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Surface Plasmon Resonance Biosensors: Advances, Applications, and Future Prospects

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Abstract. In recent years, surface plasmon resonance (SPR) biosensors have gained importance as analytical methods for biomolecular interaction studies in real-time and without the need for labels. This review encompasses the principle of SPR, the kinds of SPR biosensors, and their diverse applications ranging from medical diagnostics, environmental monitoring, food safety, and biotechnological researches. Recent advances in the development of SPR-based biosensors, including their multiple abilities and portable SPR devices, are also discussed. Furthermore, the discussion focuses on current challenges to SPR biosensors with regard to sensitivity and specificity. Besides, the future directions of research and development are also discussed, which include the possibility of novel enzyme-based SPR biosensors for direct biomarker detection. These advances clearly demonstrate that SPR biosensors, which revolutionize modern detection and monitoring techniques, are becoming increasingly significant in a number of scientific and clinical applications. As SPR technology continues to evolve, its potential to contribute to emerging areas, such as personalized medicine and environmental sustainability, is becoming increasingly apparent.

Keywords: Biosensor; Surface Plasmon Resonance; Application.

1. Introduction

Surface plasmon resonance (SPR) is a powerful optical method that can be used for the detection of changes in the refractive index close to the surface of a thin metal film. Collective oscillations of electrons induced by excitation of the metal surface with polarized light result in surface plasmons. SPR is sensitive to minute changes in the presence of biomolecules, as these oscillations are highly sensitive to shifts in the refractive index of the medium adjacent to the metal surface.

Biosensors are analytical devices containing both a biological recognition element and a physical transducer that can quantify and detect biological analytes [1]. Biosensors represent important analytical tools that play a central role in various fields, including medical diagnostics, monitoring the environment, detecting food pathogens, and biotechnology. They are invaluable addition in scientific research and practical applicability, whereby they are used to provide rapid and accurate in real-time data. SPR biosensors have such advantages as label-free detection, real-time monitoring, and high sensitivity, so they have a wide spectrum of applications [1].

This work provides a comprehensive overview of the principles and applications of SPR biosensors across various fields. It covers the latest advancements in SPR technology, including its integration with nanotechnology. It also explores the critical role in environmental monitoring, food safety, medical diagnostics, and biotechnological research.

2. Principles of SPR

2.1. Basic Theory and Mechanism

SPR occurs when an angle-polarized light beam impinges on a metal film at an angle. This generates collective oscillation of free electrons in the metal surface, known as surface plasmons. This results in a resonance condition that is very sensitive to changes in the refractive index of the medium close to the metal surface. The interaction of the biomolecules with the surface of the sensor results in a change in refractive index that in turn alters the resonance angle or intensity. In this manner, real-time monitoring of biomolecular interactions can be done using SPR without the use of any labels [1].

2.2. Advantages of SPR over Other Techniques

There are several advantages of SPR biosensors over traditional detection approaches that have made this technique invaluable for numerous analytical applications. One of the main advantages is the label-free detection capability. They do not require fluorescent or radioactive labels, reducing the complexity of the assay. SPR allows for real-time monitoring of biomolecular interactions, providing very informative kinetic data. It includes association and dissociation rates. It would be used to explain the dynamics of these interactions [1, 2]. SPR has very high sensitivity to small changes in the refractive index, which is used to identify low analyte concentrations with great accuracy. SPR can also be applied to a wide range of interaction studies, such as protein-protein, protein-DNA, and small-molecule interactions. SPR presents a very general application across a variety of applications and. Therefore, it is superior to other techniques in biomolecular detection and analysis [1].

3. Types of SPR

3.1. Nanoparticle-Enhanced SPR

The Newton Photonics (NP) SPR concept is a more specific application of prepared nanoparticles, usually made of gold or silver, for the purpose of amplification in SPR. These are basically nanoparticles with some form of unique optical properties that will amplify the local electromagnetic field when they are in proximity to the SPR sensor surface. This enhancement enables a drastic rise in the sensitivity of SPR biosensors, making it possible to detect very low analyte concentrations that would otherwise be undetectable using conventional SPR. The signal enhancement mechanism is based on the localized surface plasmon resonance of the nanoparticles. These can only be produced once the nanoparticles are illuminated by light and produce strong local electromagnetic fields. Therefore, the binding of the analyte to a receptor on the surface of SPR sensor leads to changes in the local refractive index of the medium. This change is further amplified in the presence of nanoparticles, resulting in a much more significant shift in the SPR signal [3].

3.2. SPR Imaging (SPRi)

SPR imaging is a variation of the traditional technique, using additional imaging for signal detection over an array of spots on a sensor chip. This makes it a tool for high-throughput analysis which can analyze several interactions at the same time. It provides real potential for studying biomolecular interactions with great detail. In an SPRi setup, the sensor surface is divided into multiple regions, each functionalized with different capture molecules. Thus, if a sample moves over the sensor surface, an interaction happens at different spots on the array, corresponding to specific analytes. SPRi technology simultaneously detects and processes all these interactions in real-time to produce an image where the binding event over an array is presented. Each of these spots on an image corresponds to a specific interaction, and the intensity of the signal is proportional to the number of analytes that bind to that spot [1, 4].

3.3. Localized SPR (LSPR)

Localized surface plasmon resonance (LSPR) employs metal nanostructures, such as nanorods, nanospheres, or nanostars, that strongly confine their plasmonic activity close to their surfaces. It shows higher sensitivity than traditional SPR. LSPR sensors work on the principle of small plasmon-resonant nanoparticles that cause strong sensitivity of this condition to changes in the dielectric environment. When an analyte is bonded at the surface of a metallic nanostructure, it brings about a change in the local refractive index and in the plasmon resonance wavelength. This change is quantifiable and allows conclusions about the presence or concentration of an analyte to be drawn [1, 4, 5].

