Review Article

Kamrun Nahar Fatema, Suresh Sagadevan, Ju Yong Cho, Won Kweon Jang, and Won-Chun Oh*

Graphene-based nanocomposite using new modeling molecular dynamic simulations for proposed neutralizing mechanism and real-time sensing of COVID-19

Abstract: A new virus, the coronavirus (COVID-19), is causing serious respiratory infections in humans. Rapid, specific, and sensitive diagnostic techniques for early-stage detection of SARS-CoV-2 viral protein are developing as a necessary response for effective smart diagnostics, treatment optimization, and exploration of therapeutics with better effectiveness in the fight against the COVID-19 pandemic. Keeping the considerations mentioned above, we propose a new modeling graphene nanocomposite-based biosensing device for detecting COVID-19 at the site of the epidemic as the best way to manage the pandemic. It is important to address the problems of COVID-19 management. With the challenges and aspects of COVID-19 management in mind, we present in this review a collective approach involving electrochemical COVID-19 biosensing required for early-stage COVID-19 diagnosis and the direct interaction with viral surface glycoproteins and metal nanoparticles that can enter cells and neutralize viruses by interacting directly with the viral genome (ribonucleic acid), which identifies the COVID-19 spike protein and antiviral procedure including virus inactivation, host cell receptor inactivation, electrostatic entrapment, and physicochemical destruction of viral species by
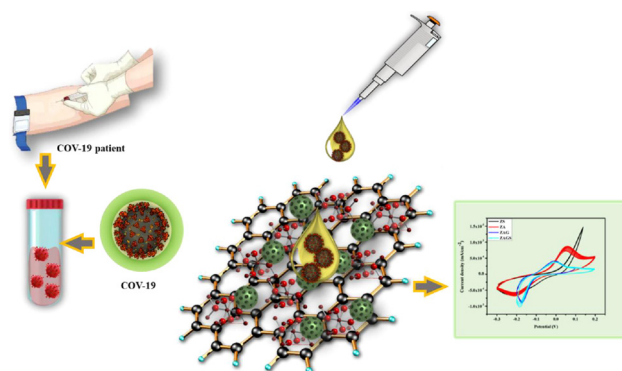
Graphical abstract

nucleotide ring opening. The interactions between the graphene composite and virus may be boosted by functionalization of the carbon surface and decoration of metallic components that enhance these interactions. Our proposed new modeling molecular dynamic simulation-based neutralizing mechanism and real-time detection of COVID-19 on graphene nanocomposite-based biosensors are suitable for point-of-care diagnostic applications, and this sensing platform can be modified for the early diagnosis of severe viral infections using real samples. For the potential application, the suggested one is the chemical reaction and bond breaking between the metallic component and molecule of COVID19 with computer simulation data.

Keywords: new modeling, real-time sensing, COVID-19, neutralizing mechanism, graphene nanocomposite, electrical signal, virus concentration

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1 Introduction

Coronavirus disease 2019 (COVID-19) is a recently emerging disease associated with severe respiratory trouble.

Global recovery from COVID-19 infection may be hampered by more recent SARS-CoV-2 mutations. If the SARS-CoV-2 virus continues to replicate, evolve, and disseminate, new strains of the virus will certainly emerge. Recent studies in India have shown that the new strains of SARS-CoV-2 that are worrisome are more lethal and spread more quickly than the original strain. These new strains have been found in the United Kingdom, Brazil, South Africa, and the United States [1–10].

Recent research discovered that COVID-19 uses angiotensin-converting enzyme II (ACE2) as a cellular receptor [11,12]. The genome of the respiratory infection virus codes for two surface glycoproteins (proteins G and F) was discovered on the viral envelope. Silver nanoparticles bind to glycoproteins found in viral films that are cysteine-rich, and these can effectively bind to thiol groups found in cysteine buildups. This interaction keeps the viral molecule at a safe distance from an endosome and helps internalize silver nanoparticles that inhibit viral protein replication, and joins them to the viral glycoprotein to avoid viral coating. Based on previously published research facility conventions [13–15], RT-PCR is currently being used to detect COVID-19. Atomic determination with RT-PCR takes at most 3 h, counting the viral ribonucleic acid (RNA) arrangement. Furthermore, the RNA planning step can have an impact on demonstrative precision.

Nanotechnology has played a key role in recent biomedical and bioengineering breakthroughs, such as developing and implementing therapeutic nanomaterials for cancer diagnostics and treatment, drug delivery, and tissue engineering. As a result, researchers worldwide have recently used various approaches to improve results by introducing some new properties into this graphene sheet. The incorporation of metal nanoparticles in the graphene sheet is one of the most prevalent approaches. Researchers are very interested in metal nanoparticles because of their potential applications in various sectors. Similarly, nanotechnology and nanoscience may open new avenues in the fight against many pathogens, including COVID-19, by various methods, including virus detection, viral illness diagnosis, and nanovaccines, such as lipid nanoparticles, for the prevention and/or treatment of infections.

Among the numerous symptomatic approaches currently available, graphene-based biosensing devices possess a few advantages, including the ability to create extremely delicate and momentary estimations by utilizing small amounts of analytes [16,17]. Graphene-based biosensors may be useful in clinical decision-making, point-of-care testing, on-site location, and sensitive immunological determination [18]. It has proven to be a valuable fabric at various detection stages due to its exceptional properties, which include high electronic conductivity, high carrier portability, and a large zone [19–21]. In general, there are two methods for using nanomaterials against viruses. One strategy considers a virus-neutralizing external stimulation. The interaction of virus surfaces with the nanomaterial utilized as an antiviral drug is the subject of another approach. As a result, studying the interactions of graphene materials with viruses should be a priority. The antibacterial activity of graphene nanomaterials can be explained by many processes, including membrane, oxidative, and/or photothermal stresses, charge transfer, and the entrapment impact of graphene materials on specific bacterial species. Due to large disparities in virus (2–300 nm) and bacteria (500–5,000 nm) size, viral studies are more difficult and expensive to undertake in contrast to bacteria.

Graphene-based biosensors can detect surface changes and provide an ideal detecting environment for ultrasensitive and low-noise locations. Silver nanoparticles (Ag-NPs) are among the most used metal nanoparticles due to their superior electrical, electrochemical, and detecting properties compared to other metal nanoparticles. Because cells treated with silver nanoparticles do not affect viral replication, Ag-NPs inactivate the virus before it enters the cell [22]. Because of its extraordinary chemical and physical properties, silver-enhanced graphene is one of the most widely used materials in various fields, including detection, energy storage, drugs, and business. The decoration of such metal nanoparticles on the graphene sheet can enhance the properties of the graphene sheet to many fold times with their applications in various fields [23–28].

In that view, we developed a graphene-based biosensing device equipped with a COVID-19 spike counteracting agent for use as a COVID-19 infection location stage. It was immobilized onto the developed device *via* *N*-hydroxysuccinimide (NHS) ester, a skilled interface coupling operator used as a linker. Most importantly, we confirmed the neutralizing mechanism and real-time detection of COVID-19 on a graphene nanocomposite-based biosensor using new modeling molecular dynamic simulations, which has the potential for clinical application by identifying COVID-19 antigen proteins in the transport medium used for blood serum, refined COVID-19 infection, and COVID-19 infection from clinical tests.

These findings demonstrate the successful development of a COVID-19 graphene nanocomposite sensor based on the integration of a COVID-19 spike counteracting agent with a graphene nanocomposite, enabling extremely sensitive location of the COVID-19 infection in clinical tests.

2 Urgency of diagnosis of COVID-19

The standard for COVID-19 nonintrusive conclusion is the location of viral nucleic acid [29–44]. In any case, because of the discovery of SARS-CoV-2, nucleic acid has high specificity and low affectability, there may be false-negative results and the testing time may be lengthy [44–60]. For the detection of COVID-19, real-time switch transcriptase-PCR (RT-PCR) is now preferred [61,62]. Coronavirus tests are based on genomic detection and immunoglobulin detection (serology). Identifying the infection in humans is based on hereditary material specific to COVID-19 infections in a person's nasopharyngeal secretions and test units use a wide range of strategies that identifies a specific portion of the viral genome [63–71]. The tissue swabbed is stacked into a standard response vial. This enables other reagents, such as synthesized RNA attaching to specific small portions of the viral genome, to access the infection. This small bound-up strand of the viral genome and reagent is then replicated numerous times for minutes to hours. At that point, another reagent specifically ties to each reproduced hereditary complex. This reagent contains a bound marker that, when enough replicated complexes are made, can be identified by the machines on their sensors. Positive results can occur in minutes to days, depending on how many infections are detected in the test [72–84]. Alternatively, if the test detects no viral material after a set period (minutes to days), the result may be a negative test. The subjective result of these tests is that either the individual is infected with COVID-19 and capable of transmitting the illness (a positive test) or the individual is negative for the infection [85–96]. This test cannot determine whether a person is resistant to previous infection, has yet to be discovered, or is still at risk [72].

