulation, and cellular function. This provides essential insights for early diagnosis, therapeutic

evaluation, and personalized treatment. Each imaging technique (PET, SPECT, MRI, optical imaging, ultrasound, etc.) possesses distinct strengths and clinical applications [6]. Table 1 outlines the principal clinical domains in which molecular imaging has been adopted, emphasizing representative scenarios, key technical advantages, and typical probes or imaging modalities. It highlights the contribution of molecular imaging to oncology, cardiovascular disease, neurology, and infection/inflammation, with particular relevance to early detection, therapeutic monitoring, and precision medicine. This table outlines the principal clinical domains in which molecular imaging has been adopted, emphasizing representative scenarios, key technical advantages, and typical probes or imaging modalities. It highlights the contribution of molecular imaging to oncology, cardiovascular disease, neurology, and infection/inflammation, with particular relevance to early detection, therapeutic monitoring, and precision medicine.

Table 1. Clinical Applications of Molecular Imaging [7-9]

Disease Area	Application Scenarios	Technical Advantages	Representative Probes and Method
Oncology	1. Early screening and diagnosis (e.g., lung cancer, esophageal cancer, lymphoma) 2. Precision therapy guidance (e.g., PSMA imaging in prostate cancer) 3. Therapeutic response evaluation and follow-up 4. Staging and metastasis assessment	1. High sensitivity for detecting small lesions 2. Ability to capture early metabolic and molecular changes 3. Companion diagnostics	1. ^{18}F-FDG PET, CT 2. ^{68}Ga-PSMA, PETCT 3. ^{89}Zr-trastuzumab, PET
Cardiovascular Diseases	1. Assessment of myocardial perfusion and viability 2. Imaging of atherosclerosis and plaque vulnerability	1. Differentiation between reversible ischemia and irreversible injury 2. Provides combined metabolic and perfusion information	1. $^{99\text{m}}\text{Tc}$-MIBI, SPECT 2. ^{18}F-FDG, PET 3. ^{13}N-ammonia, PET
Neurological Disorders	1. Early diagnosis of Alzheimer's disease 2. Functional assessment in Parkinson's disease 3. Localization and Detection of Epilepsy and Brain Tumors	1. Detects metabolic changes and protein deposition before anatomical abnormalities appear 2. High specificity in receptor imaging	1. ^{18}F-FDG, PET 2. ^{11}C-PiB / ^{18}F-Florbetapir (β-amyloid) 3. ^{123}I-ioflupane, SPECT
Infection and Inflammation	1. Localization of fever of unknown origin 2. Detection of endocarditis 3. Monitoring autoimmune diseases	1. High sensitivity for identifying occult lesions 2. Strong responsiveness to activated inflammatory cells	1. ^{18}F-FDG, PET/CT 2. Specific leukocyte-targeted probes
Precision Medicine	1. Companion diagnostics for selecting patients responsive to targeted therapies 2. Radionuclide therapy with imaging monitoring (theragnostic) 3. Tracking of stem cell and immune cell therapies	1. Enables integration of diagnosis and therapy 2. Provides tracking of cell distribution and function	1. ^{68}Ga-PSMA, PET / ^{177}Lu-PSMA therapy 2. ^{64}Cu / ^{89}Zr-labeled cell tracking

3. Overview of Biosensors in Diagnosis

3.1. Basic Principles of Biosensors

Biosensors are analytical devices that integrate a biological recognition element with a signal transduction mechanism, converting specific molecular recognition events into measurable physical or chemical signals [10]. Since their emergence in the 20th century, biosensors have played an important role in medical diagnostics, environmental monitoring, and food safety, particularly in early disease screening and precision diagnostics. With the advancement of materials science and

micro/nanotechnology, the performance of biosensors has been significantly improved, leading to the development of diverse types. Among them, optical biosensors have been widely studied due to their high sensitivity and mature imaging capabilities; nanoprobe-based biosensors utilize the unique properties of nanomaterials to achieve signal amplification and multimodal functionalities; and electrochemical biosensors, known for their high sensitivity and operational simplicity, demonstrate substantial potential for clinical translation [11].

