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2D materials as a diagnostic platform for the detection and sensing of the SARS-CoV-2 virus: a bird's-eye view

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Worldwide infections and fatalities caused by the SARS-CoV-2 virus and its variants responsible for COVID-19 have significantly impeded the economic growth of many nations. People in many nations have lost their livelihoods, it has severely impacted international relations and, most importantly, health infrastructures across the world have been tormented. This pandemic has already left footprints on human psychology, traits, and priorities and is certainly going to lead towards a new world order in the future. As always, science and technology have come to the rescue of the human race. The prevention of infection by instant and repeated cleaning of surfaces that are most likely to be touched in daily life and sanitization drives using medically prescribed sanitizers and UV irradiation of textiles are the first steps to breaking the chain of transmission. However, the real challenge is to develop and uplift medical infrastructure, such as diagnostic tools capable of prompt diagnosis and instant and economic medical treatment that is available to the masses. Two-dimensional (2D) materials, such as graphene, are atomic sheets that have been in the news for quite some time due to their unprecedented electronic mobilities, high thermal conductivity, appreciable thermal stability, excellent anchoring capabilities, optical transparency, mechanical flexibility, and a unique capability to integrate with arbitrary surfaces. These attributes of 2D materials make them lucrative for use as an active material platform for authentic and prompt (within minutes) disease diagnosis *via* electrical or optical diagnostic tools or *via* electrochemical diagnosis. We present the opportunities provided by 2D materials as a platform for SARS-CoV-2 diagnosis.

Introduction to COVID 19

The World Health Organization (WHO) received an alarming call from the national authorities in China on 21st January 2020 about an unknown infection spreading in the city of Wuhan in central China, the initial symptoms of which seemed to be like those of pneumonia. However, few details were known about the origin and transmission rate of the virus. Acknowledging the call from the Chinese authorities, a WHO team visited Wuhan and Hubei provinces and reported an unknown strain of virus (related to the Severe Acute Respiratory Syndrome human coronavirus (SARS-CoV) outbreak of 2003) on 11th February 2020 and named it "SARS-CoV-2".[1] Later, on further investigation, it was concluded that exposure to the virus 2019-nCoV leads to acute respiratory syndrome. Moreover, the amino acid sequence of the S-protein of the virus was 76.47% matched to that of the SARS-CoV virus and therefore the virus was renamed as SARS-CoV-2.[2] The process of investigation meant that it took some time to understand and realize how deadly this virus is for humans and within a short time the number of infected people rapidly increased worldwide, reaching 1,013,606 by the 3rd April 2020. By the end of January 2020, there were 9826 confirmed cases of SARS-CoV-2 and 213 deaths. However, this was just the beginning of the wide spread of SARS-CoV-2; 19 countries reported confirmed cases of SARS-CoV-2 and thus the WHO declared this outbreak of SARS-CoV-2 as a Public Health Emergency of International Concern (PHEIC) on 30th January 2020.[3,4] Further, this PHEIC was then recognized globally as a pandemic on 11th March 2020.[3]

SARS-CoV-2 was found to be related to severe acute respiratory syndrome human coronavirus (SARS-CoV) and thus is in the family of *Coronaviridae* and other similar *Nidovirale* viruses.[5] Fig. 1 shows the *Coronaviridae* family, including the sub-categories and family members related to SARS-CoV-2.

In the coronavirus family, alpha- and beta-coronaviruses are contagious to humans, while gamma- and delta-coronavirus are contagious to animals like pigs, birds, and whales.[5–8] It was

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suspected that these viruses originated from bats; however, this is just speculation as there was only 79% similarity of the genome with that of a strain collected from a bat that had SARS-CoV.[6–9] Moreover, homology modelling discloses that although there is a variation in the amino acid sequence of the SARS-CoV-2 virus in comparison to SARS-CoV, the receptor-binding domain structures are the same.[7–10] However, it is too early to say and it is not yet confirmed whether the virus originated from a bat or some seafood. The origin, mutation, and transmission of the SARS-CoV-2 virus warrant urgent investigation.

Fatality and transmission rate

In order, to understand the transmission rate of COVID-19 (SARS-CoV-2 virus), we considered some viruses that belong to the *Coronaviridae* virus family and some widely known viruses. At the time of writing this article, we found that COVID-19 has a fatality rate of ~3%, while viruses such as avian H7N9 (2013), seasonal flu, hantavirus, Spanish flu (1918), Ebola virus, H1N1 (1918), HIV, SARS-CoV, smallpox, pertussis/whooping cough, chickenpox, mumps, and measles have fatality rates of 40%, 0%, 35%, 2%, 70%, 80%, 10%, 65%, 3%, 4%, 0%, 1% and 0.3%, respectively.[11–19] While it is clear from Fig. 2 that the SARS-CoV-2 virus has a lower fatality rate compared to other widely known viruses from the same and other families, it does not mean that it will die out very soon and is harmless compared to other viruses. Untreated humans in some cases may require a ventilator in 7 days as this virus severely attacks the lungs and if a ventilator is not used then the lungs can be damaged, leading to death in 10 to 14 days.[2–7] However, some mild-symptom patients can self-heal through self-immunity.

