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A Review of Electrochemical Sensors for Biological Detection of Viruses, Glucose and Cancer Cells

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Abstract. In clinical practice, monitoring physiological indicators is essential for evaluating human health. Conventional medical devices can detect many of these signals, but their responses are often limited by insufficient selectivity and unstable output, which restricts their reliability. Electrochemical sensors have therefore attracted extensive interest in biomedical analysis as tools for assessing health status. By combining simple operation with high stability, sensitivity, and quantitative capability, electrochemical biosensors offer a promising platform for medical testing. This review provides an overview of recent developments in electrochemical biosensors for the detection of key biological targets, with a particular focus on viruses, glucose, and cancer cells. We summarize representative detection strategies and sensing materials, and highlight the main technical challenges encountered in practical applications. Finally, we discuss potential directions for the future development of electrochemical sensors in biomedical diagnostics.

Keywords: Electrochemical biosensor, Biological detection, Virus detection, Glucose sensing, Cancer cells

1. Introduction

Monitoring physiological indicators has become an integral part of both clinical practice and daily healthcare management. To track physical conditions such as metabolic status and disease-related biomarkers, a broad range of medical devices has been developed. However, the readouts of many conventional instruments are still affected by limited selectivity, unstable responses, or environmental factors such as temperature and humidity, which can compromise their diagnostic reliability. Against this background, electrochemical sensors have drawn increasing attention in biological analysis because they combine high sensitivity with relatively low cost and rapid detection.

In an electrochemical sensor, the change that occurs at the electrode-solution interface is translated into an electrical readout, such as a current response or a shift in potential [1]. In practice, the measurable signal is proportional to the amount or activity of the analyte in the sample, so it can be used to estimate the analyte concentration after proper calibration. In a typical configuration, a functional layer is deposited on the surface of the working electrode. This sensing layer is designed to interact preferentially with a given target, and the resulting interfacial process gives rise to the electrochemical response. By varying the composition, structure, or thickness of this layer, different

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sensor designs can be obtained for different analytes while still keeping the overall response reasonably stable and accurate [2]. This flexibility in electrode modification is one of the main reasons why electrochemical sensors are frequently chosen for biological measurements, including routine monitoring of health-related indicators by clinicians and researchers.

For quantitative measurements, electrochemical experiments are usually carried out in a three-electrode cell rather than a two-electrode setup, because the three-electrode arrangement provides a separate reference for potential control and thus improves the definition of the working electrode potential [3,4]. As shown in Figure 1(a,b), the cell consists of a reference electrode (RE), a working electrode (WE), and a counter electrode (CE). The RE maintains a stable and known potential; the WE is where the redox reaction of the analyte takes place; and the CE closes the circuit and supplies the current required by the measurement [5]. With these roles separated, electrochemical sensors based on the three-electrode configuration can deliver reproducible and precise data and have been adopted in many diagnostic and monitoring tasks [6]. In the following sections, we describe representative electrochemical sensing strategies and electrode materials for the detection of viruses, glucose, and cancer cells, and we outline several issues that still limit their wider use.

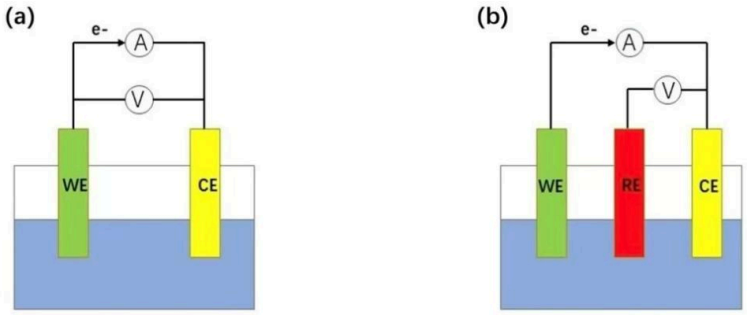

Figure 1. Schematic configurations of (a) two-electrode and (b) three-electrode electrochemical sensor systems

