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Emerging trends in point-of-care biosensing strategies for molecular architectures and antibodies of SARS-CoV-2

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ABSTRACT

COVID-19, a highly contagious viral infection caused by the occurrence of severe acute respiratory syndrome coronavirus (SARS-CoV-2), has turned out to be a viral pandemic then ravaged many countries worldwide. In the recent years, point-of-care (POC) biosensors combined with state-of-the-art bioreceptors, and transducing systems enabled the development of novel diagnostic tools for rapid and reliable detection of biomarkers associated with SARS-CoV-2. The present review thoroughly summarises and discusses various biosensing strategies developed for probing SARS-CoV-2 molecular architectures (viral genome, S Protein, M protein, E protein, N protein and non-structural proteins) and antibodies as a potential diagnostic tool for COVID-19. This review discusses the various structural components of SARS-CoV-2, their binding regions and the bioreceptors used for recognizing the structural components. The various types of clinical specimens investigated for rapid and POC detection of SARS-CoV-2 is also highlighted. The importance of nanotechnology and artificial intelligence (AI) approaches in improving the biosensor performance for real-time and reagent-free monitoring the biomarkers of SARS-CoV-2 is also summarized. This review also encompasses existing practical challenges and prospects for developing new POC biosensors for clinical monitoring of COVID-19.

1. Introduction

Infection caused by viruses is one of the major causes of increased morbidity and mortality worldwide, significantly affecting global economic conditions. The first case of a novel virus was reported in Late-December 2019. The disease was diagnosed as pneumonia with an unknown origin (Harapan et al., 2020). In March 2020, the World Health Organization (WHO) announced Coronavirus disease 2019 (COVID-19) as a global pandemic. According to the data provided by the WHO, over 753,479,439 confirmed cases, including 6,812,798 deaths were reported in 220 countries as of 31 January 2023 ("WHO Coronavirus (COVID-19) Dashboard | WHO Coronavirus (COVID-19) Dashboard With Vaccination Data," n.d.). Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the virus responsible for the current outbreak of COVID-19. The virus is the seventh species under the Coronaviridae family which infects both animals and humans. The other forms of human transmissible coronaviruses are, severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East Respiratory Syndrome (MERS-CoV) that emerged in 2002 and 2012, respectively (N. Zhu et al., 2020). SARS-CoV-2 mainly attacks the respiratory system, goblet cells in the nose, intestinal tract, kidney, and liver (Hadisi et al., 2021). Viruses in common are parasites that require a host cell to replicate. Multiple evolutions have improved the molecular mechanistic pathways of viruses entering cells and their modes of transmission. Viral infection also occurs by contacting the infected surfaces (Guo et al., 2021). Thus, understanding the structure and function of the virus causing the disease is essential in designing diagnostic assays with good selectivity. The entire viral particle is known as the virion, which consists of nucleic acids as genetic material and the outer shell layer of proteins. Most viruses have DNA or RNA as their genetic material, and the nucleic acid structure can be single-stranded or double-stranded (Perkins et al., 2017). Due to the rapid spread of this communicable

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disease, there is an urgent need to develop reliable mass screening methodologies that can be used for rapid diagnosis and contact tracing (Cui and Zhou, 2020). Detection of viral particles in the early stages of infection can help slow down the spread rate and improve the efficacy of treatment protocols to control the viral load.

The early stage of COVID-19 is diagnosed by clinical manifestations and a history of contact with potentially infected people. Since the clinical symptoms and indications of infection are not conclusive, further diagnostic and serological test is required for COVID-19 detection (Filipić et al., 2020). The importance of diagnostic tool is determined by the type of test, the time it takes to receive results, testing accuracy, and the resources necessary for testing. To put it another way, the most remarkable technique for enabling effective action and limiting transmission is to identify suspicious persons quickly. The most used strategy is to check body temperature (thermal scanner). This method is not a precise measure for COVID-19 infection as fever is correlated to different illnesses, and even those who cleared the temperature scanning were confirmed to be positive when tested using molecular or serological methods (Parihar et al., 2020). Biochemical tests such as total blood count, C-reactive protein (CRP), and cytokines can be used to improve the outcomes, although they are not highly specialized (Wrapp et al., 2020).Currently, COVID-19 detection in laboratory is enabled by enzyme-linked immunosorbent assay (ELISA), reverse transcriptase-polymerase chain reaction (RT-PCR), rapid lateral flow immunoassay (LFIA), chest computed tomography (CT), Reverse transcription loop-mediated isothermal amplification (RT-LAMP) and western blotting-based analysis (Cui and Zhou, 2020). Among these techniques, RT-PCR is a gold standard technique for COVID-19 detection as it detects the presence of nucleic acid genome. Chest-CT is more sensitive than RT-PCR in detecting patients who require further testing,

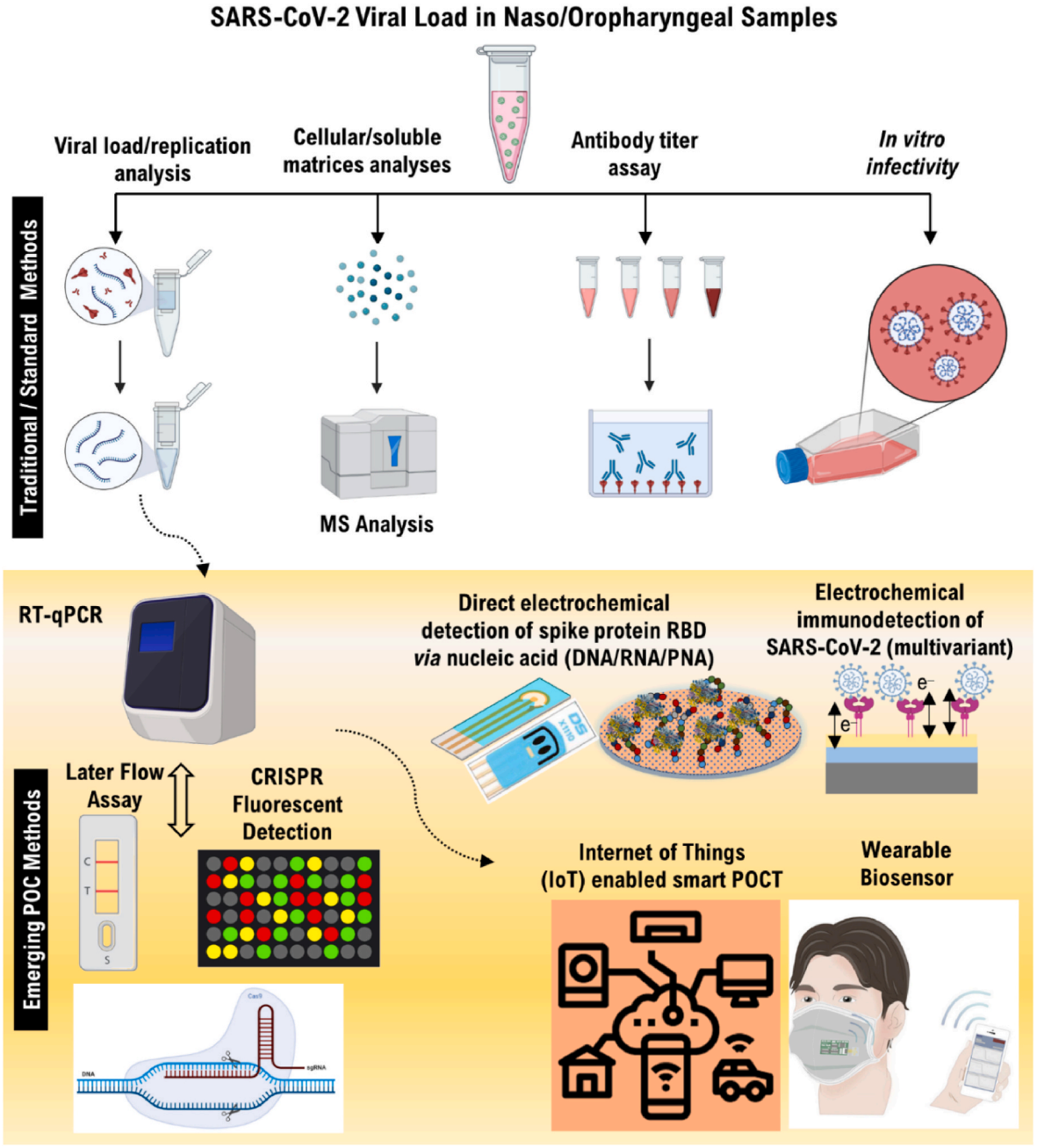

Fig. 1. Trends in detection of SARS-CoV-2. An overview of current and emerging detection platforms promising for point-of-care technology (POCT) toward early diagnosis of COVID-19.

isolation, and treatment; nevertheless, it is not specific for COVID-19 and has been associated with symptoms like coronavirus (Diagnose et al., 2020). An overview of standard methods and emerging point-of-care technologies promising for the COVID-19 detection are schematically illustrated in Fig. 1.

Although widely utilized for on-site detection, these conventional techniques are still having limitations. Despite their extensive usage, these approaches have certain drawbacks, including the necessity for expensive equipment, time-consuming protocols, trained personnel, and high purity samples. False-negative results are also acquired due to the fluctuation of the number of viruses in different samples in patients. Sample collection, storage and sample processing are the additional steps involved in the conventional technique (Carter et al., 2020; Feng et al., 2020). New platforms are being intensively researched in response to RT-PCR and chest CT constraints. Many immunoassay approaches have been developed for the diagnosis of serum antibodies and viral proteins of SARS-CoV-2 using enzyme-linked immunosorbent assay (ELISA) and rapid lateral flow immunoassay (LFIA). Immunodiagnostic techniques for detecting the presence of viral proteins are most feasible in 7–11 days after the onset of infection, or antibody-based diagnosis is generally possible in the recovery period (Abduljalil, 2020). To overcome the time limits imposed by conventional detection approaches, there is need for a rapid, portable, and cost-efficient point-of-care (POC) tool can be deployed at any place and any time. Biosensors are widely used in POC analysis for on-site health monitoring. Glucometers and pregnancy strips are well-established examples of biosensor devices in the commercial market for self-monitoring. For any pathological conditions, before identifying the complete information about the pathogenicity, multiplexed detection of biomarker panels is followed as an initial phase investigation to study the biochemical changes occurring in the body. Many biosensing devices have been used in clinical evaluation, providing an on-site measurement of biomarkers (Koteswara Rao, 2021). The Piccolo Express is a fully automated portable diagnostic device from Abbot which provides an on-site measurement of a panel of biomarkers. Similarly, the i-Stat system is a chip integrated POC diagnosis system from Abbot that allows blood profiling of biomarkers. This system uses specific chips for detecting different panels of biomarkers. In brief, biosensor devices can identify specific target molecules such as proteins, antibodies, nucleic acids through bioreceptor medicated target recognition coupled with a transducer for measuring the output signal. Biosensors can be classified based on the bioreceptors or transducers employed. Advancements around nanotechnology resulted in constructing new biosensors with unique performances (Holzinger et al., 2014). For example, nanomaterials have been integrated with the biosensors for improving detection limit, and sensitivity required for clinical analysis (Singh et al., 2016). The nanoarchitecture also provides a suitable environment for the effective immobilization of bioreceptor molecules without affecting their bio-affinity. In some cases, the nanomaterials also act as signal generating probe, as most of the target-bioreceptor interactions do not produce detectable signals.

The global epidemic situation currently leads to a massive number of publications and reviews reported for COVID-19 diagnosis. However, a clear understanding of binding sites on the SARS-CoV-2 virus in terms of detecting biomarkers at POC is still missing. The present review thoroughly summarized and discusses the SARS-CoV-2 biomarker binding sites available for efficient diagnosis. The achievements made in optical and electrochemical biosensing strategies, the two major transducing techniques used in POC devices, for detecting various molecular architectures of SARS-CoV-2 are highlighted in this review. Many review articles have been published on SARS-CoV-2 diagnostics approaches. However, these reviews need more information about the molecular architectures, targeted binding domains, and bioreceptors employed for specific detection of SARS-CoV-2. Moreover, this review is one of the first to combine the two different transduction principles (electrochemical and optical) in a single review. For example, Zhao et al. reviewed advancements and challenges associated with electrochemical biosensors for POC diagnosis of a respiratory family of viruses (Z. Zhao et al., 2021). Similarly, Mahshid et al. provided a brief overview of biomolecular recognition strategies in electrochemical signal transducers (Mahshid et al., 2021). Optical detection-based strategies for SARS-CoV-2 were also reported for POC measurement. A comprehensive update on different photonics-based techniques involved in detecting SARS-CoV family viruses (Lukose et al., 2021). These reviews, however, provide insufficient information about bioreceptors, biomarkers employed, and the binding domains targeted for specific detection. Nanomaterials play a multi-faceted role in POC devices. They can be tailored to function as immobilization matrix and signal generating probes to improve the sensor performance. Although reviews focus on nanotechnology-based approaches for COVID-19 diagnosis and therapeutics are also available (Iravani, 2020; Weiss et al., 2020), these reviews do not provide in-depth knowledge on POC sensors attempted. To provide a better understanding of the role of point-of-care biosensing strategies for molecular architectures and antibodies of SARS-CoV-2, the present review is structured into various sub-sections. The first section presents a brief overview of the different biomarkers (structural components) of SARS-CoV-2 and their binding domains. The first section also provides an understanding of SARS-CoV-2 structural features and the components of each biomarkers that need to be targeted for diagnosis. The second section lists various types of biorecognition elements (antibodies, aptamers, and molecularly imprinted polymers) used for SARS-CoV-2 biomarker detection. This section is also providing a rationale for choosing unique bioreceptors for targeted biomarkers. The third section lists various nanomaterial architectures used in sensor fabrication and their essential role in POC sensor fabrication. The fourth section encompasses different clinical specimens investigated for POC analysis of COVID-19 detection. Independent sections for comprehensive analysis of electrochemical and optical detection strategies combined with various bioreceptors and biomarkers of SARS-CoV-2 are also provided. The role of IoT and AI technologies in improving the performance of the biosensors are highlighted in this review.

2. Target regions of SARS-Cov-2

SARS-CoV-2 belongs to the family of Coronaviridae, a family of RNA viruses. The virus's genome is positive sense ssRNA ranging between 27 and 32 kb in length. The nucleotide sequence known as the genome is packed inside a protein helical capsid structure and surrounded by different structural proteins (Fig. 2). Thus, one of the approaches for developing biosensor devices for identifying SARS-CoV-2 was built upon targeting a specific region of the spike (S), nucleocapsid (N), envelope (E), and membrane (M) proteins. Apart from these critical structural proteins, the virion also has non-structural proteins (nsp), including open reading frames (ORF) and RNA dependent RNA polymerase (RdRp). While the RdRp is involved in replicating viral genome from the negative-strand RNA template, the ORFs encodes 16 different types of nsp. The nsp plays a crucial role in the transcription and replication of viruses (Gao et al., 2020). The diagnosis strategies for SARS-CoV-2 thus involves probing different structural proteins, non-structural proteins, genome sequence and the whole viral particle. Antibodies generated against these proteins are also targeted to diagnose COVID-19 (Abduljalil, 2020).

2.1. Viral proteins

The SARS-CoV-2 virus comprises four main structural proteins, viz. S, M, E, N proteins and 16 nsp (nsp1− nsp16). Among these proteins, S glycoprotein forms a protruding network on the surface of the virus envelope and provides the SARS-CoV-2 the crown-like structure. S protein is in-charge of mediating virus entry into a host cell. S protein is a 180 kDa glycoprotein that contains three different segments: (i) a large ectodomain, (ii) an intracellular tail and (iii) a small endodomain. The ectodomain further splits into S1 (receptor-binding) and S2 (membrane-

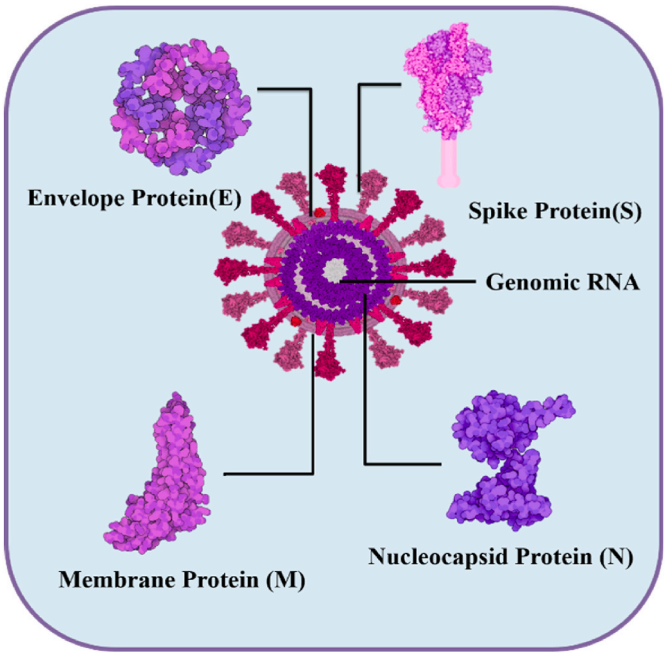

Fig. 2. The schematic diagram of four major structural protein components presents in SARS-CoV- 2 (Gardner et al., 2021).

fusion) subunits. The subunit S1 (14–685 residues) contain an extracellular N-terminal domain (14–305 residues), a short intracellular C-terminal domain and a receptor-binding domain (RBD, 319–541 residues). The RBD is a short fragment in the S1 subunit of the spike proteins. The RBD interact with the host cell receptor to facilitate cell membrane for the virus fusion. The antibodies produced against the S protein targets the RBD domain of the subunit S1. The subunit S2 (686–1273 residues) consists of a fusion peptide (FP), heptapeptide repeat (HR) sequences (HR1 and HR2), cytoplasmic domain (CT) and transmembrane domain (TM) (Pokhrel et al., 2020). The RBD attaches to the angiotensin-converting enzyme 2 (ACE 2) receptor for the viral attachment during the virus entry. Following this, the S2 subunit causes fusion in the host viral membrane for allowing the viral genome to get inside the host cell (Arndt et al., 2010). Due to its essential functions including ACE 2 receptor binding and host cell entry, the S protein is a crucial target for SARS-CoV-2 detection.

The membrane protein (M) is the more prevalent protein on the viral surface and defines the shape of the viral envelope. The M protein has about 220–260 amino acids (Huang et al., 2020). It consists of a triple-membrane spanning domain, glycosylated amino-terminal domain, and a carboxyl-terminus. It is responsible for the transmembrane nutrients transport, envelope formation, detecting the virus assembly and budding formation by interaction with other structural proteins. These characteristics make M proteins "the central organiser for coronavirus assembly" (Ruch and Machamer, 2011). M protein plays several roles in virus assembly for releasing the virus from host cells during the viral replication and maturation process. It is localised mainly at the sites of intracellular trafficking, more specifically in the endoplasmic reticulum and Golgi apparatus (Tseng et al., 2013).The E protein has a molecular weight of 8–12 kDa, with a total number of amino acids ranging from 76 to 109. The E protein comprises N terminus, C terminus and hydrophobic domains.

Nucleocapsid protein (N) encloses the genetic material inside the capsid. N proteins are highly prevalent during the initial stage of infection in the host. The N protein forms a ribonucleoprotein complex with the viral RNA for host interaction with the virus. The N protein comprises a N terminus and a C terminus domain inter-linked with a rich serine linker (Huang et al., 2004). The N proteins are bound to the single virus strand of RNA, where the genetic information is held to allow them to replicate. The N protein inhibits various host cell defence mechanisms and assists the viral genome to replicate and to create new viral particles. Apart from these structural proteins, there are 16 nsp (vide supra), and nine accessory proteins (ORF3a, 3d, 6, 7a, 7b, 8, 9b, 14, and 10) produced from five different open reading frames (ORFs) encoding accessory genes (ORF3a, ORF6, ORF7a, ORF7b, and ORF8), present in the viral particle which can be used as biomarker for SARS-CoV-2 detection.

2.2. Virus genome sequence

The genome of SARS-CoV-2 consists of a single stranded RNA (ssRNA) with ~29.9 Kb in size. The viral genome encodes a polyprotein comprised of 7096 residues. The genome sequence of SARS-CoV-2 was retrieved from the NCBI genome database (NC_045512.2)(Lu et al., 2020). The viral genome has an untranslated region (UTR), replication complexes (ORF1a and ORF1b), spike gene, envelope gene, membrane gene, and nucleocapsid gene in 5′ and several unidentified non-structural ORFs, poly-A tail in 3′. The genetic makeup comprises 38% of guanine-cytosine (GC) content, 11 coding protein genes, 12 expressed proteins and 13–15 open reading frames containing ~30,000 nucleotides (Rota, 2003). The current biosensing platforms available for diagnosing COVID-19 are targeting the RNA to improve the detection accuracy. These biosensors use hybridization DNA probes, aptamers, cDNA, and oligonucleotides for recognizing the genome.

2.3. SARS-CoV-2 antibodies

Antibodies, also known as immunoglobulins, are naturally occurring glycoproteins generated by the immune system after the onset of infection or vaccination. The human immune system produces antibodies (IgM, IgG, and IgA) against structural proteins S and N. The human defence system also produces antibodies against the subunits of S proteins. The antibodies against the proteins and subunits can readily be measured within 7–21 days after the onset of infection (Qu et al., 2020). IgG remains detectable for more extended periods in the system, while the IgM is more useful in assessing the recent infections. Although the importance of IgA in COVID-19 is not clearly understood, these proteins can also be detected in human saliva. Monoclonal antibodies such as meplazumab, 4A8, 47D11, B38, BD-23, CA1, CB6, CR3022, H4 and P2B–2F6 are also reported for targeting the subunits and structural of SARS-CoV-2 (Wang et al., 2020).

