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Properties, Detection Mechanism and Applications of AuNPs-Based Sensors in Virus Detection

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Abstract. After the outbreak of COVID-19 pandemic, infections caused by viruses have been proved to be one of the greatest global burdens that causes significant morbidity and mortality over the world. Detecting the virus as early as possible can help achieve early diagnosis of the disease. This will help doctors grasp the precious time of treating patients. Therefore, the rapid and accurate detection of viral pathogens is crucial for the effective control in the spreading of diseases, especially during such global pandemics. In the recent years, varies types of gold nanoparticles (AuNPs) based sensors have emerged since AuNPs have shown great potential in the field of viral diagnostics. This review aims to provide an overview of AuNP-based virus detection strategies. It mainly covers the properties of AuNPs, the detection mechanism, and the applications of these methods, such as colorimetric detection, surface plasmon resonance biosensors, fluorescent detection, and electrochemical detection. This work will contribute to promoting the application of AuNPs in virus diagnosis and detection.

Keywords: AuNPs; Sensor; Virus Detection; Detection Mechanism.

1. Introduction

Viral infections have been one of the greatest threats in human history. This can be proved by the recent COVID-19 pandemic and periodic outbreaks of influenza around the world [1]. Achieving rapid and accurate virus detection is crucial for controlling the diffusion of diseases. Even though traditional virus detection methods like polymerase chain reaction (PCR) and enzyme-linked immunosorbent assays (ELISA) are considered reliable, they are often time-consuming. They require specialized equipment and may not be accessible in all cases, particularly in regions that are lack of medical resources [2]. Therefore, there is a growing need for innovative, faster, and more accessible diagnostic tools.

In recent years, nanotechnology has shown its potential in the field of biosensors for viruses, offering novel solutions for virus detection. At the same time, integrating nanoparticles in traditional detection methods can also improve these methods themselves. Among the various nanomaterials which have been reported, the unique properties of AuNPs make them particularly suitable for virus detection. The surface plasmon resonance of AuNPs is considered to be a highly valuable feature for detection. In addition, AuNPs can be functionalized and endowed with rich performance, making it suitable for more detection environments. Such properties make AuNPs-based sensors highly sensitive for targeted virus detection.

In this work, the fundamental properties of AuNPs that make them particularly suitable for virus detection will be covered. Then it will be focusing on the detection mechanism of multiple types of sensors, including colorimetric detection, surface plasmon resonance biosensors, fluorescent detection, and electrochemical detection. The practical applications of these sensors in real-world virus detection scenarios will also be discussed, paving the way for future research and development in this area of AuNPs-based sensors.

2. Properties of AuNPs

2.1. Optical Properties

Localized surface plasmon resonance (LSPR) is one of the optical properties of AuNPs. When an incident light falls on the AuNPs, the oscillating electric field of the incident light interacts with the conduction electrons in AuNPs, causing them to oscillate coherently. As a result, the electron cloud deviates from its original location. The electrostatic attraction between the displaced electron cloud and the positively charged nuclei induces a restoring force on the electron cloud, which results in the oscillation of the electron cloud. When the frequency of the incident light matches the natural frequency of the electron cloud oscillations, the resonance condition is met. Thus, AuNPs are able to scatter and absorb light [3]. The resonance of AuNPs falls into the visible light range so that bright colors can be observed [3]. This property of AuNPs leads to several applications in the detection of virus, such as the colorimetric assays and surface plasmon spectroscopy.

Color change mechanism is another important property of AuNPs. Dispersed AuNPs usually demonstrate an intense red color due to their LSPR. However, when the AuNPs aggregates, the distance between AuNPs decrease. This results in the coupling of their plasmon fields. As a result, there is a shift in the surface plasmon resonance band that leads to a color change from red to blue or purple [4]. This optical property enables AuNPs to achieve visible detection of target objects to the naked eye.

