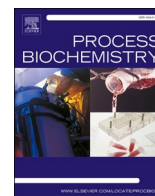




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Review

Novel electrochemical biosensor key significance of smart intelligence (IoMT & IoHT) of COVID-19 virus control management

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ABSTRACT

Recent outbreak of COVID-19 pandemic has led to the different possibilities of the development of treatment against corona virus. To know the phylogenicity of SARS-CoV, various studies have been conducted with the outcome of the results showing virulence is caused due to spike protein. Various detection techniques with clinical approach like imaging technology, RT-PCR etc. are comparatively expensively than the use of biosensors. Nano-biosensors have an excellent way of approach to track the conditions of individual and public providing information about the existing condition and treatment status. Electrochemical nano-biosensors are referred as an excellent way of detection. The use of graphene based electrochemical nano-biosensors are most advantageous due to its elevated properties. Fluorescence investigation is one of the precise ways of sensing, optical biosignals that helps in obtaining real time results with high accuracy and negligible changes. The potential application of nano-biosensors are very wide, improvised and advanced Nanotechnology helps in the use of nano-biosensors detect all possible biosignals. Significant ubiquitous IoT-enabled novel sensor technologies that can be potentially utilized to respond various facets the growing COVID-19 pandemic from diagnostic and therapeutics to the prevention stage.

1. Introduction: overviews of COVID-19 outbreak

The existing condition of world public health emergency is corona virus (SARS-CoV-2) causing pandemic due to its rapid spread all over the world. It has enormously affected public health in over 200 countries. This has caused unpredicted levels of life loss and has upset the way the world worked before 2019. Several researches have been made on the origin, phylogenicity and life cycle of corona virus, according to which it is a class of virus consisting of various different strains.

Due to mutations caused in the year of 2019, corona virus outbreak took place, giving rise to a novel coronavirus belonging to SARS which was termed as 2019-nCoV (COVID-19). Risks have been taken and efforts were put in the world to resolve the outbreak of pandemic by various modes of approach that deals with exploring the origin of the

SARS-CoV-2 viral genome. Detection of mutant corona using biosensors and to deal with effective treatment of individuals affected by COVID-19 and also in producing an effective vaccine to prevent the infection of corona virus. Upcoming will be the review that deals with various different studies of electrochemical biosensors till date SARS-CoV-2 or COVID-19 [1,2]. Significant attempts are presented to know the specific techniques to modify the surface of nano-biosensors which is one of the detection methods used in the detection of influenza virus which is also responsible for acute respiratory syndrome. These highlights latest tools and strategies are effective in diagnostic applications and key challenges of SARS-CoV-2 or COVID-19.

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2. Electrochemical biosensors: a key mechanism and potential utilities at point of care

The main moto of treatment in respiratory viral diseases caused in the pandemic of COVID-19 are protein coat of the virus (antigen), genetic material of virus [3,4]. The structure of corona virus consists of 'n' spike protein envelope and covering nucleic acid, acid the disease is caused by the virulent proteins that forms the spike. The infection is caused due to spike protein molecule to attach to the bioreceptor, which causes a particular reaction in the biological system that produces various sensations. The utilization of biosensors comes into action in this phase where a detector is used to sense the signals produced due to reactions happening in bioreceptor sites. The detector converts the signal into electrical signals where bioreceptors are used for the recognition of elements which is then transduced into information.

There are various types of biosensors being discovered based on the detector properties such as: electrochemical, mechanical, piezoelectric, magnetic, optical and thermal which are based on molecular affinity. Biosensors use properties of signals like impedance, protein structures

and immunoaffinity in different types of electrochemical biosensors. Electrochemical biosensors work on the principle of optical and surface plasmon Resonance (SPR) and quartz crystal microbalance. Depending on the molecule of target in a virus that is nucleic acid and spike protein, biosensors can be classified as nucleic acid based biosensors and antigen-antibody based electrochemical biosensors.

