Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Microchemical Journal 164 (2021) 106094

Contents lists available at ScienceDirect

Microchemical Journal

journal homepage: www.elsevier.com/locate/microc

Review Article

Biosensors promising bio-device for pandemic screening "COVID-19"

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ARTICLE INFO

Keywords:
Coronaviruses (COVID 19)
Pandemic
Biosensors
Conventional methods

ABSTRACT

Undoubtedly, the coronavirus pandemic is one of the most influential events not only in medicine but also in the economic field in the world. Rapid transmission and high mortality rates, as well as prolonged and asymptomatic communal periods, are the most important reasons for the global panic due to coronavirus. Since coronavirus treatment and specific vaccines are not yet available, early detection of the virus is critical. A rapid and accurate diagnosis can play a crucial role in the treatment and control of the COVID 19 disease. Serological, ELISA, and molecular-based tests, including PCR and RT-PCR, are among the most important routine methods for detecting coronaviruses. False-positive/negative results, low sensitivity and specificity, and the need for advanced equipment are among the disadvantages and problems of routine methods. To eliminate the drawbacks of routine methods, new technologies are being developed. Biosensors are one of the most important ones. This paper is a summary of the up-to-date states of innovative bio-sensing tools for the ultrasensitive detection of coronaviruses (COVID 19) with encouraging uses for future challenges in disease diagnosis.

1. Introduction

Coronaviruses are one of the most important and frequent sources of respiratory diseases in humans with six main species [1]. 229E (HCoV-229E), severe acute respiratory syndrome (SARS)-associated coronavirus (SARS-CoV) and HCoV-OC43 are three known human coronaviruses that commonly exist. SARS-CoV2 is most narrowly associated with two bat-derived SARS-like coronaviruses with 90% identity, and 80% and 50% identity with SARS-CoV and MERS-CoV respectively. In December 2019, numerous patients with viral pneumonia were established to be epidemiologically related to the Huanan seafood market in Wuhan, in the Hubei province of China, where several of animals such as rabbits and birds had been on sale beforehand of the epidemic. Novel coronavirus, temporarily called (2019-nCoV) and recognized with the use of next-generation sequencing, is able to cause serious infection in humans, such as unknown pneumonia which widely broken out in the world [2,3]. Due to unknown molecular and genomic regions with multiple mutations known in various genomic regions, the new coronavirus is quite dissimilar from/to both SARS-CoV and MERS-CoV [2]. Based on genomic characteristics of coronavirus, the current diagnostic tests for coronavirus, include RT- PCR, rRT-PCR (real-time reverse transcription PCR), and RT-LAMP (reverse transcription loop- mediated isothermal amplification) as well as real- time RT-LAMP [4,5]. Due to the limitations and problems related to old and modern methods of development of biosensors in recent years has received more attention of researchers [6]. Biosensor technology can be involved in optical sensor wearable sensor, smart band, cell-based sensors, plasmonic photothermal sensor, and nano-sensor which can be applied to diagnose the COVID-19 [7,8]. Findings from several studies show that biosensors are tools with high sensitivity and specificity as well as fast performance that can be a good alternative to common methods of coronavirus detection [9-11]. Even though unique features, biosensors are simple, cost-effective tools that will be very useful in pandemic screening "COVID-19" [8,11].

2. Methods in the detection of coronaviruses

2.1. Traditional methods in the detection of coronaviruses

A computerized tomography (CT) scan combines a series of X-ray images taken from different sites around the body and uses computer management to generate cross-sectional images of the various organs such as soft tissues, bones, blood vessels, and inside the body. Compared with X-ray methods, CT scan images deliver additional, comprehensive data [12,13].

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https://doi.org/10.1016/j.microc.2021.106094
Received 26 December 2020; Received in revised form 14 February 2021; Accepted 15 February 2021
Available online 19 February 2021

A CT can be used to image approximately all parts of the body, and is used to diagnose some injures or diseases as well as for radiation or surgical treatment and other medical strategies [14-16]. CT scan is extensively used as a reliable test for screening the COVID-19 patients.

As can be seen in the Fig. 1, the disease progression has appeared in images A to image H of the CT scan. The progress of the disease is characterized by a small opacity region in the right lung of the image C; with the progression of the disease after a few days, the opacity region increased and eventually involved both lungs in the image H [17]. In general, the results obtained from CT scan images are reliable but not specific because the same results are obtained from other acute respiratory diseases [14,16,18]. Although, the clinical manifestations of COVID-19 are non-specific, chest CT scan is the most important diagnostic method and its feature includes bilateral, multiple, patchy consolidation and ground-glass opacity with the sub-pleural distribution. Dynamic observation of chest CT could help rapid diagnosis, evaluate patient's condition, screen disease progress, and adjust therapeutic strategy[19]. Despite the unique and suitable features of CT scan, it seems that the most important drawback of this method is the need for advanced and expensive devices and similar and indistinguishable results with other acute respiratory diseases [20]. Finally, although routine laboratory tests, such as serological procedures, are available, CT scans are reliable, according to studies (Fig. 2).

2.2. Modern methods in the detection of coronaviruses

The polymerase chain reaction (PCR) and real-time reverse transcription–polymerase chain reaction (RT-PCR) are the most important tests and are used as gold standards for nucleic acid diagnostic biomarkers. However, such conventional tests work on a higher concentration of target molecules; they make the methodology most appropriate for highly sensitive detection and commonly needs expensive, advanced equipment and experienced personnel for the intricate process [16,21,22]. A real-time reverse transcription–polymerase chain reaction (RT-PCR) the assay was established to quickly detect the SARS-CoV based on multiple primers and probe sets in different regions of the SARS-CoV genome. This molecular method could discriminate SARS-CoV from other human and animal coronaviruses with an acceptable LOD of genomic copies per reaction [23]. During novel a novel experimental study, the authorized and fast investigative method to identify SARS-CoV-2 with Loop-Mediated Isothermal Amplification (LAMP) the assay was developed. The created system is adjusted based on isothermal amplification of the SARS-CoV-2 nucleic acids and reported as a sensitive and reliable tool [24,25]. Clustered regularly interspaced

