JoFRISE 3 (3) (2025)
Journal of Frontier Research in Science and Engineering
https://journal.riau-edutech.com/index.php/jofrise
Publisher :
Andester Riau Edutech
Pusat Inovasi Pendidikan dan Teknologi
ISSN : 3032-0348

Development of Optical Sensors Based on Surface Plasmon Resonance (SPR) for Health Applications

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Submiited: 04/09/2025
Review: 09/09/2025
Accepted: 09/09/2025
Published: 27/09/2025
Vol. 3
No. 3

Abstract- In the healthcare sector, the development of optical sensor technology has shown rapid progress, particularly through the application of the Surface Plasmon Resonance (SPR) method. SPR is an optical phenomenon that is highly sensitive to changes in the refractive index on metal surfaces, enabling real-time, non-invasive detection of biomolecules. This study aims to examine the basic principles of SPR, the main components of the sensor, and its applications in the healthcare sector through a review of the latest literature. The results of the study indicate that SPR is capable of detecting biomolecules with high sensitivity even at low concentrations, and has been successfully implemented in glucose detection via wearable sensors, identification of cancer biomarkers such as HER2 and PSA, and detection of genetic material of the SARSCoV2 virus. This technology supports efficient continuous health monitoring, but still faces challenges in cost, fabrication precision, and environmental interference. Further innovation in sensor design, microfluidic integration, and temperature compensation strategies are needed to realize accurate and affordable diagnostic systems.

Keywords: *optical sensor, Surface Plasmon Resonance, biomolecules, health technology, nanomaterials*

1. Introduction

In recent years, the world of health has been faced with various increasingly complex problems, including the increasing number of people suffering from chronic diseases, the increasing number of elderly people and the emergence of new infectious diseases that are resistant to drugs.(Sarmania & Manik, 2024)Meanwhile, environmental pollution worsens public health. This problem demonstrates that health has become a pressing global issue.(Z. Xu et al., 2015).

Along with this, technological developments, particularly in biomedicine, have experienced significant progress. Modern sensors are designed to provide fast and accurate results and can be integrated with digital systems to support more responsive healthcare services (Pratiwi & Sahal, 2024). One example of the latest biomedical sensor technology is the glucose sensor. This sensor uses electrochemistry based on a Glassy Carbon Electrode (GCE), which is developed to measure blood sugar levels.(Wardani et al., 2025). In addition, piezoelectric sensors can be used to identify respiratory tract infections by measuring lung capacity and volume.(Wardana & Adil, 2017;Nasution et al., 2021)Flexible sensors have also been developed for biomedical applications, such as monitoring the body's physiological activity in real time. Despite their advantages in terms of flexibility and ease of use, these sensors still face issues such as long-term instability and biological compatibility.(Ikbal, 2021).

One of the most prominent optical sensor technologies among the various types of biomedical sensors that have been developed is biosensors. These optical sensors are capable of non-invasive, rapid, and accurate detection. Among biosensor technologies, Surface Plasmon Resonance (SPR) techniques have gained popularity due to their high sensitivity and ability to detect molecular interactions in real time, eliminating the need for complex labeling and purification processes.(Mayasari et al., 2017)The basic

How to Cite :
Amala, S. et.al. (2025). Development of Optical Sensors Based on Surface Plasmon Resonance (Spr) for Health Applications. *Journal of Frontier Research in Science and Engineering(JoFRISE)*, 3(3), 1-7

mechanism of SPR involves the interaction between light and a metal surface. SPR occurs when light photons strike a metal surface such as gold at a specific angle. The angle of minimum reflectivity can be determined by varying the angle of incidence and recording the intensity of the reflected light during the biomolecule binding process.(Nguyen et al., 2015;Hasanah et al., 2023).

Due to the extremely small and rapid changes in refractive index, direct detection of biomolecules remains challenging (Li et al., 2023). To address this, sensor surfaces are modified using nanometer-sized recognition nanomaterials such as magnetic nanometers. These nanometers have the ability to significantly enhance SPR sensitivity and reactivity.Fe_3O_4(Mayasari et al., 2017)

In addition, SPR sensors are based on non-metal structures and have been developed for broader applications, such as detecting biomarkers of diseases such as cancer and monitoring environmental pollutants such as heavy metals and hazardous chemicals.(Ménard-moyon et al., 2021). Because of the ability of SPRs to detect changes in dielectric properties caused by molecular interactions, they have great potential for use as diagnostic and monitoring tools.(DS Wang & Fan, 2016;Das et al., 2023). Thus, the utilization and innovation of SPR technology are crucial to addressing global challenges in the health sector.