Pranay Ranjan

Dr Pranay Ranjan graduated from the Indian Institute of Technology Patna (IIT Patna) in 2019. During his doctoral training, he received an industrial award for making a methane gas sensor and, after completion of his graduation, he won Best PhD thesis award. He holds a Bachelor (BTech, Hons.) degree in Electronics and Communication Engineering. In 2020, he joined United Arab Emirates University as a Postdoctoral Researcher. His research interests include 2D materials and their hybrids, gas sensing, water desalination and filtration, and semiconductor devices.

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Prashant Kumar

Prof. Prashant Kumar received his doctorate in physics in April 2009 from the University of Hyderabad and worked with Prof. CNR. Rao at JNCASR Bangalore as a DST Nanoscience Postdoc until June 2012. He then worked as a Raytheon-funded Postdoc with Prof. Timothy S. Fisher at Purdue University, USA. From April 2013 onward, he worked as an NSF-funded Postdoc with Prof. Gary J Cheng at Purdue University. Being awarded a Ramanujan Fellowship, he started working at the Indian Institute of Technology Patna in June 2015. His research interests include novel synthetic strategies for 2D materials and their hybrids and doped nanosystems with emphasis on energy solutions.

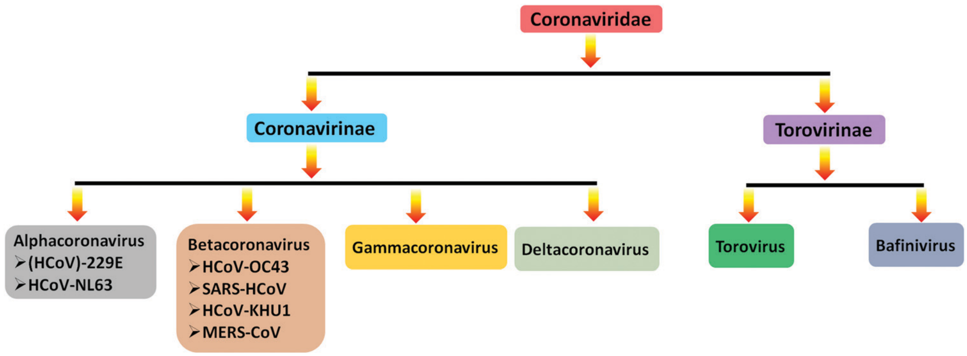

Fig. 1 Family of *Coronaviridae* viruses.[9]

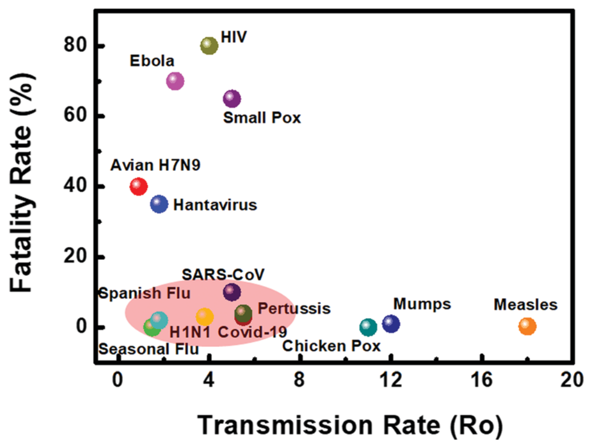

Fig. 2 Fatality and transmission rates of some viruses.[7–19]

Moreover, with a growing population, the density of people living in an area increases, therefore it will be misleading to compare the transmission rate of other known existing viruses and the SARS-CoV-2 virus. As a result, the graph in Fig. 2 is intended to develop the reader's perception of how virus transmission rates vary depending on the type of virus.

The mortality and fatality rates of these deadly viruses mean that they need to be detected at an early stage (see Fig. 3). However, testing presently relies on conventional techniques, which although being reliable take time to provide the test result. Therefore, worldwide there is a huge demand for the development of more realistic and reliable technology for the

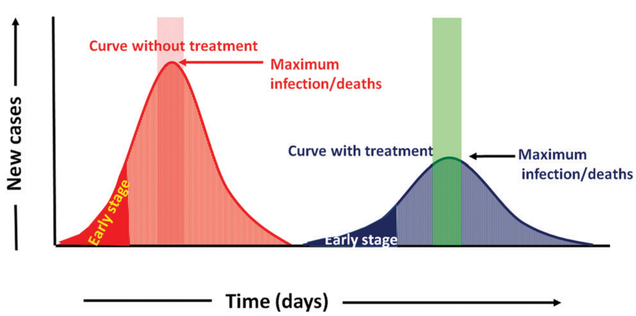

Fig. 3 Prediction of the spread, cure, and death of the SARS-Cov-2 virus in terms of sensitivity and time of detection, with and without treatment.[8]