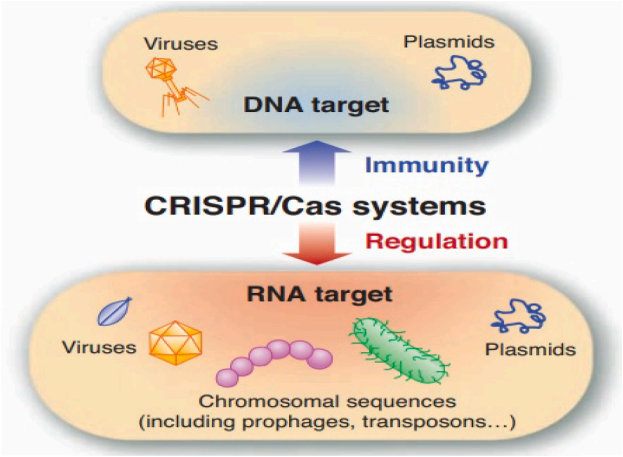

Fig. 2. The mechanism of targeting RNA and DNA by the CRISPR/Cas systems and interfering with nucleic acid sequences of viruses, phages, and plasmids, Otherwise, the capacity of CRISPR/ Cas systems to obstruct the transfer of specific nucleic acid sequences such as plasmid DNA or phage into a host might be exploited via genetic engineering to precisely prevent the distribution of adverse genetic elements, such as antibiotic-resistance markers and genes harmful to humans and other living organisms. It may also be planned to limit the intracellular extent of mobile genetic elements such as insertion sequences (IS) and transposons. On the other hand, to providing immunity, CRISPR/Cas systems that target RNA have the potential to affect the transcript stability of chromosomal elements [27].

short palindromic repeat (CRISPR) loci and their associated (Cas) proteins deliver adaptive immunity against viral infection in prokaryotes [26]. Several intrinsic features of CRISPR-based immunity have provided the most important opportunities for industrial uses such as hypervariability for typing determinations, driving viral evolution, expecting and modifying virus resistance in performing natural genetic tagging of some microbes. Additionally, CRISPR spacer content offers the potential for permanent use of industrial microbes [27,28]. Alternatively, the ability of CRISPR/ Cas systems to prevent the transfer of specific nucleic acid sequences such as a DNA phage or plasmid into a host might be exploited by genetic engineering to impede the distribution of unappealing genetic elements, such as genes damaging and antibiotic-resistance markers to/in existing organisms and humans. CRISPR/ Cas systems may also be used to limit the spread of portable genetic elements such as attachment sequences and transposons in intracellular milieu.

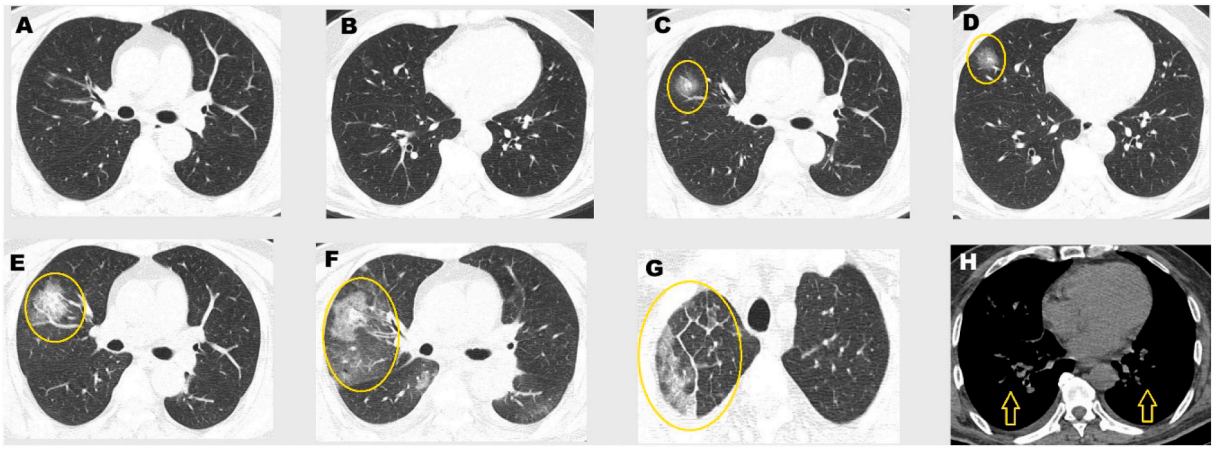

Fig. 1. CT scan of the/a COVID-19 patient, Un-enhanced CT images: A, B, Images displays ground-glass opacities in the right lung. C, D, Images attained two days later shows progressive ground-glass opacities through minor parts of consolidation in the center. E, On the sixth day, images display the amount, density, and range of lesions in the right lung enlarged extra. F, G, H, Images attained on the 9-th day exhibit that lesions grown further and complicated both lungs, with thickened interlobular septa around the lesion in the upper lobe of the right lung, and the presence of small two-sided pleural effusions [17].

CRISPR/Cas systems capable of targeting RNA sequences can affect the transcription of nucleic acid and therefore affect immunity [27].

For the first time, the CRISPR/Cas9-based method was established to detect the Zika virus in 2016 [29]. By the most novel study, CRISPR–Cas12 technology was applied for detection of SARS-CoV-2. The reported technique could qualify point-of-care analysis of the clinical diagnostic laboratory and be used in public places such as clinics, local emergency units, airports, and other locations [30]. All-In-One Dual CRISPR-Cas12a system named "AIOD-CRISPR" evaluation technique was established for ultra-sensitive, simple, and rapid detection of coronavirus (SARS-CoV-2) and HIV. This work was a visual detection platform and a pair of crRNAs was introduced to deposit dual CRISPR-Cas12a recognition and increase detection sensitivity. The AIOD-CRISPR assay system was effectively employed to detect DNA and RNA of SARS-CoV-2 and HIV with a sensitivity of low copies. Also, it was assessed by identifying HIV-1 RNA extracted from human plasma samples, attaining an equal sensitivity with real-time RT-PCR method [31].