3.2. Types of Biosensors and Performance Indicators

Table 2. Comparison of Biosensor Types and Performance Indicators [12-14]

Sensor Type	Basic Principle	Sensitivity	Selectivity	Response Time	Representative Applications
Electrochemical Biosensors	Molecular binding events induce changes in current, potential, or impedance.	High, down to fM–pM	Dependent on recognition elements (antibody/aptamer), usually high	Seconds – minutes	Blood/serum tumor markers, miRNA, ctDNA detection
Optical Biosensors	Utilization of light absorption, emission, or SPR signal variations	High, reaching single-molecule detection	High, using optical labels or label-free recognition	Seconds – minutes	Enzyme activity assays, optical imaging, environmental monitoring
Nanoprobe-based Biosensors	Nanomaterials (e.g., quantum dots, gold nanoparticles, SPIONs) generate multiple signal amplification effects	Ultra-high, femtomolar (fM)	High, depending on functionalization with biomolecules	Minutes – hours	MRI, PET, multimodal imaging, in vivo diagnostics and therapy
Enzyme-based Biosensors	Enzyme-catalyzed reactions produce detectable products	High (nM–μM)	High (determined by enzyme-substrate specificity)	Seconds – minutes	Glucose detection, cancer cell metabolism monitoring
Immunosensors	Antigen–antibody specific binding	Medium to high (pM–nM)	Very high	Minutes – 1 hour	Tumor marker detection (AFP, CEA, CA125, etc.)
Nucleic Acid Biosensors	Hybridization-based recognition of DNA/RNA	High (fM–pM)	Extremely high (sequence-specific)	Minutes	Genetic mutation detection, miRNA profiling

The performance of biosensors is typically evaluated by three parameters: sensitivity, selectivity, and response time. Owing to the differences in their signal transduction mechanisms, various types of biosensors exhibit distinct characteristics across these indicators. Table 2 provides a comparative summary of major classes of biosensors, describing their underlying principles, analytical performance characteristics, and representative biomedical applications. It demonstrates how distinct sensing strategies—including electrochemical, optical, nanoprobe-based, and enzyme-driven systems—differ in terms of sensitivity, selectivity, and response time, thereby informing their application in clinical diagnostics and translational research.

3.3. Clinical Applications in Diagnostic Testing

Biosensors have demonstrated broad application potential in clinical diagnostics, particularly in the analysis of blood, body fluids, and tissue samples, offering rapid, sensitive, and minimally invasive or even noninvasive detection. Representative application cases are summarized as follows.

3.3.1 Blood sample analysis

Blood is one of the most widely used diagnostic specimens in clinical practice, as it contains a wide range of biomarkers such as glucose, lactate, tumor markers, and circulating nucleic acids.

Electrochemical biosensors have become the cornerstone of glucose monitoring, with enzyme electrodes evolving into mature commercial products for diabetes management [15]. In addition, tumor marker detection has been significantly advanced through electrochemical or optical biosensors modified with nanomaterials, enabling sensitive analysis of serum biomarkers such as alpha-fetoprotein (AFP) and carcinoembryonic antigen (CEA), thereby facilitating early cancer diagnosis [16]. Furthermore, surface plasmon resonance (SPR)-based biosensors and electrochemical amplification strategies provide powerful tools for detecting circulating nucleic acids and proteins, including cell-free DNA and microRNAs, which are increasingly regarded as promising indicators for liquid biopsy [17].

3.3.2 Body fluid analysis

Beyond blood, body fluids such as saliva, urine, sweat, and tears have gained increasing recognition as noninvasive or minimally invasive diagnostic specimens. Electrochemical biosensors capable of measuring cortisol levels in saliva contribute to stress monitoring and the evaluation of endocrine disorders. Similarly, colorimetric and electrochemical biosensors for urinary glucose, uric acid, and creatinine serve as valuable tools for the assessment of diabetes and kidney function [18]. In addition, wearable and flexible biosensors have been designed to enable real-time monitoring of lactate and sodium ions in sweat, as well as glucose concentrations in tears (e.g., through smart contact lenses), thereby paving the way for continuous and personalized health monitoring [19].