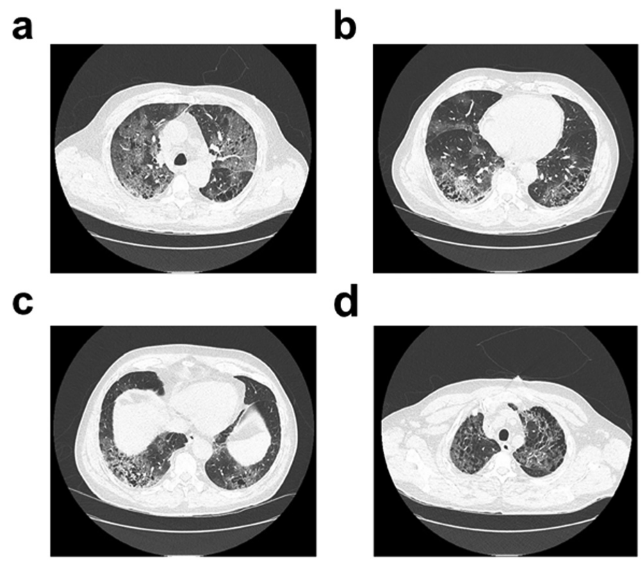

Fig. 4 CT scan of a 45 year-old COVID-19 patient demonstrating the spreading of the novel coronavirus (SARS-CoV-2) infection inside the lungs. Reproduced from Levine and Caputo,[30] JACEP Open 2020, published by Wiley Periodicals LLC on behalf of the American College of Emergency Physicians, under Creative Commons Attribution License.

detection of specific biospecies/microorganisms using very accurate diagnosis for monitoring the health of the patients. CT scan (see Fig. 4), fluorescence-based polymerase chain reaction (PCR), sequencing, and immuno/affinity reaction biosensing are some of the methods used to detect the SARS-C0V-2 virus.[20–22]

Covid-19 diagnosis

Nasopharyngeal swab sample collection is the initial step for the RT-PCR test. Contrary to the conventional PCR test, which needs an agarose gel and only gives results after a complete scan, the RT-PCR test is used to detect and quantify nucleic acids during the procession of the reaction.[23] It can also detect the amount of DNA in the sample. Detection of SARS-CoV-2 involves (a) identification of the envelope gene (E gene), the nucleocapsid protein gene (N gene), and the S gene[23–28] of the nucleic acid, and (b) selecting any two identified genes and measuring their fluorescence. This improves the sensitivity and specificity of the testing kit as it is cross-verified twice in a single run. Chan *et al.*[29] further analyzed, designed, and modified the RT-PCR assay by targeting RdRp/helicase. In comparison to the RdRp-P2 assay, the RdRp/helicase assay does not react with other members of the coronavirus family, thus increasing the sensitivity. Moreover, when the test sample is connected with PCR for the analysis, the signals for the virus are only amplified in the regions containing the virus sites.[27–29] In addition, a PCR test can only be performed by a skilled individual, thus, one can conclude that the use of PCR equipment for detecting the SARS-CoV-2 virus makes it a labour-intensive, sophisticated, time-consuming, and expensive methodology, thus limiting its use in general laboratories.[27–29]

Alongside laboratory testing, which often takes a long time for detection, a prime detection technique that nowadays is very useful for the diagnosis of COVID-19 is computed tomography imaging (CT imaging). As the SARS-CoV-2 virus attacks the lower respiratory tract, leading to pneumonia or bronchitis, it is easy to detect its presence through X-ray or chest CT imaging.

CT imaging has been shown to have a promising role in the diagnosis of COVID. The CT imaging report of a COVID-19 patient shows deterioration in his lung capacity as well as an increased multiple lobular over a while (see Fig. 4(a–d)). This kind of report is found to be similar to cases diagnosed as pneumonia. However, COVID and pneumonia cases can easily be segregated using artificial intelligence (AI). For instance, AI-driven CT images can be used to understand the signature for COVID based on high-resolution coloured images and signature of the lobular of the lungs from the CT scan. These are the key initial indicators for differentiating the results for COVID patients from those of pneumonia and can help to control the pandemic. These detection techniques are likely to reduce the fatality rate and are expected to reduce hospitalizations.

Several existing techniques for detecting COVID rapidly and with high sensitivity are shown in Fig. 5. Another promising method is the loop-mediated isothermal amplification (LAMP) test. Unlike the PCR test, which is quite complex and is not economical, LAMP is used to amplify a nucleic acid signature under isothermal conditions.[31–33] LAMP is a well-known and established technique used to detect different kinds of viruses. Le *et al.* used the LAMP technique for real-time monitoring of patients infected by influenza-like illness. The high sensitivity of >88.8% and specificity of ~100% were demonstrated by Takayama *et al.* in 2019.[34] However, the technique used by Takayama *et al.* involves a nucleic acid purification step using a commercially available RNA isolation kit as well as preparation of the reaction mixture at very low temperatures. Nakauchi *et al.*[35] proposed a much-optimized LAMP technique known as rRT-LAMP. It involves the preparation of the reaction mixture in a lyophilized form, which eases the integration into the diagnostic kits, thus reduces the time of transport and storage time during shipment of the kit to the testing laboratory. This technique is also known as the new direct rRT-LAMP assay and is predicted to be a rapid and simple solution for the molecular detection of viruses (such as COVID or influenza) as it has high sensitivity and specificity.

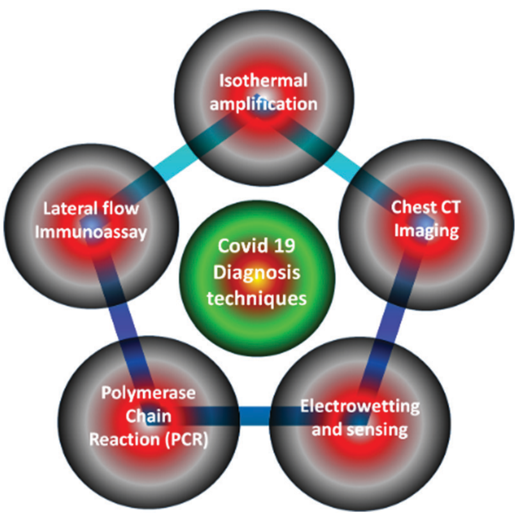

Fig. 5 COVID-19 detection techniques.