We show in Fig. 3 the principle of the AIOD-CRISPR assay, as described by X. Ding et al. In this study, the authors show that AIOD-CRISPR evaluation can be openly visualized by the naked eye. For that reason, the AIOD-CRISPR method will simplify CRISPR-based next-generation molecular diagnostics in the direction of point-of-care applications.

We show in Fig. 4 the conventional assay in detection of covid-19, as described by I. Santiago et al. In this study, the authors show that, the most important disadvantages of routine methods include low sensitivity and specificity, high cost and long-time of testing.

We summarize the main characteristics advantages, and disadvantages of conventional methods in Fig. 4 and Table 1.

Based on these studies, the main limitations are; 1- False positive and false negative results, especially (Table 2) in connection with serological tests. 2- Occurrence of cross-reactions in tests based on antibodies and serology.3- Need for advanced and expensive tools and devices 4- Need for experts to operate and interpret the results. 5- Low and unreliable sensitivity and specificity. 6- Being hard to work and time-consuming 7- Requirement to restart molecular-based techniques such as RT- PCR in the event of a mutation in the structure of nucleic acids.

To eliminate these limitations, biosensors can be ideal as advanced and modern tools.

2.3. Biosensors; nanotechnology based methods

The first biosensor, invented in 1962 by Clark and Lyons to diagnose the glosses/glasser's disease, is broadly developed, especially in connection with infectious diseases due to its technological advantages. Various types of viral targets and affinity reagents such as an antibody, aptamer, peptide nucleic acid (PNA) and whole-cell are used extensively in biosensors technology. Antigen-antibody based biosensors (Immunosensors), nucleic acid-based biosensors (Genosensors) and whole cell-based biosensors are the most developed biosensors in the detection of viral infection [6,8,36]. Due to the quick and successful isolation of antibodies in connection with broad analytes, the expansion of immunosensors has become more considerable in recent years [37]. Owing to the advantages of electrochemical biosensors, such as high sensitivity and specificity, low cost, and simple structure as well as the ability to miniaturize, electrochemical biosensors are more suitable for diagnosing viral infections [38,39]. Changes in conductivity of solutions (conductometry), provide measurable current at variable potential (voltammetry), quantifiable potential without drawing noticeable current (potentiometry) and opposition of a circuit to the current flow

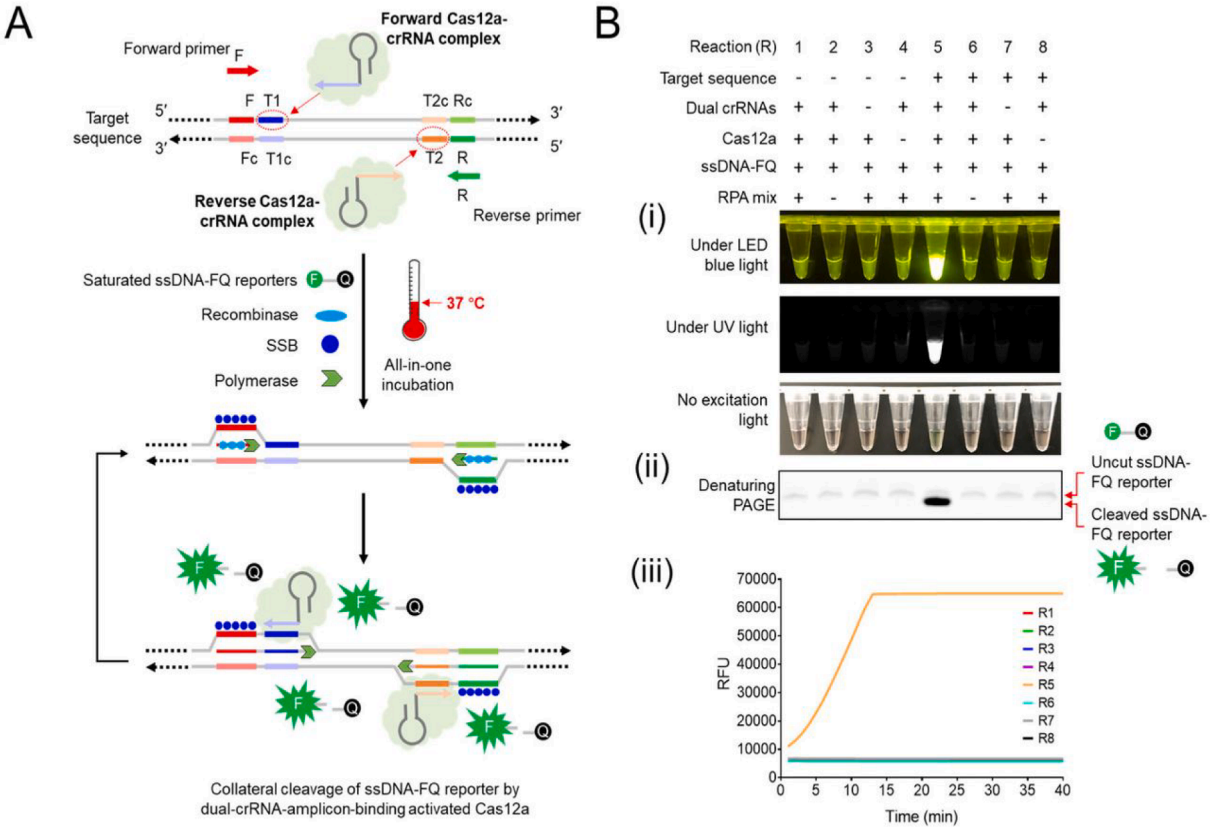

Fig. 3. Design and working principle of the AIOD-CRISPR assay, **(A)** Representation of the AIOD-CRISPR assay system. SSB, single-stranded DNA binding protein. **(B)** Improvement and assessment of the AIOD-CRISPR assay system. The ssDNA-FQ reporter was labeled by 5′ 6-FAM (Fluorescein) fluorophore and 3′ Iowa Black® FQ quencher. (i) Eight reaction systems with several components and their endpoint images after incubation. (ii) Denaturing PAGE analysis of the AIOD-CRISPR products. (iii) Real-time fluorescence detection of the AIOD-CRISPR assay for eight reaction systems with various components [31].

