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During the COVID-19 pandemic, there is an urgent need for the development of rapid and efficient detection systems. This article emphasizes the significance of biosensors in the context of COVID-19 control. It focuses on electrochemical methods for detecting COVID-19 and highlights biosensors' unique advantages and limitations compared to other detection methods. The article also discusses recent advancements in biosensor technology, their integration with digital health technologies, and potential future applications. It delves into the challenges associated with biosensors, including technical and operational obstacles, as well as risk management strategies. This comprehensive review aims to serve as a critical reference for researchers and healthcare professionals in effectively managing the pandemic.

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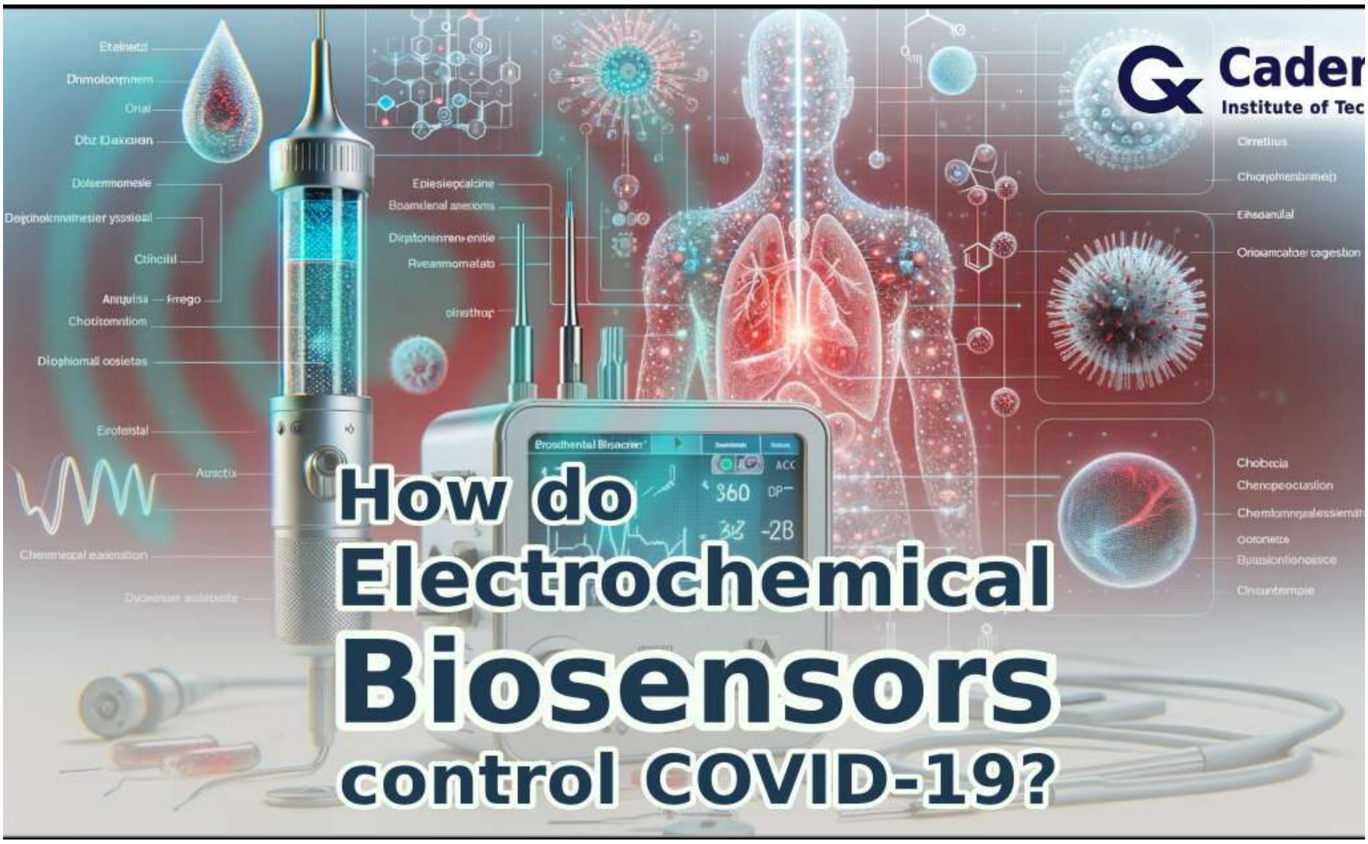