2. Different targets detected by electrochemical sensors

2.1. Electrochemical sensors for detecting viruses

Electrochemical virus sensors usually work by recognizing either proteins on the viral surface or viral nucleic acids such as DNA and RNA fragments. In the following, SARS-CoV-2 is used as a concrete example to describe typical electrochemical strategies. At the beginning of the COVID-19 outbreak, reverse transcription polymerase chain reaction (RT-PCR) was adopted almost everywhere as the standard method for confirming SARS-CoV-2 infection [7]. RT-PCR is highly specific, but in routine operation it depends strongly on experimental conditions: small changes in temperature, storage time of the nucleic-acid sample, or handling procedures can influence the readout [8]. The assay also requires well-equipped laboratories and trained staff and is sensitive to contamination, which makes it relatively slow and expensive when large numbers of samples need to be processed. Rapid antigen or antibody tests were therefore introduced for on-site screening of SARS-CoV-2. These tests are convenient, but their detection limit is higher than that of RT-PCR and false-negative results are not rare, so some infected cases may be overlooked [9]. These practical issues explain why many groups have turned to electrochemical methods for virus detection.

One type of electrochemical strategy relies on magnetic nanoparticles (MNPs) as labels or carriers for virus-related species, especially in the context of SARS-CoV-2. The sample is mixed with functionalized MNPs, and the resulting virus–nanoparticle complexes are then separated from

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the bulk solution with a magnetic field. This enrichment step shortens the pretreatment time and, at the same time, increases the electrochemical signal recorded at the electrode [8]. In other words, both sample handling and signal acquisition become easier. Another strategy links potential sweeps to a controlled modulation of the sensing interface so that the motion of target molecules is encoded in the recorded current. The measured electrochemical response is then interpreted together with the dynamic behavior of viral proteins and their probes, allowing the sensor to distinguish specific binding events, as sketched in Figure 2(a,b). When pairs of potential and current peaks are examined, only those components whose molecular motion matches the sampling frequency are kept in the analysis, which makes it possible to identify the target species with good specificity [10].

Semiconductor metal oxides form another important class of materials for virus-related electrochemical biosensors. Zinc oxide (ZnO) is a typical example. It can provide catalytic activity toward relevant redox reactions, it is compatible with many biomolecules, and it offers a surface that can adsorb and immobilize recognition elements. When ZnO is doped with other transition metals or incorporated into composite structures, its conductivity and sensing behavior can be further adjusted to suit a particular assay [11]. Spinel cobalt ferrite ($CoFe_2O_4$) represents a different kind of MNP that is often used in biosensing. After modification with chitosan, $CoFe_2O_4$ becomes less toxic to biological systems and presents a relatively large surface area with functional groups that can be tailored for binding. On this basis, an electrochemical platform using CFO@CS-Au MNPs has been reported. Owing to the hybrid material's high active area and multiple binding sites, the sensor can track the SARS-CoV-2 spike (S) protein in real time over a concentration range from 1 pg/mL to 10 μg/mL within 10 minutes [8].

Virus detection is further complicated by the fact that many viruses mutate quickly. Changes in their DNA or RNA sequences and in the chemical behavior of their proteins may reduce the response of sensors designed for earlier strains. Current electrochemical systems can still recognize several known SARS-CoV-2 variants, but ongoing viral evolution remains a practical problem [11]. Developing electrochemical sensors that keep sufficient sensitivity when new mutants appear is therefore an important task for future work.

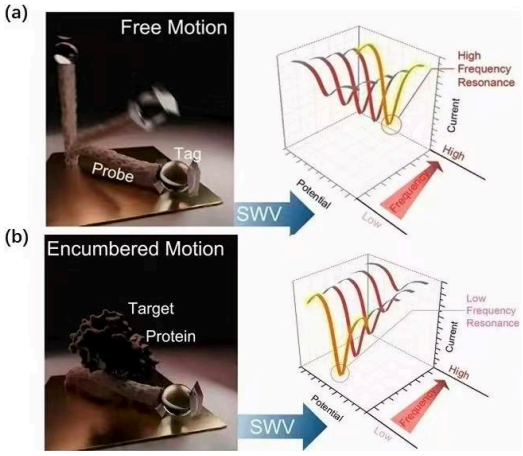

Figure 2. Schematic illustration of using sampling frequency to detect the molecular motion of a synthetic probe in the (a) absence and (b) presence of the target protein [10]

2.2. Electrochemical sensors for detecting glucose

Glucose detection is primarily used to measure human blood glucose concentration, a critical biological indicator for diabetes diagnosis. Common glucose detection methods include

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amperometry and voltammetry, which also serve as the foundation for innovations in other glucose detection technologies.