Since being introduced in the mid-1980s, lateral flow (LF) immunoassay tests, introduced in the mid-1980s are yet another technique that has been widely adopted for the detection of SARS-CoV-2. It is also known as immune-chromatographic strip tests. As the name ''lateral flow'' suggests, the technique involves fluid migration through paper or plastics. Although LF is a complex technique to detect the SARS-CoV-2 virus, due to the involvement of a number of instruments and storage of the data from each instrument, it is widely trusted and have been used to test the SARS-CoV-2 virus.[36] LF tests are also used in clinics, hospitals, and at home as they offer versatility to the manufacturers to tune the selectivity and specificity for any situation requiring rapid detection. LF tests involve the detection of disease-specific samples from urine, saliva, serum, plasma, blood, tissue, or fluids. Another prominent reason for using LF tests is the cost and time involved in making the kit. In addition to all these techniques, SERS-based detection is predicted to be the most sensitive and accurate for the diagnosis of COVID (as discussed later in this article).

Significant research efforts have been devoted to the development of new SARS-CoV-2 diagnostic tests that are faster and more reliable.[37–40] A brief comparison to understand the different detection techniques for the SARS-CoV-2 virus can be summarized as follows: the RT-PCR and immunoassay methods have sensitivities of 95% and 20–80%, respectively, but at least 4 h detection time is required in both cases. High-throughput RT-PCR kits can give results in under two hours.[41] Interestingly, LAMP and computed tomography are the only two tests with sensitivity greater than 97% and 95%, respectively. In comparison to RT-PCR, a lateral flow chromatographic immunoassay test can detect and confirm the presence of immunoglobulin G (IgG) and immunoglobulin M (IgM) antibodies in blood samples taken from a patient within 15–20 minutes,[42] while LAMP and computed tomography require only 30 min and <1 min, respectively, for detection of the SARS-CoV-2 virus.[7,8,34–42]

Ahmadivand *et al.*[37] detected (SARS)-CoV-2 virus proteins at femtomolar (fM) levels using a very effective and efficient mode of detection called plasmonic meta sensor technology.

They fabricated a miniaturized plasmonic immunosensor based on the concept of toroidal electrodynamics concept, which works in terahertz (THz) frequencies. It enables SARS-CoV-2 spike proteins to be detected at femtomolar concentrations with high precision and can detect SARS-CoV-2 proteins within ~80 min. In yet another seminal work reported by Kaushik *et al.*,[43] Mujawar *et al.*,[44] and Paliwal *et al.*,[45] detection of the SARS-CoV-2 virus using biosensing integrated with an AI- and IoT-supported platform was discussed to create a database for early-stage diagnosis, cognizance of the spread and its effect, type of strain and related disease in a sequential manner to overcome the problems associated with it. Moreover, the role of AI- and IoT-supported SARS-CoV-2 detection selectively at the low level desired for early-stage SARS-CoV-2 virus diagnostics point-of-care (POC) sensing by selecting an appropriate nanotechnology-based device and its design, packaging, integration, and sensing were discussed. POC has been further used to generate crucial information for understanding the efficacy of therapy, progression of disease, *etc.* Furthermore, Mujawar *et al.*[44] described the use of low-level targeted disease biomarker (pM level) detection, which is useful for correlating and studying the progression of the disease and its therapy. Kaushik *et al.*[46] reported an effective way of neutralizing the SARS-CoV-19 virus using manipulative magnetic nanomedicine (MMN) therapy, which offers control over drug delivery and the option to choose the desired therapeutic medicine. In another seminal work by Vicky *et al.*,[47] the authors analyzed and summarized more than 1000 articles related to SARS-CoV-19 and justified why Alzheimer's and dementia-related illness patients are more at risk from COVID-19. They reviewed 28 vaccines, their treatment protocols, and clinical trials, along with the diagnostic tools and therapeutics for SARS-CoV-19, for an effective and efficient way of handling the disease.

Suitability of 2D materials for SARS-CoV-2 virus sensing

Two-dimensional (2D) materials such as graphene, borophene, transition metal dichalcogenides (TMDCs), MXenes, plumbene, and hematene have unprecedented physical and chemical properties. They have a high surface area, weak inter-layer bonding, and strong covalent in-plane bonding, which open up a plethora of applications in sensitive, selective, and specific platforms that can rapidly detect analytes or molecules or microbes at the parts per million/billion level.[48] Amongst the family of 2D materials, graphene, borophene, and phosphorene have shown potential to address a range of global societal challenges, including healthcare-related problems. 2D materials (owing to their large surface-to-volume ratio, anchoring capability, thermal stability) play a crucial role in the detection of analytes as they provide excellent electrical, optical, mechanical, and chemical properties for device performance. Owing to their excellent optical and electronic properties, they have been considered as futuristic materials for imaging in photo-acoustic, photothermal and X-ray computed tomography. Moreover, due to their superior optoelectronic properties, they have been used in photodynamic and photothermal therapy. Transition metal dichalcogenides seem to be an obstacle for various biosensing applications due to their relatively lower carrier mobility in comparison to MXene (borophene, phosphorene, and their cousins) and graphene. The MXene family offers a tunable bandgap, which has the potential to manipulate the interaction between electromagnetic waves and the xenes, within the NIR to UV wavelength region.[49] Surprisingly, these 2D materials are used for the detection of molecules (such as germs or microbes), integrating many branches of science, including nanotechnology, chemistry, physics, and materials science, and collectively they drive bioelectronics and bioengineering.[50–53]