1- Introduction

The COVID-19 pandemic, caused by the new coronavirus SARS-CoV-2, has become a significant worldwide health pandemic. This highly contagious virus caused a worldwide emergency, impacting millions and disrupting societies and economies. The quick spread and severe effects of COVID-19 have highlighted the urgent need for fast and accurate ways to detect the virus to control its spread. Understanding and identifying the virus is crucial in fighting this global threat [1].

Traditional diagnostic approaches, such as the Enzyme-Linked Immunosorbent Assay (ELISA), antigen tests, and Reverse Transcription Polymerase Chain Reaction (RT-PCR), have been the cornerstone of COVID-19 detection efforts. Each of these methods poses its own set of advantages and limitations. For instance, RT-PCR is highly sensitive and specific but requires sophisticated laboratory infrastructure, skilled personnel, and substantial processing time, which could lead to delays in diagnosis and subsequent intervention. ELISA and antigen tests, while useful for indicating the presence of the virus or antibodies against it, also face challenges in terms of cost, accessibility, and the time needed to deliver results.

Comparatively, electrochemical biosensors, which consist of biological bioreceptors, such as aptamer, DNA, antibody, bacteriophage, endolysin protein etc. and transducers to covert biological mechanism to electrical signals, present a revolutionary approach to addressing these challenges. These biosensors offer a more straightforward, cost-effective, and rapid testing method that does not compromise on accuracy. Their design allows for the direct detection of the virus or its markers in biological samples without the need for extensive sample preparation or sophisticated equipment. This makes electrochemical biosensors particularly appealing for use in point-of-care settings, including those with limited access to laboratory facilities.

In this review, we aim to showcase the development of electrochemical biosensors, highlighting their role in medical innovation. They are crucial in tackling public health challenges, offering hope and practical strategies to manage pandemics like COVID-19.

2-Electrochemical biosensors

Electrochemical biosensors detect viruses and bacteria, translating their identification into electrical signals. This approach addresses traditional diagnostic method limitations. These biosensors quickly detect specific viral markers with high sensitivity and specificity, enabling rapid responses crucial for contact tracing and patient isolation. Their portability and ease of use make them valuable in various settings, including resource-limited or remote areas. Electrochemical biosensors play a vital role in the global response to the COVID-19 pandemic by bridging the diagnostic gap and providing a practical tool to manage and resolve this unprecedented health crisis.

One of the most significant advantages of electrochemical biosensors in combating COVID-19 is their high sensitivity and specificity. They are engineered to detect specific viral markers, allowing for accurate identification of the SARS-CoV-2 virus. This precision is critical in reducing the incidence of false negatives or positives, which are common challenges in other testing methods like antigen tests.

The rapid response time of these biosensors is another critical factor in their effectiveness. Unlike conventional diagnostic methods such as ELISA, Antigen test, and RT-PCR tests, which can take hours to days to yield results, electrochemical biosensors deliver results in a significantly shorter time frame. This speed is essential for effective contact tracing and the immediate isolation of infected individuals, which are critical strategies in curbing the spread of the virus.

In addition, the simplicity and portability of electrochemical biosensors make them a versatile tool in the fight against COVID-19. These characteristics enable their use in various settings, not just in well-equipped laboratories but also in remote or resource-poor areas. This widespread applicability is vital in ensuring equitable access to testing, especially in regions where traditional diagnostic facilities are scarce.

The comparison between electrochemical biosensors and traditional detection methods in controlling the COVID-19 pandemic is a narrative of complementary strengths and weaknesses. Conventional methods are still reliable, but biosensors' remarkable qualities, such as speed, specificity, and digital technology integration offer promising avenues for rapid, efficient, and widespread disease detection and control. The ongoing development and refinement of these biosensors will undoubtedly play a crucial role in organizing future pandemic response strategies (Table 1).