First, the core principle of amperometry involves detecting current changes when a constant potential is applied to the WE of electrochemical sensors. The recorded current varies with the relevant chemical reactions occurring at the WE, and changes in the concentration of the target analyte are proportional to the generated current. Thus, glucose concentration can be accurately measured by monitoring current changes. Second, voltammetry involves measuring potential changes at the WE and recording current variations as a function of potential. The area of the peak current is proportionally correlated with the concentration of the target analyte [12]. Based on the extent of enzyme involvement in the detection process, glucose sensors are classified into enzymatic and non-enzymatic sensors [13].

In the category of enzymatic sensors, glucose oxidase (GOx) and glucose dehydrogenase (GDH) are the primary enzymes employed. However, enzyme activity is frequently influenced by pH and temperature, which in turn impacts the detection accuracy of the sensors [14]. Therefore, non-enzymatic electrochemical sensors are widely used for glucose detection, owing to their stability and ease of fabrication. Various nanomaterials are employed as catalysts in non-enzymatic sensors [13]. At the WE surface, glucose is directly oxidized under the catalysis of nanomaterials, converting the chemical signal into a measurable electrical signal. Within a specific concentration range, the current generated by the glucose oxidation reaction is proportional to the glucose concentration—with the concentration range itself depending on the performance of the non-enzymatic electrochemical sensor. Compared with enzymatic catalysis, the catalytic performance of nanomaterials is more stable and less susceptible to external factors, indicating that non-enzymatic electrochemical sensors hold great potential for glucose detection.

Zhou et al. reported a non-enzymatic glucose electrode in which shape-controllable Fe_3O_4 nanospheres (Fe_3O_4NSs) were grown on flexible stainless steel wire mesh (SSWS) fibers and used as the catalytic layer [13]. In their design, the Fe_3O_4NSs act as the main active sites for the glucose redox process, as shown in Figure 3(a)–3(d). Fe_3O_4 contains both Fe^{3+} and Fe^{2+} ions, and electrons can shuttle between these two valence states; this internal redox couple helps to maintain good electrical conductivity within the material. By tuning the morphology of the Fe_3O_4NSs on the SSWS substrate—particularly the surface roughness and the effective surface area—the authors increased the number of accessible catalytic sites at the solid–liquid interface and, as a result, promoted the electrochemical oxidation of glucose [13].

Carbon-based materials have also attracted attention in glucose sensing because of their large specific surface area and good electrical transport properties. Taking advantage of the synergy between carbon and metals, Liu et al. synthesized a nickel–carbon composite consisting of nickel nanoparticles anchored on nitrogen-doped carbon nanotubes, which functioned as an efficient electrocatalyst for glucose oxidation [15].

Non-enzymatic sensors currently play a central role in electrochemical glucose determination, largely owing to their operational stability and tolerance to environmental fluctuations. A major drawback, however, is that many of these systems rely on substantial amounts of noble metals, which increases fabrication costs. One practical route toward low-cost, high-performance glucose sensors is therefore the rational design of composite catalysts that reduce the loading of precious metals while maintaining or improving activity. Since electrochemical glucose monitoring is required in everyday settings, translating these sensing platforms into wearable formats is particularly important. In parallel, the mechanical design of flexible devices that can withstand

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prolonged use and complex application environments should be carefully considered to ensure reliable performance over time.