Sensing *via* SERS is a more rapid and effective detection technique for the SARS-CoV-2 virus and is an integral part of bioelectronics. It saves time and money. Bioelectronics plays a crucial role in the detection of various biological microorganisms. It has opened a vibrant and vivid research field in electronics, bioengineering, and biotechnology. Detection of functional bioactive molecules such as DNA, RNA, protein, microorganisms, and antibodies[54–62] using techniques such as field-effect transistors (FETs), nanowire arrays, optical resonators, surface-enhanced Raman scattering (SERS), and electrochemical sensing (Fig. 6) has evolved over the past few decades.[63–76] Bioelectronic devices generate signals on interaction with biospecies. Typically, the signal generated is in the form of an impulse or current, voltage, resistance, conductance, or frequency.

Field-effect transistor-based sensing

In the 1970s, ion-sensitive field-effect transistors (ISFET) were invented by Bergveld *et al.*[77] It was realized that ISFET could be used for the detection of numerous biosensor targets. The subsequent time-based evolution of the technology changed the design and fabrication of FETs. Typically, a FET consists of a semiconductor path called the sensing channel, which has its two sides connected to the source (S) and drain (D) electrodes (Fig. 7). FETs are divided into two types based on the detection techniques, *i.e.*, n-type (it uses electrons as the charge carriers) and p-type (it uses holes as the charge carriers). For a typical n-type FET, if the target molecules have a positive charge and get attached to the channel then it leads to an increase in channel conductivity, while if the target molecules have a negative charge then it will lead to a decrease in the channel conductivity, and *vice versa* for a p-type FET.[78,79] It can be inferred that the anchoring, detection, and signal transmission are controlled by the channel path.

A change in the channel resistance of the FET device reveals information about the analyte. This state of the art is currently being used for wearable devices and neural interfacing technology. Li *et al.*[80] demonstrated a graphene-based FET (G-FET), in which the channel was made up of a micromechanically exfoliated graphene sheet integrated with mercury ions. Graphene, known for its high mobility and conductivity, detected 0.1 parts per billion (ppb) of mercury. Surprisingly, the graphene-based channel exceeded

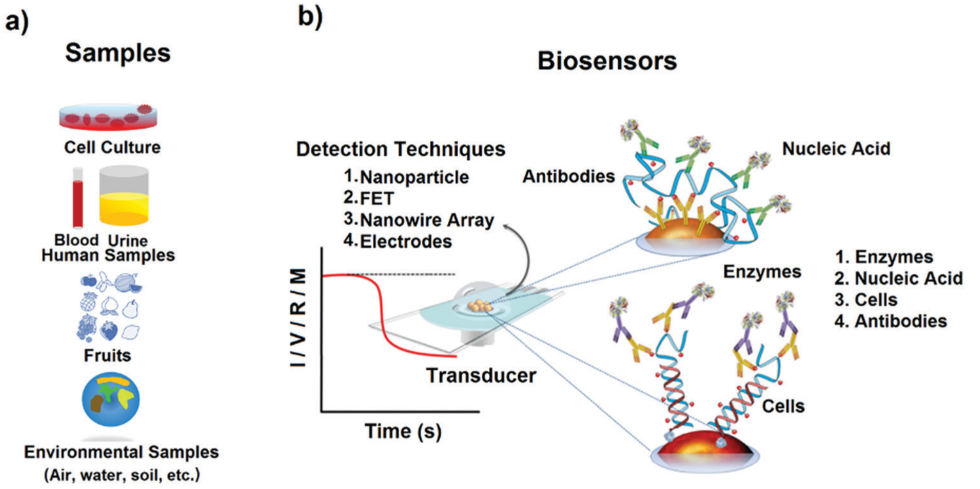

Fig. 6 (a) Targets for biosensing. (b) Schematic display of biosensors. Reproduced from Povedano *et al.*,[31] Sci Rep 2018 by Springer Nature, under Creative Commons Attribution License.

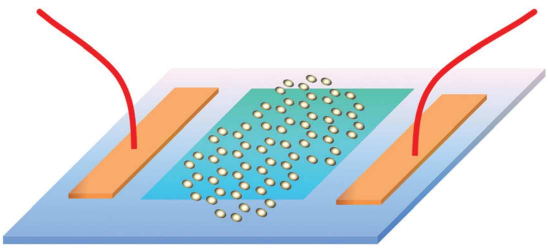

Fig. 7 Schematic diagram of a 2D material channel-based FET biosensor.