Table 1. Comparison of various approaches to recognize COVID-19

Method	Accuracy	Speed	Cost	Ease of Use	Scalability	Application	Sample Type	Point-of-Care Testing
RT-PCR	Very high	Hours to days	High	Requires trained personnel	Challenging	Laboratory-based	Respiratory	Limited
Antigen Test	Moderate, prone to errors	15-30 minutes	Lower than RT-PCR	Minimal training needed	Easier than RT-PCR	Field settings	Respiratory	Highly suitable
ELISA	High for antibodies	Several hours	Moderate	Lab expertise needed	Scalable with lab capacity	Laboratory-based	Blood	Limited
Electrochemical Biosensors	High with calibration	Minutes	Lower, especially in scale	User-friendly	Easier to deploy	Various, including remote	Various	Highly suitable

3. Advances in Electrochemical Biosensor Technology

The field of electrochemical biosensor technology is rapidly changing, driven by innovations that are revolutionizing their use in managing pandemics, particularly COVID-19. This progress is marked by several key developments demonstrating biosensor technology's transformative impact in healthcare.

One major advancement is the use of nanotechnology in biosensors. This has dramatically improved their sensitivity and specificity, allowing for the detection of pathogens at much lower levels. This increased sensitivity is key for early disease detection, such as COVID-19, leading to faster isolation and treatment.

Another important innovation is wearable biosensors. Worn on the body, these devices continuously monitor various biological markers. During a pandemic, they can provide real-time health data, helping to quickly identify signs of infection.

It is significant that the integration of biosensors with digital health technology. Smart biosensors connected to digital devices like smartphones can send data directly to healthcare providers, leading to faster responses and the prevention of illnesses like COVID-19.

Miniaturization is another advancement. Smaller, portable biosensors enable testing in various settings, not just labs. This is crucial for testing in remote areas or where immediate results are needed, such as at airports.

Electrochemical biosensors are also being used beyond detecting pathogens. They now monitor physiological parameters, like oxygen levels and breathing rates, important for managing COVID-19 patients.

Nonetheless, there are still issues, especially with large-scale manufacturing and standardization. One of the biggest challenges is making sure these cutting-edge biosensors are broadly accessible and consistently effective.

In disease detection and management. These innovations are not only useful now but are shaping future applications. The experiences from using biosensors in the COVID-19 pandemic guides research for better diagnostics in future health crises.

4. Limitation of biosensor development

Although using electrochemical biosensors is remarkable to manage COVID-19. It brings several challenges and risks, from technical issues to concerns about reliability and risk management. These challenges need strategic solutions for biosensors to be effective in public health.

A key technical challenge is ensuring biosensors work accurately in different environments. Factors like temperature and humidity can affect their performance. This reliability is hard to achieve but crucial.

Another biggest problem is calibrating and maintaining biosensors. Like all precision tools, they need regular calibration, which can be logistically tough, especially in areas with limited resources or in large public health efforts where many devices are used.

Integrating biosensors with current healthcare systems also poses challenges. They must be compatible with other health technologies, which is not always easy, particularly in less equipped healthcare settings.

Training users correctly is vital. As biosensors become more complex, educating healthcare workers and users on their proper use is essential.

Data privacy and security are major concerns with smart biosensors that transmit health data. Ensuring strong data protection is crucial to keep patient trust and meet privacy laws, especially when sharing data globally.

Scalability is another issue. Producing biosensors in large quantities, especially during a pandemic, is a huge task. This includes manufacturing and supplying the components and materials needed.

Risk management for biosensor use needs to cover these challenges comprehensively. This means not just technical solutions but also policies and standards for using, maintaining, and handling data from biosensors.

Planning for contingencies is key. This includes having protocols for device failure, data breaches, and other issues that could affect biosensor-based public health strategies.

While electrochemical biosensors have great potential in pandemic management, especially for COVID-19, their deployment faces many operational challenges and risks. Addressing these requires combining technical innovation with strategic policy and planning to maximize their benefits in public health.