Human antibodies are divided into five isotypes (IgM, IgD, IgG, IgA, and IgE) based on their H chains, which provide each isotype with distinct characteristics and roles. Immunoglobulin location tests are based on the subjective detection of IgM and IgG antibodies that are specifically produced by the body in response to COVID-19 infection [72]. IgM is typically the primary anti-inflammatory agent type produced by the body in response to the disease. At that point, the IgG antibody is produced, which replaces IgM as the dominant counteracting agent in response to the disease. Contaminations are combated by IgM and IgG antibodies that target antigens on the surface of the SARS-nCoV-2 infection. Immunoglobulin tests commonly use viral antigens to distinguish IgM and/or IgG antibodies against these antigens. If either complex is bound to the stable anti-IgM or anti-IgG, it will be captured and a signal is produced as a result. The results should be studied within 10 min and no longer than 15 min. This can tell whether the result has been discovered previously or has never been discovered for COVID-19. As a result, we proposed developing a graphene-based biosensing device that is functionalized with a COVID-19 spike counteracting agent for use as a COVID-19 infection location stage.

2.1 Design of the graphene-based COVID-19 sensor

2.1.1 Instruments

Morphologies were studied utilizing scanning electron microscopy (SEM) (JSM-76710F; JEOL, Tokyo, Japan), transmission electron microscopy (TEM) (JEM-4010; JEOL, Tokyo, Japan), and high-resolution TEM (JSM-76710F; JEOL, Tokyo, Japan) at 300 kV accelerating voltage (PG201, Potentiostat, Galvanostat, Volta lab™, Radiometer, Denmark), A computer simulation was performed using Spartan 14 software.

2.1.2 Selection of the antigen and validation of the antibody

COVID-19 encodes four auxiliary proteins: spike, envelope, lattice, and nucleocapsid [8,97]. The spike protein is best suited for use as a symptomatic antigen because it is a major transmembrane protein of the infection and is highly immunogenic. Furthermore, the spike protein exhibits amino corrosive grouping differences among coronaviruses, enabling the discovery of the COVID-19 antigen [4,8,9,11,14,15,98,99]. To distinguish this infection, a COVID-19 spike counteracting agent was used as a receptor. Immobilizing the COVID-19 spike counteracting agent onto a graphene nanocomposite-based biosensor recently confirmed the execution of this agent by the

enzyme-linked immunosorbent assay (ELISA). The findings revealed that the antagonist is bound to the COVID-19 spike protein but not to the MERS-CoV spike protein or bovine serum albumin (BSA). These perceptions confirm that the antagonist is for the COVID-19 spike protein and is thus appropriate for recognizing COVID-19. The binding agent location constraints within the ELISA stage were 4 ng/mL [8].

2.1.3 Preparation of the COVID-19 sensor

We used electrical estimations to determine the proximity of the COVID-19 spike counteracting agent on the graphene surface. Figure 1 depicts the CV and current–voltage (I–V) plots for the graphene nanocomposite-based biosensor during a recent run from 0.2 to +0.2 V after connecting *Escherichia coli*. The slopes ($\mathrm{d}I/\mathrm{d}V$) decreased after PBASE functionalization and immobilization of the counteracting agent onto the graphene channel. Thus, our proposed sensor case makes the incline fruitful presentation of the COVID-19 spike counteracting agent more

plausible. As a result, our proposed sensor case makes the incline fruitful presentation of the COVID-19 spike counteracting agent more plausible by an electrical flag with the COVID-19 sensor.

2.1.4 Fabrication of the graphene-based sensor

Graphene nanocomposite-based thin films were developed using the traditional doctor-blade method [58]. For the modified doctor-blade method, sample paste was prepared as follows: First, the synthesized material powder (1.1 g) was mixed with ethylcellulose and acetone (1.5 mL) in a mortar for 15 min. The FTO glass was shielded through the sample paste to make a thin film. Afterward, the film was dried in open air for 35 min. One drop of lubricating oil was put onto the film surface and stabilized at 374 K in the oven for 25 min to reduce cracks. The lubricating oil on the film will enable sensor/chip devices to prevent the loss of species from droplets and contamination of surfaces at points where films may break [59,100,101].
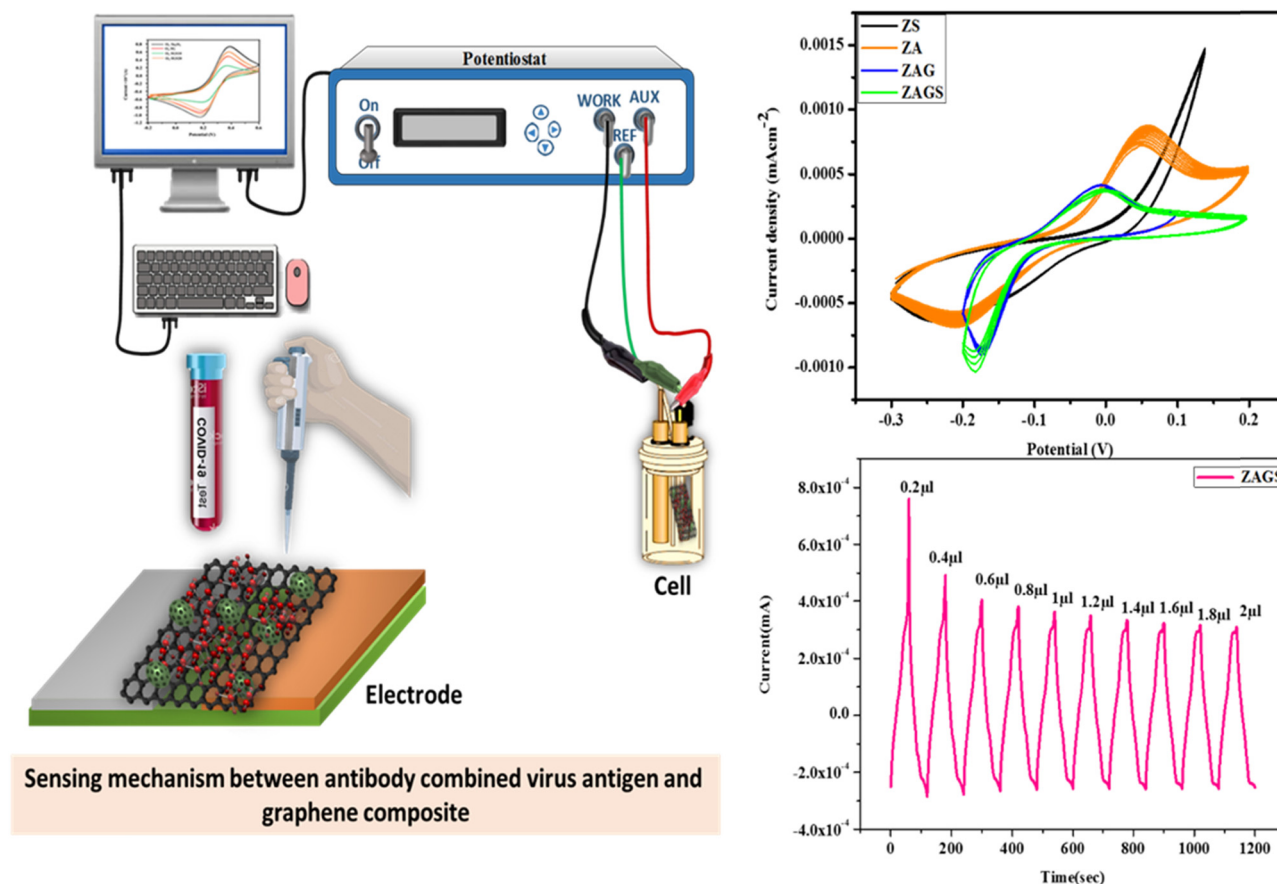

Figure 1: Graphene quaternary nanocomposite-based sensor and *cv*–*iv* curve.

3 Results and discussion

3.1 Proposed COVID-19 sensor

Graphene-based materials are used in various biomedical applications, including virus detection, personal protective equipment such as masks, gowns, and gloves, and antiviral applications. The interaction of the virus with graphene-based materials is a prevalent subject in these studies. Compared with graphene, the presence of oxygen on the edges and basal planes of GO increases its hydrophilicity, water dispersibility, and attachability. Antiviral agent binding to virus species is aided by the presence of surface functional groups on graphene materials. In contrast, molecular dynamics simulations have verified graphene's binding capabilities, indicating a high binding efficiency between pristine multilayer graphene generated by mechanical exfoliation and the SARS-CoV-2 virus's spike receptor-binding region.

Our proposed sensor case described the incline fruitful presentation of the COVID-19 spike counteracting agent. The geometry of the COVID-19 sensor was planned to use a graphene nanocomposite-based biosensor channel conjugated to the COVID-19 spike counteracting agent, andPBS (pH 7.4) buffer as the electrolyte to maintain the effective impact. In this, we report novel composites of silver nanoparticles (Ag-NPs), probably, covalently connected to thiol-functionalized GO (Figure 4a), with a COVID-19 counteracting agent, and our reenactment result too presents the modeling of the atomic structure of the GO, NSH, Ag, and our proposed component effectively (Figure 4b). First, thiolation of GO sheets was carried out through amide bonds, specifically securing the carboxylate locales of GO, empowering thiol bunches unreservedly accessible to covalently connect to Ag-NPs. Because of their high solidity, for example, against hydrolysis, amide bonds are unusually close to the composition of natural frameworks, such as protein building bonds, which is why they are often found together in natural structures. Functionalization through amide bonds was fulfilled by the coupling response utilizing NHS, under mild conditions, at room temperature and fluid medium the chemical functionalization of GO to get covalently reinforced NPs [61]. The fluid arrangement seems to distinguish COVID-19 based on the changes in the channel surface potential and comparing the impacts on the electrical reaction. We measured the exchange curves of the graphene-based sensor after each alteration cycle (Figure 5a). However, the exchange bend was shifted in the other direction, with the hypothesis being that the positive charge of the counteracting agent had an n-doping influence on the graphene after the counteracting agent had been immobilized by the exchange bend. Besides, the direct $I–V$ plots displayed profoundly steady Ohmic contact, showing that the COVID-19 sensor gave a dependable electrical signal for locating the target analytes (COVID-19 antigen protein, refined COVID-19 infection, or COVID-19 infection from clinical tests).