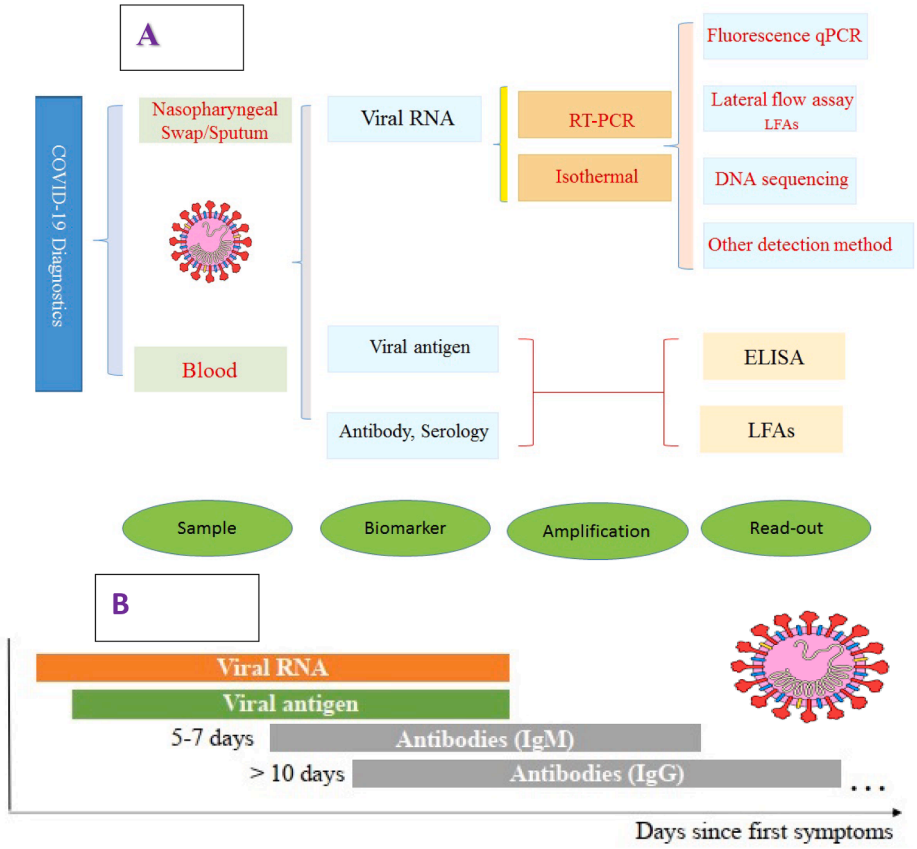

Fig. 4. Conventional methods of detecting coronavirus and the time required, **A)** Various Covid-19 detection methods, including antibody-antigenic based methods (serology) and molecular-based methods including PCR and RPCR. **B)** Duration of antibodies advent to virus infection and the possibility of serological test application[32].

Table 1
Developed conventional methods in detection of coronaviruses.

Techniques	Viral target	Advantages	Disadvantages	Refs.
LAMP	N gene F3 GCCAAAAGGCTTCTACGCA	Sensitive, Fast operation, Simple	Need for advance equipment	[24,25]
LAMP	N gene, *ORF* genes	Cost-effective, Fast operation and great point in the screening	_	[25]
RT-PCR	GTGARATGGTCATGTGTGGCGG	Reliable results	Laborious and time-consuming	[25,33]
real-time RT-PCR assay	TTA AAC CAG GTG GAA CAT CAT CCG GTG	Reliable results	Difficult and time-consuming	[23]
(mNGS) and RT-PCR	gRNA for *Orf1ab* (5′-GGGG AUUU AGAC UACC CCAA AAAC GAAG GGGA CUAA AACA AACU CUGA GGCU AUAG CUUG UAAG GUU-3′)	High sensitivity, Affordable	_	
CT scan	_	Interpretation of the pathogenesis of the virus in radiological images, high sensitivity	Non-specific results obtained, the need for advanced and expensive devices, the need for experts to interpret the results	[16,18,34]
CRISPR–Cas12	E gene and N gene	Reliable and sensitive results	Time consuming	[30]
CRISPR-Cas	5′-TAAT ACGA CTCA CTAT AGGG ACAT AAAC132 AAGC TTTG TGAA GAAA TGCT GGAC-3′	Reliable and sensitive results, Usable as therapeutic and diagnostic target	Need for advanced and extra study to reach detailed mechanisms	[35]
AIOD-CRISPR	SARS-CoV-2 and HIV virus	Comparable sensitivity with real-time RT-PCR method, has a great potential for developing next-generation point-of-care molecular diagnostics	_	[31]

(LAMP); Loop-Mediated Isothermal Amplification, **(CRISPR-Cas);** Clustered regularly interspaced short palindromic repeat (CRISPR) loci and their associated (Cas), metagenomic next-generation sequencing **(mNGS)**; All-in-One Dual CRISPR-Cas12a **(AIOD-CRISPR)**

(impedance) are the most important bio-recognition procedures in electrochemical biosensors [40]. Among the various techniques, voltammetric and impedimetric techniques will be most considered due to their high sensitivity and affinity between targets and probes interaction [41].

As shown in Fig. 5, biosensors are capable of detecting a wide range of biomarkers. Therefore, biosensor technology can be developed to diagnose a wide range of diseases, including infectious diseases, cancers, and various of disorders related to the immune system.