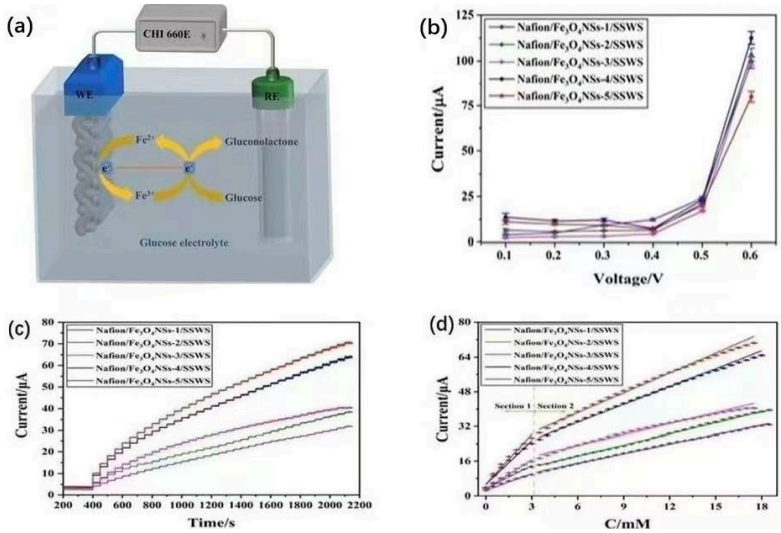

Figure 3. (a) Reaction mechanism of the Nafion/Fe_3O_4NSs/SSWS glucose sensor. (b) Effect of bias voltage on the amperometric response of the Nafion/Fe_3O_4NSs/SSWS glucose sensor. (c) Amperometric response of the Nafion/Fe_3O_4NSs/SSWS glucose sensor upon successive addition of 0.5 mM glucose into 100 mL of NaOH electrolyte. (d) Relationship between glucose concentration and response current [13]

2.3. Electrochemical sensors for detecting cancer cells

Cancer detection is undoubtedly an indispensable component of the modern medical system, as it directly influences the quality of cancer treatment for patients. This review introduces two technologies for detecting cancer cells using electrochemical sensors, using breast cancer cells as an example.

In breast cancer, the cytokine interleukin-6 (IL-6) is often used as an indicator of disease activity. Higher IL-6 concentrations are usually observed in patients with more advanced disease. Clinical reports suggest that the average IL-6 level in healthy subjects is about 5.186 pg/mL [17]. When an electrochemical sensor measures an IL-6 level clearly above this value, the result can therefore be taken as a warning signal for possible breast cancer. Vessella et al. designed an electrochemical platform in which IL-6 antibodies were immobilized on the electrode surface, so that IL-6 released by breast cancer cells could be monitored directly. The sensor reached a detection limit of 0.5 pg/mL [18], which is low enough to quantify IL-6 in the physiological range and makes earlier evaluation of disease status feasible.

Hydrogen peroxide (H_2O_2) is another marker related to metabolically active breast cancer cells. When tumor metabolism is disturbed, reactive oxygen species (ROS), including H_2O_2, are often produced in excess. Shu et al. developed a sensing interface based on coaxial Mo_2C@MoS_2 nanorods; their device showed a sensitivity of 1080 $\mu A \cdot mM^{-1} \cdot cm^{-2}$ and a detection limit of 0.2 μM for H_2O_2, as outlined in Figure 4 [19]. In a different approach, Zhang et al. fabricated an electrochemical H_2O_2 sensor using silver chloride (AgCl) nanomaterials [20]; the structure of this sensor and its operation principle are depicted in Figure 5. In both types of breast cancer–related electrochemical sensors, the analytes are typically biomolecules that are overexpressed or secreted in abnormal amounts under pathological metabolic conditions.

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Nanomaterials provide a set of tools for constructing electrochemical sensors that target cancer cells and their biomarkers. Mo_2C@MoS_2 coaxial nanorods are a representative example. In this hybrid, Mo_2C offers a noble-metal-like electronic structure and good electrical conductivity, which favor charge transfer and electrocatalytic activity in biosensing. MoS_2, on the other hand, contributes chemical and mechanical stability, helping the sensor to operate reliably. Arranging Mo_2C and MoS_2 in a coaxial nanorod geometry further improves the properties of the interface and leads to better performance in H_2O_2 detection [19]. AgCl-based systems illustrate a different design idea. Pure AgCl suffers from poor conductivity, but when it is combined with carbon nanotubes, electron transport within the sensing film is significantly improved. Making use of the deformability of carbon nanotubes, AgCl cube/porous carbon nanotube composites can be prepared. Porous multi-walled carbon nanotubes (p-MWCNTs) can assemble into cubic structures with AgCl, and the resulting composite exhibits high selectivity toward H_2O_2 [20]. Properly engineered composites therefore keep the useful features of each component and at the same time introduce cooperative effects between them.

From a practical point of view, applying these electrochemical sensors to real biological samples is more demanding than working with model solutions. Blood, sweat, urine, and other body fluids contain many additional components that can interfere with the analytical signal. It is thus necessary to further refine the sensing systems for use in such complex matrices. In parallel, careful investigations of material properties, the design of new high-performance composites, and systematic optimization of electrochemical sensitizers will be needed to improve sensor robustness and to support wider clinical application.