the World Health Organization tolerance limit for mercury of 1 ppb and in comparison to commercially available ISEs devices for detection of mercury, the sensitivity has been increased by a factor or more than 1000 times.[81,82] As well as graphene, other 2D materials, such as MoS_2, black phosphorus, and h-BN, are also used as channel materials in FET devices.[83–85] Lee *et al.* demonstrated the use of an MoS_2-based channel for the detection of DNA hybridization.[86] In comparison to the PCR detection technique, which requires continuous amplification during the testing cycle, FET-based devices give detection of low levels of targeted nucleic acids without pre-amplification.[87] Carbon nanotubes (CNTs) and silicon (Si) nanowires have also been used as channel materials in FET devices; however, the difficulty in the fabrication of nanowires and nanotubes along with the reproducibility as well as the cost of production limits their use in FET devices.[88–91] Mannoor *et al.* demonstrated whole-cell bacterial detection using chemical vapour deposition (CVD) grown graphene as a channel material for sensing.[87] They used CVD-grown layers of graphene sheets anchored with antimicrobial peptides as well as coil micro antenna on biocompatible silk to detect a single *E. coli* bacterium.[92] Further evidence of graphene and functionalized graphene for whole-cell detection was reported by Guarnieri *et al.*[93] and Pandey *et al.*,[94] who applied it for the detection of human intestinal epithelial cells and *E. coli*, respectively.

Materials for channels are, therefore, the most crucial components, which need to be evenly considered and designed. 2D materials, such as graphene, borophene, and alpha lead oxide, not only provide high conductivity, mobility, and enhanced mechanical strength but also helps in anchoring the target molecules due to the high surface-to-volume ratio and rapid, accurate, and early recognition of the molecules. 2D materials outnumber all the conventional materials used in FET as roughness in the morphology of the channel is bound to give errors and unrealizable outputs from the device due to the scattering effect. The most advantageous aspects of 2D materials in FETS are that they are rapid, economical, low-cost, and easy to use because the real-time analysis is being monitored, which can eventually be monitored and analyzed for end-user applications.

Although FET-based biosensors have many advantages over other sensors, charge screening is the most common problem faced by FET devices for biological media detection. As charge screening is mainly associated with electrolytes and the Debye length (λD) and both factors are inversely related, one of the possible solutions is ways to avoid it is by diluting the sample to a lower concentration.[94–96] However, this may lead to surface functionalization of the targeted molecules or analytes. The next possible approach is to make the targeted analyte within the size of the Debye length but this seems to be less feasible considering the size of the target and functional groups. Many new innovative and upcoming ways to avoid charge screening still need to be investigated to create a new area of futuristic research based on biomolecule-targeted FET devices.[95–98]

Surface-enhanced Raman Scattering (SERS)-based sensing

SERS is a bioelectronic technique that uses the change in frequency to provide a rapid, non-invasive way to detect the signature of biological samples with ultrahigh sensitivity. Moreover, it does not involve a complex process or require a skilled hand to obtain the results. However, in the early days, SERS platforms required complex and complicated substrates.

SERS techniques using nanostructured surfaces apply a localized electromagnetic field (EMF) near to the surface zone, resulting in the enhancement of the signal by typically 10^6 times. Usually, gold or silver nanoparticles with different sizes and shapes or cofmposite/hybrid nanoparticles with core–shell structures or periodic structures are used for SERS platforms. Lim *et al.*[99] utilized SERS for the detection of the influenza virus. Moreover, different strains of the influenza virus were easily detected through SERS. Yeha *et al.*[100] detected avian influenza A viruses using the SERS platform. In addition, it was claimed that viruses such as rhinovirus, influenza virus, and parainfluenza viruses can also be detected with their unmodified structure and with new strains. It was also revealed that SERS can give selectivity when there more than two viruses are present. The active detection of the influenza virus was also reported by Park *et al.* and Kukushkin *et al.*[101,102]

Graphene was the first 2D material to be applied for SERS (Fig. 8) and a variety of organic dyes (phthalocyanine (Pc), rhodamine 6G (R6G), PPP, and crystal violet (CV)) have been used for detection using graphene.[103–105] Early-stage detection of viral infection is the key to curing the infection but at a very early stage the SERS signal from the test molecules is very weak. To enhance the signal, therefore, one needs to enhance the laser intensity of the incident beam and at that intensity, unfortunately, test molecules get degraded. Interestingly, the high thermal conductivity of graphene comes to the rescue and helps remove interfacial heat generated upon laser exposure and thus acts as a laser shield for underlying plasmonic nanostructures on the one hand and prevents bond breaking and carbonization of test molecules on the surface on the other hand.[106,107] Atomic-scale integration of plasmonic nanostructures and graphene has been proposed and implemented for the effortless removal of heat during SERS measurement.[107–109] 2D materials hetero layers offeres tunability of the intrinsic properties of the materials behaviour, such as mobility enhancement of graphene when placed on top of an insulating boron nitride (BN). Inter-layer coupling amongst atomic sheets can be exploited to manipulate out-of-plane tunnelling behaviour[110] in these hetero-layer stacks and thus they can be implemented to attain functional fast biochips. The inception of 2D materials has completely revolutionized this field of research by providing a simple, scalable, low-cost platform. The absence of dangling bonds (out-of-plane) in 2D material makes them the most suitable platform to explore the chemical enhancement mechanism. However, 2D materials have not yet been used for the detection of viruses or microbes.