3. Bio-recognition elements for SARS-CoV-2 biomarkers

A bioreceptor or biorecognition element is a biological molecule that can bind and interact specifically with the target biomarkers. The bioreceptors used for the specific recognition of target molecule includes nucleic acids, antigens, viral proteins, antibodies, aptamers, DNA probes, peptides, and tissues (Han, 2020). Understanding the benefits and drawback of each biorecognition component and their influence on the overall biosensor performance is critical throughout the biosensor development process (Morales and Halpern, 2018). These bioreceptors are highly sensitive and could easily recognize the SARS-CoV-2 target biomarkers including whole viral particles, nucleic acids viral proteins (structural proteins and non-structural proteins), antibodies (IgM, IgG, and IgA) and enzyme encoding genes (Liang et al., 2020). As the typical affinity reaction in a biological system would not produce any detectable signal, bioreceptors are usually integrated with a nanomaterial-based transducer. The nanoarchitecture aids in converting the biological recognition event into detectable signals (electrochemical and optical) (Goode et al., 2015; Verma and Bhardwaj, 2015). A diagrammatic overview of a wide variety of bioreceptors available for recognizing SARS-CoV-2 molecular architectures and the nanomaterial signal transducing interfaces used for optical and electrochemical detection of

COVID-19 is represented in Fig. 3.

Antibodies are the most commonly used biorecognition component to identify pathogens including viruses (Sharma et al., 2016). Antibodies have recognition sites that bind to antigens selectively via a portion of the antigen known as an epitope (Patris et al., 2016). Monoclonal antibodies have mostly been used to identify antigens. Antibodies can be labelled with fluorescent probes, enzymes, and nanomaterials for generating signals. Immunosensors are biosensors that make use of antibody-based biorecognition components. For detecting SARS-CoV-2, N and S proteins are commonly employed as antigens or biomarkers, and their biorecognition molecules can be antibodies (Ahmed et al., 2020) … Aptamers are known as pseudo-natural receptors composed of single-stranded oligonucleotides of DNA or RNA with 10–100 nucleotide bases which could be customized using SELEX procedure (Bowser, 2005; Ellington and Szostak, 1990). The chemically synthesized aptamer has high specificity, stability, sensitivity, and binding affinity against the target comparable to that observed in the case of monoclonal antibodies, enabling recognition toward varieties of macromolecules (Darmostuk et al., 2015). Aptamers have been widely demonstrated in sensing, including HIV, Zika virus, influenza virus, dengue virus, Norovirus (NoV) and human papillomaviruses (Yu et al., 2021). In the current circumstance, aptamer-based biosensors can be an inexpensive and perfect tool for the SARS-CoV-2 diagnosis. Moreover, the usefulness of aptasensor in the detection of the SARS-CoV-2 virus and its structural proteins has already been demonstrated by many reports as listed in Table 1 (Lou et al., 2022; Mandal et al., 2021; Wandtke et al., 2022). The S and N proteins are the most widely used biomarker for the detection of SARS-CoV-2. Molecularly imprinted polymers (MIPs) are synthetic receptors created through a molecular imprinting process. As an alternate to biorecognition element, MIPs can solve problems associated with the stability of conventional biological receptors such as antibodies. MIPs are synthetic polymeric materials which can be used as a recognition unit for binding to a virus, bacteria, mammalian cells, or any other biomolecule (El-Schich et al., 2016; Jia et al., 2018). The approach of creating MIPs uses specific proteins, bacteria or viruses as template molecules complexed with synthetic polymers stabilized by covalent, non-covalent, ionic, semi-covalent, or metal centre coordination binding interactions (Whitcombe et al., 2014). The template molecules can then be removed from a polymerizable group, leaving behind an empty cavity capable of recognizing the target species (Manickam et al., 2016). The MIP-based approach as a cost-effective alternate tool for conventional antibody-based sensors for detecting structural proteins (N, S and E) (Raziq et al., 2021). The electrochemical polymerization process enables the controlled deposition of MIPs onto the electrode surface, allowing the creation of reproducible biosensors. MIP diagnostics Ltd. developed and commercialized the nanoMIP particles as synthetic alternatives to SARS-CoV-2 antibodies, which can be integrated with sensor surfaces (electrochemical and optical) for selectively recognizing SARS-CoV-2 antigens. The nano-MIPs able to recognize RBD spike protein as low as 5 fg/mL in a sensor surface ("COVID-19 Technical Brief — MIP Discovery," n.d.).

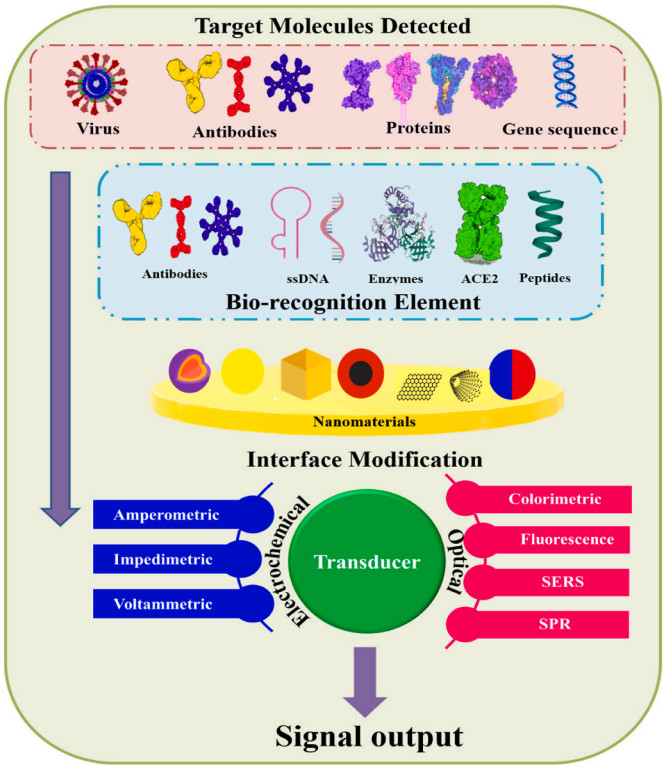

Fig. 3. Schematic representation of different SARS-CoV-2 target biomarkers, bioreceptor molecules, and transducing nanomaterials integrated platform used for Point-of-care COVID-19 diagnosis.

4. Clinical specimens used for SARS-CoV-2 detection

Rapid collection and testing of clinical specimens from suspicious patients are the important steps for managing and restricting the spread of SARS-CoV-2. During the initial stage of the pandemic, nasopharyngeal swabs were used as appropriate sampling for detection (Dawei Wang et al., 2020). Since the COVID-19 outbreak, various investigations, case reports, and meta-analyses have reported a wide range of clinical specimens in the search for an adequate specimen for early diagnosis of SARS-CoV-2. Researchers and clinical laboratories are continued to explore different types of clinical specimens for SARS-CoV-2 detection which includes upper respiratory tract samples (saliva, nasopharyngeal, oropharyngeal, and nasal swabs), lower respiratory tract samples (tracheal aspirate, bronchoalveolar lavage, sputum, and fibro bronchoscope brush biopsy), and blood products (serum and plasma)(Pan et al., 2020; Wang et al., 2020). Selecting a suitable clinical specimen for diagnosis is decided based on various parameters such as non-invasiveness, lesser risk to the health professionals, and accelerating the detection time. Combined throat and nasal swabs showed a highest positive rate (100%) of detection of SARS-CoV-2 followed by bronchoalveolar lavage (91.8%), rectal swabs (87.8%), sputum (68.1%), nasopharyngeal swab (45.5%), feces (32.8%), oropharyngeal swab (7.6%), and blood samples (1.0%) (Sharma et al., 2016). Serum, plasma, and urine samples have the lowest positive detection rate among the biological samples tested. Nasopharyngeal swab and oropharyngeal swab are the most preferred human clinical specimens for detecting the SARS-CoV-2 viral genome due to their non-invasiveness and easy accessibility of samples (Mohammadi et al., 2020). While bronchoalveolar lavage, endotracheal aspirate, fibro bronchoscope brush biopsy collection has a greater detection rate and might be the specimen of preference in hospitalized pneumonia cases, it always carries the danger of developing aerosols that might infect healthcare personnel. Furthermore, bronchoalveolar lavage cannot be used as the primary specimen in managing the COVID-19 pandemic infection. On the other hand, sputum makes things difficult not only for collection from COVID-19 patients with a dry cough but also for the low detection rate (Tong et al., 2020). Implementing combined swabs on a worldwide scale will undoubtedly aid in managing and controlling the pandemic.

5. POC sensing platforms for detecting SARS-CoV-2

Biosensors used for analysing the SARS-CoV-2 biomarkers are mostly affinity-based assays involving binding of target analyte (antigen) with specific bioreceptor molecules immobilized on the nanostructured interface at the transducer surface. Among the great variety of transducer methods, optical and electrochemical approaches have been evolved as versatile tools for the clinical detection of biomarkers. Due to

Table 1
Various aptamers reported against different target of SARS-CoV-2.

Target	Name	Aptamer sequence (5′–3′)	Affinity/Kd (nM)	Reference
N Protein	Np-A48	GCTGGATGTCGCTTACGACAATATTCCTTAGGGGCACCGCTACATTGACACATCCAGC	0.49	(L. Zhang et al., 2020)
S1 Protein	–	CGCAGCACCCAAGAACAAGGACTGCTTAGGATTGCGATAGGTTCGGTTTTT	43 ± 4	Curti et al. (2022)
N Protein	–	GCAATGGTACGGTACTTCCGGATGCGGAAACTGGCTAATTGGTGAGGCTGGGGCGGT	–	Ramanathan et al. (2022)
RBD	CoV2-RBD-1C	CAGCACCGACCTTGTGCTTTGGGAGTGCTGGTCCAAGGGCGTTAATGGACA	5.8	Song et al. (2020)
RBD	CoV2-RBD-4C	ATCCAGAGTGACGCAGCATTTCATCGGGTCCAAAAGGGGCTGCTCGGGATTGCGGATATG GACACGT	19.9	Song et al. (2020)
S Protein	SP5	GGGAGAGGAGGGAGATAGATATCAACCATGGTAGGTATTGCTTGGTAGGGATAGTGGGCT TGATGTTTCGTGGATGCCACAGGAC	14.7 ± 0.8	Schmitz et al. (2021)
S Protein	SP6	GGGAGAGGAGGGAGATAGATATCAACCCATGGTAGGTATTGCTTGGTAGGGATAGTGGGC TTGATGTTTCGTGGATGCCACAGGAC	13.9 ± 0.6	Schmitz et al. (2021)
N-terminal domain (S)	SNAP1	TCGCTCTTTCCGCTTCTTCGCGGTCATTGTGCATCCTGACTGACCCTAAGGTGCGAACATCG CCCGCGTAAGTCCGTGTGTGCGAA	39.32 ± 0.12	Kacherovsky et al. (2021)
N-terminal domain (S)	SNAP3	TCGCTCTTTCCGCTTCTTCGCGGTTAGGTACATCGTCTTCATTTCTCAAAGTCATTGTCTACA CCGCGTAAGTCCGTGTGTGCGAA	76.59 ± 0.12	Kacherovsky et al. (2021)
RBD	nCoV-S1-Apt1	CCGCAGGCAGCTGCCATTAGTCTCTATCCGTGACGGTATG	0.33 ± 0.02	(G. Yang et al., 2021)
S Protein	S14	TGGGAGCCTGGGACATAGTGGGGAAAGAGGGGAAGAGTGGGTCT	21.8	Gupta et al. (2021)
S1 Protein	MSA1	TTACGTCAAGGTGTCACTCCCACTTTCCGGTTAATTTATGCTCTACCCGTCCACCTACCGGA AGCATCTCTTTGGCGTG	0.023	(J. Li et al., 2021)
S1 Protein	MSA5	TTACGTCAAGGTGTCACTCCACGGGTTTGGCGTCGGGCCTGGCGGGGGGATAGTGCGGTGG AAGCATCTCTTTGGCGTG	0.012	(J. Li et al., 2021)
S Protein	DSA1N5	TTCCGGTTAATTTATGCTCTACCCGTCCACCTACCGGAATTTTTTTTTTTTTTTTTTTTTTTT TTTTTACGGGT TTGGCGTCGGGCCTGGCGGGGGGATAGTGCGGT	0.48 ± 0.06	(Z. Zhang et al., 2021)

their potential application in POC diagnosis, these techniques have been the subject of interest in recent days. Complex mixtures can be analysed using these techniques quickly without worrying about the extensive sample preparation techniques. However, optical, and electrochemical sensors differ in the fundamental mode of transduction and have distinctive advantages. For instance, optical assays need optic components such as the light source of a particular frequency, detector, optical waveguides or fibres, transduction moieties with biorecognition elements and integrated electronics to detect target analytes. Although more successful in the market for developing high throughput assays and multiplexed detection, the use of optical tags to make the measure the affinity binding reaction is an added step in performing optical measurement. On the other hand, electrochemical immunosensors measure the electrochemical changes during antigen-antibody binding at the electrode surface. Miniaturized modern microelectronics allows building microelectrodes that are useful for multiplexed biosensors and well suited for detecting tiny volumes of samples (microliters to nanoliters). The low-cost and large-scale production of electronic devices is another reason which makes the electrochemical approach more appealing for high-throughput analysis (Song et al., 2021).

6. Electrochemical biosensing platforms for SARS-CoV-2 detection

The electrochemical sensor platform utilizes the changes in the electrical properties of the bioreceptor-target molecule recognition for the quantification of target biomolecules. Enzymes and antibodies are the most utilized bioreceptor molecules in electrochemical biosensor design. Nanomaterials are utilized in electrochemical detection to improve the sensor's catalytic activity and sensitivity (Table 2). Electrochemical methods such as electrochemical impedance spectroscopy (EIS), square wave voltammetry (SWV), differential pulse voltammetry, amperometry, and potentiometry were utilized to determine SARS-CoV-2 (Grieshaber et al., 2008; Orooji et al., 2020). The amperometric method measures the current generated by the oxidation/reduction of electroactive analytes in real-time. Voltammetric methods provide information about the target analytes by measuring the resultant current by varying the potential. Potentiometric electrodes in an electrochemical cell detect the build-up of a charge potential at the working electrode relative to the reference electrode when no or zero current flows. The potential difference (voltage) between the working and reference electrodes is used to calculate the potentiometric signal. Impedimetric or conductometric-based sensors are useful electrochemical sensing techniques that assess changes in solution conductivity (Sheikhzadeh, 2021). The impedance approach is extremely beneficial for studying changes in electrical characteristics caused by bio-recognition events or nanomaterials at the electrode surface. Changes in conductance can be monitored at the electrode surface during various modifications or recognition components. The produced current is proportional to the concentration of the electroactive species. Conducting polymeric materials may be utilized as a transducer in the production of electrochemical sensors/biosensors, which is beneficial for attaching the biorecognition elements through the electrode (Ghazizadeh et al., 2020).

6.1. Detection of spike protein

S protein is important in viral entrance, fusion, and attachment, making it a good target for developing vaccinations, antibodies, and entry inhibitors. The S protein is employed as a diagnostic antigen due to the virus's main transmembrane protein, which is highly immunogenic. Among coronaviruses, the S protein contains amino acid sequence variation, enabling for SARS -CoV-2 detection. A low-cost gold printed circuit board (PCB)-based S protein sensing platform imitating the glucose test strip manufacturing process was developed using ACE2 as a bioreceptor molecule. The sensing platform utilizes Faradaic EIS measurement involving an external redox mediator ($[Fe(CN)_6]^{-3/-4}$) (Khan and Song, 2020). The ACE2 receptor was attached to the gold printed electrodes using a self-assembled monolayer of perfluorodecanethiol (PFDT). The level of S proteins present in saliva samples of the human subjects were measured using the biosensor in a bio-secure conditions. The sensor able detect the S protein levels as low as 1.68 ng/mL. Screen printed carbon electrode (SPCE) based portable sensing platform was also developed for S protein detection using EIS approach. Cu_2O nanocubes were integrated with the sensor substrate to provide a large surface area for antibody immobilization (Fig. 4A). Staphylococcal protein A (ProtA) is used to orient the immobilized antibodies towards efficient recognition of S proteins on the electrode surface. Bovine serum albumin

Table 2
A comprehensive table comparing the type of bioreceptor used, the biomarkers targeted, clinical sample investigated, and the transduction principle used in electrochemical POC assay for SARS-CoV-2 biomarker detection.

Target molecule	Target region	Bioreceptor	Sample type	Electrochemical technique	Type of electrode	LOD	Reference
Spike protein (S)	RBD	IgG antibody	Saliva and artificial nasal samples	EIS	SPCE - Cu_2O NCs	0.04 fg/mL	Rahmati et al. (2021)
	S1 subunit	Spike-protein capture antibody	Artificial samples	EIS	Graphene	3 ng/mL	Mojsoska et al. (2021)
	RBD	Angiotensin-converting enzyme 2 (ACE2)	Artificial samples	EIS	Palladium Nano-thin film	0.1 μg/mL	Kiew et al. (2021)
	RBD	Angiotensin-converting enzyme 2 (ACE2)	Saliva samples	EIS	PFDT-PCB gold electrode	1.68 ng/mL	Vezza et al. (2021)
	RBD	SpyTag peptide and nanobody-SpyCatcher protein	Nasopharyngeal swab	EIS	Gold electrode	23 fM	Guo et al. (2021)
	RBD	pCAGGS vector	Nasopharyngeal swabs and saliva samples	Amperometry	Co-functionalized TiO_2 nanotubes	0.7 nM	Vadlamani et al. (2020)
	RBD	DNA linker-ferrocene- CR3022 antibody	Nasopharyngeal swab	Chronoamperometry	Gold electrode	–	Yousefi et al. (2021)
	S1 subunit	S1 subunit	Serum samples	Chrono-potentiometry	gold screen-printed electrodes	1 fg/mL	Mavrikou et al. (2020)
	Spike protein	Spike monoclonal antibody and polyclonal antibody	Saliva samples	pulse method	Gold plated carbon electrode	100 pg/mL	Xian et al. (2020)
	RBD	Aptamer	Saliva samples	DPV	SPCE/AuNP	2.63 ng/mL	Sari et al. (2022)
	Spike protein	Aptamer	Oropharyngeal and nasal swab	EIS	Gold electrode	–	Lasserre et al. (2022)
	S glycoprotein	MIP	–	Chronoamperometry	Pt/Pyrrole	–	Ratautaite et al. (2022)
	Spike protein	antibody	Nasopharyngeal swab	DPV	GCE/Pd–Au nanosheets/MNP	0.0072 ng/mL	Zhao et al. (2022)
	RBD	ACE2	Saliva	DPV	MBs/AuNPs	0.35 ag/mL	Nascimento et al. (2022)
	Spike protein	Antibody	Saliva	EIS	SPCE/AuNP	3.16 pmol L^{-1}	Brazaca et al. (2022)
	RBD	Aptamer	Saliva	EIS	SPCE/AuNP/CNF	7.0 pM	(Amouzadeh Tabrizi and Acedo, 2022)
	S1 subunit	Antibody	–	EIS	Gold electrode	–	Ashur et al. (2022)
	Spike protein	Peptide	Nasopharyngeal swab	EIS	GSPE	18.2 ng/mL	Soto and Orozco (2022)
	S1 subunit	Aptamer	Nasopharyngeal swab	DPV	SWCNT-SPCEs	7 nM	Curti et al. (2022)
Nucleocapsid protein (N)	N Protein	N protein antigen	Nasopharyngeal swabs	SWV	CNF- SPCE	0.8 pg/mL	Eissa and Zourob (2021)
	N Protein- MIP	N Protein	Nasopharyngeal swab	DPV	Au-TFE	15 fM	Raziq et al. (2021)
	N Protein	Antibody	–	EIS	rGO-Au	13 fm and 2.5 p.m.	Ali et al. (2022)
	N Protein	Antibody	–	EIS	SPCE/ZnO/rGO	21 fg/mL	Haghayegh et al. (2022)
	N Protein	Antibody	Nasopharyngeal Samples	Chronoamperometry	SPCE/graphite	45 PFU/mL	Samper et al. (2022)
Antibodies	IgG monoclonal antibodies	S1 glycoprotein	Blood plasma samples	DPV	Graphene- Au nanostars SPCE	0.18×10^{-19} %V/V	Alireza Hashemi et al. (2021)
	S protein monoclonal antibodies	CR3022/SARS-CoV-2 spike RBD protein	Serum samples	EIS	Gold electrode	–	Rashed et al. (2021)
	spike S1 protein and RDB antibodies	spike S1 & RBD antigens	Artificial samples	EIS	Glass substrate with patterned gold film	1 pM and 0.001 pM	Ali et al. (2021)
	CR3022 antibody	SARS-CoV-2 S-protein RBD	Serum samples	EIS	zinc oxide nanowires (ZnO NWs)	0.4 pg/ml	(X. Li et al., 2021)
	IgG and IgM	spike protein RBD	Serum samples	SWV	graphene oxide -EDC/NHS	0.96 and 0.14 ng/mL	Yakoh et al. (2021)
	IgG and IgM	Biotin-SARS CoV-2 RBD	Serum samples	Chronoamperometry	SPCE	10.1 ng/mL and 1.64 ng/mL	(R. Peng et al., 2022)
	Antibodies	N protein	Serum samples	EIS	PEDOT/AuNPs	–	Lorenzen et al. (2022)
	IgG	RBD	Serum samples	EEVD (OCP)	G-PNR-AuNP	1.0 pg/mL	Mattioli et al. (2022)
	Antibodies	Spike protein	Serum samples	CV and EIS	Au/SAMmix		Liustrovaite et al. (2022)