2.2. Surface Functionalization

AuNPs can be functionalized with biomolecules that specifically bind with viral antigens or nucleic acids. These biomolecules include antibodies, DNA, and peptides. This property can be utilized in the detection of virus. functionalization of AuNPs with antibodies against specific proteins from the virus leads to the selective binding between them. AuNPs can also be conjugated with DNA probes complementary to viral RNA. The binding of viral RNA with the DNA probes on the AuNPs can then be detected through changes in the aggregation state or optical properties [4].

Additionally, redox-active molecules can also be covalently bonded to the surface of AuNPs using the thiol groups (-SH). With such molecules attached, the AuNPs are able to participate in redox reaction. By doing so, the electrochemical signal of the AuNPs can be greatly amplified due to the efficient electron transfer caused by the large surface area of AuNPs. In the context of virus detection, electrochemical biosensors are able to detect the change in the redox potential of redox-active molecules on the AuNPs when the virus binds to the antibody [4].

3. Detection Mechanism

3.1. Colorimetric Detection

Colorimetric detection utilizes the optical properties of AuNPs, including surface plasmon resonance. It has the ability to change color after aggregation. The binding between the functionalized AuNPs and the target virus in a sample leads to aggregation when they come closer together. Qualitative results can be obtained from a shift in the SPR band, resulting in a visible change in color from red to purple. By this way, visible phenomena which is showing that the virus is present. To obtain quantitative result, absorbance at maximum wavelength can be measured using UV-Vis spectrophotometer [5]. According to the Beer-Lambert law, the absorbance at the maximum wavelength is directly proportional to the concentration of the target virus.

There are several advantages for colorimetric detection. It is simple to perform and its qualitative result can be easily understood, making it suitable for point-of-care and field applications. It is also possible to get results within minutes, thus allowing quick detection and decision-making.

Shawky et al. developed a simple, rapid, and inexpensive colorimetric assay using unmodified AuNPs for the direct detection of unamplified Hepatitis C Virus (HCV) RNA from clinical samples. In this study, the AuNPs are citrate-coated and they demonstrate a red color. In the presence of the target HCV RNA, a specific single-stranded DNA (ssDNA) primer that is complementary to the target RNA is added to the solution. As the primer and the target RNA bind, a double-stranded structure which cannot be absorbed by the AuNPs forms. As a result, the AuNPs are not stabilised by the ssDNA primers, and the repulsive forces between the negatively charged citrate ions on their surface decrease in a saline solution. Thus, the AuNPs will aggregate which means a colour change from red to blue can be observed. If the target RNA is absent, the ssDNA primers remain unbound and freely adsorb onto the AuNPs. This adsorption stabilizes the AuNPs, preventing aggregation even in the presence of salt.

3.2. Surface Plasmon Resonance

The optical properties of AuNPs can also be applied in SPR biosensors. In this method, a monochromatic light source is shined though a prism on a thin layer of functionalized AuNPs that are immobilized on a surface of glass or polymer substrate. When the target virus binds with the functionalized AuNPs, the local refractive index changes, leading to a shift in the SPR angle. Then, a photodetector is used to measure this shift in the SPR angle [6].

SPR offers label-free and real-time analysis as SPR does not require any labels or secondary reagents. It enables real-time monitoring of binding events, providing immediate feedback.

In addition, researchers have also explored the preparation and application of nano gold with different shapes. Wang et al. developed LSPR biosensor for sensitive detection of hepatitis B virus using gold nanorod (GNR). The GNRs are functionalized with monoclonal hepatitis B surface antibodies (HBsAb) by physical adsorption. In the presence of hepatitis B surface antigens (HBsAg), the antibodies and antigens will bind specifically. This binding of HBsAg increases the effective thickness of the layer surrounding the GNRs, changing the local refractive index. The alteration in the local refractive index will lead to a shift in the LSPR wavelength to a longer wavelength which can be detected using UV-Vis spectroscopy. Beside the detection of the virus, quantification can be done since the magnitude of the LSPR shift is proportional to the amount of HBsAg present in the sample.