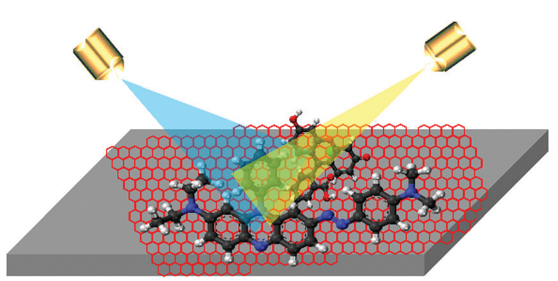

Fig. 8 Schematic diagram of 2D material-based SERS platform.

Future work and perspectives

Immediate detection of the SARS-CoV-2 virus is the need of the hour. Moreover, lack of time and available technology, as well as basic knowledge of this unknown new virus, are threats and big challenges to overcome. As the strain, size, structure, and spread rate of the virus are continuously changing, and the development of a vaccination seems to be in its nascent stage, we need to think an outside of the box solution in terms to detect the early presence of the SARS-CoV-2 virus. Materials science, especially 2D materials-based devices, is one of the ways of detecting and preventing the wide spread of the virus. Furthermore, early and rapid detection can prevent severe organ failure and reduce the death rate. Though several portable, inexpensive, invasive devices are present in the market for testing, they take time to give results for infected people. Yet, after consuming time and delaying the treatment that one infected person needs at that hour, these tests are not reliable everywhere as they need an expert and skilled operator.

2D materials-based detection techniques, such as SERS, Bio-FET, electrochemical sensing, and photoluminescence spectroscopy (Fig. 9), currently seem to be among the promising techniques for the detection of the SARS-CoV-2 virus. The absence of dangling bonds, high conductivity, mobility, luminescence (size dependent), weak van der Waals attraction between layers as well as their anchoring capability (in the case of graphene, borophene, phosphorene, and transition metal dichalcogenides) make them desirable futuristic materials for the detection of viruses. The unprecedented physical and chemical properties of 2D materials make them a platform for high sensitivity, specificity,

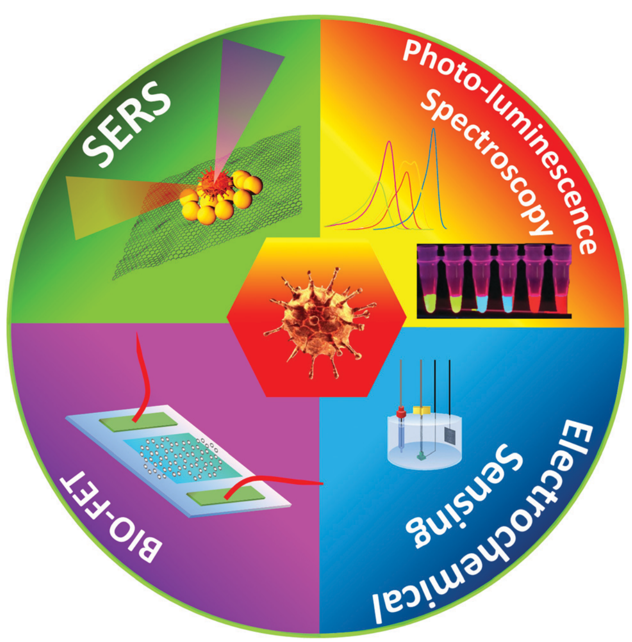

Fig. 9 2D material-based devices for detection of SARS-CoV-2.

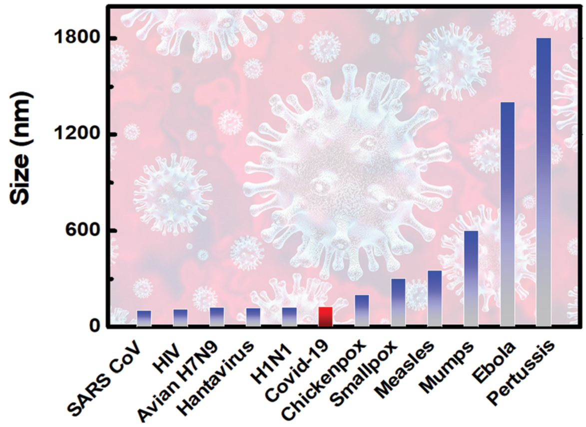

Fig. 10 Sizes of different viruses.[111–122]

and selectivity for the detection of different viruses and ensure rapid, early, effective detection of microbes. Even in a short period, 2D materials have outperformed several existing and well-recognized methods for preventing the spread of the SARS-CoV-2 virus. 2D material (graphene)-coated fabrics such as masks, PPE kit, gloves, and shoes are currently being used at the commercial level. This is possible because the inter-atomic distance of two atoms in graphene is 0.14 nm, which is far small than almost each harmful microbes, apart from their mechanical flexibility. The size of some harmful, fatal, and communicable viruses is compared with SARS-CoV-2 in Fig. 10. Graphene can even be embedded inside a polymer fabric and at a filler level higher than a threshold the fabric will be electrically conducting, which then can be used for the removal of the virus from its surface in an electrically controlled manner.[123] In case of rapid detection of any virus or analyte, mobility and charge carriers play a huge role. The electronic mobility of 2D materials relies on the size, shape, strain, atom valency, crystallinity, and chemical bonds. Therefore, the electronic mobility is an intrinsic characteristic of a material.