The sensing responses of electrochemical biosensors differs from various analysts used, ranging from smallest possible to larger biomolecular detection. The potential applications of electrochemical biosensors is referred in various different fields for its ability of recognizing of electrical signals that produce at the site of interest as shown in Fig. 1 (a) [5]. The property of electrochemical biosensors is influenced by semiconductor, dielectric and charge distribution properties. The analysis of FET-based electrochemical biosensor has many advantages when compared to biosensors using others significant properties due to its sensitivity and capability of producing instant results with very minute concentrations of bio-analytes. To obtain the best results and enhance the key property of FET-based electrochemical biosensors, the smart electronic material graphene usages as surface sensor with high

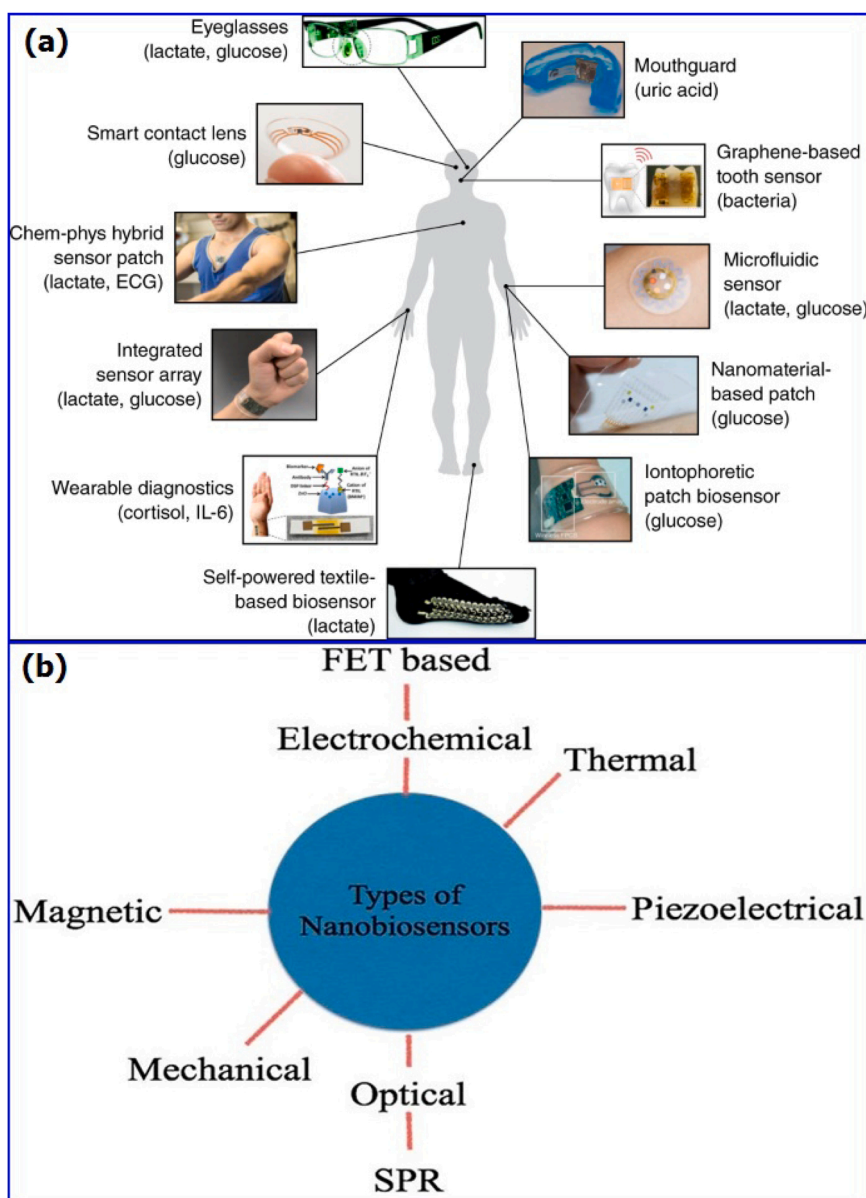


Fig. 1. (a).Versatile applications of electrochemical biosensors at the regular life cycle [5] (Copyright © 2019, Nature), and (b) Types of electrochemical biosensor activities at the point of care.

electrical conductivity, simplicity of surface functionalization with large surface area and high carrier mobility is used as the sensor in detector to obtain best results from FET-based electrochemical biosensor technique as depicted in the Fig. 1(b). Moreover, 'Surface Plasmon Resonance (SPR)' is one of the most used optical biosensor due to its property of optical based fluorescence detection. It is currently used in the 'SARS-CoV-2' or the 'corona' virus detection due to the surface system, which is extremely sensitive and has a quick response time. 'SPR' explores real time detection and is label free which has a very high accuracy even with minimum changes at the level of the nanoscale.