5- Literature review

The Max Planck Group's research in Nanobioengineering research used the electrochemical biosensors for detecting COVID-19 biomarkers focuses on personalized medicine. Their study analyses various biomarkers to diagnose and forecast the disease's progression. Emphasizing the biosensors' role in understanding SARS-CoV-2's structure and infection mechanism, this research also considers their diagnostic and prognostic potential. Furthermore, it explores integrating these biosensors with emerging technologies, advancing personalized medical approaches [2].

Biosensors, like those created by SD Biosensor for COVID-19 detection, typically use biological elements for virus identification. These elements, such as antibodies or nucleic acid probes, are designed to specifically bind to the virus's antigens or genetic material. This binding is then translated into a measurable signal, providing quick diagnostic results. This innovative technology plays a crucial role in rapidly testing and managing the pandemic effectively [3].

Yakoh et al. developed paper-based electrochemical biosensor, designed for diagnosing COVID-19, effectively detects SARS-CoV-2 antibodies and antigens, offering a swift and precise method for identifying infections. The advantages of this sensor include its low cost, ease of use, and rapid results, making it highly beneficial in resource-limited settings. However, there are some disadvantages, such as potential variability in sensitivity compared to more complex laboratory tests and a reliance on correct sample collection [4].

Lomae et al. designed the label-free electrochemical DNA Biosensor for COVID-19 diagnosis in biological samples. Its main advantage lies in its speed and simplicity, enabling faster results than traditional RT-PCR tests. However, its accuracy can be affected by sample quality and external substances, potentially leading to false results. While easier to use than some methods, it still requires technical know-how and equipment, limiting its applicability in less-equipped settings [5].

At the Institute of Radiopharmaceutical Cancer Research, Helmholtz-Zentrum Dresden-Rossendorf e.V. (HZDR), deploying electrochemical biosensors for COVID-19 detection reflects their commitment to advanced diagnostic technologies. Utilizing techniques like electrochemical impedance spectroscopy and gold nanowires, these biosensors mark a significant step in precisely detecting SARS-CoV-2 antigens and antibodies. This method boosts the efficiency of COVID-19 testing and showcases the institute's dedication to developing innovative solutions for critical medical challenges, including the pandemic [6].

Sengupta, J., and Hussain designed the Graphene-Based Electrochemical Biosensors based on identifying SARS-CoV-2 with different electrochemical approaches such as amperometry and impedance spectroscopy methods. This biosensor was sensitive and fast, which helped detect the virus earlier than usual methods. However, they need to be carefully set up and can be affected by the environment. Despite these challenges, these biosensors are a big step in fighting COVID-19, as they offer a faster and more efficient way to test for the virus [7].

AT RISE, researchers also carry out verification tests on diagnostic point-of-care analyses. A current assignment includes verification of rapid tests for measuring SARS-Cov-2 specific antibodies [8].

Meridian's antibodies detect SARS-CoV-2 various rapidly with high sensitivity. Their monoclonal antibodies specifically target the S1 protein in saliva, effective regardless of its shape. This approach, focusing on a stable region of S1, is key for diagnostics and vaccine development, offering substantial potential for neutralizing antibody production in patients [9].

5. Integration of artificial intelligence (AI) with electrochemical

biosensor

Merging artificial intelligence (AI) with electrochemical biosensor data revolutionizes in managing health, especially during crises like the COVID-19 pandemic. This means we can get quicker, smarter insights from the health data collected, helping spot disease outbreaks faster and making personalized healthcare a reality. AI can sift through many biosensor data, spotting health trends or disease markers that humans might miss, leading to early warnings and tailored health plans.

However, privacy concerns are a major topic of discussion when discussing the use of AI with health data. Ensuring the safety and security of patient information is imperative. A wide range of data must be used during training to ensure that the AI does not prefer any particular group over another. We also need to ensure that these AI systems function well everywhere and in various environments.

Recently, the potential for AI and biosensors in health is enormous. They could help us monitor our health in real time, catch diseases early, and fit into a bigger picture of digital health. But, as we move forward, we'll need to tackle the big questions about privacy, fairness, and reliability head-on to ensure these tech advances benefit everyone.