3.3.3 Tissue sample analysis

Tissue biopsy remains a cornerstone of clinical diagnostics, but traditional approaches are often time-consuming and heavily dependent on histopathology. Biosensors provide rapid alternatives by offering molecular-level insights directly from tissue samples. For instance, optical probe-based biosensors can be used intraoperatively to detect tumor metabolites, thereby assisting in the delineation of tumor margins [20]. Electrochemical immunosensors are capable of directly identifying bacterial or viral antigens in tissue, significantly reducing diagnostic time [21]. Moreover, nanoprobe-based biosensors allow for monitoring of key physiological parameters such as pH and oxygen partial pressure within the tissue microenvironment, yielding valuable information on disease mechanisms and enabling more personalized therapeutic strategies [22].

Together, Sections 3.3.1 to 3.3.3 illustrate how biosensors can be applied across diverse biological specimens to generate clinically relevant information, supporting both rapid diagnosis and long-term health monitoring.

3.4. Complementary Potential with Molecular Imaging

Biosensors and molecular imaging provide distinct yet complementary strengths in biomedical diagnostics. Biosensors excel in sensitivity, rapid response, and portability, enabling precise molecular-level analysis of small-volume samples such as blood and body fluids. However, they lack the capacity for whole-body spatial distribution and real-time visualization. In contrast, molecular imaging offers spatial localization and dynamic tracking of biomarkers or pathological processes at the tissue, organ, or systemic level, but its sensitivity often falls short in detecting extremely low-abundance targets.

Integrating these two technologies therefore enables a multidimensional diagnostic paradigm that bridges molecular quantification with spatial and temporal information. In this framework, biosensors act as prescreening tools by providing sensitive and quantitative molecular data, while molecular imaging validates spatial distribution and dynamic changes in vivo. Together, they enhance early disease detection, individualized therapy planning, and therapeutic evaluation. For instance, electrochemical biosensors detecting circulating tumor DNA or specific proteins can be coupled with imaging techniques to localize tumor lesions, forming a “liquid biopsy + imaging localization” strategy that significantly improves diagnostic accuracy [23, 24].

This complementary relationship highlights the synergistic potential of combining biosensors and molecular imaging, providing a logical transition toward cross-application strategies discussed in Section 3.

4. Cross-Applications of Molecular Imaging and Biosensors

Molecular imaging, which enables *in vivo* visualization at the molecular level, has been widely applied in early disease diagnosis and therapeutic evaluation [25]. However, it still faces limitations in sensitivity and specificity, particularly in the detection of low-abundance molecules. In contrast, biosensors demonstrate remarkable advantages in biomedical detection due to their high sensitivity, rapid response, and excellent selectivity [10].

In recent years, the integration of these two approaches has attracted increasing attention in the medical field. For example, optical biosensors exploit established fluorescence and photoacoustic imaging for real-time visualization; nanoscale probe-based sensors, leveraging the multimodal properties of nanomaterials, have promoted the development of theragnostic; the electrochemical biosensors, primarily used for *in vitro* assays, provide complementary information to imaging readouts. Collectively, the cross-application of molecular imaging and biosensors opens new avenues for precision medicine.

4.1. Application Scenarios

The integration of molecular imaging and biosensors has demonstrated potential across multiple major diseases. Early cancer screening represents the most illustrative example. By combining *in vitro* biosensors for detecting circulating tumor biomarkers (e.g., ctDNA, miRNA, exosomes) with *in vivo* molecular imaging probes, both early detection and precise localization can be achieved [11]. In neurological disorders, biosensors can monitor neurotransmitters or amyloid proteins, while imaging techniques provide spatial lesion information, thereby linking molecular detection with functional imaging [26]. In infectious disease monitoring, electrochemical or optical biosensors allow rapid pathogen detection, whereas molecular imaging can track infection progression *in vivo*, offering guidance for anti-infective therapies [27].

4.2. System Integration

At the system level, the synergy between molecular imaging and biosensors primarily lies in the complementary roles of *in vitro* detection and *in vivo* imaging. *In vitro* biosensors enable highly sensitive molecular detection, such as low-abundance biomarker analysis in blood, while *in vivo* imaging probes provide spatial localization and dynamic visualization. Together, they establish a “diagnostic loop”: initial alerts are generated via *in vitro* assays, followed by *in vivo* imaging for localization and validation, thereby significantly improving diagnostic accuracy and reliability [28].