There is no doubt, that the detection limit (LOD) is one of the most important performance characteristics of an analytical procedure. Progress in analytical chemistry might well be measured by the shift of

Table 2
Developed biosensors for the detection of coronaviruses.

Transducer/Techniques (s)	Viral Target	Nanoparticles	Samples Form	Linear range	LOD	Refs..
PPT/LSPR	_	AuNIs	_	0.01 pM to 50 μM	2.26 × 107	[51]
LSPCF	Np	_	Human serum	0.1 pg/mL to 1 ng/mL	1 pg/mL	[52]
SELEX	Np	_	Clinical	NA	2 pg/m	[53]
Label-Free, Electrical	Np	In_2O_3 nanowire	BSA	_	44 μM	[54]
SPR	Oligonucleotides	_	Throat swab	1 nM to 1 μM	2 nM	[55]
FRET	Antibody	MoS_2 is a 2-D nanosheet	Human serum	10^2–10^6 EID50	1.0 × 10–5 ng/mL	[62]
SPR	SCVme	_	_	10 g mL^{-1}	200 ng mL-1	
Immunosensor	HCoV and MERS-CoV proteins	Au	Spiked nasal	0.001 to 100 ng.mL-1	0.4 and 1.0 pg. mL-1	[57]
Luciferase-Based Biosensors	PLpro and 3CLpro	_	Spiked	NA	NA	[58]
FRET-based biosensors	Protein-protein interactions	Au	Spiked	1–10 nm	NA	[59]
Field-Effect Transistor-BasedBiosensor	Antigen protein	_	Clinical samples	1.6 × 10^1 pfu/ml to 1.6 × 10^4 pfu/ml	1.6 × 10^1 pfu/ml	[60]

NA: Not available, **PPT/LSPR:** Plasmonic photothermal/ Localized Surface Plasmon Resonance, **(AuNIs):** gold nanoislands, **(LSPCF),** localized surface plasmon coupled fluorescence, **(SELEX)** systematic evolution of ligand by exponential enrichment, **(Np):** N protein, **(SPR),** surface plasmon resonance, **(FRET),** fluorescence resonance energy transfer, **(SCVme);** Coronaviral surface antigen.

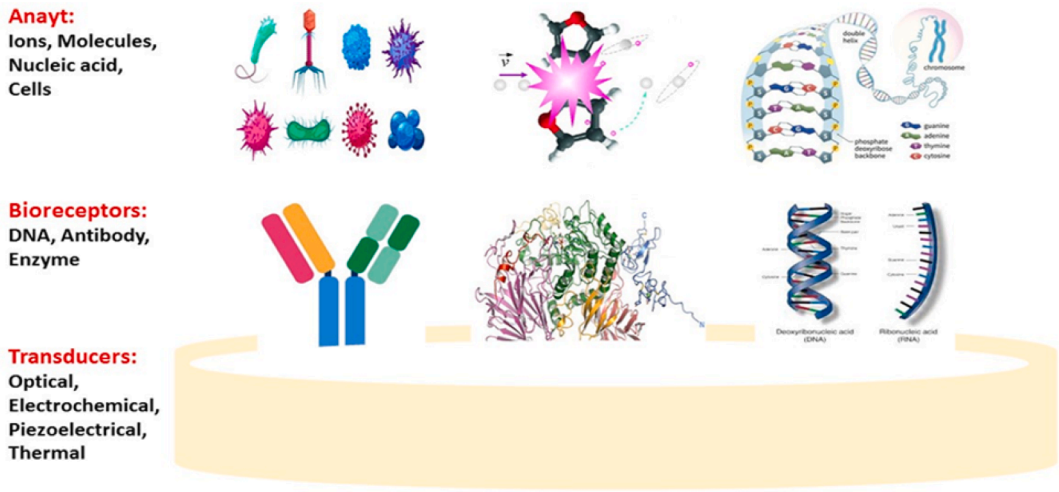

Fig. 5. Schematic illustration of biosensors and components on a proposed platform. The figure includes the introduction of various analyzers, bio-receptors and transducers used in biosensors technology.

the LOD towards lower values. Of course, the picture emerging would reflect only part of the progress [42,43]. Certainly, many problems in analytical chemistry are problems related to detecting and determining elements or compounds in small amounts of sample (micro-analysis), very low concentrations or small amounts in the larger specimen (trace analysis), or even of determining low concentrations in small samples. In the most cases a method is assumed to be very sensitive when the LOD is low, and the LOD and sensitivity in many cases in point are considered synonymous [44]. However, in other divisions of science, the sensitivity is defined as the slope of the curve that is acquired when the result of the measurement is plotted against the amount that is to be determined. In analytical chemistry, the sensitivity defined in this way is equal to the slope of the analytical calibration curve, and the definition of the sensitivity will be used in biosensor technology. The lower LOD is exactly understood as the limit below which detection is impossible [43,44].

2.3.1. *Developed coronaviruses biosensors*

Innovative biosensors used to detect RNA-viruses include nucleic-acid based, CRISPR-Cas9 based paper strips, optical biosensor, aptamer-based, antigen-Au/Ag nanoparticles-based electrochemical biosensors, and Surface Plasmon Resonance (SPR), Fig. 6 [11,45]. Biosensors might be effective bio-device for rapid, accurate, portable, and more promising diagnosis in the existing pandemic that has exaggerated the world humanity and economies [46,47].