Formulation of the problem

1. What is the working principle of Surface Plasmon Resonance (SPR) technology in optical sensors?
2. How is SPR applied in the health sector

Research purposes

1. Explain the basic concepts and working principles of SPR in optical sensor systems.
2. Examining the application of SP R in early detection of problems

2. Research methods

The method used in this research is a literature review with a qualitative approach. The purpose of this study is to review and analyze various previous research findings relevant to the topic of developing Surface Plasmon Resonance (SPR)-based optical sensors. The sources used include trusted national and international journals that discuss the working principles, development, and application of SPR in the health sector. The selected literature must be directly related to the research topic and published in Indonesian and English between 2015 and 2025.

The collected data will be analyzed qualitatively by comparing and synthesizing the contents of the literature, to find general patterns, important findings, advantages, disadvantages, and development of SPR technology in health applications.

As a basis for the study, an optical phenomenon called Surface Plasmon Resonance occurs when electromagnetic waves of light interact with a metal surface, such as gold or silver, causing resonance with free electrons on the metal surface.(Mauludi et al., 2024)This resonance occurs at specific angles or wavelengths, which are sensitive to the refractive index near the metal surface. This allows for real-time detection of biomolecular interactions without additional labeling.(Nguyen et al., 2015;Rajabiah, 2017).

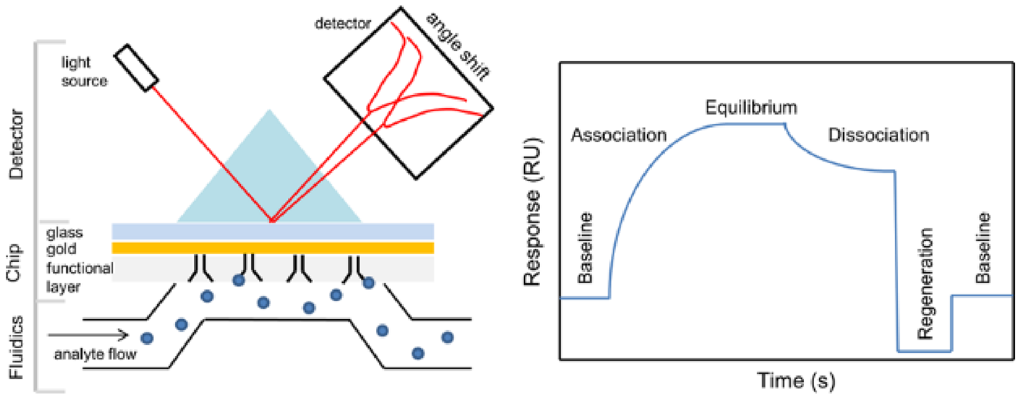

Figure 1: Basic principles of Surface Plasmon Resonance (SPR) (Source:Damborský et al., 2016)

Mathematically, SPR involves an evanescent electric field that oscillates along the metal-dielectric interface and undergoes an exponential decay perpendicular to the surface. Figure 1 shows that when p-polarized light is reflected from a prism (with a high refractive index) toward a liquid medium through a thin metal film, this evanescent field can couple with a surface plasmon wave. Coupling occurs when the wave vector and frequency of the evanescent field match those of the plasmon, resulting in a decrease in light reflection at a certain angle called the resonance angle. The change in refractive index due to the binding of the target molecule to the ligand on the sensor surface causes a shift in the resonance angle, which can be monitored as an optical signal.(Damborský et al., 2016;(Novitasari et al., 2022).

In an SPR biosensor system, a light source, a gold-coated sensor chip, an optical detector, and a microfluidic system are some of the main components of an SPR instrument. Ligand molecules are first fixed to the sensor surface through a specific chemical technique, and then an analyte solution is flowed across the surface. The refractive index changes caused by both are described as shifts in the light reflection angle. The results are depicted in the form of a sensorgram graph that reflects the stages of association, equilibrium, and regeneration.(Schasfoort, 2017).

Various SPR configurations have been successfully used for the detection of specific biomolecules, such as glucose and cancer biomarkers. The choice of ligand and immobilization technique significantly determines the sensitivity and specificity of the sensor used. The sensor is then applied to a real biological sample, such as blood serum, to directly detect disease biomarkers. Validation of the results is performed using standard reference methods such as ELISA or PCR to ensure accuracy and potential clinical use.(Kuruvilla Thomas et al., 2024).

3. Results and Discussion

Based on the results of the literature review that has been conducted, it shows that Surface Plasmon Resonance (SPR) is one of the most effective optical sensor methods for detecting biomolecular interactions in real-time without the need for additional dyes or labels. The principle behind SPR is the change in the refractive index around the sensor surface. This occurs due to the binding of target molecules (analytes) with materials placed on a metal surface, such as gold. This change causes a shift in the resonance angle which is then recorded as an optical signal. The advantage of this technology is its ability to detect biomolecules with high sensitivity, even at very low concentrations.