In this study, we proposed a graphene nanocomposite-based biosensor. We custom-fitted the graphene sensor surface for the label-free location of the COVID-19 antigen by chemically adjusting graphene with antibodies. Figure 4(a) shows the graphene film exposed to the serum test, conducting channels were used. The electrical properties of graphene exposed to the antigen-containing serum and those of graphene that was not exposed show differences. To the best of our knowledge, the twofold conductance peak has not yet been used in biosensing applications. The appearance of this highlight and how it changes when an antigen is presented to the graphene surface allow for their discovery.

3.2 Working principle of the COVID-19 sensor

In the COVID-19 immunosensor realization and planning, the biosensor consists of a competitive immunoassay performed on graphene nanocomposite cathodes to enable the multiplexed detection of distinct COVID-19 antigens; however, our proposed cathodes can also be used to immobilize COVID-19 antigens for more multiplexed detection in the future. It is worth noting that the cost of our proposed terminal is extremely low. In this article, we proposed using a COVID-19 counteracting agent as a biomarker for sensor development. This protein contains 719 amino acids and has an estimated atomic weight of 79.9 kDa. The biosensor is based on circular competition between the free infection virus within the test and the immobilized COVID-19 counteracting agent for a fixed concentration of the included antigen in the test. After each step, the location measured the diminishment peak current of the PBS redox couple. The binding of the antigen to the immobilized counteracting agent would result in a decrease in the CV peak current. This decrease in the top current is attributed to the anode surface's scope with the measured bulky antibodies (the antibodies in common have an atomic weight of roughly 150 kDa). This scope of the surface with the counteracting agent obstructs the access of the PBS

redox couple to the conductive surface and thus reduces the electron exchange productivity, resulting in a decrease in current. The sensor reaction is then identified by observing the change in the peak current when different concentrations of the COVID-19 antigen are added.

3.3 Real-time detection of the COVID-19 antigen protein

Figure 2 shows the COVID-19 RNA structure. Nucleobases are susceptible to oxidation, which is mediated by radical and nonradical receptive oxygen species. The N-oxide arrangement is peculiar from the point of metal coordination because it reduces the basicity of the nitrogen included. Within the setting of nucleobases, the presence of an extra oxygen atom at the ring nitrogen changes the coordination chemistry, compared to the unmodified nucleobase. We can observe from Figure 2 that COVID-19 is a single-stranded RNA-enveloped virus [64]. An RNA-based metagenomic next-generation sequencing approach has been applied to characterize its entire genome, which is 29,881 bp in length (GenBank no. MN908947), encoding 9860 amino acids [102]. Gene fragments express structural and nonstructural proteins. The S, E, M, and N genes encode structural proteins, whereas nonstructural proteins,

such as 3-chymotrypsin-like protease, papain-like protease, and RNA-dependent RNA polymerase, are encoded by the open reading frame region [103] (Figure 3).

Many glycosylated S proteins cover the surface of SARS-CoV-2 and bind to the host cell receptor angiotensin-converting enzyme 2 (ACE2), mediating viral cell entry [104]. When the S protein binds to the receptor, TM protease serine 2 (TMPRSS2), a type 2 TM serine protease located on the host cell membrane, promotes virus entry into the cell by activating the S protein. Once the virus enters the cell, the viral RNA is released, polyproteins are translated from the RNA genome, and replication and transcription of the viral RNA genome occur *via* protein cleavage and assembly of the replicase–transcriptase complex. Viral RNA is replicated, and structural proteins are synthesized, assembled, and packaged in the host cell, after which viral particles are released [96,97,105,106].

We can assess the sensor's energetic reaction to the spike protein to examine the execution of the COVID-19 graphene nanocomposite-based sensor. To begin, we determined the sensor's LOD for the spike protein. The sensor responded to 0.2 L of COVID-19 spike protein in PBS, which indicates the sensor's LOD. However, without the graphene-based gadget with COVID-19 spike protein conjugation, there was no significant flag change after the presentation of different test concentrations (orange and dark lines in the figure). The control study shows that
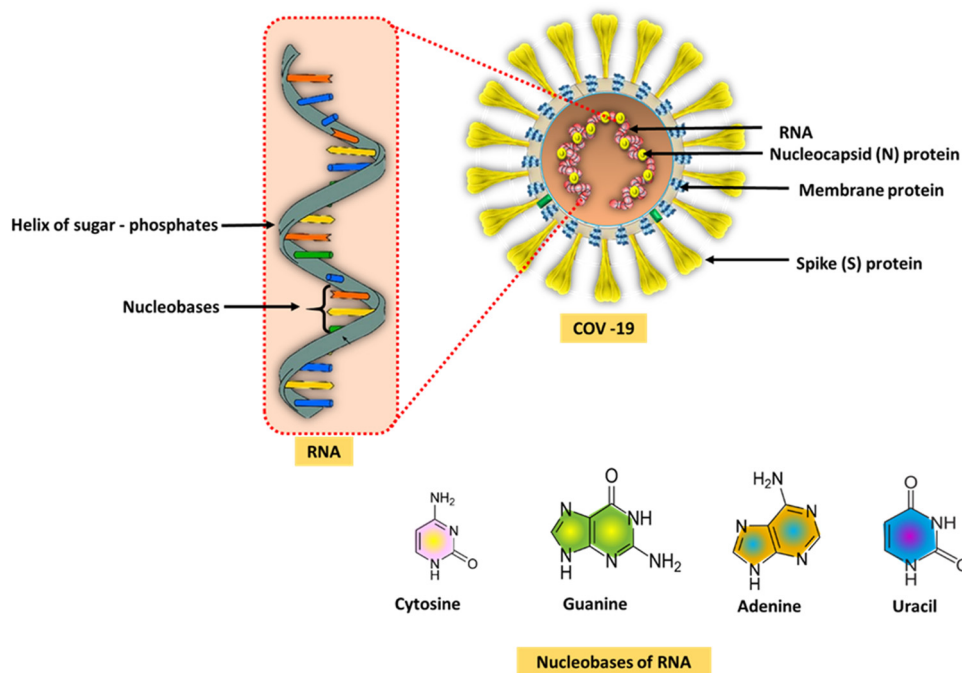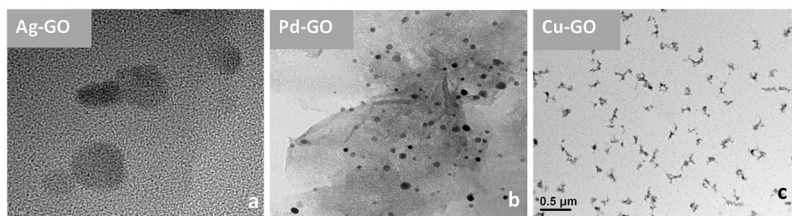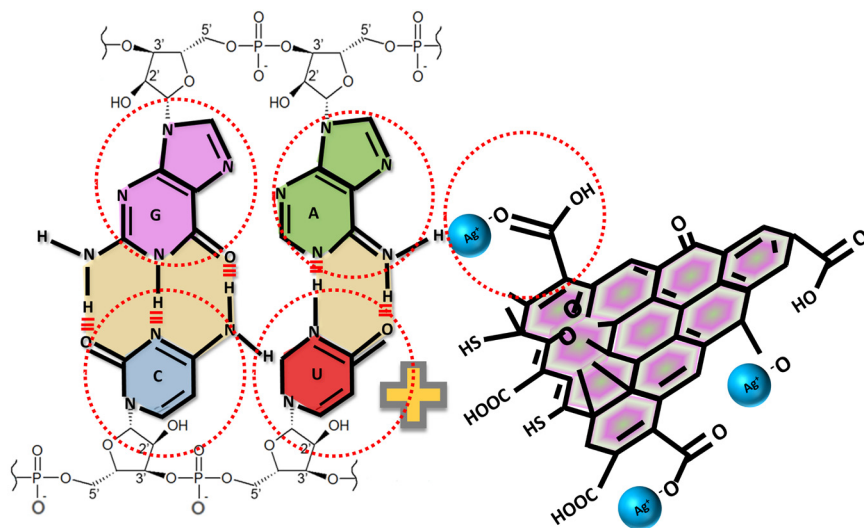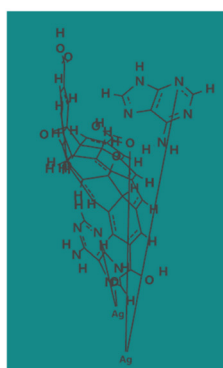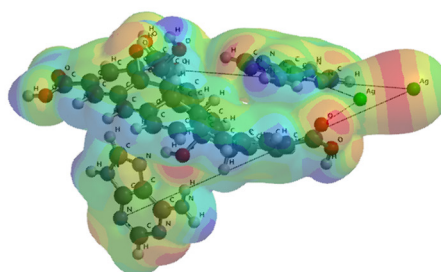