In order to develop diagnostic coronavirus biosensors, a dual-functional plasmonic biosensor with the plasmonic photothermal (PPT) effect combined with localized surface plasmon resonance (LSPR) sensing transduction was fabricated as a hopeful solution for the clinical severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) diagnosis. The two-dimensional gold nanoislands (AuNIs) functionalized with complementary DNA receptors can perform a sensitive detection of the selected sequences from COVID-19 through nucleic acid hybridization. High sensitivity and specificity are unique features of the developed system [51]. Nucleocapsid (N) protein in the SARS-CoV is the most important protein and aids as an analytical marker for ultra-sensitive detection of the virus. Localized surface plasmon coupled fluorescence (LSPCF) fiber-optical bio-sensing tools were fabricated for the detection of nucleocapsid protein of SARS-CoV N in human serum as an appropriate clinical approach. The created platform has a simple structure and operation, with a suitable linear range and limit of detection [52]. During experimental studies, the systematic evolution of ligand by exponential enrichment (SELEX) technique was performed for detection of N protein of coronaviruses. Aptamer–antibody hybrid based immunoassay was used as a fast and sensitive method in the detection of SARS-CoV N protein [53]. Antibody mimetic proteins (AMPs) are useful polypeptides with high affinity and specificity that bind to their target analytes. Compared to routine methods, these types of peptides can be

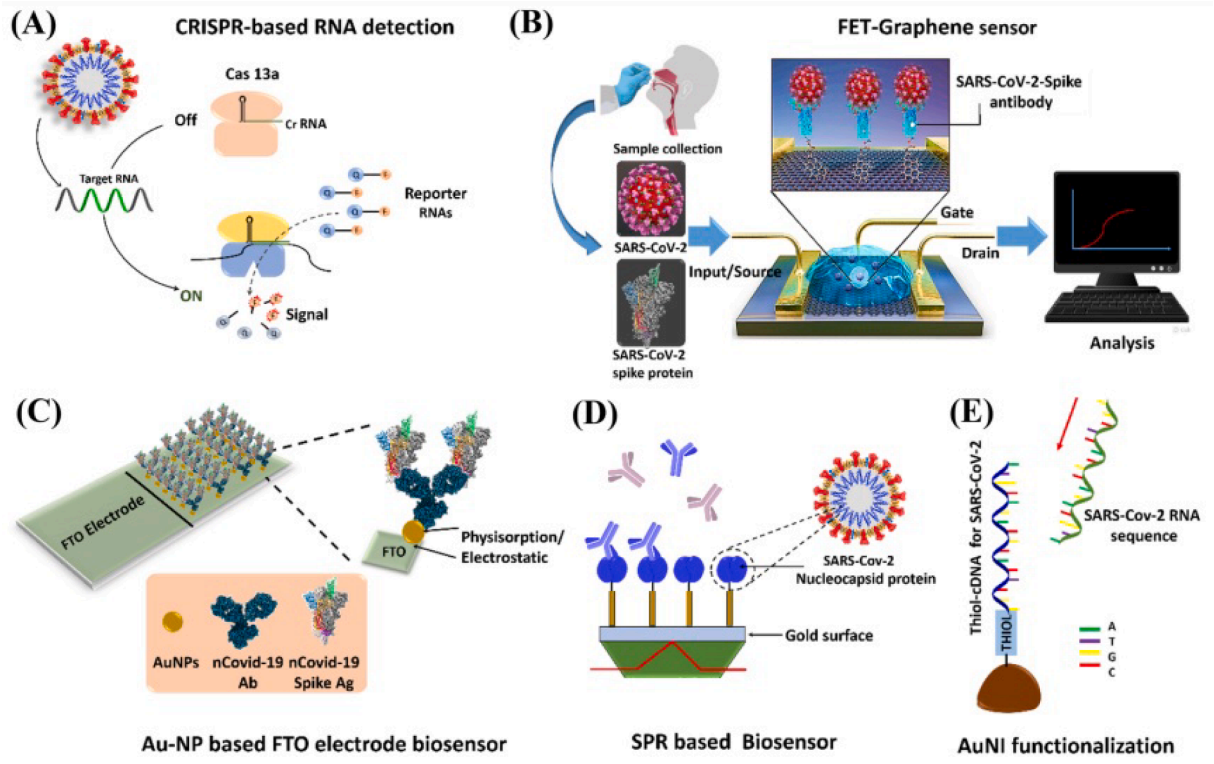

Fig. 6. Various type of the biosensors for SARS-CoV-2 virus detection [47]. **A)** CRISPR based nucleic acid (RNA) detection [48]. **B)** FET based biosensor operation [49], **C)** AuNPs based FTO electrode biosensor [50], **D)** Surface Plasmon Resonance (SPR) based biosensor, **E)** 2D gold Nano-islands (AuNIs) functionalized biosensors [47].

used in very small amounts. AMPs were applied in a nano-biosensor platform to detect N protein of SARS. Employing of this biosensor, N protein was identified at a low concentration in bovine serum albumin (BSA) [54]. A novel surface plasmon resonance (SPR) based biosensor was created for sensitive and specified detection of SARS and common respiratory viruses. This system was developed by immobilizing virus-specific oligonucleotides in an SPR chip. To increase the biosensor sensitivity, biotin and streptavidin were used to label the PCR primer and amplify the signal more after hybridization. Accordingly, the created biosensor can sensitively recognize the SARS and some respiratory viruses [55]. A simple and effective technique for assembly of SPR based sensing platforms was established for selective and sensitive recognition of SARS coronaviral surface antigen (SCVme) Fig. 7 [56].

An electrochemical immunosensor was fabricated for sensitive and selective detection of MERS-CoV in single-step. The created system displayed suitable stability and acceptable, good selectivity compared to other non-specific targets such as the flu virus. The high sensitivity of

the immunosensor is attributed to the application of AuNP modified carbon array electrodes, which leads to improved electron transfer efficacy and electrode surface area. Moreover, the use of a disposable electrode decreases the cost of the assay and allows the multiplexed and simultaneous detection of HCoV and MERS-CoV. In summary, the fabricated immunosensor was effectively applied to detect HCoV and MERS-CoV proteins in spiked nasal samples presenting acceptable recovery percentages Fig. 8 [57].