(*continued on next page*)

Table 2 (*continued*)

Target molecule	Target region	Bioreceptor	Sample type	Electrochemical technique	Type of electrode	LOD	Reference
						2.53 nM and 1.99 nM	
	IgG and IgM	Spike protein	Serum samples	DPV	laser-induced graphene	–	Oliveira et al. (2022)
	Antibodies	Spike protein	saliva and oropharyngeal swab	SWV	GCE/Au	9.3 ag/mL	Liv and Kayabay (2022)
	IgG	Spike protein	Serum samples	EIS	SPCE/SWCNT	0.7 pg/mL	Cardoso et al. (2022)
Virus genome sequence	N and S genes	DNA conjugated Si-Avidin	Nasopharyngeal swab	DPV	SPCE	1 copy/μL	Chaibun et al. (2021)
	ORF1ab	SARS-CoV-2 ssDNA	Sputum, throat, blood, saliva samples	DPV	SPCE	3 aM	(H. Zhao et al., 2021)
	RdRP	SARS-CoV-2 probe sequence	Sputum samples	DPV	Carbon paste electrode	0.3 pM	Farzin et al. (2021)
	N-gene	Biotin- peptides-labelled probes	Serum samples	DPV	GCE- PANI nanowires	3.5 fM	Song et al. (2021)
	RdRP	Probe DNA	Artificial samples	EIS	platinum/titanium electrodes	–	Hwang et al. (2021)
	cDNA	SARS-CoV-2 Primers	Artificial samples	SWV	Gold electrode (TriSilix)	0.02 pg	Nunez-Bajo et al. (2020)
	viral RNA or cDNA	Thiolated nucleotide probes	Artificial samples	Amperometry	Au onto Ti substrate	–	Tripathy and Singh (2020)
	viral RNA (N gene)	graphene-ssDNA-AuNPs	Nasal swab and saliva samples	signal conditioner circuit	Gold electrode	6.9 copies/μL	Moitra et al. (2020)
	RNA	CHA and TdT DNA strants	serum and saliva samples	EIS and DPV	Gold electrode	26 fM	(Y. Peng et al., 2021)
	N-gene	Aptamer and antibody	Blood and throat swab	EIS	TAPP-DPDD-POP/AE	0.59 fg/mL and 0.17 fg/mL	Cui et al. (2022)
	RNA	ssDNA	–	DPV	Graphene/polylactic acid	15 M	Crevillen et al. (2022)
	RdRP	ssDNA	–	CV and EIS	Graphene Oxide Nanocolloids	–	Ang et al. (2022)
	ORF and S genes	RNA	Artificial saliva	DPV	AuNF/NC/SPCE	4.4×10^{-2} and 8.1×10^{-2} fg/mL	Heo et al. (2022)
	RNA	ssDNA	Nasopharyngeal swab	DPV	SPCE/AuNTs	22.2 fM	del Caño et al. (2022)
SARS-CoV-2 virus	Spike Antigen	nCovid-19 monoclonal Ab	Saliva samples	DPV	FTO electrode-AuNPs/SPCE	0.01 pM	Mahari et al. (2020)
	Spike Antigen	S spike glycoproteins	Blood, saliva, and oropharyngeal swab	DPV	GO-8H-EDC–NHS–Au NS	1.68×10^{-22} μg mL^{-1}	Alireza Hashemi et al. (2021)
	N protein antigen	N protein	Nasopharyngeal swabs	SWV	CNF- SPCE	0.8 pg/mL	Eissa and Zourob (2021)
	N and S protein antigen	N and S Proteins	Saliva samples	DPV	screen-printed graphite electrodes	19 ng/mL, 8 ng/mL	Fabiani et al. (2021)
	Antigen	N protein, S1 (IgG and IgM) and CRP	Blood and Saliva samples	DPV and OCP-EIS	laser-engraved graphene (LEG)	–	Torrente-Rodríguez et al. (2020)
	Spike Antigen	Spike antibody	Nasopharyngeal swabs	2634B semiconductor analyzer	graphene sheets FET	1 fg/mL	Seo et al. (2020)

(BSA) was used as a blocking agent to avoid non-specific binding caused by the non-analyte proteins in the blood samples. The portable EIS based electrochemical device allows the measurement of S protein in 20 min (Rahmati et al., 2021). Amperometric methods measure the current response produced by an electroactive redox reaction at the working electrode. This method is mainly used for biocatalytic and affinity-based biosensors for their low detection limit and high selectivity towards the target. An amperometric electrochemical approach for detecting RBD of spike protein accumulated on the surface of the SARS-CoV-2 virus is developed. The electrode was fabricated by cobalt functionalized TiO_2 nanotubes (Vadlamani et al., 2020). Recently, Mahari et al. reported a two electrode-based electrochemical approach for detecting S protein. Two types of biosensors were fabricated for the study. The first involves the immobilization of S-protein specific monoclonal antibodies on gold nanoparticles and fluorine-doped tin oxide and the second one involves the immobilization of SARS-CoV-2 antibodies on the screen-printed electrode. These biosensors are efficient in detecting at fM concentration in saliva and buffer solution within 10–30 s (Mahari et al., 2020).

The field-effect transistor (FET) type immunosensing platforms are potentially considered in POC testing for their ability to measure a small number of analytes and are highly sensitive. FET-based sensing platform for detecting SARS-CoV-2 using spike specific antibody as a bioreceptor was reported by Seo et al. In this method, FET surface was modified with graphene sheets and followed by immobilization of anti-spike protein antibodies using N-hydroxysuccinimide ester-based coupling agent (Fig. 5B). The FET biosensor detects SARS-CoV-2 antigen present in transport medium containing nasopharyngeal swab samples. The sensor detected the antigen as low as 1 fg/mL (Seo et al., 2020). Aptamers have sparked widespread interest in the development of electrochemical biosensors capable of detecting a variety of target biomolecules. Idili et al. developed a label-based electrochemical aptasensor for S protein detection based on an Au electrode modified with methylene blue derivative (MB2) tagged aptamer. The binding event of S protein with the aptamer causes aptamer conformation to change, which in turn changes the location of the redox label MB2. The change in conformation produced a quantifiable electrochemical signal associated to the fluctuation of S protein concertation. With great sensitivity, the aptasensor detected the picomolar level of S Protein (Idili et al., 2021). Curti et al. developed

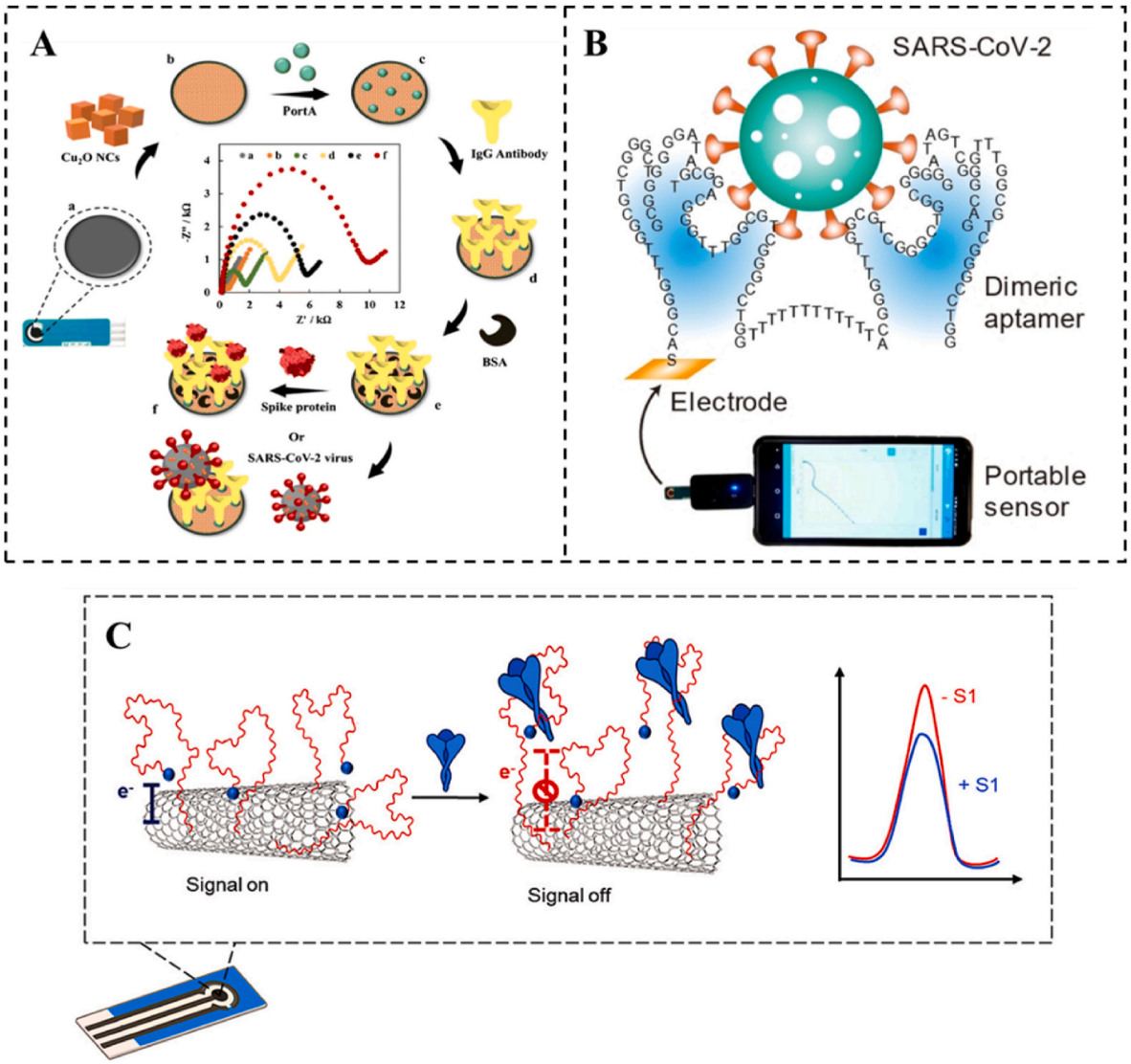

Fig. 4. (A) Schematic representation of SPCE based device for monitoring S protein (reproduced with permission from Springer (Rahmati et al., 2021)), **(B)** Schematic of the electrochemical sensor for the detection of SARS-CoV-2 using spike protein specific aptamer (reproduced with permission from John Wiley and Sons (Z. Zhang et al., 2021)), and **(C)** The operating concept of the aptasensor is illustrated schematically by the conformational change in a redox-tagged SARS-CoV-2 aptamer following engagement with the target S1 protein (reproduced with permission from American Chemical Society (Curti et al., 2022)).

a label-based aptasensor based on single-walled carbon nanotube screen-printed electrodes (SWCNT-SPEs) functionalized with a redox-tagged DNA aptamer (Fig. 4C). The aptasensor allows the detection of S proteins as low as 7 nM with good selectivity and specificity (Curti et al., 2022).

Using MIPs, Ayankojo et al. created an electrochemical biosensor for detecting S protein detection based on a disposable Au-based thin-film electrodes. The selectivity of MIP sensor for SP protein was obtained by using a covalent imprinting method between the S protein and 1,2-diol moieties and 3-aminophenyl boronic acid groups. The sensor's operating concept is based on the modulation of charge transfer between the Au-thin film electrodes and redox probe via imprinted pathways established within the sensor (Ayankojo et al., 2022).

6.2. Detection of nucleocapsid protein

Using stencil-printed carbon electrodes (SPCEs), Samper et al. established a highly sensitive and label-based electrochemical immunoassay for quantitative detection of N protein. The numerous carboxyl groups (-COOH) on the SPCEs allowed anti-SARS-CoV-2 N protein to be immobilized through EDC/NHS coupling. Following that, the target N protein was connected to the sensor's surface using an antibody-antigen key-lock system, which allowed the anchoring of HRP labelled anti-SARS-CoV-2 N protein (Samper et al., 2022). Cotton swabs were widely as a swabbing tool for collecting pathogenic samples. To improve the sample collection efficiency of the electrochemical sensor, the SPCE were modified with functionalized cotton-based carbon nanofibers (CNF). The SPCE coated with adsorbing cotton pads are immobilized with N protein specific antibodies for the detection of SARS-CoV-2 in Nasopharyngeal swabs. Apart from improving the sample collection efficiency, the functionalized cotton-based CNF allowed the immobilization of the antibodies through diazonium chemistry. The immunosensor was calibrated using spiked nasal fluids and validated using clinical Nasopharyngeal swabs collected from patients (Fig. 5A). SWV voltammetry technique is used the POC electrochemical measurement to interrogate the immunosensor. The sensor was able to detect the N proteins as low as 0.8 pg/mL (Eissa and Zourob, 2021).

Aptamer and MIP based sensor also involved in the detection of N protein. Qi et al. presented a low-cost microelectrode array (MEA) chip-based aptasensor for N protein detection. With a sensitivity of pM, this

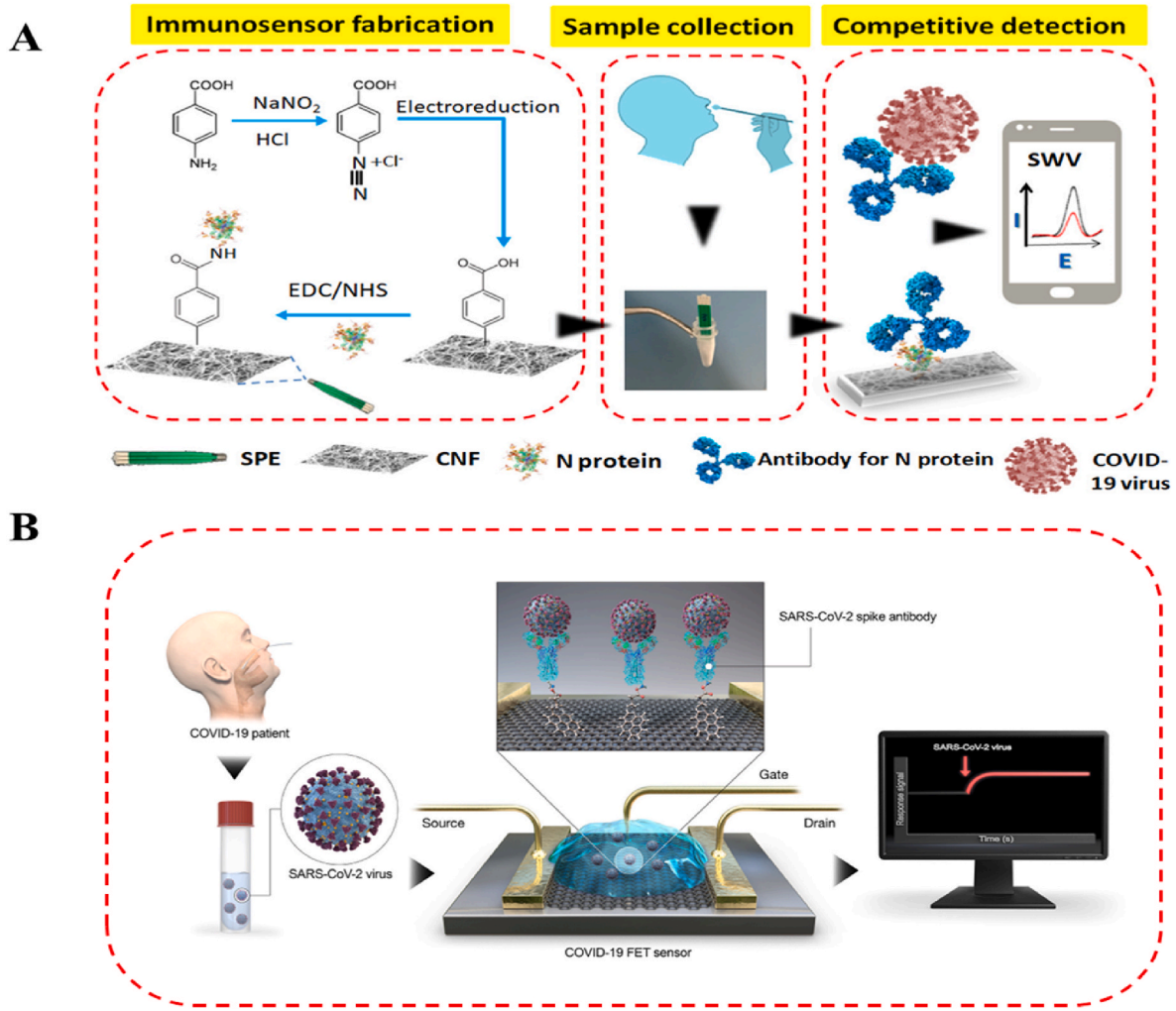

Fig. 5. (A) Graphics of cotton-tipped electrochemical immunosensor for COVID-19 detection using SWV Technique (reproduced with permission from American Chemical Society (Eissa and Zourob, 2021)) and **(B)** Schematic representation spike antibody immobilized FET-Graphene based electrochemical detection of SARS-CoV-2 (reproduced with permission from American Chemical Society (Seo et al., 2020)).

aptamer-modified MEA caused a change in capacitance at the solid-liquid interface following the N protein binding. When combined with an efficient microfluidic enrichment, the sensor detected N protein in 15 s with a wide linear range and low LOD (Qi et al., 2022). Raziq et al. used the DPV technique to develop MIPs integrated electrochemical sensors to detect N protein. The capability of the biosensor for detecting N protein in nasopharyngeal swab samples of COVID-19 positive patients is also demonstrated (Raziq et al., 2021).

6.3. Detection of antibodies (immunoglobulins)

Human immune system produces antibodies such as IgG, IgM, and IgA in COVID-19 patients' bodily fluids and utilized to identify SARS-CoV-2. According to a recent immuno-chromatographic study, both IgG and IgM antibodies have 11.1%, 92.9%, and 96.8% sensitivity for SARS-CoV-2 detection at the early stage (several days to weeks after the COVID-19 infection), intermediate stage (1–2 weeks after the onset), and late stage (more than 2 weeks) of infection. Yakoh et al. recently developed an electrochemical paper-based analytical device (ePAD) to detect SARS-CoV-2 immunoglobulins (IgG and IgM). (Yakoh et al., 2021). Similarly, Li et al. studied a microfluidic PAD (μ-PAD) for highly selective and label-free detection of SARS-CoV-2 utilizing an EIS biosensor. In this system, zinc oxide nanowires (ZnO NWs) were grown atop a working electrode to improve its function with Faradaic processes that use iron-based electron mediators. The μ-PAD biosensors were calibrated using various morphologies of ZnO NWs that achieved a low LOD of 0.4 pg/mL. The EIS biosensor has the capacity to discriminate the amounts of IgG antibody CR3022 specific to SARS-CoV-2 in human serum samples; the findings obtained demonstrated the usefulness of the EIS-biosensor for detecting COVID-19 (X. Li et al., 2021).

6.4. Detection of viral nucleic acid

The clinical usefulness of antibody-based biosensors for detecting SARS-CoV-2 is limited due to the risk of false-negative findings during the early stage of illness. Since the antibody production in human bodily fluids might take many days after the onset of infection, individuals begin to exhibit various symptoms. Rapid antigen assays for SARS-CoV-2 are often less sensitive than nucleic acid-based testing. As a result, nucleic acid testing is the most reliable way for determining COVID-19 infection. Considering these difficulties and limits of the RT-PCR approach, as well as advancements in molecular biology and nano-technology, electrochemical biosensors for SARS-CoV-2 detection have shown interesting potential.

Electrochemical approaches also find applications in detecting RdRP sequence as a target for probing SARS-CoV-2. The complementary probe sequence against the RdRP was used as a recognition element. A macrocyclic crown ether ligand complexed with Ag^{+} ion is used as a

redox reporter. The redox reporter is further modified with silicon quantum dots coated with chitosan-poly (amidoamine) (PAMAM) dendrimer to immobilize the target sequence on the electrode surface through amine cross-linking reaction. Calibration and measurement in simulated sputum samples were performed using differential pulse voltammetry The nanosensor allowed the detection of RdRP sequence as low as 0.3 pM in spiked sputum samples (Farzin et al., 2021). Recently, Chaibun et al. reported an isothermal rolling circle amplification (RCA) based electrochemical approach for detection of S and N genes of RNA. The assay was prepared by hybridization of RCA amplicons with

Table 3
A comprehensive table comparing the type of bioreceptor used, the biomarkers targeted, clinical sample investigated, and the transduction principle used in optical POC assay for SARS-CoV-2 biomarker detection.