Figure 2: COVID-19 RNA structure [16].
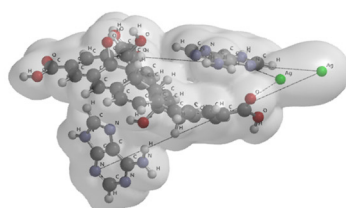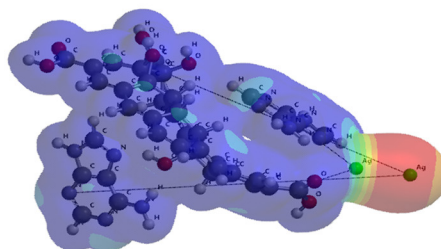
(a)

Molecular structure

Electrostatic potential map

Density

Local Ionization potential map

(b)

Figure 3: (a) Schematic presentation of the synthesis of N9-propyladenine N1-oxide with silver possible coordination mode, model structure, and (b) electron density, interaction potential, and dynamic simulation of GO, NSH, Ag and GO, Ag and adenine.

the COVID-19 spike protein is required for authoritative with the COVID-19 antigen. Furthermore, the COVID-19 graphene nanocomposite-based sensor was extremely sensitive for spike antigen protein. In the clinic, COVID-19 is determined using nasopharyngeal swabs suspended in a common transport medium (UTM). The UTM contains various reagents that will influence sensor execution, such as Hank's adjusted salts and BSA. Therefore, we tested the graphene nanocomposite-based sensor's response to antigens. The results revealed that the graphene nanocomposite-based sensor appears to effectively identify COVID-19 spike antigen proteins at concentrations as low as 0.1 μL. This demonstrates that the COVID-19 graphene nanocomposite-based sensor can detect antigens in clinical tests without any prior planning or processing. To further investigate the normalized affectability of the COVID-19 graphene nanocomposite-based sensor, the changes in affectability as a function of COVID-19 antigen protein concentration were characterized by fitting each data point, as shown in Figure 4. This finding indicates that the graphene nanocomposite-based sensor has the potential to be used for COVID-19 detection.

3.4 New modeling for molecular dynamic simulations

Graphene materials' antiviral properties could be explained by their chemical/physical interactions with viruses. According to this, the opposite surface charges of antiviral species (GO and GO–Ag) on one side and both viruses on the other could induce graphene materials and viruses to bind together. GO could interact with the enclosed virus's lipid components in this situation. In both enclosed and nonenveloped viruses, the binding of Ag and –SH groups of viral proteins offers additional interaction. This binding is essential for IBDV infection management. In the case of GO–Ag and nonenveloped viruses, GO nanosheets play a minor role in the nanocomposite's overall antiviral activity. GO, on the other hand, helps the antiviral agent's overall efficacy by providing a substrate for silver particles to spread evenly and without noticeable agglomeration.

In this article, Figure 4(a) presents the novel composites of silver nanoparticles (Ag-NPs), linked to thiol-functionalized GO, with COVID 19 acting as a counteracting agent, and our result shows the modeling of the atomic
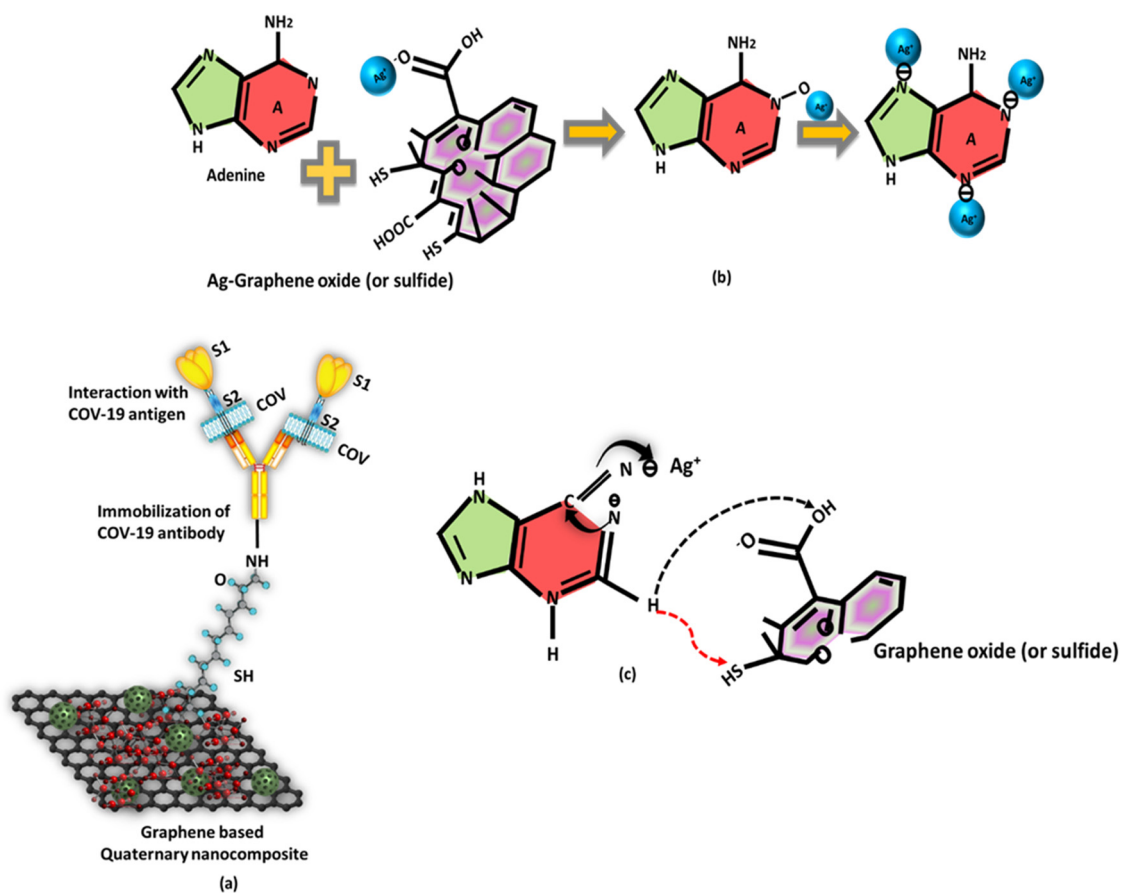
Figure 4: (a) Schematic presentation of the COVD-19 viral antigen binding with graphene nanocomposite sensor with coordination with antibody, (b) proposed binding mechanism, and (c) adenine ring opening by silver nanoparticles on the graphene surface.
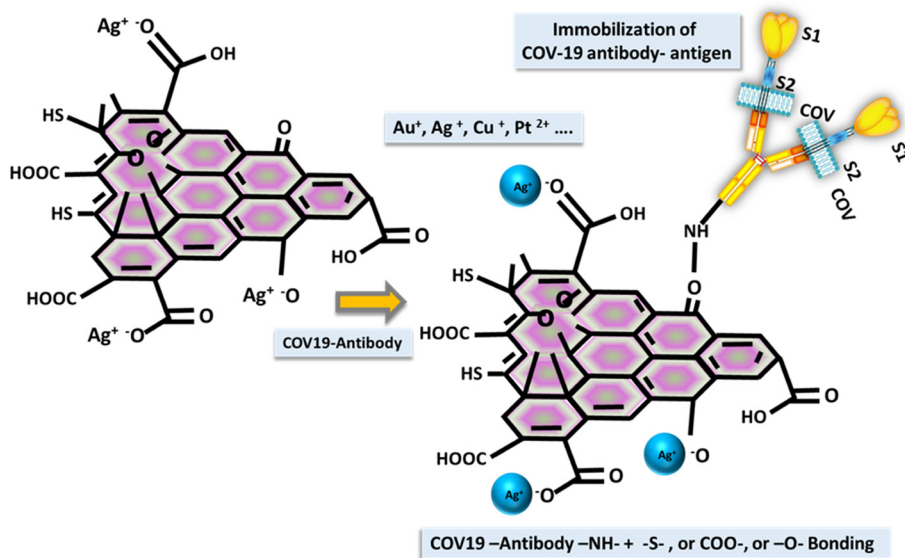
(a)
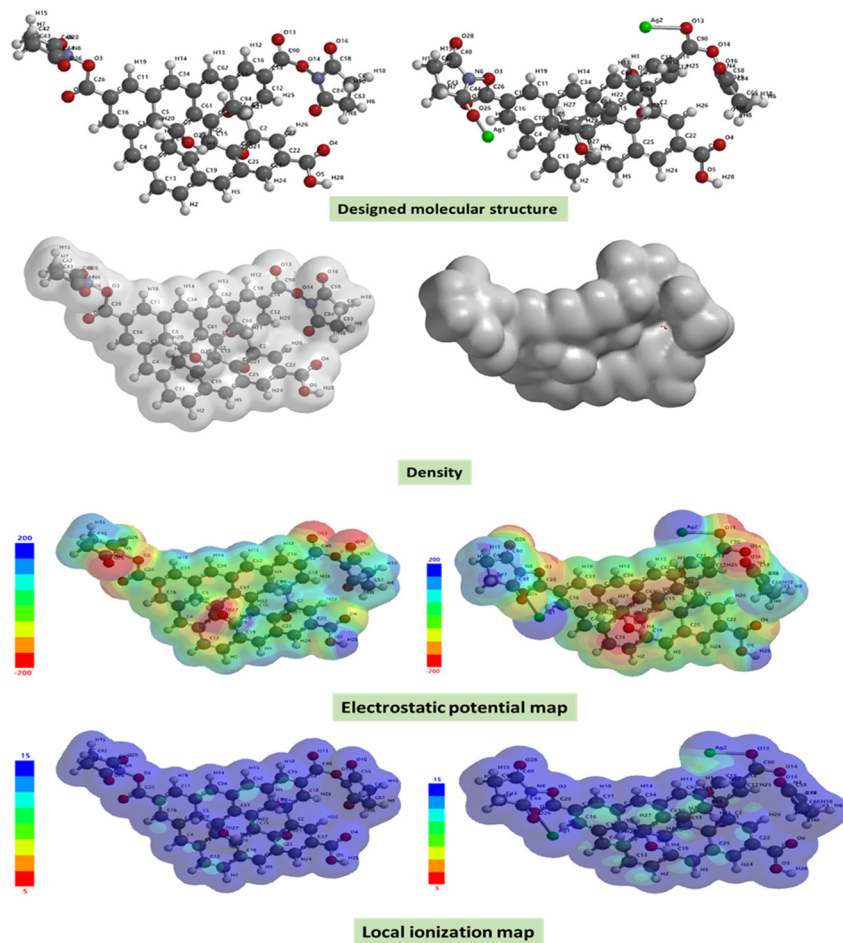
(b)