4. Applications

SPR biosensors are widely applied in medical diagnostics for detecting disease biomarkers. They provide a rapid, sensitive, and non-invasive method for identifying a wide range of biomarkers present in bodily fluids, such as blood, urine, and saliva. For example, SPR biosensors have been developed to detect biomarkers for cancer, cardiovascular diseases, and infectious diseases. It provided crucial information for early diagnosis and treatment monitoring [2].

Drug discovery and development are critical functions in the pharmaceutical industry for SPR biosensors. These tools find application in prospective drug candidates being screened, taking measurements of binding affinity and kinetics toward target proteins. Such information helps identify the most promising compounds and further optimize the interactions. SPR biosensors have also found applications in drug-target interaction studies for elucidating mechanisms and monitoring drug effects on biological systems [2].

SPR biosensors are strong analytical tools for environmental monitoring, especially for detecting pollutants and hazardous substances in water, air, and soil. They can recognize trace heavy metals, pesticides, and organic contaminants in real-time for environmental protection and regulatory compliance. For example, SPR biosensors have been used to detect mercury (Hg) in contaminated water sources with detection limits as low as 0.5 ppb, providing crucial data for environmental safety standards. Additionally, SPR-based sensors have been developed to detect lead (Pb) in drinking water at concentrations below the U.S. Environmental Protection Agency (EPA) action level of 15 ppb, helping to prevent lead poisoning in vulnerable populations. Furthermore, cadmium (Cd) detection using SPR biosensors has shown effectiveness in monitoring agricultural runoff, where cadmium contamination from fertilizers poses a significant risk to both the environment and human health [3].

Food safety is a significant global concern. SPR biosensors are regarded as one of the reliable means to detect pathogens and contaminants in food products. For instance, a biosensor based on SPR has been developed for the detection of Salmonella enterica, a foodborne pathogen, from poultry products at a detection limit as low as 10^3 CFU/mL to prevent salmonellosis outbreaks. The SPR biosensors have also been applied to detect the mycotoxin aflatoxin B1 in peanuts and corn at the parts per billion (ppb) level to ensure food products are safe and free of toxic contaminants. SPR biosensors have also been used to detect Escherichia coli in beef products within a short period of time to prevent foodborne infections [4].

Protein-protein interaction forms the basis of biotechnological research and pharmacology. At the base of the research lies the detection and study of interactions between biological molecules, by interacting with SPR biosensors in real time to give data on their binding affinities, kinetics, and stoichiometry. For example, SPR biosensors have been used in the investigation of the interaction between tumor suppressor protein p53 which is a critical interaction in cancer biology. The study allows the researcher to screen for potential inhibitors, which could be new anticancer drugs. SPR biosensors have also been applied in the studies of antibody-antigen binding interaction during therapeutic monoclonal antibody development. Therefore, important kinetic data are acquired for antibody-based therapies optimization. SPR biosensors have further been utilized in the investigation of interaction between HIV-1 proteins and cellular proteins of hosts to shed light on possible viral mechanisms of infection and the associated potential therapeutic targets [1, 4, 6].

SPR biosensors are applied in nucleic acid analysis through the detection of DNA sequences, hybridization kinetics studies, and genetic mutation identification. This method allows label-free, real-time monitoring of nucleic acid interactions, making it a valuable tool in genomics, diagnostics, and personalized medicine [1, 6].

5. Advancements in SPR Biosensors

5.1. Nanotechnology Integration

Recent advances in the integration of nanotechnology into SPR biosensors have significantly improved their performance. The surface area and the sensitivity of SPR sensors have been enhanced through modifications by nanostructures. For example, gold nanoparticles amplify the local electromagnetic field, resulting in a much stronger SPR signal. Due to the increased surface area and signal output, SPR biosensors can detect low-abundance analytes, increasing their overall durability [5].

5.2. Portable SPR Devices

Recent research and development have produced portable SPR devices. Those research enabling the technology for use in point-of-care testing and field applications. These portable devices maintain the sensitivity and specificity of conventional SPR systems but introduce the convenience of on-site analysis. They are highly useful in remote areas, environmental monitoring, and rapid medical diagnostics [1, 5].

6. Challenges and Future Directions

Despite the enormous advantages of SPR biosensors over other techniques, they are limited by sensitivity and specificity. Non-specific binding and complex sample matrices can interfere with measurements. Designing better surface chemistry, advanced signal processing, and new recognition elements are efforts put forth to address this problem [1, 4].

The incorporation of artificial intelligence and machine learning in data analysis is among the upcoming innovations in SPR biosensors. In addition, the hybrid sensors that include SPR technology along with other detection methods are worthy of further investigation. Besides, exploring new materials for sensor surfaces are also considered as an efficient way to enhance the performance of sensors. These innovations are expected to expand the capabilities of SPR biosensors further, making them indispensable tools for scientific research and practical applications [5, 6].

7. Conclusion

SPR biosensors can be used in many different fields, including medical diagnostics, environmental monitoring, food safety, and biotechnologies. New horizons involving nanotechnology, along with developments in multiplexing and portability, have evolved and enhanced its overall performance. However, it faces some challenges concerning with the sensitivity and specificity. Addressing these issues in the future with sustained research and innovation would further cement SPR biosensors as imperative tools for detection and monitoring applications.

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