Target molecule detected	Target region	Bio receptor	Sample Type	Optical Technique	Substrate	LOD	Reference
Spike protein (S)	RBD	ACE2 or SARS-CoV-2 mAbs	Nasopharyngeal swab and saliva	LSPR	AuNPs	370 vp/mL	Huang et al. (2021)
	S glycoprotein	ACE2	Artificial samples	SPR	Rutile prism/BK7/ ITO film/tellurene/ MoS_2–COOH	–	Peng et al. (2020)
	RBD	ACE2	Throat swabs, saliva, and sputum samples	Fluorescence detection	Carbon nanotubes	12.59 nM	Pinals et al. (2021)
	RBD	Biotin-aptamer	Artificial samples	SPR	Gold nanofilm- POF	37 nM	Cennamo et al. (2021)
	RBD	ACE2	Artificial samples	SERS	silver-nanorod	–	(D. Zhang et al., 2020)
	RBD	Aptamers (Biotin-RBD-1C)	Artificial samples	SERS	AgNPs	–	Zavyalova et al. (2021)
	RBD	DNA aptamers	Artificial samples	SRS and SERS	AgNPs	250 nM	Stanborough et al. (2021)
	S1 Subunit	S1 antibody	Artificial samples	Plasmonic metasensor	AuNPs	4.2 fM	Ahmadivand et al. (2021)
	RBD	DNA aptamers	Nasopharyngeal smear	SERS	Au nanopopcorn	~10 PFU/mL	Chen et al. (2021)
Nucleocapsid protein (N)	–	N protein antibody	Saliva sample	SPR	AuNPs	Attomolar (10^{-18}M)	Murugan et al. (2020)
Antibodies	S Protein Antibody	Spike protein	Plasma samples	LSPR	Gold nanospikes	0.08 ng/mL	Funari et al. (2020)
	S, E, and M antibodies	S, E, and M proteins	Nasal and throat swab Samples	Colorimetric detection	AuNPs	–	Ventura et al. (2020)
	IgM and IgG antibodies	Recombinant antigen	Blood samples	Colorimetric detection	AuNPs	–	Li et al. (2020)
	IgG antibody	N protein	Serum samples	Fluorescence detection	Lanthanide-doped polystyrene nanoparticles		Chen et al. (2020)
	IgM and IgG	S protein	Serum samples	Fluorescence detection	SiO_2–Au-QD	1:10^6 dilution	Wang et al. (2020)
	N Protein antibody	Nucleoprotein (N)	Artificial samples	SPR	Au chip	1.02 pM	Bong et al. (2020)
	Anti-SARS-CoV-2 IgM/IgG	Spike protein (S)	Serum samples	SERS	Ag shell on SiO_2	1.28×10^7 dilution	Liu et al. (2021)
	IgA antibody	N Protein antigen	Saliva and serum samples	Colorimetric and chemiluminescence	AuNPs	–	Roda et al. (2021)
Virus genome sequence	RdRp, ORF1ab and E genes	SARS-CoV 2 cDNA	Artificial samples	LSPR	Gold nanoisland	0.220 pM	Qiu et al. (2020)
	N gene	RNA sequence	Oropharyngeal swab	Colorimetric detection	Thiol-modified ASO-capped AuNPs	0.18 ng/μL	Moitra et al. (2020)
	RdRp gene	Oligo probe	Nasopharangeal samples	Colorimetric detection	AuNPs	0.5 ng	Kumar et al. (2022)
	N gene	RNA sequence	nasopharyngeal swabs	SERS	AgNPs	1 fM	Liang et al. (2021)
	N1, N2 and RPP30 genes	RNA	Pharyngeal and sputum samples	Fluorescence detection	Au seed-coated magnetic core	–	Cheong et al. (2020)
	ORF1ab and N gene	ssDNA primers	Artificial samples	SPR	AuNPs	–	(W. S. Zhang et al., 2021)
	RdRp, ORF1ab, E and N genes	DNA probes	Artificial samples	colorimetric/SERS/ fluorescence	AuNPs	0.58 pM, 2.17 pM, 1.11 pM.	Diao et al. (2021)
SARS-CoV-2 virus	–	RNA	Artificial samples	Colorimetric detection	AuNPs	50 RNA copies/ reaction	Jiang et al. (2021)
	S, E, M Protein antigens	Antibody	Nasal and Throat Swabs	Colorimetric detection	AuNPs	–	Ventura et al. (2020)
	–	S Antibody and DNA probes	Throat swabs and sputum samples	Fluorescence detection	Europium-chelate-FNPs	1000 TU ml^{-1}	Wang et al. (2020)
	–	Antibody	nasopharyngeal aspirates	SERS	AuNPs	2.56 fg/mL	Cha et al. (2022)
	ORF1ab, E and N antigen	Monoclonal antibody and Probe DNA	Nasopharyngeal swab	Fluorescence detection	europium-chelate FNPs	–	Diao et al. (2021)
	–	Antibody	Nasopharyngeal swabs	SPR	Sialic acid-Au NPs	–	Alfassam et al. (2021)

acridine orange (AO), M) and integrated silica nanoparticles (Chaibun et al., 2021). Peng et al. developed an electrochemical sensor to monitor SARS-CoV-2 RNA, in which the presence of a target sequence triggers the catalytic hairpin assembly circuit and subsequently begins terminal deoxynucleotidyl transferase-mediated DNA polymerization. As a result, several lengthy single-stranded DNA products can be generated. Due to electrostatic adsorption, these negatively charged DNA products can hybridize with many positively charged electroactive molecules. The inclusion of $Ru(NH_3)_6^{3+}$ resulted in a considerable improvement in electrochemical signals for sensitive detection of SARS-CoV-2 RNA. The biosensor's capacity to discriminate was tested using complicated matrices as well as clinical samples from patients (Y. Peng et al., 2021).

7. Optical biosensing platforms for SARS-CoV-2 detection

Optical biosensor is a powerful tool in viral infection detection because of its sensitivity, reliability, and selectivity, which eliminates the necessity of nucleic acid amplification. Previously, optical methods were employed to detect HIV, Ebola, norovirus, and influenza viruses. The optical biosensor comprises a transducer and bioreceptor to probe the interaction between the bioreceptor and target. The optical transducer converts the biological event into an optical signal by absorption, transmission, reflection, refraction, amplitude, frequency, or light in response to the physical/chemical change created by the biorecognition element. Most of the optical-based approaches for SARS-CoV-2 identification methods uses antibody-antigen interaction and probe sequence hybridization. Only a few optical biosensors for viral detection are now on the market to the best of our knowledge. More work is required to get these innovations from the lab to the market. This review looks at various optical methods and their uses in SARS-CoV-2 detection (Table 3). Among the biosensing approaches plasmonic-based approach is promising for the POC measurement of SARS-CoV-2 (Mejía-Salazar and Oliveira, 2018). It allows label-free, fast, and real-time detection of biological analytes. The rapid development in the field of nanobiotechnology has created an infinite number of possibilities for the development of new diagnosis technologies, particularly the emergence of nanofluorescent materials, which offers a wide range of opportunities for the application of novel fluorescence detection techniques. Optical biosensing strategies based on fluorescence colorimetric, SERS and SPR-based measurements provide quick and high-sensitivity biological detection capabilities, which are critical for detecting SARS-CoV-2 in a timely manner (Xu et al., 2022).

7.1. Colorimetric sensors

Colorimetric sensors are among the most sophisticated and outstanding devices for POC measurement of SARS-CoV-2 (Maddali et al., 2021). Colorimetric approach can detect the presence of certain compounds through a ligand-target complex, and it creates a colour shift that may be seen with the naked eye or by a simple portable optical detector (Choi et al., 2018). The colour changes in optical detection strategy are caused by noble metal NPs, metal oxide NPs, carbon nanotubes, and conducting polymers (CPs)(Song et al., 2011). Metal oxide NPs and carbon nanotubes can change the colour by stimulating a peroxidase substrate response or by having inherent peroxidase activity. A colour shift caused by conformational transitions or aggregation may be seen in various CPs. On the other hand, AuNPs are the perfect particles for colorimetric detection of SARS-CoV-2 because of their colour may be modified by their aggregated or non-aggregated orientation (Liu et al., 2018). In this regard, Ventura et al. demonstrated a colorimetric based biosensor for detecting S, E and M proteins using colloidal AuNPs modified with specific antibodies targeting multiple SARS-CoV-2 proteins (S, E, and M proteins). The method can be adapted to detect viral load in throat and nasal swab samples (Ventura et al., 2020). Recently, naked-eye-based colorimetric detection of the whole virus particle (SARS-CoV-2) was developed by immobilizing AuNPs with N-gene specific thiol-modified antisense oligonucleotides (Fig. 6A). The assay did not produce any significant drift in the presence of MERS-CoV RNA and showed a LOD of 0.18 ng/μL (Moitra et al., 2020),Similarly, Kumar et al. utilized AuNPs to detect the RNA-dependent RNA polymerase (RdRp) gene of SARS-CoV-2 by forming an oligo probe-target hybrid. It leads to a change in colour from pink to blue in assay containing nasopharyngeal RNA sample. The assay colour did not change from pink when the test included COVID-19 negative subjects or human papillomavirus (Kumar et al., 2022). All these assays involve using AuNPs as signal generating probes for visible detection.

7.2. Fluorescence based sensor

Wang et al. developed an amplification-free nucleic acid lateral flow strip to detect SARS-CoV-2 RNA in less than 1 h. The assay utilizes DNA probes specific to ORF1ab, E protein and N protein regions, and the europium chelate-based fluorescent nanoparticle labelled monoclonal antibody complex. The assay achieved sensitivities of 100% and specificities of 99% for throat swab and sputum samples (Daming Wang et al., 2020). Nanoparticles also act as fluorescent signal generating probes. Single-walled carbon nanotubes (SWCNT) based optical detection principle was demonstrated by Pinals et al. for S protein detection. The sensor was constructed by non-covalently functionalizing SWCNTs with ACE2 for tuning the binding affinity with spike protein. The sensor exhibits turn-on response (up to 73%) in the presence of S protein particles within 5 s of exposure (Pinals et al., 2021). Recently, Chen et al. reported a sensitive and fast approach in the form of lateral flow immunoassay (LFIA), which could anti-SARS-CoV-2 (IgG) in human serum (Chen et al., 2020). Lanthanide-doped polystyrene nanoparticles integrated with recombinant nucleocapsid dispensed nitrocellulose membrane was used to bind and measure specific IgG. Quantum dots (QDs) are the one among candidate nanomaterial with a good dispersion, stable quantum activity and outstanding photoluminescence performance. For example, Bardajee et al. developed a CdTe–ZnS QDs were used in conjunction with DNA to precisely detect the COVID-19 virus's DNA or RNA using the FRET technique. The QDs-DNA functions as a donor molecule, while the BHQ2-DNA was synthesized to operate as an acceptor molecule in the FRET process. When coupled with target RNA, BHQ2-DNA can completely quench the fluorescence of QDs-DNA in 25 min at an excitation of 325 nm. (Bardajee et al., 2022). In the recent study Alexaki et al. have reported on the development of an upconversion nanoparticles/graphene-based biosensor for the quick detection of viral oligonucleotide (Fig. 6B). An oligonucleotide is used to functionalize the upconversion material. When graphene is present, the oligonucleotide aromatic bases will interact with the graphene oxide (GO), causing fluorescence to be quenched. When the target virus is present, the functional upconversion nanoparticles preferentially attach to the target RNA, minimizing fluorescence quenching. The entire detection procedure takes 30 min, and the system's minimal detection limit is 5 fM (Alexaki et al., 2022).

7.3. Surface plasmons based sensor

Plasmonic sensing approaches detect molecular interactions by exploiting nanostructures distinctive optical characteristics for signal generation and quantification (Kussrow et al., 2011). Surface plasmon resonance (SPR) and localized surface plasmon resonance (LSPR) are the two essential methods involved in the Surface plasmons based sensing approaches. SPR detection can be regulated based on changes in intensity, refractive index, wavelength, and resonance angle (Maddali et al., 2021). The LSPR detection approach is based on the target-ligand binding event causing local refractive index changes around metal nanostructures (Mayer and Hafner, 2011). Djaileb et al. developed a SPR sensors coated with polypeptide and SARS-CoV-2 recombinant S protein produced by several cell lines to detect SARS-CoV-2 IgG antibodies in clinical samples (Fig. 7A). The N protein has minimal influence on

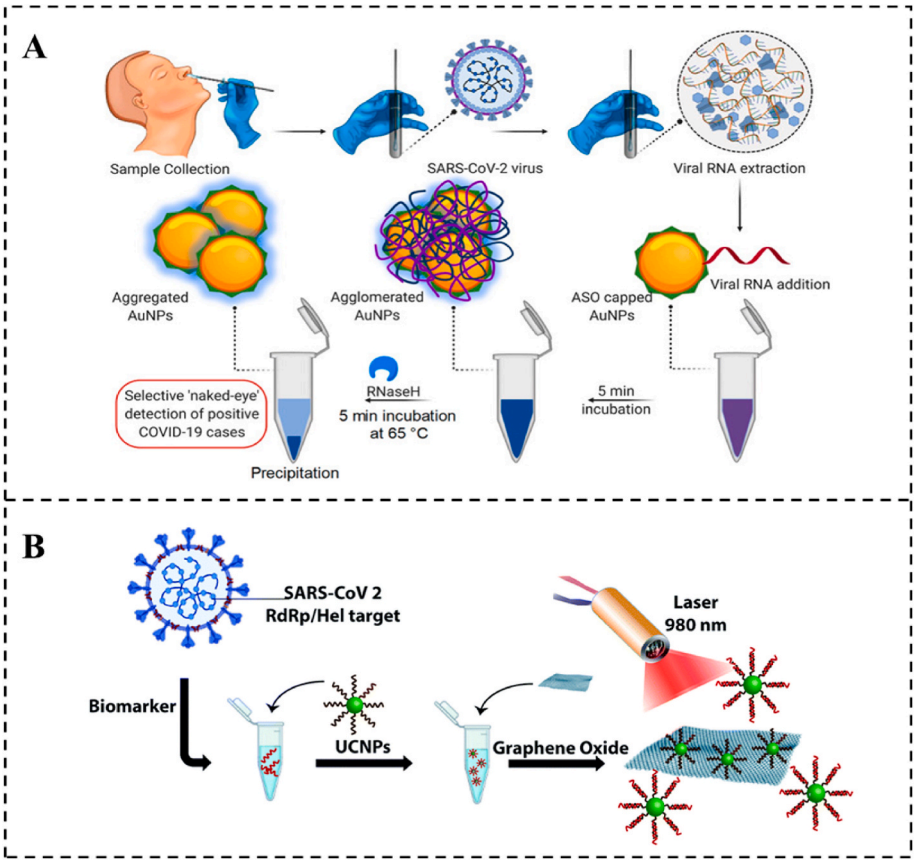

Fig. 6. (A) Visible detection of SARS-CoV-2 virus mediated by AuNPs functionalized oligonucleotides (reproduced with permission from American Chemical Society (Moitra et al., 2020)), and **(B)** Detection of the RdRp/Hel gene sequence of SARS-CoV-2 via an upconversion nanoparticles/graphene associated oligonucleotide based biosensor (reproduced with permission from Royal Society of Chemistry (Alexaki et al., 2022)).

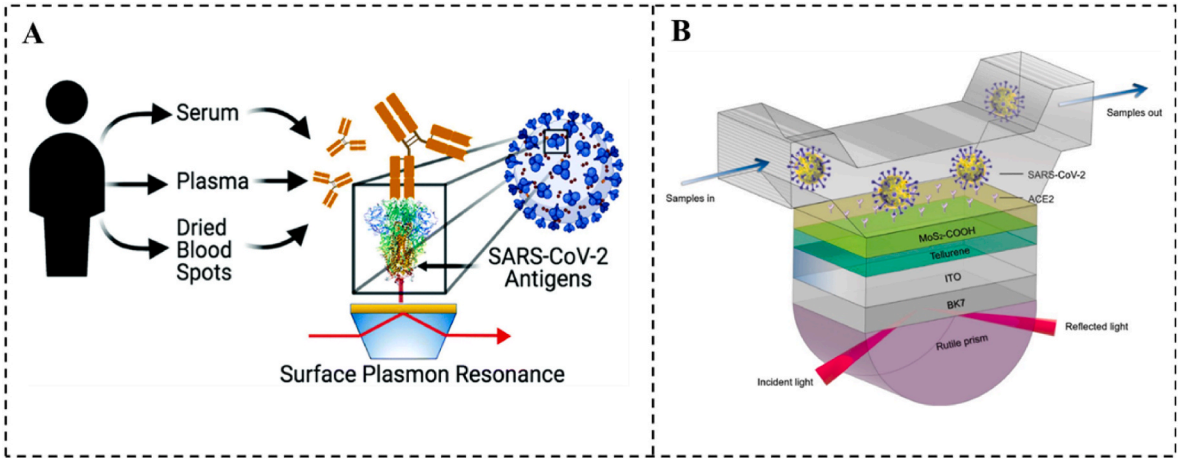

Fig. 7. (A) Schematic representation for the detection of human antibodies from diverse blood products (serum, plasma, or dried blood spots) obtained from COVID positive or negative persons, different SPR sensors customized with a variety of SARS-CoV-2 antigens (reproduced with permission from Royal Society of Chemistry (Djaileb et al., 2021)), and **(B)** Schematic diagram of rutile prism/BK7/ITO film/tellurene/MoS_2–COOH biosensor (reproduced with permission from IOPSCIENCE (Peng et al., 2020)).

antibody detection in different cell lines, but the S protein in the CHO cell line performs better. The biological investigation used a portable SPR device that can detect four samples in 30 min. SARS-CoV-2 detection also makes extensive use of optical fiber SPR biosensors (Djaileb et al., 2021).Peng et al. reported the detection of S protein by immobilizing ACE2 receptor in ITO film using SPR based plasmonic biosensor (Fig. 7B). The biosensor showed excellent detection sensitivity in saliva, urine, and other bodily fluid (Peng et al., 2020). Utilizing a similar principle, Cennamo et al. reported the detection of SARS-CoV-2 S protein by immobilizing RBD specific aptamer sequence using polyethyleneglycol (PEG) interface on gold nano-film deposited on a D-shaped plastic optical fibre (POFs) probe. The binding interaction between the RBD specific aptamer and the S protein was monitored by measuring the SPR signal changes. The optical sensor showed good LOD

(37 nM), and preliminary tests in diluted human serum were also attempted (Cennamo et al., 2021).

By combining the plasmonic photothermal (PPT) effect with the LSPR sensing transduction, Qiu et al. provided an alternative and promising strategy for the clinical diagnosis of COVID-19. Gold nano-islands (AuNIs) surface modification with complementary DNA receptors may identify specific sequences from the SARS-CoV-2 via nucleic acid hybridization. The thermoplasmonic heat is created by its plasmonic resonance frequency on the same AuNI chip to boost sensing capability. The localized PPT heat permits in situ hybridization of two identical gene sequences, improving precision and discriminating. Our dual-function LSPR biosensor has higher sensitivity for selected SARS-CoV-2 sequences, allowing the specified target to be identified correctly in a multigene mixture with a lower LOD up to 0.22 pM(Qiu et al., 2020). Funari et al. designed an Opto-microfluidic sensing platform for rapid detection of antibodies against the SARS-CoV-2 spike protein. The sensing platform involves a microfluidic device coupled with an optical probe that targets the LSRP generated by gold nano-spikes. The platform takes up to 30 min to detect antibodies in human plasma and buffer solution with a LOD of 0.08 ng/mL (Funari et al., 2020).

7.4. Surface-enhancing Raman scattering based sensor

Surface-enhancing Raman scattering (SERS) is based on amplifying an analyte's Raman response when it interacts with the surface plasmon of nano metals (Vo-Dinh et al., 2010). SERS has been used to identify influenza, Adeno, West Nile, and rift valley fever virus, among other things, and has more significant responses and chemical specificities than other optical detection methods (Luo et al., 2014). In this regard, Zavyalova and co-workers developed SERS based nucleic acid sensor for S protein using colloidal silver nanoparticles (Fig. 8A). The aptamer RBD-1C showed a high affinity to RBD of spike protein and was tagged with silver nanoparticles. A sandwich immune complex formation of silver nanoparticle tagged aptamer with SARS-CoV-2 antibodies leads to the formation of aggregates. This method presented simple, fast (7 min), and has a LOD of 5.5 × 104 TCID50/mL (Zavyalova et al., 2021). Similarly, Chen et al. developed a SERS-based aptasensor technology for sensing SARS-CoV-2 lysate spike protein. A DNA aptamer was employed as a receptor in this sensor, modified on an Au nanopopcorn surface for a SERS detecting substrate. Within 15 min, this approach can identify SARS-CoV-2 with a limit of detection (LoD) of fewer than 10 PFU/mL (Chen et al., 2021). The new sensor uses an ACE2-functionalized gold nano "forest" structure to selectively collect SARS-CoV-2, with detection sensitivity approaching that of a single virus (Fig. 8B). Because of the unusual nano "forest" structure and the strong affinity of ACE2 for the S protein of SARS-CoV-2, the sensor has a 106-fold improved capacity to enrich viruses in water. Furthermore, machine learning technologies are used to build viral diagnostic signal criteria and procedures. It's ideal LOD for SARS-CoV-2 detection is 80 copies/mL, and the detection time is under 5 min, which is critical for SARS-CoV-2 clinical testing (Y. Yang et al., 2021).