One of the currently widely developed SPR applications relates to blood glucose detection. This technology utilizes the enzyme glucose oxidase (GOx) placed on the sensor surface as a ligand (Fauza, 2025). When glucose molecules in the sample interact with the enzyme, the sensor measures the change in refractive index. In general, SPR sensors designed for glucose detection have a high level of sensitivity, short detection times, and can operate without further chemical processing. A special feature of this technology is its ability for continuous monitoring, eliminating the need for additional chemical processing.(Q. Wang et al., 2024).

Figure 2. a.) Flow diagram of the nanopillar functionalization process using 4-MPBA, b.) Schematic illustration of a watch device that optically detects glucose.

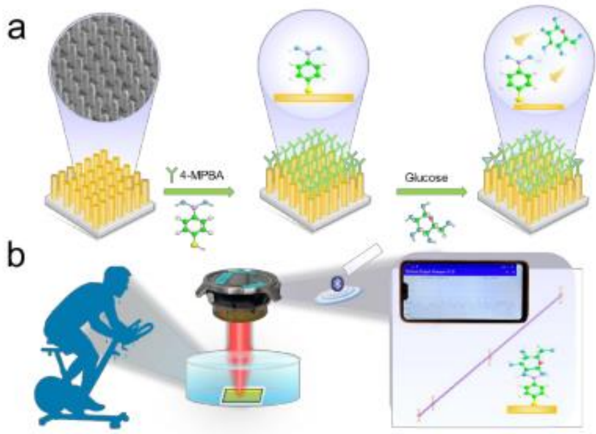

Figure 2. Illustrates The Operation Of A Nanopillar-Based SPR Sensor For Glucose Detection.

Part (a) shows the functionalization process of the nanopillar using the compound 4-MPBA (4-Mercaptophenylboronic Acid), which is capable of binding to glucose molecules. When glucose interacts with the functional layer, a change in the refractive index occurs, which can be recognized by the SPR system as an optical signal. Meanwhile, part (b) illustrates the application of this technology in the form of a wearable device used during physical activity. Signals from the sensor are sent wirelessly to a mobile device for real-time display and monitoring. This technology shows great potential in the development of a practical and efficient optical-based, non-invasive glucose monitoring system.(Liu et al., nd;Wu et al., 2023;Ambaye et al., 2024).

As an exampleLiu et al.who successfully developed a wearable SPR-based sensor for glucose monitoring through sweat. This sensor uses a silver-coated silicon nanowire substrate functionalized with 4-mercaptophenylboronic acid (4-MPBA), enabling glucose detection with high sensitivity down to 0.12 mM and good selectivity within the physiological sweat concentration range. In fact, this sensor has been integrated in a watch format with wireless data transmission to a mobile app, demonstrating its great potential for non-invasive health monitoring.

In addition to glucose detection, SPR is also widely used in detecting cancer biomarkers, such as HER2, PSA, or CEA.(Chen et al., 2022)In this application, antibodies against cancer biomarkers are placed on the sensor surface. If the patient sample contains the appropriate antigen, specific binding occurs, generating an SPR signal. Research byBellassai et al.AndDas et al.demonstrated that SPR biosensors can detect the presence of cancer antigens at very low concentrations, even down to the picogram per millimeter (pg/mL) scale, making them a highly potential tool for early cancer detection. Furthermore, Gold Nanoparticles (GNPs) are also often used as additives in SPR systems due to their unique plasmonic properties. Research byAgarwal et al.shows that GNP can be usedto increase the effectiveness of cancer therapy, especially in the treatment of prostate cancer with photothermal techniques, without damaging the surrounding critical tissue.

Another application of SPR is the detection of biomarkers of kidney disease, such as albumin in urine.Bergmann et al.reported the use of a Localized Surface Plasmon Resonance (LSPR) sensor with hexagonal gold nanoparticles to detect albumin. By varying the lateral size and thickness of the nanoparticles, the optimal sensitivity of the sensor reached 391 nm/RIU. In fact, by modifying the combination of AuNPs with silicon nanoparticles, the sensitivity increased to 651 nm/RIU. This shows that the design and modification of the nanoparticle structure in the SPR sensor can significantly improve the sensor performance.

In addition, SPR has also been used to detect genetic material such as RNA or DNA of viruses, including HIV, hepatitis viruses, and SARS-CoV-2.(Mauriz, 2020). Specific RNA/DNA probes are immobilized on the sensor surface, so that interaction with the viral genetic target in the sample generates an SPR signal. This technology holds great promise for rapid detection of infectious diseases, with high sensitivity and short response times. Recent research has demonstrated the ability of SPR to detect SARS-CoV-2 RNA in less than 10 minutes at femtomolar concentrations using a portable chip.(W. Xu et al., 2021).