3.3. Fluorescent Detection

The surface plasmon resonance of AuNPs can be applied in fluorescent detection as well. The SPR of AuNPs is capable of quenching or enhancing the fluorescence of nearby fluorophores depending on the distance between the AuNPs and fluorophores. If the fluorophores are in a close proximity (around 1-10 nm), the energy from the excited fluorophores will be transferred to the AuNPs, causing a decrease in the fluorescence intensity. Thus, the fluorophores are quenched. On the other hand, enhancement occurs when the fluorophores are further away from the AuNPs. The amplification of the local electromagnetic field will increase the excitation rate of the nearby fluorophores, leading to a higher fluorescence intensity. As a result, the change in fluorescence intensity can be measured using a fluorescence spectrometer. The intensity at a specific wavelength is recorded and analyzed [7].

In the study conducted by Chang et al., enhancing mechanism is used to detect hemagglutinin (HA) proteins present on the surface of the H1N1 virus. The core of the biosensor is made by attaching antibodies that is specific to the H1N1 HA protein on an exposed optical fiber. When HA protein is introduced, the HA antigens bind to the immobilized capture antibodies on the fiber surface. Then, another type of detection antibody, which is labelled with a fluorophore and adsorbed onto gold nanoparticles will specifically bind with a different epitope on the HA antigen, forming a sandwich structure. As the sandwich structure is formed, the optical fiber is exposed to a laser to excite the

fluorophores, while the AuNPs enhance the fluorescence signal. The intensity of the fluorescence signal is directly proportional to the concentration of the target HA protein in the sample.

The use of AuNPs in this biosensor greatly improved the detection limit due to the enhanced fluorescence intensity. The increased sensitivity can result in early and accurate diagnosis of H1N1.

3.4. Electrochemical Detection

There are multiple ways in which AuNPs are used in electrochemical detection such as impedance spectroscopy and voltametric sensors. In this paper, the mechanism of voltametric sensors will be discussed. A voltametric sensor measures the current as a function of an applied potential. Since AuNPs demonstrate catalytic activity, high surface area, and excellent conductivity, they are able to greatly enhance the efficiency of electron transfer. Thus, AuNPs can amplify the signal produced. If the AuNPs are functionalized with redox-active molecules, the binding of viral particles can lead to the change in peak currents or potentials which indicates the presence of target virus [4].

Martínez-Paredes et al. use of a gold nanostructured screen-printed carbon electrode (SPCE) to detect the presence of SARS-CoV RNA [8]. A thiolated DNA probe that is complementary to a specific sequence of the SARS-CoV RNA, is immobilized on the gold nanostructured surface located on the SPCE. When the target RNA binds with the DNA probe, the setup will trigger an enzymatic reaction that reduces sliver ion to silver metal deposited on the SPCE. The deposited silver is then detected by anodic stripping voltammetry (ASV) where electrode potential is swept. The metallic silver will be oxidized back to sliver ion. The current generated during oxidation is detected and it is proportional to the amount of silver deposited, which also correlates with the amount of target RNA present [9].

4. Conclusion

AuNPs have been found to be efficient tools in developing advanced virus detection techniques, providing high sensitivity, specificity, and rapid detection. The use of different platforms like colorimetric detection, SPR biosensors, fluorescence-based detections and electrochemical procedures has shown the potential of AuNP-based sensors for mitigating the impact of viral outbreaks by enabling early detection. However, there are still some challenges facing AuNP-based sensors. Fundamental issues include controlled synthesis as well as surface modification of AuNPs. The performance of these sensors can be strongly affected by changes occurring due to variations in their size, shape or surface functionalization. These may cause specificity and sensitivity impact on them. Furthermore, AuNPs can remain in the environment and accumulate in organisms. This may create some harmful long-term ecological effects. The potential for biomagnification to occur raises concerns about their impact on wildlife and human health. Thus, addressing such issues would enable fuller potential realization of AuNPs so that there will be more accessible and reliable detection methods in the future.

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