3. Role of electrochemical biosensors in virus (SARS-CoV-2/ COVID-19) control management

In the existing COVID-19 pandemic, the use of biosensors has excellently worked in the detection of SARS-CoV when compared to conventional methods like RT-PCR, ELISA and other expensive methods like imaging technology etc. [6,7]. Depending on the molecule of target in a virus that is nucleic acid and spike protein, biosensors can be classified as nucleic acid-based biosensors and antigen-antibody based biosensors. The sensing of electrochemical biosensors differs from various analytes used, ranging from smallest possible to larger biomolecular detection.

'Surface Plasmon Resonance (SPR)' is the most effective tools as used in optical biosensors due to its emerging optical property of fluorescence detection. It is currently used in the 'SARS-CoV-2' or the 'corona' virus detection due to the surface system, which is extremely sensitive and has a quick response time. SPR explores real time detection and is label free which has a very high accuracy even in minimum changes at the level of nanoscale [8,9].

Typical gold nanoparticles (AuNPs), gold nanoislands (AuNIs), graphene as well as the assembly of nanowires are most essential for the detection of 'corona' virus protection further nanomaterials affinity-based biosensors (ABBS) modulation techniques as illustrated in the schematic diagram of the Fig. 2(a). While, in the Fig. 2(b) demonstrates nanowires assembly covalent immobilization onto F_n probe, as well as *in-vitro* identification mechanisms are done by AMPs which is more reliable in an extensive range of pH compared to traditional antibodies.

3.1. Viral antigen detection: nucleic acids- and protein-based biosensor

The nucleic acids of virus are used to obtain cDNA which is utilized for the detection in graphene based FET device, which allows us to know the severity of the condition suffering from COVID-19. The efficiency of

the biosensor was tested and compared to real clinical sample testing that usages nasopharyngeal swab specimen of both -CoV-2 or COVID and normal subjects. The modification of the biosensor can be done to enhance or amplify the electrochemical CRISP biosensor [10,11].

3.2. Antibody detection: immunoglobulin (Ig)-based biosensor

In approaches made considering the antigen protein where the detection can also be made using an antibody that is produced in the patients is done. The biosensors must be highly specific to sense the functionalization of 'COVID-19' diagnostic signals where the infection of pathogen to an individual shoot up the development of antibodies such as IgM, TgA and IgG, where in first three weeks that is day 4 to day 25 on the onset of fever and illness, the peakinh og IgA and IgM takes place and in the later days that is 21–25 shows the surging of IgG, therefore helping in diagnosing the condition at both early and later stages accordingly [12]. Considering the uncertain life span of antibodies like immunoglobulin that protects against the infection of 'SARS-CoV-2' or 'COVID-19', tests must be done within the assigned number of days.

Herein, this consequence, we also explored in depth studies on the privilege of novel 'Laser-Scribed Graphene (LSG)' biosensor modulation scheme for corona virus control management during the year of 2019 interfacing via gold nanoparticle assisted smart biosensor electrodes were customize with spike 'SARC-CoV-2' spike protein serum actually followed by the surface topology adjustment. Henceforth, integrated smartphone enabled point-of-care (POC) operating system is the most intriguing as well as environmentally reliable diagnostic platform for convenient accessibility, user friendly and systematic memorandums diagnosis as explored in the Fig. 3 [13].

3.3. Implimentation of biosensors at Internet of healthcare and mobile things (IoHT and IoMT)

The IoT (Internet of Things) has applications in health care and medical services leading to formation of the devices that uses software applications which can be managed via an internet connection contributing an excellent information technology, such devices are also called as 'IoHT' (*Internet of Health Care Things*). The 'IoT' or 'IoHT' consists of capabilities to collect, save and use data provide information about the symptoms and trends making remote care possible by tracking the medication orders, which are used as wearable devices. This helps in sharing of health information to the respective health care professionals [14,15,17]. Investigations have shown the improvisation in function with the help of dedicated, smart phone applications, enabling data analysis by tracking and storing patient health status. This is excessively put in use, providing technological solution supports which may lead to efficiently control the spread of the 'corona' virus. The above 'IoT' or 'IoHT' are used in various countries such as South Korea, China, Singapore and other Asian countries. Various countries are yet to introduce biosensors due to the privacy concerns limiting the control of existing pandemic [16].