Figure 5: (a) Overall steps for the targeted COV19 −Antibody −NH⁻ + −S⁻, or COO⁻, or ⁻O-bonding formation of the GO-based composites; (b) model structure, electron density, interaction potential and dynamic simulation.

structure of the GO, NHS, Ag, and our proposed component effectively in Figure 4(b).

To begin, focused thiolation of GO sheets was performed using amide bonds, specifically securing the carboxylate locales of GO, making thiol bunches open to covalently connect to Ag NPs. Indeed, amide bonds are peculiarly due to their high solidity, for example, against hydrolysis, advocating their closeness within the composition of natural frameworks, *e.g.*, protein building bonds. The coupling response utilizing NHS under mild conditions, at room temperature, and in a fluid medium for the chemical functionalization of GO to obtain covalently reinforced NPs was completed [107–110]. The fluid arrangement appears to distinguish COVID-19 based on changes in channel surface potentials and comparing impacts on the electrical reaction. We measured the graphene-based sensor's exchange curves after each cycle. However, the exchange rate was moved in the opposite direction, implying that the positive charge of the counteracting agent had an n-doping impact on graphene after the counteracting agent was immobilized. Furthermore, the direct IV plots demonstrated profoundly consistent Ohmic contact, indicating that the COVID-19 sensor provided a reliable electrical signal for the location of the target analytes (COVID-19 antigen protein, refined COVID-19 infection, or COVID-19 infection from clinical tests).

Figure 5(a and b) depicts the binding of N9-propyladenine N1-oxide with silver conceivable coordination mode, showing structure (b) depicts GO, Ag, and adenine to contemplate the electron thickness, interaction, and energetic behavior of these useful materials. To find an electron in the vicinity of a molecule or particle of GO, Ag, or adenine, graphical representations of electron thickness were performed using a computer program. Locations of extensive electron thickness are frequently found around the particles as well as their holding in GO, Ag, and adenine particles. Electron thickness is related to chemical bonds and electronic properties. Furthermore, the electron thickness provides more information about the atomic estimate of the band structure of GO and Ag. It is concluded that GO and Ag showed large electron thickness, which is included in the bond arrangement with adenine. The GO, Ag, and Adenine interaction potential outline may be used to distinguish between the interaction vitality. This indicates that the charge exchange potential has the effect of bringing the states closer to the GO and Ag surface. Furthermore, the active recreation of GO, Ag, and adenine was used to investigate the behavior of a single layer of graphene at Ag (Figure 6).
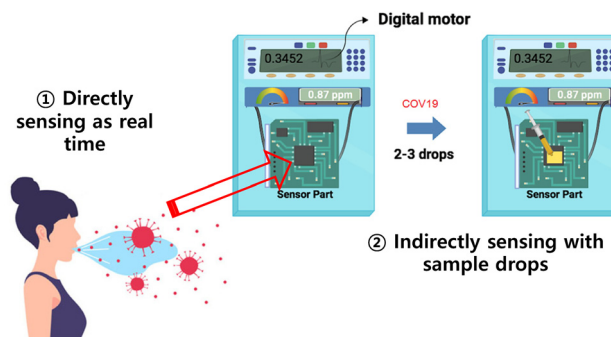

Figure 6: Graphene-based COVID-19 proposed sensor; the sensor system is working as real time in droplet transmission conditions or with sample drops obtained from cases.

3.5 Proposed neutralizing mechanism

COVID-19 viruses are among the biggest threats to humanity, with the current pandemic showing how these pathogens can shut down countries, halt entire industries, and cause untold human suffering as they spread through communities. COVID-19 viruses have also evolved in such a way that they are difficult to neutralization [111–113]. The odd makeup of these infectious agents is part of what makes them difficult to defeat. Compared to other pathogens, such as bacteria, viruses are minuscule. Because they have none of the hallmarks of living things a metabolism or the ability to reproduce on their own, for example, they are harder to target with drugs. Antibiotics, which are used to fight bacterial infections, attack the bacteria's cell walls, block protein production, and stop bacteria from reproducing. However, they are not effective against viral infections because viruses do not carry out any of these processes on their own. Rather, viruses need to invade and take over host cells to replicate.

Various emerging infectious diseases caused by viruses, including severe acute respiratory syndrome coronavirus COVID19. Silver nanoparticles (Ag-NPs) have been proven to be the most effective antimicrobial agents against bacteria and viruses because of their high surface-area-to-volume ratio and unique chemical and physical properties, even though they have shown cytotoxicity at high concentrations The major antiviral mechanism of Ag-NPs has not been investigated extensively, but the most frequently observed method by which Ag-NPs may inhibit viruses is the physical binding between the virus and Ag-NPs to block the entry of the viruses into cells. Ag-NPs could inhibit the *in vitro* production of viral RNA and extracellular virions by interacting with the viral particles.

Ag NPs bind to glycoproteins early in viral infection and inhibit binding and fusion. Because Ag-NPs have a natural tendency to bind the disulfide bonds in each monomer of hemagglutinin protein on the surface of virus and block its host receptor binding sites, Ag-NPs can inhibit the absorption of virus. Numerous factors can determine the antiviral efficacy of Ag-NPs, including size, shape, and capping agents. Previous studies have found that the most effective size of Ag-NPs is <10 nm and that a spherical shape is superior to a tubular shape or aggregation. Furthermore, previous studies have revealed that capping agents limiting the release of free Ag-NPs would exhibit lower viral inhibition. Therefore, a novel material for the capping and support agents of Ag-NPs is required for a superior application of Ag-NPs.

Graphene, a single atomic plane of graphene with two-dimensional extension, is promising as a next-generation nanomaterial due to its unique high carrier mobility, effective optical transparency, large surface area, and biocompatibility. GO is employed in the production of graphene family nanomaterials for various applications. The antibacterial activity of well-dispersed GO sheets has been evaluated, and a few studies have reported that graphene-based materials can inhibit the entry and replication of enveloped DNA virus (herpesvirus) and RNA virus (coronavirus) in their target cells. The pertinent findings of previous studies on the nanocomposites formed by Ag-NPs and GO sheets against bacteria can be applied to investigations of the antiviral activity of nanocomposites composed of GO sheets and Ag-NPs (GO–Ag). The GO sheets can serve as a supporting and stabilizing agent in preventing the agglomeration of the Ag-NPs and consequently in preventing a reduction of the antibacterial activity. The Ag-NPs supported on GO sheets showed a spherical-like morphology and an average size of 7.5 nm, which is suitable for antiviral activity. The most significant advantage of GO–Ag nanocomposites over free Ag-NPs is that the immobilization of Ag-NPs on GO sheets prevents the movement of the nanoparticles, thus increasing the material's biocompatibility and reducing the toxicological effects and the environmental impact associated with metallic nanoparticles. In addition, the GO–Ag matrix is highly dispersible in water, contains a large specific surface area, shows excellent bactericidal activity at extremely low concentrations, and exhibits no corrosive characteristics [12,102,114–125].

Graphene materials, including RNA and DNA viruses, show outstanding antiviral inhibitory effects against enclosed and nonenveloped viruses. These properties, which are related to the surfaces' physicochemical features, can be used to control the COVID-19 pandemic. It is important that graphene materials have the ability to be functionalized and used as a substrate for the homogeneous loading of various antiviral drugs. The surface area, charge density, concentration of graphene materials, the kind and size of loaded particles, as well as the type and degree of functional groups are all factors to be considered. Graphene materials' antiviral properties are influenced by their features. However, virus characteristics such as enveloped or nonenveloped viruses, as well as the period of nanomaterial use (virus pre-treatment, virus co-treatment, cell pre-, and post-treatment) all have a role in defining the antiviral activity of graphene-based materials.