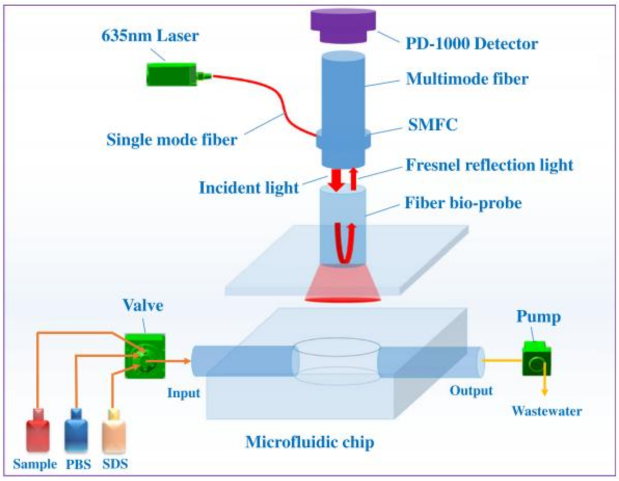

Figure 3. Schematic of the FRMB system, including the fiber optic system, microfluidic chip, fiber optic bio-probe, and fluids (pumps and valves).
(Source: Wenjuan et al., 2021)

Figure 3 shows the configuration of a fiber-optic Surface Plasmon Resonance (SPR) sensor system integrated with a microfluidic chip. The system consists of a 635 nm laser light source coupled to a single-mode optical fiber (SMF) and then connected to a multimode fiber (MMF) to transmit light to the fiber bioprobe. The reflected light (Fresnel reflection) from the fiber tip will change depending on the interaction of the target molecules at the bioprobe tip in contact with the sample. The PD-1000 detector receives the reflection and converts it into an electrical signal for analysis.(W. Xu et al., 2021;W. Wang et al., 2024).

The system is equipped with a microfluidic chip that regulates the flow of three fluids: sample, PBS (phosphate-buffered saline), and SDS (cleaning detergent). Through valves and pumps, the fluids are controlled into the detection chamber and then exit as waste. This system enables rapid, real-time biomolecule detection with very small sample volumes. The integration of fiber optics and microfluidics is ideal for point-of-care applications because the device is compact, sensitive, and portable.(Li et al., 2023).

Some of the main advantages of SPR include:

1. Real-time and label-free detection, without the need for additional chemicals as in the ELISA method.
2. High sensitivity, even at low concentrations (pg/mL scale).
3. Reusability of sensors after surface regeneration process, thus saving operational costs.
4. Application flexibility, as it can be adapted to detect various types of biomolecules such as proteins, enzymes, antigens, and DNA/RNA.

However, despite its advantages, SPR also has several limitations, such as:

1. Requires sophisticated optical equipment, such as microfluidic control systems and sensitive light detectors, which increases installation and operational costs.

2. The process of immobilizing the ligand on the sensor surface must be carried out with great precision so that the detection results remain accurate.
3. SPR sensors are susceptible to physical and environmental disturbances, such as mechanical vibrations, changes in temperature, or medium composition, which can affect signal stability.

Overall, the literature review indicates that SPR technology holds significant potential for the development of modern diagnostic devices. Its ability to detect biomolecules quickly, precisely, and non-invasively supports applications in various healthcare fields, such as glucose monitoring, cancer detection, and infectious disease diagnosis. Several scientific journals published between 2015 and 2025 also reported advances in metal layer optimization, nanoparticle design, optical system integration, and the development of portable SPR-based devices. Although challenges such as cost and system stability remain significant, future developments in SPR technology are expected to provide faster, more accurate, and more affordable diagnostic solutions, even in resource-limited regions.

4. Conclusion

Based on the literature review that has been conducted, it can be concluded that Surface Plasmon Resonance (SPR) technology is one of the optical sensor methods that is very effective in detecting biomolecules in real-time and without labels (label-free). SPR works on the principle of detecting changes in the refractive index on the surface of a metal sensor due to biomolecule interactions, thus enabling sensitive detection even at low concentrations, such as on the picogram per milliliter scale. This technology has been successfully implemented in various medical applications, including non-invasive glucose detection using nanopillar-based wearable sensors functionalized with 4-Mercaptophenylboronic Acid (4-MPBA), detection of cancer biomarkers such as HER2 and PSA with high sensitivity, and monitoring infectious diseases through the detection of viruses such as HIV, Hepatitis, and SARS-CoV-2. However, SPR technology still has several limitations, such as the need for sophisticated optical equipment, sensitivity to environmental disturbances, and the ligand immobilization process that requires precise conditions. Therefore, further development is needed to improve sensor stability, reduce production costs, and expand access to its use, especially in areas with limited resources. Overall, SPR is a very promising technology for biomolecule detection applications in healthcare. With research advances in sensor design, material functionalization, and integration with portable electronic devices, SPR has the potential to become a fast, accurate, and practical diagnostic solution for the future, supporting the development of more effective and efficient health monitoring systems.

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