Luciferase-Based Biosensors were developed for the detection of coronavirus Papain-Like (PLpro) and 3-chymotrypsin-like protease (3C-Like Proteases) properly. PLpro and 3CLpro from MERS-CoV are the two most important proteins which can be applied as therapeutic target biomarkers in the diagnostic approach. Accordingly, in the optimum expression of MERSCoV PLpro and 3CLpro, established luciferase-based biosensor will monitor and identify effective small-molecule inhibitors and protease activity for MERSCoV and other future emerging coronaviruses [58]. In the last decade, major technological successes have been made in bio-assay, such as the recognition approaches, transduction devices, and signal amplification. Innovative biosensor technology was established for the improvement of COVID-19 diagnosis in clinical labs through the present greater specificity and sensitivity, with user-friendly design in a short time. This platform can similarly be used to improve monitor devices, for instance by being attached to the severe care ventilators, they may help to reveal the spread route of the SARS-covid-2 viruses [59]. Ultra-sensitivity, rapid measurements and being usable with a low quantity of analytes, are the advantages of field-effect transistor (FET)-based biosensors. FET-based biosensors are considered useful devices in clinical diagnosis. Graphene-based FET biosensors are capable of sense surrounding alterations on their surface and therefore offering an ideal sensing environment for

minimum noise detection and high sensitivity. From this point of view, graphene-based FET tools

are suitable for applications associated with the sensitive immunological diagnosis. Accordingly, FET based biosensor functionalized with SARS-CoV-2 spike antibody was established for the detection of coronaviruses. The created system shows acceptable LOD and is used detect of the virus antigen-protein in transport medium from nasopharyngeal swabs from clinical samples [60]. The proposed bio-sensing platform illustrated in Fig. 9.

CRISPR–Cas9 based biosensor on a graphene field-effect transistor was created for the detection of unamplified target genes. Similar work can be considered as a modern bio-sensing tool for the detection of viral targets such as covid-19 nucleic acids [61].

The most important challenge associated with Covid-19 disease is the rapid transmission, asymptomatic and long-term incubation in carriers. Due to the simple and low-cost structure, easy operation process, high sensitivity, and specificity, biosensor technology could be the best alternative to conventional methods in the detection of covid-19; however, the development of genosensors should be considered more closely due to their high sensitivity and specificity.

The disadvantages and advantages of routine methods with

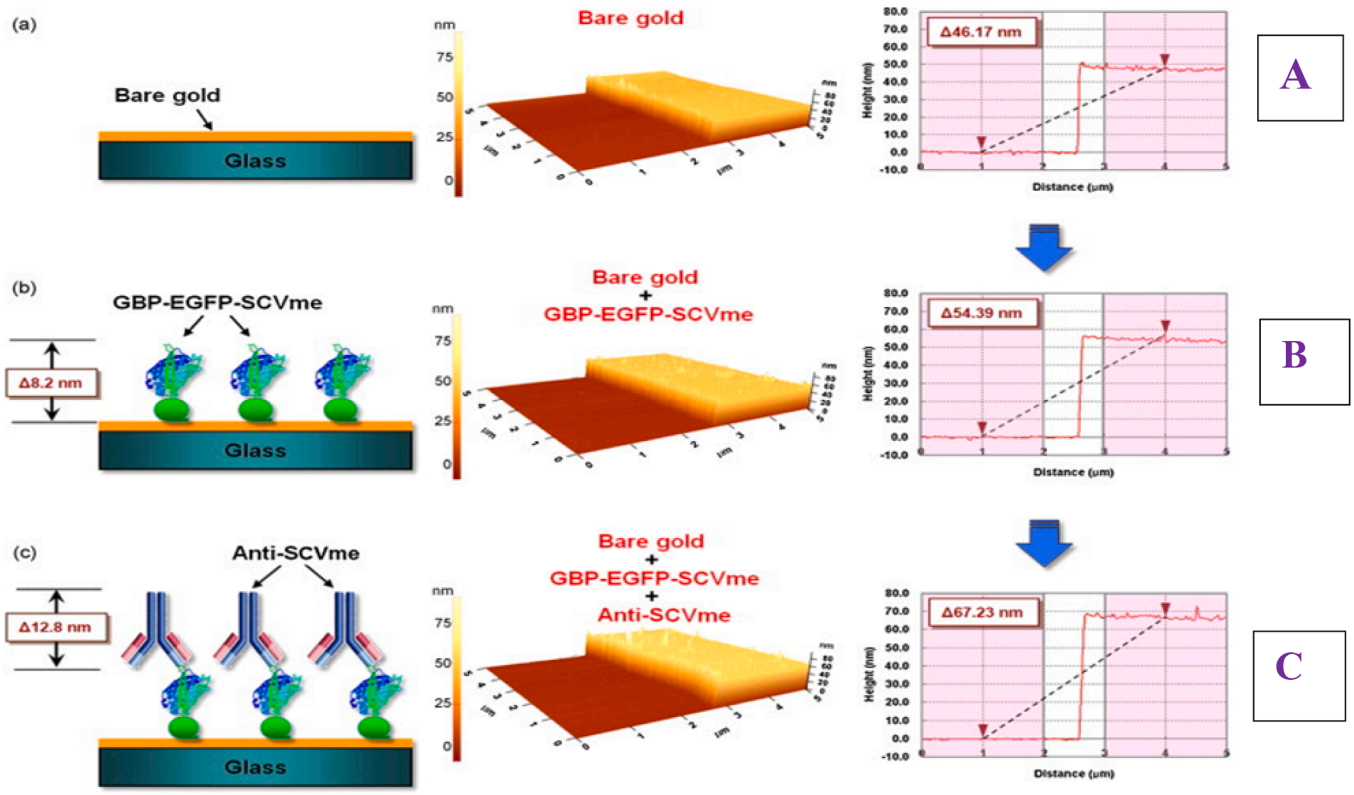

Fig. 7. Illustration of proposed SPR based biosensor for detection of coronaviral surface antigen (SCVme), AFM images of the sequential binding of GBP-E-SCVme and anti-SCVme on the gold-micro-patterned surface. **(A)** Bare gold surface, **(B)** binding of the GBP-E-SCVme fusion proteins onto the gold surface, and **(C)** subsequent binding of the anti-SCVme antibodies on the GBP-E-SCVme layer. Left, representation plans for the successive binding of GBP-E-SCVme and anti-SCVme on the gold micro-patterns; middle, three-dimensional topological images; right, the cross-sectional contours of samples a–c, sequentially (these are average height differences of the individual scan lines from each area) [56].