4 Conclusion

According to this study, developing a biosensor for point-of-care (POC) COVID-19 detection is of utmost importance. Overall, a smart sensor for SARS-CoV-2 virus protein detection is discussed carefully and critically in this review. We proposed the new modeling for real-time detecting and neutralizing mechanism of COVID-19, with graphene-based nanocomposite in the base of computer simulation. A graphene nanocomposite-based sensor for COVID-19 detection in which a COVID-19 spike counteracting agent is conjugated to a graphene sheet serves as the detecting region and generates a significant electrical signal. Through the use of two unique points of rate, the sensor was able to distinguish between COVID-19 virus in a clinical sample with neutralizing mechanism. As a result, in clinical tests, our functionalized graphene-based sensor platform provides a basic, quick, and extremely responsive position of the COVID-19 virus. This proposed graphene nanocomposite biosensor can provide a dependable and simple conclusion step in real time to increase the virus concentration in clinical samples and reduce the load on PCR-based tests. As a result, this review concentrated on the antiviral properties of selected nanomaterials, with special emphasis on graphene-based materials. Finally, graphene-based materials can have multifunctional properties, sensing and neutralizing, hence boosting their efficiency in environmental protection.

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References

[1]	Hanaei S, Rezaei N. COVID-19: developing from an outbreak to a pandemic. Arch Med Res. 2020;51:582.

[2]	Wu F, Zhao S, Yu B, Chen YM, Wang W, Song ZG, et al. A new coronavirus associated with human respiratory disease in China. Nature. 2020;579:265–9.

[3]	Gorbalenya AE, Baker SC, Baric RS, de Groot RJ, Drosten C, Gulyaeva AA. The species severe acute respiratory syndrome-related coronavirus: classifying 2019-nCoV and naming it SARS-CoV-2. Nat Microbiol. 2020;5(4):536–44.

[4]	Seo G, Lee G, Kim MJ, Baek SH, Choi M, Ku KB, et al. Rapid detection of COVID-19 causative virus (SARS-CoV-2) in human nasopharyngeal swab specimens using field-effect transistor-based biosensor. ACS Nano. 2020;14:5135–42.

[5]	Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, et al. Early transmission dynamics in Wuhan, China, of novel corona-virus–infected pneumonia. N Engl J Med. 2020;382:13.

[6]	Li G, Fan Y, Lai Y, Han T, Li Z, Zhou P, et al. Coronavirus infections and immune responses. J Med Virol. 2020;92:424–32.

[7]	De Wit E, Van Doremalen N, Falzarano D, Munster VJ. SARS, and MERS: recent insights into emerging coronaviruses. Nat Rev Microbiol. 2016;148:523–34.

[8]	Lu R, Zhao X, Li J, Niu P, Yang B, Wu H, et al. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. Lancet. 2020;395:565–74.

[9]	Li W, Moore MJ, Vasilieva N, Sui J, Wong SK, Berne MA, et al. Angiotensin-converting enzyme 2 is a functional receptor for the SARS coronavirus. Nature. 2003;426:450–4.

[10]	Gage A, Brunson K, Morris K, Wallen SL, Dhau J, Gohel H, et al. Perspectives of Manipulative and High-Performance Nanosystems to Manage Consequences of Emerging New Severe Acute Respiratory Syndrome Coronavirus 2 Variants. Front Nanotechnol. 2021;3:45.

[11]	Tian X, Li C, Huang A, Xia S, Lu S, Shi Z, et al. Potent binding of 2019 novel coronavirus spike protein by a SARS corona-virus-specific human monoclonal antibody. Emerg Microbes Infect. 2020;9:382–5.

[12]	Wrapp D, Wang N, Corbett KS, Goldsmith JA, Hsieh CL, Abiona O, et al. Cryo-EM structure of the 2019-nCoV spike in the prefusion conformation. Science. 2020;367:1260–3.

[13]	World Health Organization. Coronavirus disease (COVID-19); 2021.

[14]	Zou L, Ruan F, Huang M, Liang L, Huang H, Hong Z, et al. SARS-CoV-2 viral load in upper respiratory specimens of infected patients. N Engl J Med. 2020;382:1177–9.

[15]	Bai Y, Yao L, Wei T, Tian F, Jin DY, Chen L, et al. Presumed asymptomatic carrier transmission of COVID-19. Jama. 2020;323:1406–7.

[16]	Goldsmith BR, Locascio L, Gao Y, Lerner M, Walker A, Lerner J, et al. Digital biosensing by foundry-fabricated graphene sensors. Sci Rep. 2019;9:1.

[17]	Hwang MT, Heiranian M, Kim Y, You S, Leem J, Taqieddin A, et al. Ultrasensitive detection of nucleic acids using deformed graphene channel field effect biosensors. Nat Commun. 2020;11:1.

[18]	Cooper DR, D'Anjou B, Ghattamaneni N, Harack B, Hilke M, Horth A, et al. Experimental review of graphene. Int Sch Res Not. 2012;2012:56.

[19]	Geim AK, Novoselov KS. The rise of graphene. J Nanosci Nanotechnol Nat. 2010;6:11–9.

[20]	Lei YM, Xiao MM, Li YT, Xu L, Zhang H, Zhang ZY, et al. Detection of heart failure-related biomarker in whole blood with graphene field effect transistor biosensor. Biosens Bioelectron. 2017;91:1–7.

[21]	Zhou L, Mao H, Wu C, Tang L, Wu Z, Sun H, et al. Label-free graphene biosensor targeting cancer molecules based on non-covalent modification. Biosens Bioelectron. 2017;87:701–7.

[22]	Khandelwal N, Kaur G, Kumar N, Tiwari A. Application of silver nanoparticles in viral inhibition: a new hope for antivirals. DJNB. 2014;9:1.

[23]	Bhujel R. Capacitive and sensing responses of biomass derived silver decorated graphene. Sci Rep. 2019;1:1–14.

[24]	Lin Y, Zhou Q, Tang D, Niessner R, Yang H, Knopp D. Silver nanolabels-assisted ion-exchange reaction with CdTe quantum dots mediated exciton trapping for signal-on photoelectrochemical immunoassay of mycotoxins. Anal Chem. 2016;88:7858–66.

[25]	Tang J, Tang D, Su B, Li Q, Qiu B, Chen G. Silver nanowire–graphene hybrid nanocomposites as label for sensitive electrochemical immunoassay of alpha-fetoprotein. Electrochim Acta. 2011;56:8168–75.

[26]	Zhou Q, Lin Y, Zhang K, Li M, Tang D. Reduced graphene oxide/BiFeO$_3$ nanohybrids-based signal-on photoelectro-chemical sensing system for prostate-specific antigen detection coupling with magnetic microfluidic device. Biosens Bioelectron. 2018;101:146–52.

[27]	Cai G, Yu Z, Ren R, Tang D. Exciton–plasmon interaction between AuNPs/graphene nanohybrids and CdS quantum dots/TiO$_2$ for photoelectrochemical aptasensing of prostate-specific antigen. ACS Sens. 2018;3:632–9.

[28]	Li J, Kuang D, Feng Y, Zhang F, Xu Z, Liu M. A graphene oxide-based electrochemical sensor for sensitive determination of 4-nitrophenol. J Hazard Mater. 2012;201:250–9.

[29]	Zhang Y, Zhang J, Chen Y, Luo B, Yuan Y, Huang F, et al. The ORF8 protein of SARS-CoV-2 mediates immune evasion through potently downregulating MHC-I. BioRxiv. 2020.

[30]	Liu Y, Ning Z, Chen Y, Guo M, Liu Y, Gali NK, et al. Aerodynamic analysis of SARS-CoV-2 in two Wuhan hospitals. Nat. 2020;582:557–60.

[31]	Ma J, Qi X, Chen H, Li X, Zhan Z, Wang H, et al. Exhaled breath is a significant source of SARS-CoV-2 emission. MedRxiv. 2020.

[32] Faridi S, Niazi S, Sadeghi K, Naddafi K, Yavarian J,
      Shamsipour M, et al. A field indoor air measurement of
      SARS-CoV-2 in the patient rooms of the largest hospital
      in Iran. Sci Total Env. 2020;725:138401.

[33] Cheng VC, Wong SC, Chan VW, So SY, Chen JH, Yip CC, et al.
      Air and environmental sampling for SARS-CoV-2 around
      hospitalized patients with coronavirus disease 2019
      (COVID-19). Infect Control Hosp Epidemiol.
      2020;41:1258–65.

[34] Ong SW, Tan YK, Chia PY, Lee TH, Ng OT, Wong MS, et al. Air,
      surface environmental, and personal protective equipment
      contamination by severe acute respiratory syndrome
      coronavirus 2 (SARS-CoV-2) from a symptomatic patient.
      Jama. 2020;323:1610–2.

[35] Suzuki M, Kamiya H, Okamoto K, Yamagishi T, Kakimoto K,
      Takeda M, et al. Environmental sampling for severe acute
      respiratory syndrome coronavirus 2 (SARS-CoV-2) during
      a coronavirus disease (COVID-19) outbreak aboard a
      commercial cruise ship. MedRxiv. 2020.

