Evolution and Challenges of Surface Plasmon Resonance (SPR) Biosensors

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Abstract. Surface Plasmon Resonance (SPR) biosensors have evolved into effective tools for real-time, label-free biomolecular interaction sensing. Their sensitivity, specificity, and variety of applications have significantly expanded since their introduction due to developments in materials, tools, and surface chemistry. This study explores the evolution of SPR biosensors over time, emphasizing important technological turning points and their consequences for environmental monitoring, drug research, and diagnostics. Notwithstanding their achievements, SPR biosensors have a number of challenges, such as non-specific binding, signal stability, cost-effectiveness, and downsizing. Additionally examined are cutting-edge approaches like data analysis based on artificial intelligence and the integration of nanomaterials. Gaining insight into the strengths and weaknesses of SPR biosensors is essential for directing future studies and enhancing their usefulness in a range of industrial and biomedical applications.

Keywords. Surface Plasmon Resonance, Biosensors, Sensor Evolution, Detection Sensitivity, Biomedical Applications, Technological Challenges

1. Introduction

Liedeberg and Nylander illustrated the value of Surface Plasmon Resonance (SPR) as an optical biosensor in 1982. Since then, surface chemistry has benefited from SPR, which has allowed chemistry, physics, and biology to share a similar platform [1]. Several businesses have commercialized SPR as an optical biosensor under several trade names [3]. The application of SPR biosensors has grown in popularity in a variety of fields, including environmental and agricultural monitoring, drug development, clinical diagnosis, health science research, and basic biological studies. SPR is rapidly gaining traction in the field of quantitative analyses for POC diagnostics in clinical laboratories, such as immunoassay analysis, mutation detection, and therapeutic drug monitoring (TDM) for dosage control and toxicity risk management to improve drug therapies with exceptional reutilization performance and reproducibility [3].

SPR provides real-time, label-free measurements of the kinetics and affinity of bimolecular binding. SPR offers a number of benefits over radioactive or fluorescent labeling methods, including as cost effectiveness, direct determination of binding constant and affinity, less reagent consumption, and the possibility of label impairment in binding. [4].

Label-free biomolecular interaction investigations have grown to rely heavily on Surface Plasmon Resonance (SPR) biosensors due to their high sensitivity, real-time detection capabilities, and versatility in a variety of biochemical and biomedical applications. Since their inception in the early 1980s and subsequent commercialization in the 1990s, SPR biosensors have experienced significant technological advancement, expanding their use in drug discovery, clinical diagnostics, food safety, and environmental monitoring [5,6]. The basic element of SPR biosensors is surface plasmon resonance, a physical phenomenon that occurs at the interface between a metal (often gold) and a dielectric medium. It allows for the detection of minute changes in refractive index close to the sensor surface [7]. Because SPR is sensitive to changes in the local refractive index, it can be used to monitor biomolecular interactions without the use of labels or secondary markers while maintaining the analyte's natural behaviour [8].

Despite their advantages, SPR biosensors face several challenges that limit their broader implementation, especially in complex biological matrices. Issues such as non-specific binding, limited multiplexing capabilities, integration with microfluidic systems, and the need for miniaturization and cost reduction continue to hinder their scalability and adaptability [9,10]. Furthermore, while traditional SPR configurations have excelled in laboratory settings, the transition toward portable and point-of-care devices demands innovative solutions in materials science, sensor design, and data processing algorithms.

This study is to investigate the technological development of SPR biosensors, analyze the current obstacles preventing their broad use, and talk about new approaches to get over these obstacles. This work aims to provide a thorough perspective in order to direct future advancements and promote interdisciplinary cooperation in the advancement of SPR technology toward next-generation biosensing applications.

2. Sensor Design and Configuration

The Kretschmann configuration, which used large prism-based optical systems, was the main basis for earlier SPR biosensors [10]. Because of their size and expense, these sensors needed to be precisely aligned and were mostly used in laboratory settings. With the use of photonic integrated circuits (PICs), grating couplers, and optical fibers, modern systems have developed toward integrated and compact designs. By lowering the instrument footprint and improving user accessibility, these developments support portable and point-of-care applications [16,19].

3. Sensitivity and Detection limit

For many biochemical interactions, traditional SPR sensors' detection limits were in the nanomolar range; nevertheless, they were insufficient for analytes with ultra-low concentrations

[6]. Recent methods use localized surface plasmon resonance (LSPR), 2D materials (such as graphene and MoS_2), and nanostructured surfaces to increase sensitivity. The picomolar and femtomolar ranges are now the detection limits due to these changes [18,12].

4. Multiplexing capability

Because early devices were one-channel, conventional SPR sensors could only detect one analyte per experiment. Multiple targets can now be detected simultaneously using SPR imaging (SPRi) and microarray formats, boosting throughput and opening up applications such as biomarker panels for disease diagnostics [15].