8. Impact of nanotechnology in electrochemical and optical biosensing of SARS-CoV-2

In recent years, the outstanding developments in nanotechnology have created a paradigm in therapeutic methods, diagnosis, and prognosis of viral infections (Saylan et al., 2019). Nanomaterials have unique properties, such as size, surface characteristics, multi-functionality, and enhanced solubility, which are being exploited in developing effective vaccine, drug delivery system, tissue therapies, personalised medicines, and rapid diagnostic tools (Maduraiveeran et al., 2018). The promise of nanotechnology is undeniable in the present COVID-19 pandemic

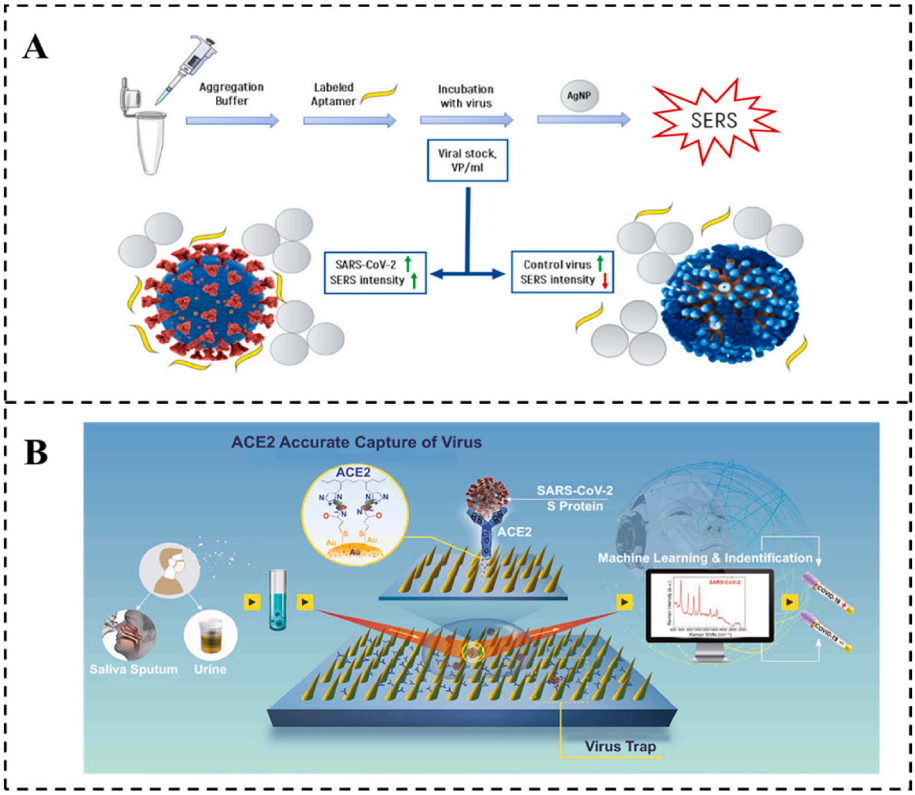

Fig. 8. (A) Schematic representation colloidal SERS based aptasensor for spike protein measurement (reproduced with permission from MDPI(Zavyalova et al., 2021)), and **(B)** Schematic representation of SERS based biosensor for the detection of SARS-CoV-2 by virus traps nanoforests and ACE2 protein composite (reproduced with permission from Springer (Y. Yang et al., 2021)).

predicament. Nanotechnology also finds applications in creating efficient disinfectants, surface coatings, self-sterilising personal protective equipment (PPE) for healthcare staff to prevent the transmission of the virus (Chintagunta et al., 2021). As the COVID-19 is a highly human-human transmittable infection, an accurate and sensitive POC device that can rapidly detect the infection is essential for on-site monitoring. Nanotechnology offers numerous solutions for addressing the challenges associated with the biosensing devices. During biosensor device construction, their reactive capacity in proportion to their bulk shape is crucial. Nanomaterial's size and shape can be readily customised for surface modification/immobilization with various receptors via covalent or non-covalent bonding. This can improve biosensing characteristics such as low detection limit, high sensitivity, selectivity, and rapid response against target (Tang et al., 2021). The size of metals and metal oxide nanoparticles are significantly suitable for biosensors due to their unique optical and electric properties (Sahoo et al., 2007).

Nanomaterial-based diagnostic devices amplify detection signals suitable for sensitive, rapid, and cost-efficient POC methods for identifying SARS-CoV-2 target molecules and identifying COVID-19 (Morales-Narváez and Dincer, 2020). Tunable optical, electrical, mechanical and magnetic properties of nanomaterials offer unique function in biosensor design and application (Mokhtarzadeh et al., 2017). Transducer surface modification is an essential aspect of the biosensor fabrication process. This enhances the affinity and interaction between biorecognition elements and target analytes. Nanomaterials also help build biosensors with large biocompatible areas for immobilizing bioreceptors like antibodies, enzymes, DNA, cells, and proteins (Ozer et al., 2019). In some cases, the nanomaterial interfaces act as signal generating probes, where the biorecognition process (receptor-target binding) does not produce any detectable signals. In this case, the variations in the *in-situ* signal produced by the nanomaterial interface are probed for quantifying the biorecognition process. In recent years, several nanomaterials have been investigated to measure SARS-CoV-2. Among the wide varieties of nanomaterials, carbon nanotubes (CNTs), graphene-based nanomaterials, metals (Au, Ag, Pt, Pd, Co, Fe and Cu), metal oxides (ZnO, TiO_2, SnO_2 and MnO_2), in different nanoarchitectures such as nanowire, nanorods, nanofibers, nanocubes, MXenes and quantum dots (QDs) have been explored (Fig. 9). The

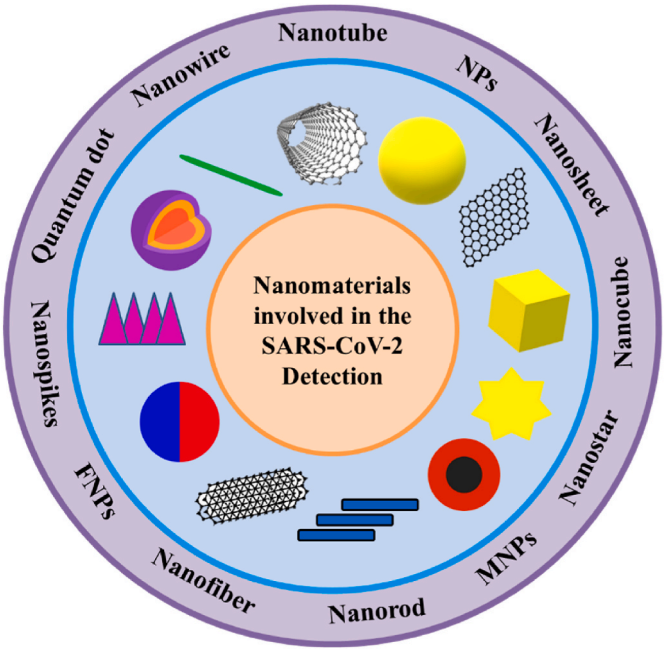

Fig. 9. Various type of nanoarchitectures involved in SARS-CoV-2 diagnosis by electrochemical and optical methods.

following sections of this review will discuss the use of nano-sized materials for COVID-19 infection prevention, early detection, and treatment options. This evaluation may assist in highlighting the benefits of nanotechnology to exploit their potential in resolving the pandemic crisis. Among the various nanoarchitectures, gold-based nano architectures have been widely employed to develop viral detection methods due to their unique photonic, catalytic, and electric capabilities and the molecular interaction selectivity of several biomolecules such as antibodies, RNA aptamers, and single-stranded DNA (Draz and Shafiee, 2018). They also have exceptional multiplexing capabilities, making them ideal for optical and electrochemical signal transducers to create a biosensor. Mahari et al. described an electrochemical biosensor based on Au nanoparticles for detecting spike S1 protein antigen within ~1 min (Mahari et al., 2020). Due to their high electrical conductivity, Au-NPs were employed as signal amplifiers in this biosensor.

Similarly, Xiang et al. reported the biosensing efficacy of colloidal gold immunochromatographic (GICA) and enzyme-linked immunoassay (ELISA) kits for detecting SARS-CoV-2 infection (Xiang et al., 2020). The colorimetric testing can be a simple and accurate method using AuNPs for detecting viral infections. Thiol-modified AuNPs were hybridized with aptamers for preventing salt aggregation. As a result, colour changes occur within 10 min in the platform, visually detectable by naked eye (Kumar et al., 2022; Moitra et al., 2020). Lateral flow immunoassay (LFIA) system based on AuNPs can detect SARS-CoV-2 antibodies (IgM and IgG) in blood samples within 15 min. Furthermore, the LIFA showed high clinical detection sensitivity (88.66%) and specificity (90.63%), suggesting that it might be helpful in the early identification of COVID-19 infections (Li et al., 2020). Throughout the pandemic, we have seen significant progress in developing COVID-19 diagnostic tests. However, the hunt for novel solutions continues, and nanosensor have made significant contributions to transform *in vitro* systems into *in vivo* systems. The action of the corona protein, which occurs when a specific set of biomolecules quickly covers the surface of NPs in the presence of biological fluids, has been widely researched for nanosensor fabrication. NPs can work by precisely attracting viral biomarkers when functionalized with the right receptors (Santiago, 2020). As a result, success in nanosensor research requires an ultra-sensitive detection system that can combine low-cost, high-speed, and simple equipment. In this context, the future for these nanotechnology-based systems is to investigate the integration of multiple features (optical, magnetic, electrochemical, and biological) to encourage a more precise and rapid diagnosis response (Z. Zhu et al., 2020). Fusion technology integrating the nanomaterial science and instrumentation engineering has been intensively researched in creating novel detection systems, as evidenced throughout this article.

9. Conclusion and future prospect

Socio-economic turbulence due to COVID pandemics has triggered global government to create policies to rationalise regulatory guidelines, prompt the research communities to design novel therapeutic approaches, cost-effective diagnostics to combat the impacts of pandemics. Priorities were devoted to developing PPEs/kits, disinfectants, anti-viral drug repurposing, and vaccine development to support the healthcare needs. Researchers were continuously working to create novel tech solutions such as robotics enabled accelerated supply, online surveillance, e-learning and mobile app for improving the lifestyle and behavioural health. At the initial stage of the pandemic, clinical investigations like chest CT, ultrasound sonography and X-ray provided insights on COVID-19 disease state. In the meantime, multiplexed analysis of inflammation-associated biomarkers such as procalcitonin, C-reactive protein, interleukin-6, and ferritin enables clinicians to rationalise theragnostic to manage COVID-19. The key biomarkers like lactate dehydrogenase, aspartate aminotransferase and alanine aminotransferase were played crucial role in assessing the pathophysiological status of COVID-19 victims. The primary concern in healthcare is the structural and

genomic mutations in SARS-CoV-2, which leads to the generation of new variants such as delta, gamma, omicron and XE. The variants facilitate infection with high transmissibility, virulence, mortality, and a decrease in the effectiveness of public health and social measures (Chaudhary et al., 2022a). WHO is collaborating with various health agencies worldwide to monitor and assess the evolution of SARS-CoV-2 to understand the impact of the virus mutation on human health. Researchers have developed a massive library for monitoring how mutation to the virus can affect the specificity of the biorecognition elements used in the biosensors. Their library has ~8000 amino acid substitutions for possible virus mutation, which enable the design of novel synthetic biorecognition elements. These libraries may help to detect future mutations and guide for optimal prevention methods (Frank et al., 2022).

Though RT-PCR-based confirmatory assays of S, E, and N-gene are regarded for SARS-CoV-2 testing, there is still a need for advancement in signal amplification based on multiplex tandem PCR(Attwood et al., 2020). RT-nanopore target sequencing provides complementary detection feasibility for COVID-19 and other respiratory viral variant detection (Wang et al., 2020). These techniques provide detailed information of the infection state. The gold standard RT-PCR testing comprises the massive part of observation testing, worn out the working environment, and takes 4–6 h to get results. The accuracy of RT-PCR results principally depends on the type of clinical sample involved in the diagnosis process between oropharyngeal swabs (32–48%), nasopharyngeal swabs (63%), bronchoalveolar lavage fluid (79–93%), sputum (72–76%) and stool (29%)(Kevadiya et al., 2021).

In response to the limitations posed by RT–PCR testing for POC measurement and for screening asymptomatic COVID-19 cases, developing rapid and inexpensive techniques for selective and early detection of the viral infection is imperative. Early detection of viral infection can help slow down the spreading rate and improve the efficacy of treatment protocols to control the viral load. Targeting appropriate regions of SARS-CoV-2 is essential in devising protocols for early detection and timely treatment. The viral genomic sequence (UTR) and replication complexes (ORF1a and ORF1b) are the most critical targets for selective detection of the virus in the early stages (first week) because, during the initial stage of viral infection, the nucleic acid present in the biofluids. The levels of viral particles will decrease in the upper respiratory tract after 7–10 days of the onset of the infection, which leads to negative swab results among the SARS-CoV-2 infected people. Many portable LFIA methods have been developed for detecting nucleic acid, S, N, and E proteins and SARS-CoV-2 antibodies. These portable paper-based devices allow the measurement of antibodies or protein biomarkers in less than 30 min. However, the LFIA face sensitivity issues when the concentrations of SARS-CoV-2 are less in the clinical specimen. In such cases, the nucleic acid amplification strategy is coupled with the LFIA, where the LFIA is used to interpret the nucleic acid amplification results visually. In some patients, the antibodies were detectable as early as one day after the onset of infection. Detection of antibodies in serological samples is recommended only after two weeks of the infection (Lino et al., 2022). The antibodies (IgG and IgM) levels are relatively lower during the first two weeks of infection and gradually increase till the next four to five weeks. After that, the concentration of antibodies decreases and reaches the initial level. The levels of IgG increase rapidly in the initial state compared to the IgM levels. Another challenge for serological antibody testing is the low immunity response from people with mild infections.

The selection of suitable POC measurement for early diagnosis also depends on the concentration of the target biomarker as well as the sampling protocol involved. There is room to develop smart sensors for rapid and selective detection of SARS-CoV-2 structural proteins at the picomolar levels for enabling POC for early diagnosis. Nanomaterials-based electrochemical and optical biosensors showed to be potential in detecting SARS-CoV-2 biomarkers in various clinical specimens, including nasopharyngeal swabs, saliva blood and sputum samples. Efforts have been made to simplify the sample collection protocol required for screening and diagnostics. The clinical specimens should be collected in a non-invasive manner and must be used with no further purification to enable the point-of-site measurement. The current practice of collecting naso/oro-pharyngeal swab specimens often require further purification. This can be avoided by the utilization of alternative sample collection protocols, such as saline gargles from frontline workers (Goldfarb et al., 2021). Peptide-based electrochemical biosensor devising customized human ACE-2 oligopeptides as probe to target receptor binding domains of spike proteins of SARS-CoV-2 directly from naso/oro-pharyngeal swab specimens (Kumar et al., 2023). Amplification free electrochemical based detection of DNA or RNA specific region sequences from RdRp and spike protein (Spike) region genes of SARS-CoV-2 using gold nanotriangles functionalized with oligonucleotides (del Caño et al., 2022). These methods can detect SARS-CoV-2 within 10 min–100 min and enables early and rapid diagnosis of COVID-19 cases. Sensor to sensor variation is another issue in going forward with the clinical manifestation of electrochemical sensors. For instance, POC detection performed using screen-printed electrodes produces variation corresponding to electrode batch, contamination, and surface roughness, affecting the overall quantification result. Although visual-based diagnostic tools provide POC solutions, the plasmonic-based optical detection techniques require specialized instruments for the detection process that create issues related to portability. The intervention of nanomaterial scientists' and biomedical researchers offered valuable contributions in POC diagnosis. Stability of the bioreceptors and cost per assay hamper the utilization of POC detection of SARS-CoV-2. Accessibility and affordability of any clinical investigation, whether provided by the government agencies as a part of a welfare scheme or at paid services, genuinely depend on the cost-effectiveness of the assay method. Therefore, the efficient design of materials (nanomaterials, bioreceptors and transducers) involved in device construction is critical for widespread applications. Nucleotide based detection strategies and emerging CRISPR system-based approach aid in producing efficient, stable, and cost-effective bioassays.

To oversee the COVID-19 widespread, intelligent new technologies are required to perform diagnostics, therapeutics, and optimisation of expectation. Machine learning (ML), artificial intelligence (AI), and IoT approaches would help in analysing the large set of sensor data through novel strategies to create meaningful results (Kaushik et al., 2020). The advancement in the nanotechnology makes a modern era of biosensor and face mask respirators for the airborne disease driven by Internet-of-nano-things (IoNT) (Chaudhary et al., 2022b, 2022c). The MXene hybrid biosensors are demonstrated as an intelligent and smart sensing techniques for the infectious disease detection. In addition, these techniques integrated with 5G communication, internet-of-medical-things (IoMT), artificial intelligence (AI), and data clouding to make new era toward hospital-on-chip (HOC) solutions (Chaudhary et al., 2023). The post COVID monitoring is another important problem the world facing, after diagnosed with SARS-CoV-2, patients experiencing certain difficulties in their life like short of breathing, irregularity in bowel movement, loss of appetite, diabetes, sleep disorder, fatigue, muscle, and joint pain, etc. These make a global concern over the government to monitor the people but monitoring huge amount of people in the hospitals is not a possible one. As a result, there is an urgent need for a quick monitoring system that is broadly accessible to the public and allows for repeated high-precision assessments. Wearable sensor technology may be a viable technique for identifying post-COVID-19 disorders and developing COVID-19 infection in large population. COVID-19 management system in which wearable sensors monitor users' body temperature, heart rate, oxygen level, and respiratory rate, which may then be processed in real time for risk assessment and eventual diagnosis (Cherusseri et al., 2022; Khondakar and Kaushik, 2023). Nevertheless, nanotechnology and materials engineering science can provide promising opportunities for better POC diagnosis in both *in vitro* and *in vivo* conditions. Lessons learned from the COVID-19 pandemic gave us future research perspectives in managing any

remerging pathogenic disease. This includes but is not limited to the need for collaborative research integrating bioinformatics, material science, and electronics experts to reach a global-standard diagnostic device. As a result, efforts should be undertaken to enhance this technique to reap the rich payoff in the fight against the COVID-19 pandemic. Furthermore, a low detection limit, high stability, and quick reaction time may be achieved using the POC devices, thanks to surface modification of sensing electrodes and recombinant technology. However, this may not be the case in clinical analysis. Factors such as LOD, stability, and response time may not be as promising when the sensing device is challenged for clinical specimen analysis. The sensitivity and selectivity of the POC biosensing platform are highly reliant on multiple variables, including antigen, antibody, protein, nanomaterials, and other biomolecules (Srivastava et al., 2021). These parameters play an active role and, as a result, can considerably impact the overall performance of nanomaterials-based biosensing devices. As a result, developing new nanomaterials enabled biosensing devices for SARS-CoV-2 detection necessitates a strong theoretical and experimental understanding of these aspects, which must be thoroughly investigated. We are still in the early stages of nanomaterials-enabled biosensing technology for COVID-19 diagnosis and in-depth research on nanotechnology enabled theragnostic is still required. Finally, it would be technically advantageous to build universal nanomaterials-based biosensors coupled with synthetic bioreceptors as an alternate tool for detecting SARS-CoV-2 infection in clinical samples, such as urine, blood, saliva, and nasopharyngeal swabs. These findings, connected to sampling, sample collection duration, and active infection against post-infection seroconversion, helps in mitigating the issues associated with the current generation of POC sensing devices.

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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.

Data availability

No data was used for the research described in the article.

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References

Abduljalil, J.M., 2020. Laboratory diagnosis of SARS-CoV-2: available approaches and limitations. New Microbes New Infect. 36, 100713 https://doi.org/10.1016/j.nmni.2020.100713.

Ahmadivand, A., Gerislioglu, B., Ramezani, Z., Kaushik, A., Manickam, P., Ghoreishi, S. A., 2021. Functionalized terahertz plasmonic metasensors: femtomolar-level detection of SARS-CoV-2 spike proteins. Biosens. Bioelectron. 177, 112971 https://doi.org/10.1016/j.bios.2021.112971.

Ahmed, S.F., Quadeer, A.A., McKay, M.R., 2020. Preliminary identification of potential vaccine targets for the COVID-19 coronavirus (SARS-CoV-2) based on SARS-CoV immunological studies. Viruses 12. https://doi.org/10.3390/v12030254.

Alexaki, K., Kyriazi, M.E., Greening, J., Taemaitree, L., El-Sagheer, A.H., Brown, T., Zhang, X., Muskens, O.L., Kanaras, A.G., 2022. A SARS-Cov-2 sensor based on upconversion nanoparticles and graphene oxide. RSC Adv. 12, 18445–18449. https://doi.org/10.1039/D2RA03599E.

Alfassam, H.A., Nassar, M.S., Almusaynid, M.M., Khalifah, B.A., Alshahrani, A.S., Almughem, F.A., Alshehri, A.A., Alawad, M.O., Massadeh, S., Alaamery, M., Aldeailej, I.M., Alamri, A.A., Binjomah, A.Z., Tawfik, E.A., 2021. Development of a colorimetric tool for SARS-CoV-2 and other respiratory viruses detection using sialic acid fabricated gold nanoparticles. Pharmaceutics 13, 502. https://doi.org/10.3390/pharmaceutics13040502.

Ali, M.A., Hu, C., Jahan, S., Yuan, B., Saleh, M.S., Ju, E., Gao, S.-J., Panat, R., 2021. Sensing of COVID-19 antibodies in seconds via aerosol jet nanoprinted reduced-graphene-oxide-coated 3D electrodes. Adv. Mater. 33, e2006647–e2006647 https://doi.org/10.1002/adma.202006647.

Ali, M.A., Hu, C., Zhang, F., Jahan, S., Yuan, B., Saleh, M.S., Gao, S.-J., Panat, R., 2022. N protein-based ultrasensitive SARS-CoV-2 antibody detection in seconds via 3D nanoprinted, microarchitected array electrodes. J. Med. Virol. 94, 2067–2078. https://doi.org/10.1002/jmv.27591.

Alireza Hashemi, S., Bahrani, S., Mojtaba Mousavi, S., Omidifar, N., Ghaleh Golab Behbahan, N., Arjmand, M., Ramakrishna, S., Bagheri Lankarani, K., Moghadami, M., Shokripour, M., Firoozsani, M., Chiang, W.-H., 2021. Ultra-precise label-free nanosensor based on integrated graphene with Au nanostars toward direct detection of IgG antibodies of SARS-CoV-2 in blood. J. Electroanal. Chem. 894, 115341 https://doi.org/10.1016/j.jelechem.2021.115341.

Amouzadeh Tabrizi, M., Acedo, P., 2022. An electrochemical impedance spectroscopy-based aptasensor for the determination of SARS-CoV-2-RBD using a carbon nanofiber–gold nanocomposite modified screen-printed electrode. Biosensors 12. https://doi.org/10.3390/bios12030142.

Ang, W.L., Lim, R.R.X., Ambrosi, A., Bonanni, A., 2022. Rapid electrochemical detection of COVID-19 genomic sequence with dual-function graphene nanocolloids based biosensor. FlatChem 32, 100336. https://doi.org/10.1016/j.flatc.2022.100336.