High yield fabrication of smart nanomaterials assembled novel biosensor materializes throughout the *in-vitro* investigations of biosensing highly sophisticated worldwide research. The increasing performance of biosensor sensitivity is an amazing avenue of traditional research during 'corona' virus pandemic all over the world. Overall surveys in this comprehensive review article our main intensions to reflect on the *Nanoscience and Nanotechnology* enabled integrated device manufacturing of various nanoscale morphology utilizes smart biosensor implementations in diagnostics tools for cancer treatment via *Internet of healthcare things and mobile things (IoHT and IoMT)* [17] of details machine learning operating system of biosensor activities are depicted in Fig. 4 [18]. Additionally, a mobile friendly user interface (UI) application was developed for medical inspections as well as healthcare perception. As it stands, an integration of inconspicuous

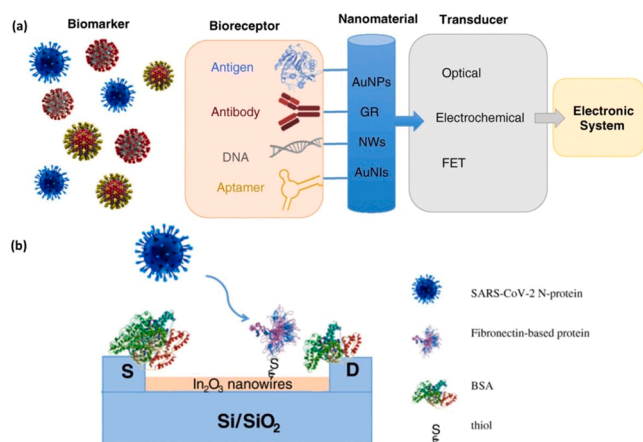


Fig. 2. Schematic illustration of (a) gold nanoparticles, gold nanoislands, graphene self-assembly nanomaterials-based affinity biosensors modulation for the detection of coronavirus, and (b) In_2O_3 induced Field Effect Transistor (FET)-based immune sensor for corona virus control management.

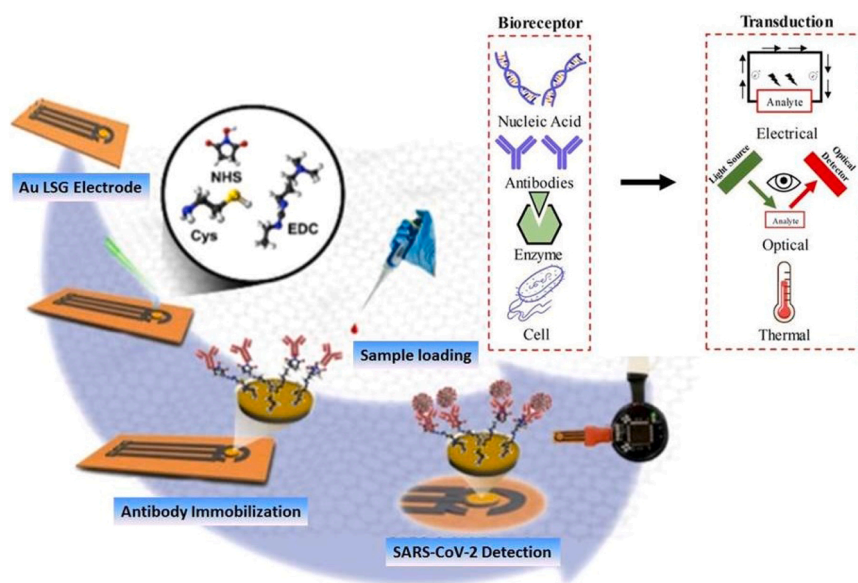


Fig. 3. Schematic presentation of LSG-based electrochemical sensing, antibody immobilization and COVID virus point of detection (POD) scheme [13] (Copyright © 2021, American Chemical Society).