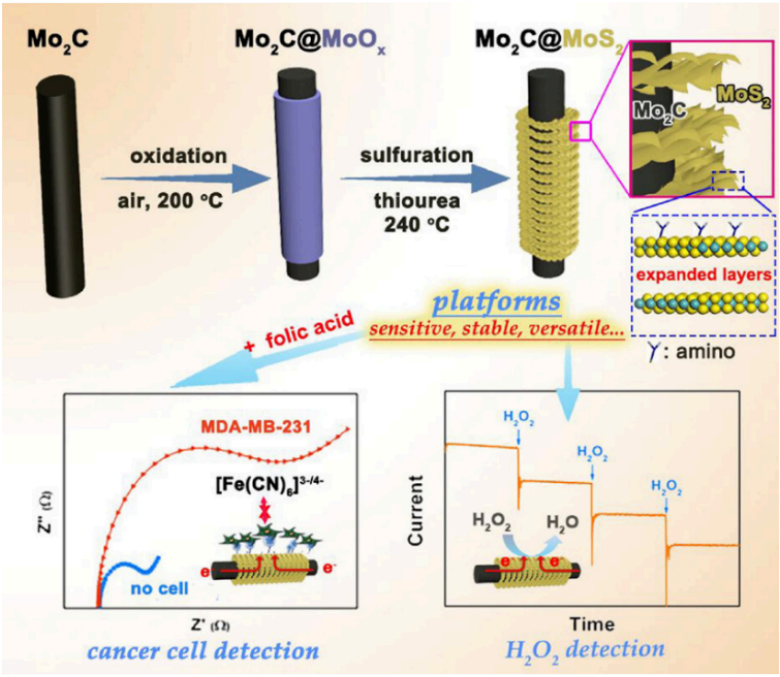

Figure 4. Schematic illustration of the preparation of hierarchical Mo_2C@MoS_2 nanorods as a biosensing platform [19]

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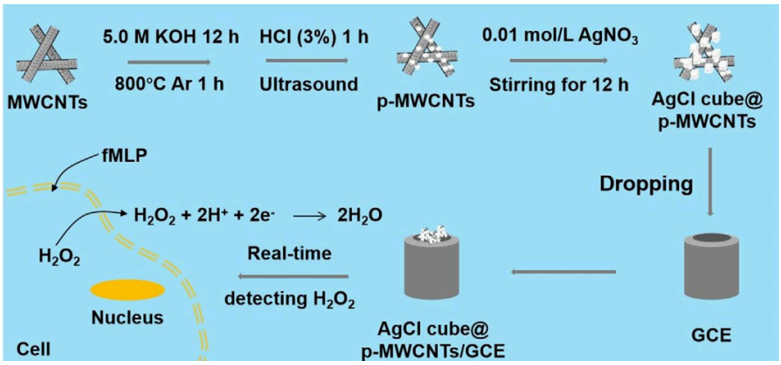

Figure 5. Schematic illustration of the fabrication of the MWCNT-based sensor and its application in detecting H_2O_2 released from living cells [20]

3. Conclusion

Electrochemical sensing has become an important direction in biomedical analysis, particularly for monitoring viruses, glucose levels, and cancer-related biomarkers. Drawing on representative examples, this work has outlined how different detection strategies and electrode interfaces can be adapted to specific biological targets, and how practical issues—such as selectivity, stability, and matrix effects—still constrain sensor performance. The reported devices show that electrochemical platforms are capable of delivering sensitive and reliable signals for clinically relevant analytes, often with better stability and lower detection limits than many traditional transduction methods. Nevertheless, established analytical techniques continue to play a role in routine testing, and their limitations, including slow response and interference from coexisting species, highlight why further innovation in electrochemical sensor design remains necessary.

At the same time, developments in wearable and portable healthcare systems are reshaping the context in which electrochemical biosensors will be used. Flexible devices and nanomaterial-based architectures offer a way to combine mechanical compliance with high analytical performance. When nanomaterials are integrated into flexible substrates, the sensor can retain sensitivity while operating under bending, stretching, or other complex conditions. Carefully designed nanocomposites help balance the weaknesses of individual components, and deliberate structural tuning of nanomaterials can enhance charge transport and signal generation. Continued work along these lines is likely to extend electrochemical biosensors into more demanding diagnostic settings and to support their gradual migration from controlled laboratory environments toward real-world clinical and personal health applications.

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