Arndt, A.L., Larson, B.J., Hogue, B.G., 2010. A conserved domain in the coronavirus membrane protein tail is important for virus assembly. J. Virol. 84, 11418–11428. https://doi.org/10.1128/JVI.01131-10.

Ashur, I., Alter, J., Werbner, M., Ogungbile, A., Dessau, M., Gal-Tanamy, M., Vernick, S., 2022. Rapid electrochemical immunodetection of SARS-CoV-2 using a pseudo-typed vesicular stomatitis virus model. Talanta 239, 123147. https://doi.org/10.1016/j.talanta.2021.123147.

Attwood, L.O., Francis, M.J., Hamblin, J., Korman, T.M., Druce, J., Graham, M., 2020. Clinical evaluation of AusDiagnostics SARS-CoV-2 multiplex tandem PCR assay. J. Clin. Virol. 128, 104448 https://doi.org/10.1016/j.jcv.2020.104448.

Ayankojo, A.G., Boroznjak, R., Reut, J., Öpik, A., Syritski, V., 2022. Molecularly imprinted polymer based electrochemical sensor for quantitative detection of SARS-CoV-2 spike protein. Sensors Actuators B Chem. 353, 131160 https://doi.org/10.1016/j.snb.2021.131160.

Bardajee, G.R., Zamani, M., Mahmoodian, H., Elmizadeh, H., Yari, H., Jouyandeh, L., Shirkavand, R., Sharifi, M., 2022. Capability of novel fluorescence DNA-conjugated CdTe/ZnS quantum dots nanoprobe for COVID-19 sensing. Spectrochim. Acta Part A Mol. Biomol. Spectrosc. 269, 120702 https://doi.org/10.1016/j.saa.2021.120702.

Bong, J.-H., Kim, T.-H., Jung, J., Lee, S.J., Sung, J.S., Lee, C.K., Kang, M.-J., Kim, H.O., Pyun, J.-C., 2020. Pig sera-derived anti-SARS-CoV-2 antibodies in surface plasmon resonance biosensors. BioChip J. 14, 358–368. https://doi.org/10.1007/s13206-020-4404-z.

Bowser, M.T., 2005. SELEX: just another separation? Analyst 130, 128–130. https://doi.org/10.1039/B412492H.

Brazaca, L.C., Imamura, A.H., Gomes, N.O., Almeida, M.B., Scheidt, D.T., Raymundo-Pereira, P.A., Oliveira, O.N., Janegitz, B.C., Machado, S.A.S., Carrilho, E., 2022. Electrochemical immunosensors using electrodeposited gold nanostructures for detecting the S proteins from SARS-CoV and SARS-CoV-2. Anal. Bioanal. Chem. 414, 5507–5517. https://doi.org/10.1007/s00216-022-03956-1.

Cardoso, A.R., Alves, J.F., Frasco, M.F., Piloto, A.M., Serrano, V., Mateus, D., Sebastião, A.I., Matos, A.M., Carmo, A., Cruz, T., Fortunato, E., Sales, M.G.F., 2022. An ultra-sensitive electrochemical biosensor using the Spike protein for capturing antibodies against SARS-CoV-2 in point-of-care. Mater. Today Bio 16, 100354. https://doi.org/10.1016/j.mtbio.2022.100354.

Carter, L.J., Garner, L.V., Smoot, J.W., Li, Y., Zhou, Q., Saveson, C.J., Sasso, J.M., Gregg, A.C., Soares, D.J., Beskid, T.R., Jervey, S.R., Liu, C., 2020. Assay techniques and test development for COVID-19 diagnosis. ACS Cent. Sci. 6, 591–605. https://doi.org/10.1021/acscentsci.0c00501.

Cennamo, N., Pasquardini, L., Arcadio, F., Lunelli, L., Vanzetti, L., Carafa, V., Altucci, L., Zeni, L., 2021. SARS-CoV-2 spike protein detection through a plasmonic D-shaped plastic optical fiber aptasensor. Talanta 233, 122532. https://doi.org/10.1016/j.talanta.2021.122532.

Cha, H., Kim, H., Joung, Y., Kang, H., Moon, J., Jang, H., Park, S., Kwon, H.-J., Lee, I.-C., Kim, S., Yong, D., Yoon, S.-W., Park, S.-G., Guk, K., Lim, E.-K., Park, H.G., Choo, J., Jung, J., Kang, T., 2022. Surface-enhanced Raman scattering-based immunoassay for severe acute respiratory syndrome coronavirus 2. Biosens. Bioelectron. 202, 114008 https://doi.org/10.1016/j.bios.2022.114008.

Chaibun, T., Puenpa, J., Ngamdee, T., Boonapatcharoen, N., Athamanolap, P., O'Mullane, A.P., Vongpunsawad, S., Poovorawan, Y., Lee, S.Y., Lertanantawong, B., 2021. Rapid electrochemical detection of coronavirus SARS-CoV-2. Nat. Commun. 12, 802. https://doi.org/10.1038/s41467-021-21121-7.

Chaudhary, V., Bhadola, P., Kaushik, A., Khalid, M., Furukawa, H., Khosla, A., 2022a. Assessing temporal correlation in environmental risk factors to design efficient area-specific COVID-19 regulations: Delhi based case study. Sci. Rep. 12, 12949 https://doi.org/10.1038/s41598-022-16781-4.

Chaudhary, V., Gautam, A., Silotia, P., Malik, S., de Oliveira Hansen, R., Khalid, M., Khosla, A., Kaushik, A., Mishra, Y.K., 2022b. Internet-of-nano-things (IoNT) driven intelligent face masks to combat airborne health hazard. Mater. Today 60, 201–226. https://doi.org/10.1016/j.mattod.2022.08.019.

Chaudhary, V., Kaushik, A., Furukawa, H., Khosla, A., 2022c. Review—towards 5th generation AI and IoT driven sustainable intelligent sensors based on 2D MXenes and borophene. ECS Sensors Plus 1, 13601. https://doi.org/10.1149/2754-2726/ac5ac6.
Chaudhary, V., Khanna, V., Ahmed Awan, H.T., Singh, K., Khalid, M., Mishra, Y.K., Bhansali, S., Li, C.-Z., Kaushik, A., 2023. Towards hospital-on-chip supported by 2D MXenes-based 5th generation intelligent biosensors. Biosens. Bioelectron. 220, 114847 https://doi.org/10.1016/j.bios.2022.114847.
Chen, H., Park, S.-G., Choi, N., Kwon, H.-J., Kang, T., Lee, M.-K., Choo, J., 2021. Sensitive detection of SARS-CoV-2 using a SERS-based aptasensor. ACS Sens. 6, 2378–2385. https://doi.org/10.1021/acssensors.1c00596.
Chen, Z., Zhang, Z., Zhai, X., Li, Y., Lin, L., Zhao, H., Bian, L., Li, P., Yu, L., Wu, Y., Lin, G., 2020. Rapid and sensitive detection of anti-SARS-CoV-2 IgG, using lanthanide-doped nanoparticles-based lateral flow immunoassay. Anal. Chem. 92, 7226–7231. https://doi.org/10.1021/acs.analchem.0c00784.
Cheong, J., Yu, H., Lee, C.Y., Lee, J., Choi, H.-J., Lee, J.-H., Lee, H., Cheon, J., 2020. Fast detection of SARS-CoV-2 RNA via the integration of plasmonic thermocycling and fluorescence detection in a portable device. Nat. Biomed. Eng. 4, 1159–1167. https://doi.org/10.1038/s41551-020-00654-0.
Cherusseri, J., Savio, C.M., Khalid, M., Chaudhary, V., Numan, A., Varma, S.J., Menon, A., Kaushik, A., 2022. SARS-CoV-2-on-Chip for long COVID management. Biosensors 12. https://doi.org/10.3390/bios12100890.
Chintagunta, A.D., S.K, M., Nalluru, S., N. S, S.K, 2021. Nanotechnology: an emerging approach to combat COVID-19. Emergent Mater. 4, 119–130. https://doi.org/10.1007/s42247-021-00178-6.
Choi, Y., Hwang, J.H., Lee, S.Y., 2018. Recent trends in nanomaterials-based colorimetric detection of pathogenic bacteria and viruses. Small Methods 2, 1700351. https://doi.org/10.1002/smtd.201700351.
COVID-19 technical brief — MIP Discovery [WWW Document], n.d. URL. https://mipdiscovery.com/covid19-technical-brief.
Crevillen, A.G., Mayorga-Martinez, C.C., Vaghasiya, J.V., Pumera, M., 2022. 3D-Printed SARS-CoV-2 RNA genosensing microfluidic system. Adv. Mater. Technol. 7, 2101121 https://doi.org/10.1002/admt.202101121.
Cui, F., Zhou, H.S., 2020. Diagnostic methods and potential portable biosensors for coronavirus disease 2019. Biosens. Bioelectron. 165, 112349 https://doi.org/10.1016/j.bios.2020.112349.
Cui, J., Kan, L., Cheng, F., Liu, J., He, L., Xue, Y., Fang, S., Zhang, Z., 2022. Construction of bifunctional electrochemical biosensors for the sensitive detection of the SARS-CoV-2 N-gene based on porphyrin porous organic polymers. Dalton Trans. 51, 2094–2104. https://doi.org/10.1039/D1DT03869A.
Curti, F., Fortunati, S., Knoll, W., Giannetto, M., Corradini, R., Bertucci, A., Careri, M., 2022. A folding-based electrochemical aptasensor for the single-step detection of the SARS-CoV-2 spike protein. ACS Appl. Mater. Interfaces 14, 19204–19211. https://doi.org/10.1021/acsami.2c02405.
Darmostuk, M., Rimpelova, S., Gbelcova, H., Ruml, T., 2015. Current approaches in SELEX: an update to aptamer selection technology. Biotechnol. Adv. 33, 1141–1161. https://doi.org/10.1016/j.biotechadv.2015.02.008.
del Caño, R., García-Mendiola, T., García-Nieto, D., Álvaro, R., Luna, M., Iniesta, H.A., Coloma, R., Díaz, C.R., Milán-Rois, P., Castellanos, M., Abreu, M., Cantón, R., Galán, J.C., Pineda, T., Pariente, F., Miranda, R., Somoza, Á., Lorenzo, E., 2022. Amplification-free detection of SARS-CoV-2 using gold nanotriangles functionalized with oligonucleotides. Microchim. Acta 189, 171. https://doi.org/10.1007/s00604-022-05272-y.
Diagnose, C., Cancer, E.O., Tanabe, K., Ikeda, M., Hayashi, M., Matsuo, K., Yasaka, M., 2020. Comprehensive Serum Glycopeptide Spectra Analysis Combined with Artificial Intelligence.
Diao, B., Wen, K., Zhang, J., Chen, J., Han, C., Chen, Y., Wang, S., Deng, G., Zhou, H., Wu, Y., 2021. Accuracy of a nucleocapsid protein antigen rapid test in the diagnosis of SARS-CoV-2 infection. Clin. Microbiol. Infect. 27, 289.e1–289.e4. https://doi.org/10.1016/j.cmi.2020.09.057.
Djaileb, A., Hojjat Jodaylami, M., Coutu, J., Ricard, P., Lamarre, M., Rochet, L., Cellier-Goetghebeur, S., Macaulay, D., Charron, B., Lavallée, É., Thibault, V., Stevenson, K., Forest, S., Live, L.S., Abonnenc, N., Guedon, A., Quessy, P., Lemay, J.-F., Farnós, O., Kamen, A., Stuible, M., Gervais, C., Durocher, Y., Cholette, F., Mesa, C., Kim, J., Cayer, M.-P., de Grandmont, M.-J., Brouard, D., Trottier, S., Boudreau, D., Pelletier, J.N., Masson, J.-F., 2021. Cross-validation of ELISA and a portable surface plasmon resonance instrument for IgG antibody serology with SARS-CoV-2 positive individuals. Analyst 146, 4905–4917. https://doi.org/10.1039/D1AN00893E.
Draz, M.S., Shafiee, H., 2018. Applications of gold nanoparticles in virus detection. Theranostics 8, 1985–2017. https://doi.org/10.7150/thno.23856.
Eissa, S., Zourob, M., 2021. Development of a low-cost cotton-tipped electrochemical immunosensor for the detection of SARS-CoV-2. Anal. Chem. 93, 1826–1833. https://doi.org/10.1021/acs.analchem.0c04719.
El-Schich, Z., Abdullah, M., Shinde, S., Dizeyi, N., Rosén, A., Sellergren, B., Wingren, A. G., 2016. Different expression levels of glycans on leukemic cells—a novel screening method with molecularly imprinted polymers (MIP) targeting sialic acid. Tumor Biol. 37, 13763–13768. https://doi.org/10.1007/s13277-016-5280-y.
Ellington, A.D., Szostak, J.W., 1990. In vitro selection of RNA molecules that bind specific ligands. Nature 346, 818–822. https://doi.org/10.1038/346818a0.
Fabiani, L., Saroglia, M., Galatà, G., De Santis, R., Fillo, S., Luca, V., Faggioni, G., D'Amore, N., Regalbuto, E., Salvatori, P., Terova, G., Moscone, D., Lista, F., Arduini, F., 2021. Magnetic beads combined with carbon black-based screen-printed electrodes for COVID-19: a reliable and miniaturized electrochemical immunosensor for SARS-CoV-2 detection in saliva. Biosens. Bioelectron. 171, 112686 https://doi.org/10.1016/j.bios.2020.112686.
Farzin, L., Sadjadi, S., Sheini, A., Mohagheghpour, E., 2021. A nanoscale genosensor for early detection of COVID-19 by voltammetric determination of RNA-dependent RNA polymerase (RdRP) sequence of SARS-CoV-2 virus. Microchim. Acta 188, 121. https://doi.org/10.1007/s00604-021-04773-6.
Feng, W., Newbigging, A.M., Le, C., Pang, B., Peng, H., Cao, Y., Wu, J., Abbas, G., Song, J., Wang, D.-B., Cui, M., Tao, J., Tyrrell, D.L., Zhang, X.-E., Zhang, H., Le, X.C., 2020. Molecular diagnosis of COVID-19: challenges and research needs. Anal. Chem. 92, 10196–10209. https://doi.org/10.1021/acs.analchem.0c02060.
Filipić, A., Gutierrez-Aguirre, I., Primc, G., Mozetič, M., Dobnik, D., 2020. Cold plasma, a new hope in the field of virus inactivation. Trends Biotechnol. 38, 1278–1291. https://doi.org/10.1016/j.tibtech.2020.04.003.
Frank, F., Keen, M.M., Rao, A., Bassit, L., Liu, X., Bowers, H.B., Patel, A.B., Cato, M.L., Sullivan, J.A., Greenleaf, M., Piantadosi, A., Lam, W.A., Hudson, W.H., Ortlund, E.A., 2022. Deep mutational scanning identifies SARS-CoV-2 Nucleocapsid escape mutations of currently available rapid antigen tests. Cell 185. https://doi.org/10.1016/j.cell.2022.08.010, 3603–3616.e13.
Funari, R., Chu, K.-Y., Shen, A.Q., 2020. Detection of antibodies against SARS-CoV-2 spike protein by gold nanospikes in an opto-microfluidic chip. Biosens. Bioelectron. 169, 112578 https://doi.org/10.1016/j.bios.2020.112578.
Gao, Y., Yan, L., Huang, Y., Liu, F., Zhao, Y., Cao, L., Wang, T., Sun, Q., Ming, Z., Zhang, L., Ge, J., Zheng, L., Zhang, Y., Wang, H., Zhu, Y., Zhu, C., Hu, T., Hua, T., Zhang, B., Yang, X., Li, J., Yang, H., Liu, Z., Xu, W., Guddat, L.W., Wang, Q., Lou, Z., Rao, Z., 2020. Structure of the RNA-dependent RNA polymerase from COVID-19 virus. Science (80- 368, 779–782. https://doi.org/10.1126/science.abb7498.
Gardner, A., Autin, L., Fuentes, D., Maritan, M., Barad, B.A., Medina, M., Olson, A.J., Grotjahn, D.A., Goodsell, D.S., 2021. CellPAINT: turnkey illustration of molecular cell biology. Front. Bioinf. 1, 660936 https://doi.org/10.3389/fbinf.2021.660936.
Ghazizadeh, E., Moosavifard, S.E., Daneshmand, N., 2020. Impediometric electrochemical sensor based on the inspiration of carnation Italian ringspot virus structure to detect an Attommolar of miR. Sci. Rep. 10, 1–9.
Goldfarb, D.M., Tilley, P., Al-Rawahi, G.N., Srigley, J.A., Ford, G., Pedersen, H., Pabbi, A., Hannam-Clark, S., Charles, M., Dittrick, M., Gadkar, V.J., Pernica, J.M., Hoang, L.M.N., 2021. Self-collected saline gargle samples as an alternative to health care worker-collected nasopharyngeal swabs for COVID-19 diagnosis in outpatients. J. Clin. Microbiol. 59 https://doi.org/10.1128/JCM.02427-20.
Goode, J.A., Rushworth, J.V.H., Millner, P.A., 2015. Biosensor regeneration: a review of common techniques and outcomes. Langmuir 31, 6267–6276. https://doi.org/10.1021/la503533g.
Grieshaber, D., MacKenzie, R., Vörös, J., Reimhult, E., 2008. Electrochemical biosensors - sensor principles and architectures. Sensors 8, 1400–1458. https://doi.org/10.3390/s80314000.
Guo, K., Wustoni, S., Koklu, A., Díaz-Galicia, E., Moser, M., Hama, A., Alqahtani, A.A., Ahmad, A.N., Alhamlan, F.S., Shuaib, M., Pain, A., McCulloch, I., Arold, S.T., Grünberg, R., Inal, S., 2021. Rapid single-molecule detection of COVID-19 and MERS antigens via nanobody-functionalized organic electrochemical transistors. Nat. Biomed. Eng. https://doi.org/10.1038/s41551-021-00734-9.
Gupta, A., Anand, A., Jain, N., Goswami, S., Anantharaj, A., Patil, S., Singh, R., Kumar, A., Shrivastava, T., Bhatnagar, S., Medigeshi, G.R., Sharma, T.K., 2021. A novel G-quadruplex aptamer-based spike trimeric antigen test for the detection of SARS-CoV-2. Mol. Ther. Nucleic Acids 26, 321–332. https://doi.org/10.1016/j.omtn.2021.06.014.
Hadisi, Z., Walsh, T., Dabiri, S.M.H., Seyfoori, A., Hamdi, D., Mirani, B., Pagan, E., Jardim, A., Akbari, M., 2021. Management of coronavirus disease 2019 (COVID-19) pandemic: from diagnosis to treatment strategies. Adv. Ther. 4, 2000173 https://doi.org/10.1002/adtp.202000173.
Haghayegh, F., Salahandish, R., Hassani, M., Sanati-Nezhad, A., 2022. Highly stable buffer-based zinc oxide/reduced graphene oxide nanosurface Chemistry for rapid immunosensing of SARS-CoV-2 antigens. ACS Appl. Mater. Interfaces 14, 10844–10855. https://doi.org/10.1021/acsami.1c24475.
Han, B., 2020. Nanosensors for Smart Cities. Elsevier, Waltham.
Harapan, H., Itoh, N., Yufika, A., Winardi, W., Keam, S., Te, H., Megawati, D., Hayati, Z., Wagner, A.L., Mudatsir, M., 2020. Coronavirus disease 2019 (COVID-19): a literature review. J. Infect. Public Health 13, 667–673. https://doi.org/10.1016/j.jiph.2020.03.019.
Heo, W., Lee, K., Park, S., Hyun, K.-A., Jung, H.-I., 2022. Electrochemical biosensor for nucleic acid amplification-free and sensitive detection of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) RNA via CRISPR/Cas13a trans-cleavage reaction. Biosens. Bioelectron. 201, 113960 https://doi.org/10.1016/j.bios.2021.113960.
Holzinger, M., Le Goff, A., Cosnier, S., 2014. Nanomaterials for biosensing applications: a review. Front. Chem. 2 https://doi.org/10.3389/fchem.2014.00063.
Huang, L., Ding, L., Zhou, J., Chen, S., Chen, F., Zhao, C., Xu, J., Hu, W., Ji, J., Xu, H., Liu, G.L., 2021. One-step rapid quantification of SARS-CoV-2 virus particles via low-cost nanoplasmonic sensors in generic microplate reader and point-of-care device. Biosens. Bioelectron. 171, 112685 https://doi.org/10.1016/j.bios.2020.112685.
Huang, Q., Yu, L., Petros, A.M., Gunasekera, A., Liu, Z., Xu, N., Hajduk, P., Mack, J., Fesik, S.W., Olejniczak, E.T., 2004. Structure of the N-terminal RNA-binding domain of the SARS CoV nucleocapsid protein. Biochemistry 43, 6059–6063. https://doi.org/10.1021/bi036155b.
Huang, Y., Yang, C., Xu, X., Xu, W., Liu, S., 2020. Structural and functional properties of SARS-CoV-2 spike protein: potential antivirus drug development for COVID-19. Acta Pharmacol. Sin. 41, 1141–1149. https://doi.org/10.1038/s41401-020-0485-4.
Hwang, C., Park, N., Kim, E.S., Kim, M., Kim, S.D., Park, S., Kim, N.Y., Kim, J.H., 2021. Ultra-fast and recyclable DNA biosensor for point-of-care detection of SARS-CoV-2 (COVID-19). Biosens. Bioelectron. 185, 113177 https://doi.org/10.1016/j.bios.2021.113177.

Idili, A., Parolo, C., Alvarez-Diduk, R., Merkoçi, A., 2021. Rapid and efficient detection of the SARS-CoV-2 spike protein using an electrochemical aptamer-based sensor. ACS Sens. 6, 3093–3101. https://doi.org/10.1021/acssensors.1c01222.