4.3. Data Analysis and Signal Integration

The integration of multimodal signals presents both challenges and opportunities. Biosensors typically output quantitative data (e.g., current, fluorescence intensity), whereas molecular imaging provides spatiotemporal information. Machine learning and multimodal data fusion can facilitate a deeper understanding of complex biological processes. For instance, combining quantitative data from electrochemical biosensors with spatial information from MRI or PET enables not only precise localization but also concentration quantification, thereby enhancing diagnostic sensitivity and specificity [29].

4.4. Clinical Cases and Research Progress

Several studies have investigated the clinical potential of this integrated approach. For example, the combination of photoacoustic imaging and nanoscale probe-based biosensors has successfully enabled early detection of breast and prostate cancers in animal models [30]. In neurodegenerative

diseases, fluorescent probes combined with molecular imaging have been applied to in vivo visualization of amyloid plaques associated with Alzheimer's disease [31]. Moreover, the integration of electrochemical biosensors with PET imaging has shown promise for early monitoring of infectious diseases [32]. These advances suggest that the cross-application of molecular imaging and biosensors is gradually advancing from experimental research toward clinical translation.

5. Challenges and Limitations

Despite the significant potential of integrating molecular imaging with biosensors, multiple challenges remain in both fundamental research and clinical translation. These challenges are primarily associated with probe and sensor delivery efficiency, signal quality, translational bottlenecks, and data processing.

5.1. Probe and Sensor Delivery

Achieving efficient and precise in vivo delivery of probes or sensors remains a critical challenge. Rapid clearance of nanoprobe in the circulatory system, nonspecific uptake, and physiological barriers can all reduce their accumulation efficiency in target tissues [33]. Moreover, the insufficient stability of biosensors and imaging probes in complex biofluid environments further hinders their translational potential.

5.2. Signal Intensity and Noise

Signal attenuation and background noise interference are major factors limiting sensitivity and specificity during imaging and detection. For example, optical signals are often affected by tissue autofluorescence and light scattering, while electrochemical sensors are prone to interference from nonspecific adsorption [34, 35]. Optimizing signal-to-noise ratios and enhancing specificity remain major directions for future research.

5.3. Clinical Translation Barriers: Safety, Cost, and Ethical Concerns

Clinical applications require not only high sensitivity and accuracy but also safety and affordability. Nanoprobes may pose risks of long-term toxicity and immune responses, while the complex fabrication processes of advanced biosensors contribute to higher costs [36]. Additionally, studies involving genetic analysis and in vivo imaging face ethical and regulatory challenges, thereby limiting large-scale clinical translation.

5.4. Data Processing and Multimodal Integration

The integration of molecular imaging with biosensors often generates multidimensional, large-volume datasets that combine quantitative analytical signals with spatial imaging information. Efficient data processing and multimodal signal fusion are therefore critical bottlenecks for clinical applicability. Artificial intelligence and machine learning have been increasingly employed to integrate multimodal imaging and sensing data [37]. However, challenges remain in algorithm standardization and clinical validation.

6. Conclusion

The convergence of molecular imaging and biosensors establishes a multidimensional diagnostic paradigm that unites molecular quantification with spatial and temporal insights, thereby advancing early detection, precise monitoring, and personalized therapeutic strategies. Despite significant progress, critical challenges remain in probe and sensor delivery, signal optimization, clinical translation, and multimodal data integration. Overcoming these hurdles requires advances in nanotechnology, artificial intelligence, and system-level integration. Looking ahead, the synergistic development of molecular imaging and biosensors is expected to accelerate clinical adoption,

transforming diagnostic medicine and contributing to the realization of precision and predictive healthcare. Looking forward, the synergistic development of molecular imaging and biosensors is poised to transform clinical diagnostics, supporting precision medicine and predictive healthcare.