Even though boron nitride (BN) is an insulator and has a low mobility of 0.05 cm^2 V^{-1} s^{-1} (see Fig. 11),[76] 2D semimetals such as graphene, metals such as borophene, and semiconductors such as MoS_2 exhibit excellent mobility enhancement when placed on an atomically smooth, dangling-bond-free and charge-passivated BN layer. With the recent surge in 2D material Moire superlattices as tunable metamaterials, different hetero-layers composed of 2D materials have been proposed as active surfaces for authentic SARS-CoV-2 virus detection *via* two probe, 4 probe, and FET measurements, as well as SERS-based molecular sensing in liquid phase containing blood, tears, sweat or saliva (see Fig. 12). Nanomaterials in general and atomic sheets, in particular, are thus proposed to have tremendous potential in prompt detection and prevention of the SARS-CoV-2 virus. Research in this direction has just commenced worldwide and as a materials platform, 2D materials are destined to bestow the best performance in times to come. Even though recent literature on the use of nanotechnology motivates research along these directions and due implementation, the present review on employing two-dimensional materials along with their doped

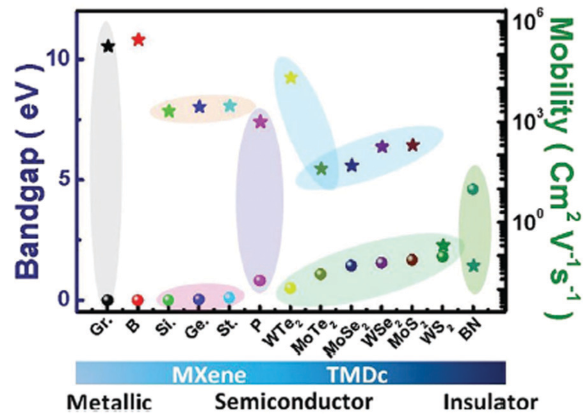

Fig. 11 Bandgap *versus* mobility of various 2D materials Reproduced with permission from Ranjan *et al.*,[76] Adv Mater 2020, Copyright 2020, Wiley-VCH. Amongst the Xene family, graphene and borophene have electronic mobilities of 180 000 and 280 000 cm^2 V^{-1} s^{-1}, respectively. These values are the highest amongst 2D materials. Cousins of graphene, *viz.* silicene, germanene, stanene, and phosphorene, however, have moderate mobilities of 2100 cm^2 V^{-1} s^{-1}, 2800 cm^2 V^{-1} s^{-1}, 3000 cm^2 V^{-1} s^{-1}, 1000 cm^2 V^{-1} s^{-1}, respectively.[70,76] In general, semiconductor 2D materials from the transition metal dichalcogenides (TMDCs) family have low mobility, however, this is compensated for by the carrier concentration.[70,76] Thus, even though these 2D semiconductors may not be apt for ultrafast detection, the electrical signal will be enhanced as conductivity is the product of mobility and carrier concentration.

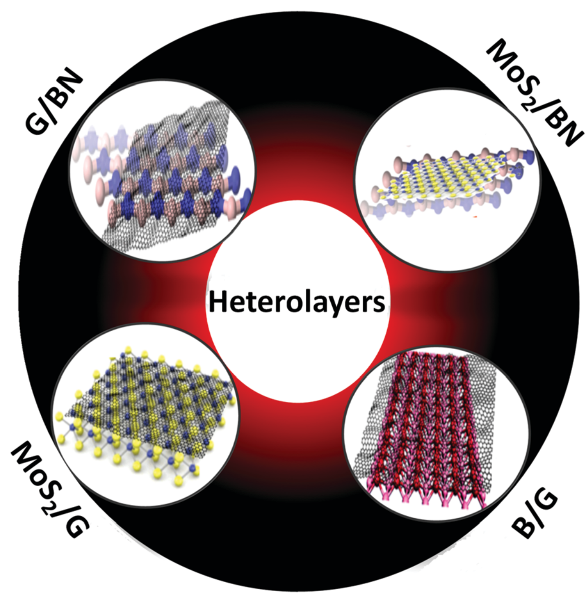

Fig. 12 2D material heterostructures as active materials in FET devices.

and hybrid versions should inspire on-demand prompt diagnosis and treatments.[123–133]

Conclusion

It is evident that the SARS-CoV-2 virus is a modified form of SARS-CoV and the alpha-coronaviruses, and that beta-coronavirus are contagious to humans. Moreover, the fatality rate of SARS-CoV-2 (nearly 3%) has been found to be lower than those for HIV, Ebola, smallpox, and avian H7N9. In addition, the transmission rate of SARS-CoV-2 is comparable with that for pertussis and is far less than those for mumps and measles. Detection of the SARS-CoV-2 virus seems to be practically possible with various sensing techniques, such as PCR, electro-wetting and sensing, and LAMP test. However, it was found that the RT-PCR test was the best amongst all existing techniques considering time and sensitivity. Detection of the SARS-CoV-2 virus also seems to be possible with the use of 2D materials as the sensing platform. In this respect, different 2D materials, such as graphene and borophene, have been deemed to be effective in SERS and biosensing (FET) for the detection of the SARS-CoV-2 virus. Biosensing with 2D materials can be applied for rapid detection, analysis, and research on the SARS-CoV-2 virus. Materials like graphene, MXene, borophene, and their hybrids are futuristic materials for developing testing kits for viruses.

Author contributions

All authors were involved in the literature data collection, conceptualization, writing, editing, and proofreading of this review manuscript.

Conflicts of interest

The authors declare no conflict of interest.

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