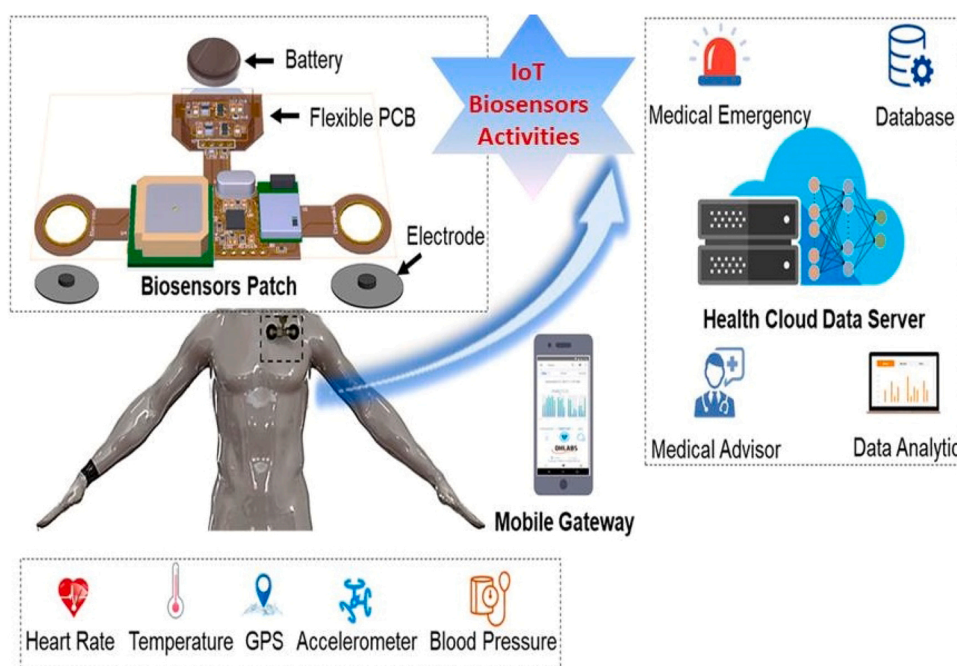


Fig. 4. A schematic overview of the wearable biosensor patch with H-IoT and IoMT applications [18] (Copyright © 2022, MDPI).

biosensor resulted due to IoMT development and precautionary healthcare assessment IoHT platform are most fascinating. Throughout the scalability is especially a significant impediment to IoHT and IoMT’s application fight against the pandemic as various sensing important signs of patients and making the availability of the cloud server. As compared to global therapeutics of COVID-19 brimming to capacity as well as IoMT implementation requires the ability to deal with a scenario on such an unprecedented scale.

4. Conclusions and future outlook

Summarizes to the COVID-19 global pandemic outbreak, all possible diagnostic methods have been made for the detection of victims of

COVID-19. The common diagnostic methods like imaging, blood test, RT-PCR, etc. has their own limitations such as high costs, not so sensitive in every case, less specificity, lack of preparation and failure of detection in early stages. Researches are conducted to overcome these limitations with the usages of Nanotechnology giving rise to electrochemical biosensors that might help in prevention and diagnosing COVID-19 infections. In spite of having discovered the vaccines due to the failure in detection of the existing infections might result in the unknown outbreak of the virulent virus leading to failure in the systems. Electrochemical biosensors possessing various benefits that helps in the effective detection with high performance, accuracy, portability, etc. Indeed, sensors helps in the identification of analyte of interest such as pathogen, protein, nucleic acid, antibodies, surface signal transducers,

biosensing interfaces etc. to increase the specificity and sensitivity through the investigation of electrochemical biosensors, the researchers have materialized various shape dependent nanocomposites such as nanopillars, nanorods, nanowires, quantum dots and many more. Developing the 3D-structures of electrochemical biosensors leads to the detection of multi-microbial activity or multi-platform activity. Thus, the efficient utilization of electrochemical biosensors e.g. 'IoT' is the most helpful in obtaining the information via, internet to patients and professional's smart phone. The alarming property of IoT enabled novel electrochemical biosensors is very much beneficial in early detection and prevention of the any critical viral diseases.

Conflicts of interest

All authors have declared that there is no conflict and any financial interest for research work publications.

Data Availability

Data will be made available on request.

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