References

- [1] K.-H. Jung and K.-H. Lee, "Molecular Imaging in the Era of Personalized Medicine," *Journal of Pathology and Translational Medicine*, vol. 49, no. 1, pp. 5-12, 2015.
- [2] S. P. Rowe and M. G. Pomper, "Molecular imaging in oncology: Current impact and future directions," *CA: A Cancer Journal for Clinicians*, vol. 72, no. 4, pp. 333-352, 2021.
- [3] V. Ntziachristos, "Going deeper than microscopy: the optical imaging frontier in biology," *Nature Methods*, vol. 7, no. 8, pp. 603-614, 2010.
- [4] V. P. B. Grover, J. M. Tognarelli, M. M. E. Crossey, I. J. Cox, S. D. Taylor-Robinson, and M. J. W. McPhail, "Magnetic Resonance Imaging: Principles and Techniques: Lessons for Clinicians," *Journal of Clinical and Experimental Hepatology*, vol. 5, no. 3, pp. 246-255, 2015.
- [5] J. E. Aldrich, "Basic physics of ultrasound imaging," *Critical Care Medicine*, vol. 35, no. Suppl, pp. S131-S137, 2007.
- [6] R. Weissleder and M. J. Pittet, "Imaging in the era of molecular oncology," *Nature*, vol. 452, no. 7187, pp. 580-589, 2008.
- [7] J. Trotter et al., "Positron Emission Tomography (PET)/Computed Tomography (CT) Imaging in Radiation Therapy Treatment Planning: A Review of PET Imaging Tracers and Methods to Incorporate PET/CT," *Adv Radiat Oncol*, vol. 8, no. 5, p. 101212, Sep-Oct 2023.
- [8] M. Palihati, J. P. Das, R. Yeh, and K. Capaccione, "Emerging PET Imaging Agents and Targeted Radioligand Therapy: A Review of Clinical Applications and Trials," *Tomography*, vol. 11, no. 8, Jul 28 2025.
- [9] D. Albano, A. Rizzo, A. Guarneri, L. Leccisotti, C. Rodella, and G. Treglia, "Emerging PET-radiotracers in cardiovascular, neuro-inflammation, lung and rheumatological diseases: a narrative review," *EJNMMI Rep*, vol. 9, no. 1, p. 28, Aug 11 2025.
- [10] A. P. F. Turner, "Biosensors: sense and sensibility," *Chemical Society Reviews*, vol. 42, no. 8, 2013.
- [11] D.-E. Lee, H. Koo, I.-C. Sun, J. H. Ryu, K. Kim, and I. C. Kwon, "Multifunctional nanoparticles for multimodal imaging and theragnosis," *Chem. Soc. Rev.*, vol. 41, no. 7, pp. 2656-2672, 2012.
- [12] J. Quinchia, D. Echeverri, A. F. Cruz-Pacheco, M. E. Maldonado, and J. Orozco, "Electrochemical Biosensors for Determination of Colorectal Tumor Biomarkers," *Micromachines (Basel)*, vol. 11, no. 4, Apr 14 2020.
- [13] V. N. Palakollu, Y. Veera Manohara Reddy, M. I. Shekh, S. V. P. Vattikuti, J. Shim, and R. Karpoormath, "Electrochemical immunosensing of tumor markers," *Clin Chim Acta*, vol. 557, p. 117882, Apr 15 2024.
- [14] S. Basu, A. Hendler-Neumark, and G. Bisker, "Monitoring Enzyme Activity Using Near-Infrared Fluorescent Single-Walled Carbon Nanotubes," *ACS Sens*, vol. 9, no. 5, pp. 2237-2253, May 24 2024.
- [15] J. Wang, "Electrochemical Glucose Biosensors," *Chemical Reviews*, vol. 108, no. 2, pp. 814-825, 2007.
- [16] Y. Guo and L. Feng, "Highly Sensitive Detection of Carcinoembryonic Antigen via an Electrochemical Platform Fabricated by AuNPs/Streptavidin/Reduced Graphene Oxide," *Frontiers in Chemistry*, vol. 10, 2022.
- [17] M. Labib, E. H. Sargent, and S. O. Kelley, "Electrochemical Methods for the Analysis of Clinically Relevant Biomolecules," *Chemical Reviews*, vol. 116, no. 16, pp. 9001-9090, 2016.
- [18] E. M. McBride et al., "Paper spray ionization: Applications and perspectives," *TrAC Trends in Analytical Chemistry*, vol. 118, pp. 722-730, 2019/09/01/ 2019.
- [19] J. Kim, A. S. Campbell, B. E.-F. de Ávila, and J. Wang, "Wearable biosensors for healthcare monitoring," *Nature Biotechnology*, vol. 37, no. 4, pp. 389-406, 2019.
- [20] S. A. Toms, W.-C. Lin, R. J. Weil, M. D. Johnson, E. D. Jansen, and A. Mahadevan-Jansen, "Intraoperative Optical Spectroscopy Identifies Infiltrating Glioma Margins with High Sensitivity," *Operative Neurosurgery*, vol. 57, pp. 382-391, 2005.