Iravani, S., 2020. Nano- and biosensors for the detection of SARS-CoV-2: challenges and opportunities. Mater. Adv. 1, 3092–3103. https://doi.org/10.1039/D0MA00702A.

Jia, M., Zhang, Z., Li, J., Ma, X., Chen, L., Yang, X., 2018. Molecular imprinting technology for microorganism analysis. TrAC, Trends Anal. Chem. 106, 190–201. https://doi.org/10.1016/j.trac.2018.07.011.

Jiang, Y., Hu, M., Liu, A.-A., Lin, Y., Liu, L., Yu, B., Zhou, X., Pang, D.-W., 2021. Detection of SARS-CoV-2 by CRISPR/Cas12a-Enhanced colorimetry. ACS Sens. 6, 1086–1093. https://doi.org/10.1021/acssensors.0c02365.

Kacherovsky, N., Yang, L.F., Dang, H.V., Cheng, E.L., Cardle, I.I., Walls, A.C., McCallum, M., Sellers, D.L., DiMaio, F., Salipante, S.J., Corti, D., Veesler, D., Pun, S. H., 2021. Discovery and characterization of spike N-terminal domain-binding aptamers for rapid SARS-CoV-2 detection. Angew Chem. Int. Ed. Engl. 60, 21211–21215. https://doi.org/10.1002/anie.202107730.

Kaushik, A.K., Dhau, J.S., Gohel, H., Mishra, Y.K., Kateb, B., Kim, N.-Y., Goswami, D.Y., 2020. Electrochemical SARS-CoV-2 sensing at point-of-care and artificial intelligence for intelligent COVID-19 management. ACS Appl. Bio Mater. 3, 7306–7325. https://doi.org/10.1021/acsabm.0c01004.

Kevadiya, B.D., Machhi, J., Herskovitz, J., Oleynikov, M.D., Blomberg, W.R., Bajwa, N., Soni, D., Das, S., Hasan, M., Patel, M., Senan, A.M., Gorantla, S., McMillan, J.E., Edagwa, B., Eisenberg, R., Gurumurthy, C.B., Reid, S.P.M., Punyadeera, C., Chang, L., Gendelman, H.E., 2021. Diagnostics for SARS-CoV-2 infections. Nat. Mater. https://doi.org/10.1038/s41563-020-00906-z.

Khan, N.I., Song, E., 2020. Lab-on-a-Chip Systems for Aptamer-Based Biosensing. Micromachines. https://doi.org/10.3390/mi11020220.

Khondakar, K.R., Kaushik, A., 2023. Role of wearable sensing technology to manage long COVID. Biosensors 13. https://doi.org/10.3390/bios13010062.

Kiew, L.-V., Chang, C.-Y., Huang, S.-Y., Wang, P.-W., Heh, C.-H., Liu, C.-T., Cheng, C.-H., Lu, Y.-X., Chen, Y.-C., Huang, Y.-X., Chang, S.-Y., Tsai, H.-Y., Kung, Y.-A., Huang, P.-N., Hsu, M.-H., Leo, B.-F., Foo, Y.-Y., Su, C.-H., Hsu, K.-C., Huang, P.-H., Ng, C.-J., Kamarulzaman, A., Yuan, C.-J., Shieh, D.-B., Shih, S.-R., Chung, L.-Y., Chang, C.-C., 2021. Development of flexible electrochemical impedance spectroscopy-based biosensing platform for rapid screening of SARS-CoV-2 inhibitors. Biosens. Bioelectron. 183, 113213 https://doi.org/10.1016/j.bios.2021.113213.

Koteswara Rao, V., 2021. Point of care diagnostic devices for rapid detection of novel coronavirus (SARS-nCoV19) pandemic: a review. Front. Nanotechnol. 2 https://doi.org/10.3389/fnano.2020.593619.

Kumar, V., Mishra, S., Sharma, R., Agarwal, J., Ghoshal, U., Khanna, T., Sharma, L.K., Verma, S.K., Mishra, P., Tiwari, S., 2022. Development of RNA-based assay for rapid detection of SARS-CoV-2 in clinical samples. Intervirology 65,181-187. doi:10.1159/000522337.

Kumar, T.H.V., Srinivasan, S., Krishnan, V., Vaidyanathan, R., Babu, K.A., Natarajan, S., Veerapandian, M., 2023. Peptide-based direct electrochemical detection of receptor binding domains of SARS-CoV-2 spike protein in pristine samples. Sensors Actuators B Chem. 377, 133052 https://doi.org/10.1016/j.snb.2022.133052.

Kussrow, A., Baksh, M.M., Bornhop, D.J., Finn, M.G., 2011. Universal sensing by transduction of antibody binding with backscattering interferometry. Chembiochem 12, 367–370. https://doi.org/10.1002/cbic.201000671.

Lasserre, P., Balansethupathy, B., Vezza, V.J., Butterworth, A., Macdonald, A., Blair, E. O., McAteer, L., Hannah, S., Ward, A.C., Hoskisson, P.A., Longmuir, A., Setford, S., Farmer, E.C.W., Murphy, M.E., Flynn, H., Corrigan, D.K., 2022. SARS-CoV-2 aptasensors based on electrochemical impedance spectroscopy and low-cost gold electrode substrates. Anal. Chem. 94, 2126–2133. https://doi.org/10.1021/acs.analchem.1c04456.

Li, J., Zhang, Z., Gu, J., Stacey, H.D., Ang, J.C., Capretta, A., Filipe, C.D.M., Mossman, K. L., Balion, C., Salena, B.J., Yamamura, D., Soleymani, L., Miller, M.S., Brennan, J.D., Li, Y., 2021. Diverse high-affinity DNA aptamers for wild-type and B.1.1.7 SARS-CoV-2 spike proteins from a pre-structured DNA library. Nucleic Acids Res. 49, 7267–7279. https://doi.org/10.1093/nar/gkab574.

Li, X., Qin, Z., Fu, H., Li, T., Peng, R., Li, Z., Rini, J.M., Liu, X., 2021. Enhancing the performance of paper-based electrochemical impedance spectroscopy nanobiosensors: an experimental approach. Biosens. Bioelectron. 177, 112672 https://doi.org/10.1016/j.bios.2020.112672.

Li, Z., Yi, Y., Luo, X., Xiong, N., Liu, Y., Li, S., Sun, R., Wang, Y., Hu, B., Chen, W., Zhang, Y., Wang, J., Huang, B., Lin, Y., Yang, J., Cai, W., Wang, X., Cheng, J., Chen, Z., Sun, K., Pan, W., Zhan, Z., Chen, L., Ye, F., 2020. Development and clinical application of a rapid IgM-IgG combined antibody test for SARS-CoV-2 infection diagnosis. J. Med. Virol. 92, 1518–1524. https://doi.org/10.1002/jmv.25727.

Liang, J., Teng, P., Xiao, W., He, G., Song, Q., Zhang, Y., Peng, B., Li, G., Hu, L., Cao, D., Tang, Y., 2021. Application of the amplification-free SERS-based CRISPR/Cas12a platform in the identification of SARS-CoV-2 from clinical samples. J. Nanobiotechnol. 19, 273. https://doi.org/10.1186/s12951-021-01021-0.

Liang, K.-H., Chang, T.-J., Wang, M.-L., Tsai, P.-H., Lin, T.-H., Wang, C.-T., Yang, D.-M., 2020. Novel biosensor platforms for the detection of coronavirus infection and severe acute respiratory syndrome coronavirus 2. J. Chin. Med. Assoc. 83, 701–703. https://doi.org/10.1097/JCMA.0000000000000337.

Lino, A., Cardoso, M.A., Gonçalves, H.M.R., Martins-Lopes, P., 2022. SARS-CoV-2 detection methods. Chemosensors 10. https://doi.org/10.3390/chemosensors10060221.

Liu, G., Lu, M., Huang, X., Li, T., Xu, D., 2018. Application of gold-nanoparticle colorimetric sensing to rapid food safety screening. Sensors 18, 4166. https://doi.org/10.3390/s18124166.

Liu, H., Dai, E., Xiao, R., Zhou, Z., Zhang, M., Bai, Z., Shao, Y., Qi, K., Tu, J., Wang, C., Wang, S., 2021. Development of a SERS-based lateral flow immunoassay for rapid and ultra-sensitive detection of anti-SARS-CoV-2 IgM/IgG in clinical samples. Sensors Actuators B Chem. 329, 129196 https://doi.org/10.1016/j.snb.2020.129196.

Liustrovaite, V., Drobysh, M., Rucinskiene, A., Baradoke, A., Ramanaviciene, A., Plikusiene, I., Samukaite-Bubniene, U., Viter, R., Chen, C.-F., Ramanavicius, A., 2022. Towards an electrochemical immunosensor for the detection of antibodies against SARS-CoV-2 spike protein. J. Electrochem. Soc. 169, 37523 https://doi.org/10.1149/1945-7111/ac5d91.

Liv, L., Kayabay, H., 2022. An electrochemical biosensing platform for the SARS-CoV-2 spike antibody detection based on the functionalised SARS-CoV-2 spike antigen modified electrode. ChemistrySelect 7, e202200256. https://doi.org/10.1002/slct.202200256.

Lorenzen, A.L., dos Santos, A.M., dos Santos, L.P., da Silva Pinto, L., Conceição, F.R., Wolfart, F., 2022. PEDOT-AuNPs-based impedimetric immunosensor for the detection of SARS-CoV-2 antibodies. Electrochim. Acta 404, 139757. https://doi.org/10.1016/j.electacta.2021.139757.

Lou, B., Liu, Y., Shi, M., Chen, J., Li, K., Tan, Y., Chen, L., Wu, Y., Wang, T., Liu, X., Jiang, T., Peng, D., Liu, Z., 2022. Aptamer-based biosensors for virus protein detection. TrAC, Trends Anal. Chem. 157, 116738 https://doi.org/10.1016/j.trac.2022.116738.

Lu, R., Zhao, X., Li, J., Niu, P., Yang, B., Wu, H., Wang, W., Song, H., Huang, B., Zhu, N., Bi, Y., Ma, X., Zhan, F., Wang, L., Hu, T., Zhou, H., Hu, Z., Zhou, W., Zhao, L., Chen, J., Meng, Y., Wang, J., Lin, Y., Yuan, J., Xie, Z., Ma, J., Liu, W.J., Wang, D., Xu, W., Holmes, E.C., Gao, G.F., Wu, G., Chen, W., Shi, W., Tan, W., 2020. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. Lancet 395, 565–574. https://doi.org/10.1016/S0140-6736(20)30251-8.

Lukose, J., Chidangil, S., George, S.D., 2021. Optical technologies for the detection of viruses like COVID-19: progress and prospects. Biosens. Bioelectron. 178, 113004 https://doi.org/10.1016/j.bios.2021.113004.

Luo, S.-C., Sivashanmugan, K., Liao, J.-D., Yao, C.-K., Peng, H.-C., 2014. Nanofabricated SERS-active substrates for single-molecule to virus detection in vitro: a review. Biosens. Bioelectron. 61, 232–240. https://doi.org/10.1016/j.bios.2014.05.013.

Maddali, H., Miles, C.E., Kohn, J., O'Carroll, D.M., 2021. Optical biosensors for virus detection: prospects for SARS-CoV-2/COVID-19. Chembiochem 22, 1176–1189. https://doi.org/10.1002/cbic.202000744.

Maduraiveeran, G., Sasidharan, M., Ganesan, V., 2018. Electrochemical sensor and biosensor platforms based on advanced nanomaterials for biological and biomedical applications. Biosens. Bioelectron. 103, 113–129. https://doi.org/10.1016/j.bios.2017.12.031.

Mahari, S., Roberts, A., Shahdeo, D., Gandhi, S., 2020. eCovSens-Ultrasensitive Novel In-House Built Printed Circuit Board Based Electrochemical Device for Rapid Detection of nCovid-19 Antigen, a Spike Protein Domain 1 of SARS-CoV-2. Bioengineering.

Mahshid, S.S., Flynn, S.E., Mahshid, S., 2021. The potential application of electrochemical biosensors in the COVID-19 pandemic: a perspective on the rapid diagnostics of SARS-CoV-2. Biosens. Bioelectron. 176, 112905 https://doi.org/10.1016/j.bios.2020.112905.

Mandal, M., Dutta, N., Dutta, G., 2021. Aptamer-based biosensors and their implications in COVID-19 diagnosis. Anal. Methods 13, 5400–5417. https://doi.org/10.1039/D1AY01519B.

Manickam, P., Pasha, S.K., Snipes, S.A., Bhansali, S., 2016. A reusable electrochemical biosensor for monitoring of small molecules (cortisol) using molecularly imprinted polymers. J. Electrochem. Soc. 164 https://doi.org/10.1149/2.0781702jes. B54–B59.

Mattioli, I.A., Castro, K.R., Macedo, L.J.A., Sedenho, G.C., Oliveira, M.N., Todeschini, I., Vitale, P.M., Ferreira, S.C., Manuli, E.R., Pereira, G.M., Sabino, E.C., Crespilho, F.N., 2022. Graphene-based hybrid electrical-electrochemical point-of-care device for serologic COVID-19 diagnosis. Biosens. Bioelectron. 199, 113866 https://doi.org/10.1016/j.bios.2021.113866.

Mavrikou, S., Moschopoulou, G., Tsekouras, V., Kintzios, S., 2020. Development of a portable, ultra-rapid and ultra-sensitive cell-based biosensor for the direct detection of the SARS-CoV-2 S1 spike protein antigen. Sensors 20, 3121. https://doi.org/10.3390/s20113121.

Mayer, K.M., Hafner, J.H., 2011. Localized surface plasmon resonance sensors. Chem. Rev. 111, 3828–3857. https://doi.org/10.1021/cr100313v.

Mejía-Salazar, J.R., Oliveira, O.N., 2018. Plasmonic Biosensing. Chem. Rev. 118, 10617–10625. https://doi.org/10.1021/acs.chemrev.8b00359.

Mohammadi, A., Esmaeilzadeh, E., Li, Y., Bosch, R.J., Li, J.Z., 2020. SARS-CoV-2 detection in different respiratory sites: a systematic review and meta-analysis. EBioMedicine 59. https://doi.org/10.1016/j.ebiom.2020.102903.

Moitra, P., Alafeef, M., Dighe, K., Frieman, M.B., Pan, D., 2020. Selective naked-eye detection of SARS-CoV-2 mediated by N gene targeted antisense oligonucleotide capped plasmonic nanoparticles. ACS Nano 14, 7617–7627. https://doi.org/10.1021/acsnano.0c03822.

Mojsoska, B., Larsen, S., Olsen, D.A., Madsen, J.S., Brandslund, I., Alatraktchi, F.A., 2021. Rapid SARS-CoV-2 detection using electrochemical immunosensor. Sensors 21, 390. https://doi.org/10.3390/s21020390.

Mokhtarzadeh, A., Eivazzadeh-Keihan, R., Pashazadeh, P., Hejazi, M., Gharaatifar, N., Hasanzadeh, M., Baradaran, B., de la Guardia, M., 2017. Nanomaterial-based biosensors for detection of pathogenic virus. TrAC, Trends Anal. Chem. 97, 445–457. https://doi.org/10.1016/j.trac.2017.10.005.

Morales-Narváez, E., Dincer, C., 2020. The impact of biosensing in a pandemic outbreak: COVID-19. Biosens. Bioelectron. 163, 112274 https://doi.org/10.1016/j.bios.2020.112274.

Morales, M.A., Halpern, J.M., 2018. Guide to selecting a biorecognition element for biosensors. Bioconjugate Chem. 29, 3231–3239. https://doi.org/10.1021/acs.bioconjchem.8b00592.

Murugan, D., Bhatia, H., Sai, V.V.R., Satija, J., 2020. P-FAB: a fiber-optic biosensor device for rapid detection of COVID-19. Trans. Indian Natl. Acad. Eng. 5, 211–215. https://doi.org/10.1007/s41403-020-00122-w.

Nascimento, E.D., Fonseca, W.T., de Oliveira, T.R., de Correia, C.R.S.T.B., Faça, V.M., de Morais, B.P., Silvestrini, V.C., Pott-Junior, H., Teixeira, F.R., Faria, R.C., 2022. COVID-19 diagnosis by SARS-CoV-2 Spike protein detection in saliva using an ultrasensitive magneto-assay based on disposable electrochemical sensor. Sensors Actuators B Chem. 353, 131128 https://doi.org/10.1016/j.snb.2021.131128.

Nunez-Bajo, E., Kasimatis, M., Cotur, Y., Asfour, T., Collins, A., Tanriverdi, U., Grell, M., Kaisti, M., Senesi, G., Stevenson, K., Güder, F., 2020. Ultra-Low-Cost Integrated Silicon-Based Transducer for On-Site, Genetic Detection of Pathogens. Bioengineering.

Oliveira, M.E., Lopes, B.V., Rossato, J.H.H., Maron, G.K., Gallo, B.B., La Rosa, A.B., Balboni, R.D.C., Alves, M.L.F., Ferreira, M.R.A., da Silva Pinto, L., Conceição, F.R., Piva, E., de Pereira, C.M.P., Escote, M.T., Carreño, N.L.V., 2022. Electrochemical biosensor based on laser-induced graphene for COVID-19 diagnosing: rapid and low-cost detection of SARS-CoV-2 biomarker antibodies. Surfaces 5, 187–201. https://doi.org/10.3390/surfaces5010012.

Orooji, Y., Sohrabi, H., Hemmat, N., Oroojalian, F., Baradaran, B., Mokhtarzadeh, A., Mohaghegh, M., Karimi-Maleh, H., 2020. An overview on SARS-CoV-2 (COVID-19) and other human coronaviruses and their detection capability via amplification assay, chemical sensing, biosensing, immunosensing, and clinical assays. Nano-Micro Lett. 13, 18. https://doi.org/10.1007/s40820-020-00533-y.

Ozer, T., Geiss, B.J., Henry, C.S., 2019. Review—chemical and biological sensors for viral detection. J. Electrochem. Soc. 167, 37523 https://doi.org/10.1149/2.0232003jes.

Pan, Y., Zhang, D., Yang, P., Poon, L.L.M., Wang, Q., 2020. Viral load of SARS-CoV-2 in clinical samples. Lancet Infect. Dis. 20, 411–412. https://doi.org/10.1016/S1473-3099(20)30113-4.

Parihar, A., Ranjan, P., Sanghi, S.K., Srivastava, A.K., Khan, R., 2020. Point-of-Care biosensor-based diagnosis of COVID-19 holds promise to combat current and future pandemics. ACS Appl. Bio Mater. 3, 7326–7343. https://doi.org/10.1021/acsabm.0c01083.

Patris, S., Vandeput, M., Kauffmann, J.-M., 2016. Antibodies as target for affinity biosensors. TrAC, Trends Anal. Chem. 79, 239–246. https://doi.org/10.1016/j.trac.2015.12.005.

Peng, X., Zhou, Y., Nie, K., Zhou, F., Yuan, Y., Song, J., Qu, J., 2020. Promising near-infrared plasmonic biosensor employed for specific detection of SARS-CoV-2 and its spike glycoprotein. New J. Phys. 22, 103046 https://doi.org/10.1088/1367-2630/abbe53.

Peng, R., Pan, Y., Li, Z., Qin, Z., Rini, J.M., Liu, X., 2022. SPEEDS: a portable serological testing platform for rapid electrochemical detection of SARS-CoV-2 antibodies. Biosens.Bioelectron.197,113762. doi:10.1016/j.bios.2021.113762.

Peng, Y., Pan, Y., Sun, Z., Li, J., Yi, Y., Yang, J., Li, G., 2021. An electrochemical biosensor for sensitive analysis of the SARS-CoV-2 RNA. Biosens. Bioelectron. 186, 113309 https://doi.org/10.1016/j.bios.2021.113309.

Perkins, M.D., Dye, C., Balasegaram, M., Bréchot, C., Mombouli, J.-V., Røttingen, J.-A., Tanner, M., Boehme, C.C., 2017. Diagnostic preparedness for infectious disease outbreaks. Lancet 390, 2211–2214. https://doi.org/10.1016/S0140-6736(17)31224-2.

Pinals, R.L., Ledesma, F., Yang, D., Navarro, N., Jeong, S., Pak, J.E., Kuo, L., Chuang, Y.-C., Cheng, Y.-W., Sun, H.-Y., Landry, M.P., 2021. Rapid SARS-CoV-2 spike protein detection by carbon nanotube-based near-infrared nanosensors. Nano Lett. 21, 2272–2280. https://doi.org/10.1021/acs.nanolett.1c00118.

Pokhrel, P., Hu, C., Mao, H., 2020. Detecting the coronavirus (COVID-19). ACS Sens. 5, 2283–2296. https://doi.org/10.1021/acssensors.0c01153.

Qi, H., Hu, Z., Yang, Z., Zhang, J., Wu, J.J., Cheng, C., Wang, C., Zheng, L., 2022. Capacitive aptasensor coupled with microfluidic enrichment for real-time detection of trace SARS-CoV-2 nucleocapsid protein. Anal. Chem. 94, 2812–2819. https://doi.org/10.1021/acs.analchem.1c04296.

Qiu, G., Gai, Z., Tao, Y., Schmitt, J., Kullak-Ublick, G.A., Wang, J., 2020. Dual-functional plasmonic photothermal biosensors for highly accurate severe acute respiratory syndrome coronavirus 2 detection. ACS Nano 14, 5268–5277. https://doi.org/10.1021/acsnano.0c02439.