6. Electrochemical biosensors in point-of-care devices: future trends

Advanced electrochemical biosensors become more popular approach in the fight against COVID-19, indicating the potential of cutting-edge technologies to revolutionize public health. These biosensors enable rapid disease detection, providing crucial data for managing infectious diseases and facilitating quicker responses to outbreaks. Their ability to deliver real-time insights into infection rates and trends has proven invaluable for public health decision-making, especially in controlling the spread of viruses and managing healthcare resources efficiently.

In patient care, electrochemical biosensors offer immediate diagnostics, reducing the burden on healthcare facilities and improving access in under-resourced areas. The forward-looking applications of these technologies extend into personalized medicine, where biosensors could tailor treatments to individual patient profiles, and the development of global health networks that leverage biosensor data for early warning systems, potentially averting future pandemics.

The integration of artificial intelligence (AI) with biosensor data holds promise for transforming public health through advanced data analysis, enabling predictive modeling of disease spread and enhancing public health planning. This synergy could lead to more informed and proactive health strategies, emphasizing the importance of continuous research and development to keep pace with evolving health challenges.

However, realizing the full potential of electrochemical biosensors in public health requires overcoming significant hurdles, including data privacy concerns, the need for technology standardization, and ensuring equitable access to these advancements. Addressing these challenges is critical for harnessing the transformative power of biosensors in healthcare, indicating a future where data, efficiency, and proactive measures drive public health strategies.

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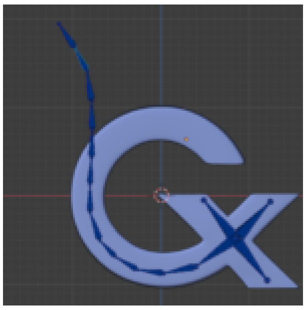
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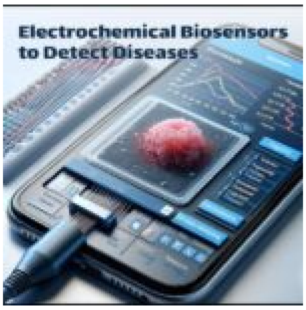

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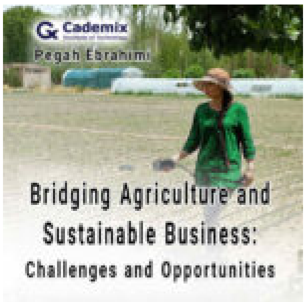

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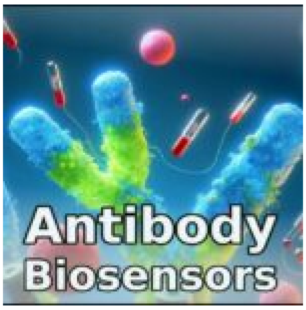

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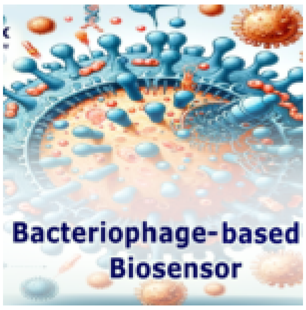

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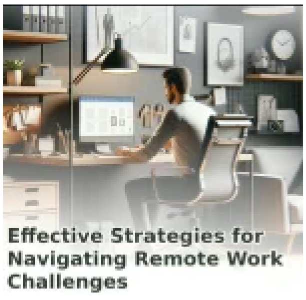

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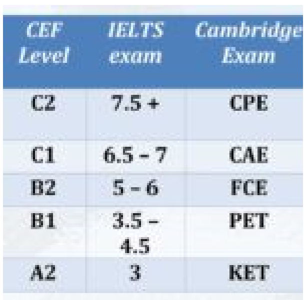

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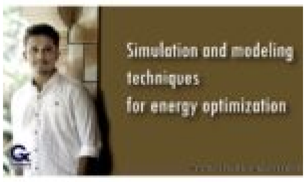

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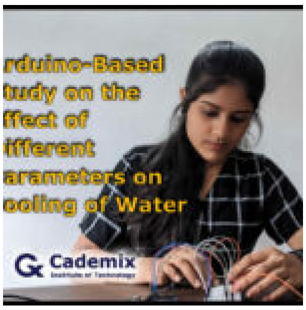

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