5. Integration with Microfluids

Manual sample delivery was necessary for early SPR setups, and fluidic integration attempts were rudimentary and vulnerable to fouling or sample loss. Microfluidic chips are frequently used in modern SPR biosensors, allowing for automated sample processing, real-time flow control, and lower reagent volumes. This is essential for in-field and point-of-care diagnostics [14,10].

6. Data Analysis and Interpretation

Basic kinetics fitting was used for data interpretation, necessitating manual sensorgram interpretation by skilled users. For remote monitoring and real-time analytics, modern systems integrate cloud integration, AI-based analysis, and sophisticated signal processing, which makes them more intuitive and perceptive [11].

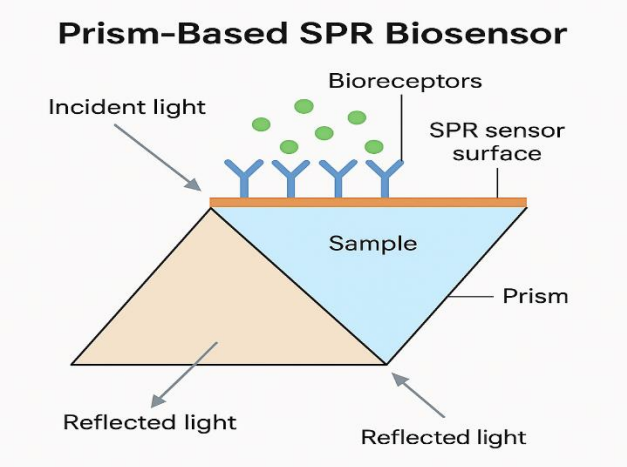

Fig. 1

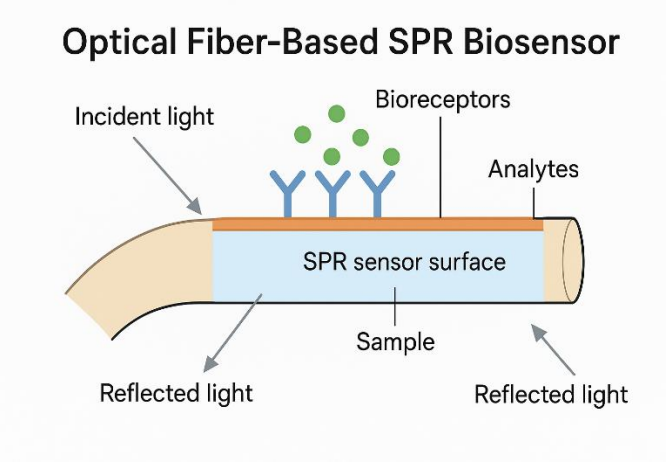

Fig. 2

7. Discussion

The demand for real-time, label-free biomolecular contact detection has led to a major evolution in Surface Plasmon Resonance (SPR) biosensors since their inception. Originally limited

to laboratory-scale uses, modern SPR systems are now employed in a wide range of sectors, including food safety, medical diagnostics, and environmental monitoring. Improvements in sensitivity, specificity, and downsizing brought about by developments in surface chemistry, nanotechnology, and microfabrication have made this shift easier [13]. The transition from conventional prism-based configurations to more portable, compact systems like optical fiber-based SPR and localized SPR (LSPR) using nanoparticles is one of the most significant advancements in SPR biosensors. These developments have made it possible to include SPR biosensors into wearable technology and point-of-care (POC) diagnostic systems [20]. In certain situations, the use of nanostructured materials like graphene and gold nanoparticles has improved detection limits to the femtomolar range by greatly increasing the surface area for biomolecular interactions [21].

Even with these developments, a number of issues still exist. The nonspecific adsorption of molecules onto the sensor surface, which causes signal drift and decreased repeatability, is still a significant drawback. Polyethylene glycol (PEG) coatings and other surface functionalization approaches have been used to solve this problem, but their long-term efficacy has been restricted [22]. Furthermore, SPR is limited to identifying events that are surface-bound due to the intrinsically small penetration depth of evanescent fields (~200 nm), which makes it less appropriate for researching intricate, multi-layered biological systems.

Moreover, the extensive use of SPR technology is restricted by the high expense of equipment and the need for qualified workers, particularly in environments with limited resources. Although commercial maturity is currently lacking, efforts are being made to democratize the technology through the development of low-cost, smartphone-integrated SPR devices [23]. The quantitative interpretation of SPR signals in complex matrices, such blood or serum, where background noise is introduced by variations in viscosity, temperature, and refractive index, is another crucial difficulty. To distinguish between selective binding and nonspecific interactions, sophisticated data processing algorithms—such as machine learning techniques—are being investigated; however, these need more standardization and validation [24].

8. Conclusion

In conclusion, even though SPR biosensors have advanced significantly, major obstacles in surface chemistry, instrumentation cost, and data interpretation must be addressed before their full promise can be realized in clinical and field contexts. To overcome these constraints and expand the potential of SPR technology, multidisciplinary research must continue.

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