- [21] G. Seo et al., "Rapid Detection of COVID-19 Causative Virus (SARS-CoV-2) in Human Nasopharyngeal Swab Specimens Using Field-Effect Transistor-Based Biosensor," *ACS Nano*, vol. 14, no. 4, pp. 5135-5142, 2020.
- [22] L. Wang and C. Li, "pH responsive fluorescence nanoprobe imaging of tumors by sensing the acidic microenvironment," *Journal of Materials Chemistry*, vol. 21, no. 40, 2011.
- [23] R. Weissleder and M. Nahrendorf, "Advancing biomedical imaging," *Proceedings of the National Academy of Sciences*, vol. 112, no. 47, pp. 14424-14428, 2015.
- [24] J. V. Jokerst and S. S. Gambhir, "Molecular Imaging with Theranostic Nanoparticles," *Accounts of Chemical Research*, vol. 44, no. 10, pp. 1050-1060, 2011.
- [25] R. Weissleder, "Molecular Imaging in Cancer," *Science*, vol. 312, no. 5777, pp. 1168-1171, 2006.
- [26] A. V. Leopold, D. M. Shcherbakova, and V. V. Verkhusha, "Fluorescent Biosensors for Neurotransmission and Neuromodulation: Engineering and Applications," *Frontiers in Cellular Neuroscience*, vol. 13, 2019.
- [27] M. Banakar et al., "Electrochemical Biosensors for Pathogen Detection: An Updated Review," *Biosensors*, vol. 12, no. 11, 2022.
- [28] M. A. Eckert et al., "Novel Molecular and Nanosensors for In Vivo Sensing," *Theranostics*, vol. 3, no. 8, pp. 583-594, 2013.
- [29] S. R. Stahlschmidt, B. Ulfenborg, and J. Synnergren, "Multimodal deep learning for biomedical data fusion: a review," *Briefings in Bioinformatics*, vol. 23, no. 2, 2022.
- [30] S. Han, T. Ninjabdar, M. Kang, C. Kim, and J. Kim, "Recent Advances in Photoacoustic Agents for Theranostic Applications," *Nanomaterials*, vol. 13, no. 4, 2023.
- [31] H. Tong, K. Lou, and W. Wang, "Near-infrared fluorescent probes for imaging of amyloid plaques in Alzheimer's disease," *Acta Pharmaceutica Sinica B*, vol. 5, no. 1, pp. 25-33, 2015.
- [32] E. Cesewski and B. N. Johnson, "Electrochemical biosensors for pathogen detection," *Biosensors and Bioelectronics*, vol. 159, 2020.
- [33] E. Blanco, H. Shen, and M. Ferrari, "Principles of nanoparticle design for overcoming biological barriers to drug delivery," *Nature Biotechnology*, vol. 33, no. 9, pp. 941-951, 2015, doi: 10.1038/nbt.3330.
- [34] A. M. Smith, M. C. Mancini, and S. Nie, "Second window for in vivo imaging," *Nature Nanotechnology*, vol. 4, no. 11, pp. 710-711, 2009.
- [35] J. Wang, "Electrochemical biosensors: Towards point-of-care cancer diagnostics," *Biosensors and Bioelectronics*, vol. 21, no. 10, pp. 1887-1892, 2006.
- [36] M. A. Dobrovolskaia and S. E. McNeil, "Immunological properties of engineered nanomaterials," *Nature Nanotechnology*, vol. 2, pp. 469-478, Aug. 2007.
- [37] Y. Tian, L. Du, P. Zhu, Y. Chen, W. Chen, C. Wu, P. Wang, and P. Wang, "Recent progress in micro/nano biosensors for shellfish toxin detection," *Biosensors and Bioelectronics*, vol. 161, p. 112899, 2020.