[36] Döhla M, Wilbring G, Schulte B, Kümmerer BM, Diegmann C,
      Sib E, et al. SARS-CoV-2 in environmental samples of
      quarantine households. medRxiv. 2020.

[37] Wu S, Wang Y, Jin X, Tian J, Liu J, Mao Y. Environmental
      contamination by SARS-CoV-2 in a designated hospital
      for coronavirus disease 2019. Am J Infect Control.
      2020;48:910–4.

[38] Ding Z, Qian H, Xu B. Toilets dominate environmental
      detection of SARS-CoV-2 virus in a hospital. medRxiv.
      2020;7.

[39] Cheng VC, Wong SC, Chen JH, Yip CC, Chuang VW, Tsang OT,
      et al. Escalating infection control response to the rapidly
      evolving epidemiology of the coronavirus disease 2019
      (COVID-19) due to SARS-CoV-2 in Hong Kong. Infect Control
      Hosp Epidemiol. 2020;41:493–8.

[40] Bullard J, Dust K, Funk D, Strong JE, Alexander D, Garnett L,
      et al. Predicting infectious severe acute respiratory syndrome
      coronavirus 2 from diagnostic samples. Arch Clin Infect Dis.
      2020;71:2663–6.

[41] Durante-Mangoni E, Andini R, Bertolino L, Mele F,
      Bernardo M, Grimaldi M, et al. Low rate of severe acute
      respiratory syndrome coronavirus 2 spread among
      health-care personnel using ordinary personal protection
      equipment in a medium-incidence setting. Clin Microbiol
      Infect. 2020;26:1269–70.

[42] Wong SC, Kwong RS, Wu TC, Chan JW, Chu MY, Lee SY, et al.
      Risk of nosocomial transmission of coronavirus disease
      2019: an experience in a general ward setting in Hong Kong.
      J Hosp Infect. 2020;105:119–27.

[43] Leclerc QJ, Fuller NM, Knight LE, Funk S, Knight GM. CMMID
      covid-19 Working Group. settings have been linked SARS-
      CoV-2. Transm Clust Wellcome Open Res. 2020;5:83.

[44] Lu J, Gu J, Li K, Xu C, Su W, Lai Z, et al. Early release-COVID-19
      outbreak associated with air conditioning in restaurant,
      Guangzhou, China. Emerg Infect Dis -CDC. 2020;26:46.

[45] Jang S, Han SH, Rhee JY. Cluster of coronavirus disease
      associated with fitness dance classes, South Korea.
      Emerg Infect Dis. 2020;26:1917.

[46] Dillon A. Clustering and superspreading potential of severe
      acute respiratory syndrome coronavirus 2 (SARS-CoV-2)
      infections in Hong Kong. Research Square; 2020.

[47] Matson MJ, Yinda CK, Seifert SN, Bushmaker T, Fischer RJ,
      van Doremalen N, et al. Effect of environmental conditions
      on SARS-CoV-2 stability in human nasal mucus and sputum.
      Emerg Infect Dis. 2020;26:2276.

[48] Pastorino B, Touret F, Gilles M, de Lamballerie X, Charrel RN.
      Prolonged infectivity of SARS-CoV-2 in fomites. Emerg Infect
      Dis. 2020;26:2256.

[49] Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical
      characteristics of coronavirus disease 2019 in China. N Engl J
      Med. 2020;382:1708–20.

[50] Pan Y, Zhang D, Yang P, Poon LL, Wang Q. Viral load of
      SARS-CoV-2 in clinical samples. Lancet Infect Dis.
      2020;20:411–2.

[51] Wang W, Xu Y, Gao R, Lu R, Han K, Wu G, et al. Detection of
      SARS-CoV-2 in different types of clinical specimens. Jama.
      2020;323:1843–4.

[52] Wu Y, Guo C, Tang L, Hong Z, Zhou J, Dong X, et al. Prolonged
      presence of SARS-CoV-2 viral RNA in faecal samples. Lancet
      Gastroenterol Hepatol. 2020;5:434–5.

[53] Zheng S, Fan J, Yu F, Feng B, Lou B, Zou Q, et al. Viral load
      dynamics and disease severity in patients infected with
      SARS-CoV-2 in Zhejiang province, China, January–March
      2020: retrospective cohort study. Br Med J. 2020;369.

[54] Sun J, Zhu A, Li H, Zheng K, Zhuang Z, Chen Z, et al. Isolation
      of infectious SARS-CoV-2 from urine of a COVID-19 patient.
      Emerg Microbes Infect. 2020;9:991–3.

[55] Xiao F, Sun J, Xu Y, Li F, Huang X, Li H, et al. Infectious
      SARS-CoV-2 in feces of patient with severe COVID-19.
      Emerg Infect Dis. 2020;26:1920.

[56] Zhang Y, Chen C, Zhu S, Shu C, Wang D, Song J, et al.
      Isolation of 2019-nCoV from a stool specimen of a laboratory-
      confirmed case of the coronavirus disease 2019 (COVID-19).
      China CDC Wkly. 2020;2:123–4.

[57] Le Chang LZ, Gong H, Wang L, Wang L. severe acute
      respiratory syndrome coronavirus 2 RNA detected in blood
      donations. Emerg Infect Dis. 2020;26:1631.

[58] Andersen KG, Rambaut A, Lipkin WI, Holmes EC, Garry RF. The
      proximal origin of SARS-CoV-2. Nat Med. 2020;26:450–2.

[59] Sharma PK, Kim ES, Mishra S, Ganbold E, Seong RS,
      Kaushik AK, et al. Ultrasensitive and Reusable Graphene
      Oxide-Modified Double-Interdigitated Capacitive (DIDC)
      Sensing Chip for Detecting SARS-CoV-2. ACS Sens.
      2021;6(9):3468–76.

[60] Serrano-Aroca Á, Takayama K, Tuñón-Molina A, Seyran M,
      Hassan SS, Pal Choudhury P, et al. Carbon-based nanoma-
      terials: promising antiviral agents to combat COVID-19 in the
      microbial-resistant era. ACS nano. 2021;15(5):8069–86.

[61] Roy R, Rahman MS, Raynie DE. Current research in green
      and sustainable chemistry. South Dakota State
      University; 2020.

[62] Kaushik AK, Dhau JS, Gohel H, Mishra YK, Kateb B, Kim NY,
      et al. Electrochemical SARS-CoV-2 sensing at point-of-care
      and artificial intelligence for intelligent COVID-19 manage-
      ment. ACS Appl Bio Mater. 2020;3(11):7306–25.

[63] Corman VM, Müller MA, Costabel U, Timm J, Binger T,
      Meyer B, et al. Assays laboratory confirmation Nov Hum
      coronavirus (hCoV-EMC) Infect. Eurosurveillance.
      2012;17:20334.

[64] Drosten C, Günther S, Preiser W, Van Der Werf S, Brodt HR,
      Becker S, et al. Identification of a novel coronavirus in

patients with severe acute respiratory syndrome. N Engl J Med. 2003;348:1967–76.

[65] Corman VM, Eickmann M, Landt O, Bleicker T, Brünink S, Eschbach-Bludau M, et al. Specific detection by real-time reverse-transcription PCR assays of a novel avian influenza A (H7N9) strain associated with human spillover infections in China. Eurosurveillance. 2013;18:20461.

[66] Corman VM, Eckerle I, Bleicker T, Zaki A, Landt O, Eschbach-Bludau M, et al. Detection of a novel human coronavirus by real-time reverse-transcription polymerase chain reaction. Eurosurveillance. 2012;17:20285.

[67] Panning M, Charrel RN, Mantke OD, Landt O, Niedrig M, Drosten C. Coordinated implementation of Chikungunya virus reverse transcription–PCR. Emerg Infect Dis. 2009;15:469.

[68] Corman VM, Rasche A, Baronti C, Aldabbagh S, Cadar D, Reusken CB, et al. Assay optimization for molecular detection of Zika virus. Bull World Health Organ. 2016;94:880.

[69] Drexler JF, Gloza-Rausch F, Glende J, Corman VM, Muth D, Goettsche M, et al. Genomic characterization of severe acute respiratory syndrome-related coronavirus in European bats and classification of coronaviruses based on partial RNA-dependent RNA polymerase gene sequences. J Virol. 2010;84:11336–49.

[70] Muth D, Corman VM, Roth H, Binger T, Dijkman R, Gottula LT, et al. Attenuation of replication by a 29-nucleotide deletion in SARS-coronavirus acquired during the early stages of human-to-human transmission. Sci Rep. 2018;8:1.

[71] Corman VM, Muth D, Niemeyer D, Drosten C. Hosts, and sources of endemic human coronaviruses. Adv Virus Res. 2018;100:163–88.

[72] Drexler JF, Corman VM, Drosten C. Ecology, evolution, and classification of bat coronaviruses in the aftermath of SARS. Antivir Res. 2014;101:45–56.

[73] Chan JF, Yuan S, Kok KH, To KK, Chu H, Yang J, et al. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. Lancet. 2020;395:514–23.

[74] Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020;395:497–506.