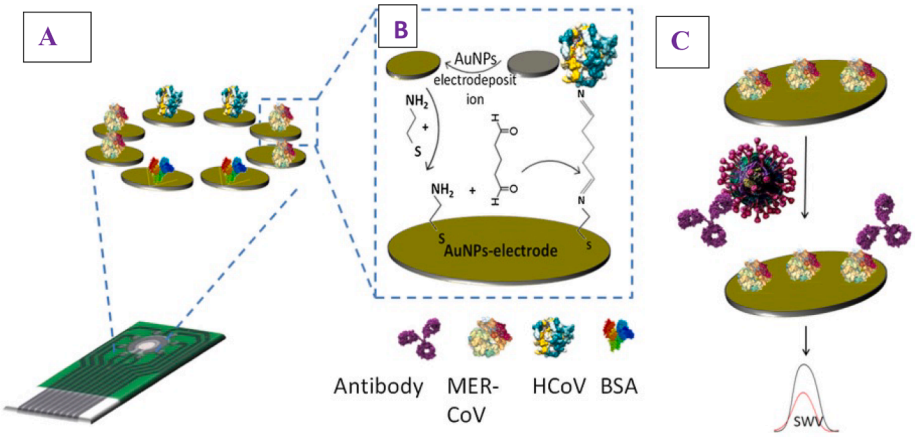

Fig. 8. Illustration of immunosensor for detection of HCoV and MERS-CoV proteins, (**A**) COV immunosensor array chip (**B**), The immunosensor fabrication steps (**C**) The detection process of the competitive immunosensor for the virus [57].

biosensor technology are summarized in Table 3.

As revealed in several studies rapid detection is the main feature of biosensors technology compared to routine diagnosis methods. In addition to biosensors, other diagnostic methods are being developed for rapid detection of the COVID-19, for example, rapid antigen diagnostic (RAD) test was developed as an immunoassay approach [63]. Although rapid diagnosis is a necessary factor, especially in relation to COVID-19, it should be noted that the sensitivity and specificity of a diagnostic method are more important than a rapid diagnosis. For instance, serological methods are the main rapid diagnostic techniques in virology, but unfortunately its false positive and negative results have limited its use [64].

3. Conclusion

The most important results obtained from this review study are; 1. Future technology and diagnostic methods, especially in connection with infectious and contagious diseases, should be in line with simple, low-cost methods with high sensitivity and specific diagnostic methods so that they can be effective in the face of a similar covid-19 pandemic.

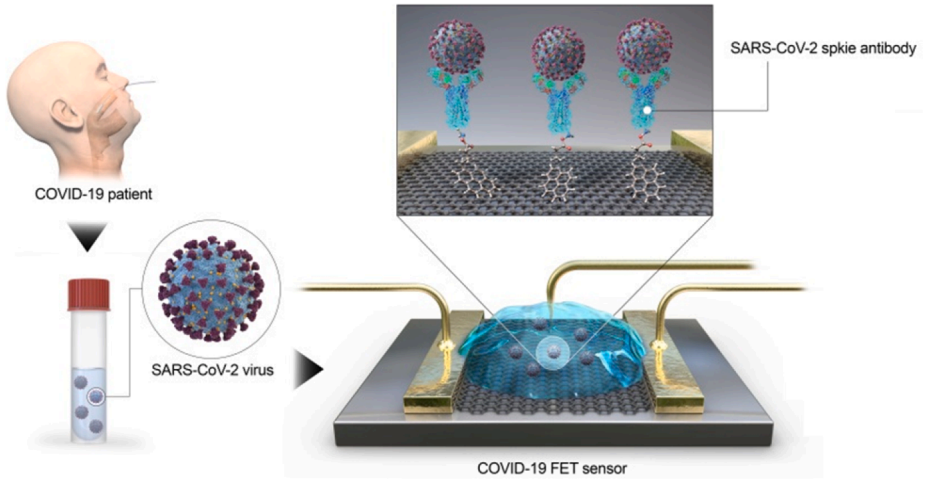

Fig. 9. A field-effect transistor (FET)-based biosensors for detection of SARS-CoV-2 spike antibody, Graphene as a sensing material is selected and SARS-CoV-2 spike an antibody is conjugated on the graphene sheet by 1-pyrenebutyric acid n-hydroxysuccinimide ester, which is an interfacing molecular as a probe linker [60].

Table 3
Comparison of routine methods with biosensor technology.

	Biosensor technology	Routine methods
Need for advanced tools	No Need	Need
Operation time	Fast	Slow
Sensitivity and specificity	High	Low
Interpretation of results	Easy	Difficult
Cost of testing	Low	High

2. Future diagnostic approaches should be rapidly approved by the doctors and clinicians, which can affect the treatment line of COVID-19 and other similar infections. 3. Future technology should be used to integrate entirely medical plans, strategies and treatment processes. 4. According to the latest studies in the field of COVID-19 diagnostic techniques, the most significant drawbacks of conventional methods include high cost and low sensitivity/specificity due to the presence of false positive/negative results and the occurrence of cross-reactions. On the other hand, rapid diagnosis is one of the basic requirements in the treatment and control of the disease, while routine tests are very time consuming and in some cases, the results of the diagnosis are prepared after a few days. 5. CRISPR-Cas mediated adaptive immunity, is promising as a diagnostic and therapeutic target; however, comprehensive and appropriate research is needed to achieve medicine approval. 6. Even though molecular-based methods such as PCR, and RT-PCR have been highly sensitive compared to conventional methods to date, biosensor technology, mainly CRISPR-Cas mediated biosensors, appears to be a golden alternative in diagnosis and therapeutic approaches in the near future.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgment

The authors would like to thank the Aging Research Institute and the Physical Medicine Rehabilitation Research Center of Tabriz University of Medical Sciences.

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