Qu, J., Wu, C., Li, X., Zhang, G., Jiang, Z., Li, X., Zhu, Q., Liu, L., 2020. Profile of immunoglobulin G and IgM antibodies against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Clin. Infect. Dis. 71, 2255–2258. https://doi.org/10.1093/cid/ciaa489.

Rahmati, Z., Roushani, M., Hosseini, H., Choobin, H., 2021. Electrochemical immunosensor with Cu2O nanocube coating for detection of SARS-CoV-2 spike protein. Microchim. Acta 188, 105. https://doi.org/10.1007/s00604-021-04762-9.

Ramanathan, S., Gopinath, S.C.B., Ismail, Z.H., Md Arshad, M.K., Poopalan, P., 2022. Aptasensing nucleocapsid protein on nanodiamond assembled gold interdigitated electrodes for impedimetric SARS-CoV-2 infectious disease assessment. Biosens. Bioelectron. 197, 113735 https://doi.org/10.1016/j.bios.2021.113735.

Rashed, M.Z., Kopechek, J.A., Priddy, M.C., Hamorsky, K.T., Palmer, K.E., Mittal, N., Valdez, J., Flynn, J., Williams, S.J., 2021. Rapid detection of SARS-CoV-2 antibodies using electrochemical impedance-based detector. Biosens. Bioelectron. 171, 112709 https://doi.org/10.1016/j.bios.2020.112709.

Ratautaite, V., Boguzaite, R., Brazys, E., Ramanaviciene, A., Ciplys, E., Juozapaitis, M., Slibinskas, R., Bechelany, M., Ramanavicius, A., 2022. Molecularly imprinted polypyrrole based sensor for the detection of SARS-CoV-2 spike glycoprotein. Electrochim. Acta 403, 139581. https://doi.org/10.1016/j.electacta.2021.139581.

Raziq, A., Kidakova, A., Boroznjak, R., Reut, J., Öpik, A., Syritski, V., 2021. Development of a portable MIP-based electrochemical sensor for detection of SARS-CoV-2 antigen. Biosens. Bioelectron. 178, 113029 https://doi.org/10.1016/j.bios.2021.113029.

Roda, A., Cavalera, S., Di Nardo, F., Calabria, D., Rosati, S., Simoni, P., Colitti, B., Baggiani, C., Roda, M., Anfossi, L., 2021. Dual lateral flow optical/chemiluminescence immunosensors for the rapid detection of salivary and serum IgA in patients with COVID-19 disease. Biosens. Bioelectron. 172, 112765 https://doi.org/10.1016/j.bios.2020.112765.

Rota, P.A., 2003. Characterization of a novel coronavirus associated with severe acute respiratory syndrome. Science (80- 300, 1394–1399. https://doi.org/10.1126/science.1085952.

Ruch, T.R., Machamer, C.E., 2011. The hydrophobic domain of infectious bronchitis virus E protein alters the host secretory pathway and is important for release of infectious virus. J. Virol. 85, 675–685. https://doi.org/10.1128/JVI.01570-10.

Sahoo, S.K., Parveen, S., Panda, J.J., 2007. The present and future of nanotechnology in human health care. Nanomed. Nanotechnol. Biol. Med. 3, 20–31. https://doi.org/10.1016/j.nano.2006.11.008.

Samper, I.C., McMahon, C.J., Schenkel, M.S., Clark, K.M., Khamcharoen, W., Anderson, L.B.R., Terry, J.S., Gallichotte, E.N., Ebel, G.D., Geiss, B.J., Dandy, D.S., Henry, C.S., 2022. Electrochemical immunoassay for the detection of SARS-CoV-2 nucleocapsid protein in nasopharyngeal samples. Anal. Chem. 94, 4712–4719. https://doi.org/10.1021/acs.analchem.1c04966.

Santiago, I., 2020. Trends and innovations in biosensors for COVID-19 mass testing. Chembiochem 21, 2880–2889. https://doi.org/10.1002/cbic.202000250.

Sari, A., Hartati, Y., Gaffar, S., Anshori, I., Hidayat, D., Wiraswati, H., 2022. The optimization of an electrochemical aptasensor to detect RBD protein S SARS-CoV-2 as a biomarker of COVID-19 using screen-printed carbon electrode/AuNP: scientific paper. J. Electrochem. Sci. Eng. 12, 219–235. https://doi.org/10.5599/jese.1206.

Saylan, Y., Erdem, Ö., Ünal, S., Denizli, A., 2019. An alternative medical diagnosis method: biosensors for virus detection. Biosensors 9. https://doi.org/10.3390/bios9020065.

Schmitz, A., Weber, A., Bayin, M., Breuers, S., Fieberg, V., Famulok, M., Mayer, G., 2021. A SARS-CoV-2 spike binding DNA aptamer that inhibits pseudovirus infection by an RBD-independent mechanism. Angew. Chem., Int. Ed. 60, 10279–10285. https://doi.org/10.1002/anie.202100316.

Seo, G., Lee, G., Kim, M.J., Baek, S.-H., Choi, M., Ku, K.B., Lee, C.-S., Jun, S., Park, D., Kim, H.G., Kim, S.-J., Lee, J.-O., Kim, B.T., Park, E.C., Kim, S. Il, 2020. Rapid detection of COVID-19 causative virus (SARS-CoV-2) in human nasopharyngeal swab specimens using field-effect transistor-based biosensor. ACS Nano 14, 5135–5142. https://doi.org/10.1021/acsnano.0c02823.

Sharma, S., Byrne, H., O'Kennedy, R.J., 2016. Antibodies and antibody-derived analytical biosensors. Essays Biochem. 60, 9–18. https://doi.org/10.1042/EBC20150002.

Sheikhzadeh, E., 2021. Electrochemical biosensors for COVID-19. Culture 1, 1.

Singh, P., Pandey, S.K., Singh, J., Srivastava, S., Sachan, S., Singh, S.K., 2016. Biomedical perspective of electrochemical nanobiosensor. Nano-Micro Lett. 8, 193–203. https://doi.org/10.1007/s40820-015-0077-x.

Song, Y., Song, J., Wei, X., Huang, M., Sun, M., Zhu, L., Lin, B., Shen, H., Zhu, Z., Yang, C., 2020. Discovery of aptamers targeting the receptor-binding domain of the SARS-CoV-2 spike glycoprotein. Anal. Chem. 92, 9895–9900. https://doi.org/10.1021/acs.analchem.0c01394.

Song, Y., Wei, W., Qu, X., 2011. Colorimetric biosensing using smart materials. Adv. Mater. 23, 4215–4236. https://doi.org/10.1002/adma.201101853.

Song, Z., Ma, Y., Chen, M., Ambrosi, A., Ding, C., Luo, X., 2021. Electrochemical biosensor with enhanced antifouling capability for COVID-19 nucleic acid detection in complex biological media. Anal. Chem. 93, 5963–5971. https://doi.org/10.1021/acs.analchem.1c00724.

Soto, D., Orozco, J., 2022. Peptide-based simple detection of SARS-CoV-2 with electrochemical readout. Anal. Chim. Acta 1205, 339739. https://doi.org/10.1016/j.aca.2022.339739.

Srivastava, M., Srivastava, N., Mishra, P.K., Malhotra, B.D., 2021. Prospects of nanomaterials-enabled biosensors for COVID-19 detection. Sci. Total Environ. 754, 142363 https://doi.org/10.1016/j.scitotenv.2020.142363.

Stanborough, T., Given, F.M., Koch, B., Sheen, C.R., Stowers-Hull, A.B., Waterland, M.R., Crittenden, D.L., 2021. Optical detection of CoV-SARS-2 viral proteins to sub-picomolar concentrations. ACS Omega 6, 6404–6413. https://doi.org/10.1021/acsomega.1c00008.

Tang, Z., Zhang, X., Shu, Y., Guo, M., Zhang, H., Tao, W., 2021. Insights from nanotechnology in COVID-19 treatment. Nano Today 36, 101019. https://doi.org/10.1016/j.nantod.2020.101019.

Tong, Y., Bao, A., Chen, H., Huang, J., Lv, Z., Feng, L., Cheng, Y., Wang, Y., Bai, L., Rao, W., Zheng, H., Wu, Z., Qiao, B., Zhao, Z., Wang, H., Li, Y., 2020. Necessity for detection of SARS-CoV-2 RNA in multiple types of specimens for the discharge of the patients with COVID-19. J. Transl. Med. 18, 411. https://doi.org/10.1186/s12967-020-02580-w.

Torrente-Rodríguez, R.M., Lukas, H., Tu, J., Min, J., Yang, Y., Xu, C., Rossiter, H.B., Gao, W., 2020. SARS-CoV-2 RapidPlex: a graphene-based multiplexed telemedicine platform for rapid and low-cost COVID-19 diagnosis and monitoring. Matter 3, 1981–1998. https://doi.org/10.1016/j.matt.2020.09.027.

Tripathy, S., Singh, S.G., 2020. Label-free electrochemical detection of DNA hybridization: a method for COVID-19 diagnosis. Trans. Indian Natl. Acad. Eng. 5, 205–209. https://doi.org/10.1007/s41403-020-00103-z.

Tseng, Y.-T., Chang, C.-H., Wang, S.-M., Huang, K.-J., Wang, C.-T., 2013. Identifying SARS-CoV membrane protein amino acid residues linked to virus-like particle assembly. PLoS One 8, e64013. https://doi.org/10.1371/journal.pone.0064013.

Vadlamani, B.S., Uppal, T., Verma, S.C., Misra, M., 2020. Functionalized TiO2 nanotube-based electrochemical biosensor for rapid detection of SARS-CoV-2. Sensors 20, 5871. https://doi.org/10.3390/s20205871.

Ventura, B. Della, Cennamo, M., Minopoli, A., Campanile, R., Censi, S.B., Terracciano, D., Portella, G., Velotta, R., 2020. Colorimetric test for fast detection of SARS-CoV-2 in nasal and throat swabs. ACS Sens. 5, 3043–3048. https://doi.org/10.1021/acssensors.0c01742.

Verma, N., Bhardwaj, A., 2015. Biosensor technology for pesticides—a review. Appl. Biochem. Biotechnol. 175, 3093–3119. https://doi.org/10.1007/s12010-015-1489-2.

Vezza, V.J., Butterworth, A., Lasserre, P., Blair, E.O., MacDonald, A., Hannah, S., Rinaldi, C., Hoskisson, P.A., Ward, A.C., Longmuir, A., Setford, S., Farmer, E.C.W., Murphy, M.E., Corrigan, D.K., 2021. An electrochemical SARS-CoV-2 biosensor inspired by glucose test strip manufacturing processes. Chem. Commun. 57, 3704–3707. https://doi.org/10.1039/D1CC00936B.

Vo-Dinh, T., Wang, H.-N., Scaffidi, J., 2010. Plasmonic nanoprobes for SERS biosensing and bioimaging. J. Biophot. 3, 89–102. https://doi.org/10.1002/jbio.200910015.

Wandtke, T., Wędrowska, E., Szczur, M., Przybylski, G., Libura, M., Kopiński, P., 2022. Aptamers—diagnostic and therapeutic solution in SARS-CoV-2. Int. J. Mol. Sci. 23 https://doi.org/10.3390/ijms23031412.

Wang, C., Yang, X., Gu, B., Liu, H., Zhou, Z., Shi, L., Cheng, X., Wang, S., 2020. Sensitive and simultaneous detection of SARS-CoV-2-specific IgM/IgG using lateral flow immunoassay based on dual-mode quantum dot nanobeads. Anal. Chem. 92, 15542–15549. https://doi.org/10.1021/acs.analchem.0c03484.

Wang, D., He, S., Wang, X., Yan, Y., Liu, J., Wu, S., Liu, S., Lei, Y., Chen, M., Li, L., Zhang, J., Zhang, L., Hu, X., Zheng, X., Bai, J., Zhang, Y., Zhang, Y., Song, M., Tang, Y., 2020. Rapid lateral flow immunoassay for the fluorescence detection of SARS-CoV-2 RNA. Nat. Biomed. Eng. 4, 1150–1158. https://doi.org/10.1038/s41551-020-00655-z.

Wang, D., Hu, B., Hu, C., Zhu, F., Liu, X., Zhang, J., Wang, B., Xiang, H., Cheng, Z., Xiong, Y., Zhao, Y., Li, Y., Wang, X., Peng, Z., 2020. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus–infected pneumonia in Wuhan, China. JAMA 323, 1061. https://doi.org/10.1001/jama.2020.1585.

Wang, M., Fu, A., Hu, B., Tong, Y., Liu, R., Liu, Z., Gu, J., Xiang, B., Liu, J., Jiang, W., Shen, G., Zhao, W., Men, D., Deng, Z., Yu, L., Wei, W., Li, Y., Liu, T., 2020. Nanopore targeted sequencing for the accurate and comprehensive detection of SARS-CoV-2 and other respiratory viruses. Small 16, 2002169. https://doi.org/10.1002/smll.202002169.

Wang, X., Gopinath, S.C.B., Li, J., 2020. Anxiety determination by antibody-conjugated nanoparticles on an interdigitated electrode sensor. 3 Biotech 10, 377. https://doi.org/10.1007/s13205-020-02370-7.

Weiss, C., Carriere, M., Fusco, L., Capua, I., Regla-Nava, J.A., Pasquali, M., Scott, J.A., Vitale, F., Unal, M.A., Mattevi, C., Bedognetti, D., Merkoçi, A., Tasciotti, E., Yilmazer, A., Gogotsi, Y., Stellacci, F., Delogu, L.G., 2020. Toward nanotechnology-enabled approaches against the COVID-19 pandemic. ACS Nano 14, 6383–6406. https://doi.org/10.1021/acsnano.0c03697.

Whitcombe, M.J., Kirsch, N., Nicholls, I.A., 2014. Molecular imprinting science and technology: a survey of the literature for the years 2004–2011. J. Mol. Recogn. 27, 297–401.

WHO coronavirus (COVID-19) dashboard | WHO coronavirus (COVID-19) dashboard with vaccination data [WWW Document], n.d. URL. https://covid19.who.int/. (Accessed 2 January 2023).

Wrapp, D., Wang, N., Corbett, K.S., Goldsmith, J.A., Hsieh, C.-L., Abiona, O., Graham, B. S., McLellan, J.S., 2020. Cryo-EM structure of the 2019-nCoV spike in the prefusion conformation. Science 367, 1260–1263. https://doi.org/10.1126/science.abb2507.

Xian, M., Carey, P.H., Fares, C., Ren, F., Shan, S.-S., Liao, Y.-T., Esquivel-Upshaw, J.F., Pearton, S.J., 2020. Rapid electrochemical detection for SARS-CoV-2 and cardiac troponin I using low-cost, disposable and modular biosensor system. In: 2020 IEEE Research and Applications of Photonics in Defense Conference (RAPID). IEEE, pp. 1–2. https://doi.org/10.1109/RAPID49481.2020.9195689.

Xiang, J., Yan, M., Li, H., Liu, T., Lin, C., Huang, S., Shen, C., 2020. Evaluation of enzyme-linked immunoassay and colloidal gold-immunochromatographic assay kit for detection of novel coronavirus (SARS-Cov-2) causing an outbreak of pneumonia (COVID-19). medRxiv 2020. https://doi.org/10.1101/2020.02.27.20028787, 02.27.20028787.

Xu, M., Li, Y., Lin, C., Peng, Y., Zhao, S., Yang, X., Yang, Y., 2022. Recent advances of representative optical biosensors for rapid and sensitive diagnostics of SARS-CoV-2. Biosensors 12. https://doi.org/10.3390/bios12100862.

Yakoh, A., Pimpitak, U., Rengpipat, S., Hirankarn, N., Chailapakul, O., Chaiyo, S., 2021. Paper-based electrochemical biosensor for diagnosing COVID-19: detection of SARS-CoV-2 antibodies and antigen. Biosens. Bioelectron. 176, 112912 https://doi.org/10.1016/j.bios.2020.112912.

Yang, G., Li, Z., Mohammed, I., Zhao, L., Wei, W., Xiao, H., Guo, W., Zhao, Y., Qu, F., Huang, Y., 2021. Identification of SARS-CoV-2-against aptamer with high neutralization activity by blocking the RBD domain of spike protein 1. Signal Transduct. Targeted Ther. 6, 227. https://doi.org/10.1038/s41392-021-00649-6.

Yang, Y., Peng, Y., Lin, C., Long, L., Hu, J., He, J., Zeng, H., Huang, Z., Li, Z.-Y., Tanemura, M., Shi, J., Lombardi, J.R., Luo, X., 2021. Human ACE2-functionalized gold "virus-trap" nanostructures for accurate capture of SARS-CoV-2 and single-virus SERS detection. Nano-Micro Lett. 13, 109. https://doi.org/10.1007/s40820-021-00620-8.

Yousefi, H., Mahmud, A., Chang, D., Das, J., Gomis, S., Chen, J.B., Wang, H., Been, T., Yip, L., Coomes, E., Li, Z., Mubareka, S., McGeer, A., Christie, N., Gray-Owen, S., Cochrane, A., Rini, J.M., Sargent, E.H., Kelley, S.O., 2021. Detection of SARS-CoV-2 viral particles using direct, reagent-free electrochemical sensing. J. Am. Chem. Soc. 143, 1722–1727. https://doi.org/10.1021/jacs.0c10810.

Yu, H., Alkhamis, O., Canoura, J., Liu, Y., Xiao, Y., 2021. Advances and challenges in small-molecule DNA aptamer isolation, characterization, and sensor development. Angew. Chem., Int. Ed. 60, 16800–16823. https://doi.org/10.1002/anie.202008663.

Zavyalova, E., Ambartsumyan, O., Zhdanov, G., Gribanyov, D., Gushchin, V., Tkachuk, A., Rudakova, E., Nikiforova, M., Kuznetsova, N., Popova, L., Verdiev, B., Alatyrev, A., Burtseva, E., Ignatieva, A., Iliukhina, A., Dolzhikova, I., Arutyunyan, A., Gambaryan, A., Kukushkin, V., 2021. SERS-based aptasensor for rapid quantitative detection of SARS-CoV-2. Nanomaterials 11, 1394. https://doi.org/10.3390/nano11061394.

Zhang, D., Zhang, X., Ma, R., Deng, S., Wang, X., Zhang, X., Huang, X., Liu, Y., Li, G., Qu, J., Zhu, Y., Li, J., 2020. Ultra-fast and onsite interrogation of severe acute respiratory syndrome Coronavirus 2 (SARS-CoV-2) in environmental specimens via Surface enhanced Raman Scattering (SERS). Infect. Dis. (except HIV/AIDS).

Zhang, L., Fang, X., Liu, X., Ou, H., Zhang, H., Wang, J., Li, Q., Cheng, H., Zhang, W., Luo, Z., 2020. Discovery of sandwich type COVID-19 nucleocapsid protein DNA aptamers. Chem. Commun. 56, 10235–10238. https://doi.org/10.1039/D0CC03993D.

Zhang, W.S., Pan, J., Li, F., Zhu, M., Xu, M., Zhu, H., Yu, Y., Su, G., 2021. Reverse transcription recombinase polymerase amplification coupled with CRISPR-cas12a for facile and highly sensitive colorimetric SARS-CoV-2 detection. Anal. Chem. 93, 4126–4133. https://doi.org/10.1021/acs.analchem.1c00013.

Zhang, Z., Pandey, R., Li, J., Gu, J., White, D., Stacey, H.D., Ang, J.C., Steinberg, C.-J., Capretta, A., Filipe, C.D.M., Mossman, K., Balion, C., Miller, M.S., Salena, B.J., Yamamura, D., Soleymani, L., Brennan, J.D., Li, Y., 2021. High-affinity dimeric aptamers enable the rapid electrochemical detection of wild-type and B.1.1.7 SARS-CoV-2 in unprocessed saliva. Angew. Chem., Int. Ed. 60, 24266–24274. https://doi.org/10.1002/anie.202110819.

Zhao, H., Liu, F., Xie, W., Zhou, T.-C., OuYang, J., Jin, L., Li, H., Zhao, C.-Y., Zhang, L., Wei, J., Zhang, Y.-P., Li, C.-P., 2021. Ultrasensitive supersandwich-type electrochemical sensor for SARS-CoV-2 from the infected COVID-19 patients using a smartphone. Sensors Actuators B Chem. 327, 128899 https://doi.org/10.1016/j.snb.2020.128899.

Zhao, J., Fu, Z., Li, H., Xiong, Y., Cai, S., Wang, C., Chen, Y., Han, N., Yang, R., 2022. Magnet-assisted electrochemical immunosensor based on surface-clean Pd-Au nanosheets for sensitive detection of SARS-CoV-2 spike protein. Electrochim. Acta 404, 139766. https://doi.org/10.1016/j.electacta.2021.139766.

Zhao, Z., Huang, C., Huang, Z., Lin, F., He, Q., Tao, D., Jaffrezic-Renault, N., Guo, Z., 2021. Advancements in electrochemical biosensing for respiratory virus detection: a review. TrAC, Trends Anal. Chem. 139, 116253 https://doi.org/10.1016/j.trac.2021.116253.

Zhu, N., Zhang, D., Wang, W., Li, X., Yang, B., Song, J., Zhao, X., Huang, B., Shi, W., Lu, R., Niu, P., Zhan, F., Ma, X., Wang, D., Xu, W., Wu, G., Gao, G.F., Tan, W., 2020. A novel coronavirus from patients with pneumonia in China, 2019. N. Engl. J. Med. 382, 727–733. https://doi.org/10.1056/NEJMoa2001017.

Zhu, Z., Lian, X., Su, X., Wu, W., Marraro, G.A., Zeng, Y., 2020. From SARS and MERS to COVID-19: a brief summary and comparison of severe acute respiratory infections caused by three highly pathogenic human coronaviruses. Respir. Res. 21, 224. https://doi.org/10.1186/s12931-020-01479-w.