[75] Burke RM, Midgley CM, Dratch A, Fenstersheib M, Haupt T, Holshue M, et al. Active monitoring of persons exposed to patients with confirmed COVID-19 – United States, January–February 2020. Morb Mortal Wkly Rep. 2020;69:245.

[76] Hamner L. High SARS-CoV-2 attack rate following exposure at a choir practice. Morb Mortal Wkly Rep. 2020;69:606–10.

[77] Ghinai I, McPherson TD, Hunter JC, Kirking HL, Christiansen D, Joshi K, et al. First known person-to-person transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in the USA. Lancet. 2020;395:1137–44.

[78] Pung R, Chiew CJ, Young BE, Chin S, Chen MI, Clapham HE, et al. Investigation of three clusters of COVID-19 in Singapore: implications for surveillance and response measures. Lancet. 2020;395:1039–46.

[79] Luo L, Liu D, Liao X, Wu X, Jing Q, Zheng J. Modes of contact and risk of transmission in COVID-19 among close contacts (pre-print). MedRxiv. 2020.

[80] Mittal R, Ni R, Seo JH. The flow physics of COVID-19. J Fluid Mech. 2020;894.

[81] Bourouiba L. Turbulent gas clouds and respiratory pathogen emissions: potential implications for reducing transmission of COVID-19. Jama. 2020;323:1837–8.

[82] Asadi S, Bouvier N, Wexler AS, Ristenpart WD. The coronavirus pandemic and aerosols: Does COVID-19 transmit *via* expiratory particles Taylor & Francis, Aerosol Science and Technology; 2020.

[83] Morawska L, Cao J. Airborne transmission of SARS-CoV-2: The world should face the reality. Env Int. 2020;139:105730.

[84] Gralton J, Tovey ER, McLaws ML, Rawlinson WD. Respiratory virus RNA is detectable in airborne and droplet particles. J Med Virol. 2013;85:2151–9.

[85] Stadnytskyi V, Bax CE, Bax A, Anfinrud P. The airborne lifetime of small speech droplets and their potential importance in SARS-CoV-2 transmission. Proc Natl Acad Sci. 2020;117:11875–7.

[86] Somsen GA, van Rijn C, Kooij S, Bem RA, Bonn D. Small droplet aerosols in poorly ventilated spaces and SARS-CoV-2 transmission. Lancet Respir Med. 2020;8:658–9.

[87] Asadi S, Wexler AS, Cappa CD, Barreda S, Bouvier NM, Ristenpart WD. Aerosol emission and superemission during human speech increase with voice loudness. Sci Rep. 2019;9:1.

[88] Van Doremalen N, Bushmaker T, Morris DH, Holbrook MG, Gamble A, Williamson BN, et al. Aerosol and surface stability of SARS-CoV-2 as compared with SARS-CoV-1. N Engl J Med. 2020;382:1564–7.

[89] Fears AC, Klimstra WB, Duprex P, Hartman A, Weaver SC, Plante KS, et al. Persistence of severe acute respiratory syndrome coronavirus 2 in aerosol suspensions. Emerg Infect Dis. 2020;26:2168.

[90] Chia PY, Coleman KK, Tan YK, Ong SW, Gum M, Lau SK, et al. Detection of air and surface contamination by SARS-CoV-2 in hospital rooms of infected patients. Nat Commun. 2020;11:1–7.

[91] Guo ZD, Wang ZY, Zhang SF, Li X, Li L, Li C, et al. Aerosol and surface distribution of severe acute respiratory syndrome coronavirus 2 in hospital wards, Wuhan, China, 2020. Emerg Infect Dis. 2020;26:1586.

[92] Santarpia JL, Rivera DN, Herrera V, Morwitzer MJ, Creager H, Santarpia GW. Transmission potential of SARS-CoV-2 in viral shedding observed at the University of Nebraska Medical Center (pre-print). MedRxiv. 2020.

[93] Nguyen TV, Lee HC, Yang OB. The effect of pre-thermal treatment of TiO2 nanoparticles on the performances of dye-sensitized solar cells. Sol Energy Mater Sol. 2006;90:967–81.

[94] Kleinert J, Srinivasan V, Rival A, Delattre C, Velev OD, Pamula VK. The dynamics and stability of lubricating oil films during droplet transport by electrowetting in microfluidic devices. Biomicrofluidics. 2015;9:034104.

[95] Cui J, Li F, Shi ZL. Origin and evolution of pathogenic coronaviruses. Nat Rev Microbiol. 2019;17:181–92.

[96] Liu J, Liao X, Qian S, Yuan J, Wang F, Liu Y, et al. Community transmission of severe acute respiratory syndrome coronavirus 2. Emerg Infect Dis. 2020;26:1320.

[97] Litman GW, Rast JP, Shamblott MJ, Haire RN, Hulst M, Roess W, et al. Phylogenetic diversification of

immunoglobulin genes and the antibody repertoire. Mol Biol Evol. 1993;10:60–72.

[98] Zhou P, Yang XL, Wang XG, Hu B, Zhang L, Zhang W, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature. 2020;579:270–3.

[99] WHO. Coronavirus disease (COVID-19) technical guidance: laboratory testing for 2019-nCoV in humans; 2020.

[100] Fatema KN, Biswas MR, Bang SH, Cho KY, Oh WC. Electroanalytical characteristic of a novel biosensor designed with graphene–polymer-based quaternary and mesoporous nanomaterials. Bull Mater Sci. 2020;43:1–3.

[101] Fatema KN, Liu Y, Cho KY, Oh WC. Comparative study of electrochemical biosensors based on highly efficient mesoporous ZrO_2-Ag-G-SiO_2 and In_2O_3-G-SiO_2 for rapid recognition of *E. coli* O157: H7. ACS Omega. 2020;5:22719–30.

[102] Chen YN, Hsueh YH, Hsieh CT, Tzou DY, Chang PL. Antiviral activity of graphene–silver nanocomposites against non-enveloped and enveloped viruses. Int J Environ Res public health. 2016;13(4):430.

[103] Chen L, Liu W, Zhang Q, Xu K, Ye G, Wu W, et al. RNA based mNGS approach identifies a novel human coronavirus from two individual pneumonia cases in 2019 Wuhan outbreak. Emerg Microbes Infect. 2020;9:313–9.

[104] Chan JF, Kok KH, Zhu Z, Chu H, To KK, Yuan S, et al. Genomic characterization of the 2019 novel human-pathogenic coronavirus isolated from a patient with atypical pneumonia after visiting Wuhan. Emerg Microbes Infect. 2020;9:221–36.

[105] Letko M, Marzi A, Munster V. Functional assessment of cell entry and receptor usage for SARS-CoV-2 and other lineage B betacoronaviruses. Nat Microbiol. 2020;5:562–9.

[106] Fehr AR, Perlman S. Coronaviruses: an overview of their replication and pathogenesis. Coronaviruses. 2015;1282:1–23.

[107] Orth ES, Fonsaca JE, Domingues SH, Mehl H, Oliveira MM, Zarbin AJ. Targeted thiolation of graphene oxide and its utilization as precursor for graphene/silver nanoparticles composites. Carbon. 2013;61:543–50.

[108] Chan JF, To KK, Tse H, Jin DY, Yuen KY. Interspecies transmission, and emergence of novel viruses: lessons from bats and birds. Trends Microbiol. 2013;21:544–55.

[109] Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al. A novel coronavirus from patients with pneumonia in china, 2019. N Engl J Med. 2020;382:727–33.

[110] Wu A, Peng Y, Huang B, Ding X, Wang X, Niu P, et al. Genome composition and divergence of the novel coronavirus (2019-nCoV) originating in China. Cell Host Microbe. 2020;27:325–8.

[111] Singh A, Kaushik A, Dhau JS, Kumar R. Exploring coordination preferences and biological applications of pyridyl-based organochalcogen (Se, Te) ligands. Coord Chem Rev. 2022;450:214254.

[112] Tiwari S, Juneja S, Ghosal A, Bandara N, Khan R, Wallen S, et al. Antibacterial and antiviral high-performance nano-

systems to mitigate new SARS-CoV-2 variants of concerns. Curr OpBiomed Eng. 2021;21:100363.

[113] Sadique MA, Yadav S, Ranjan P, Verma S, Salammal ST, Khan MA, et al. High-performance antiviral nano-systems as a shield to inhibit viral infections: SARS-CoV-2 as a model case study. J Mater Chem B. 2021;9:4620–42.

[114] Prajapati RK, Kumar J, Verma S. Counteranion-directed structural consequences in silver–adenine N-oxide complexes. CrystEngComm. 2013;15:9316–9.

[115] Hoffmann M, Kleine-Weber H, Krüger N, Müller M, Drosten C, Pöhlmann S. The novel coronavirus 2019 (2019-nCoV) uses the SARS-coronavirus receptor ACE2 and the cellular protease TMPRSS2 for entry into target cells. BioRxiv. 2020.

[116] Subbaram K, Kannan H, Gatasheh MK. Emerging develop-ments on pathogenicity, molecular virulence, epidemiology, and clinical symptoms of current Middle East respiratory syndrome coronavirus (MERS-CoV). Hayati. 2017;24:53–6.

[117] Zhang XW, Yap YL. The 3D structure analysis of SARS-CoV S1 protein reveals a link to influenza virus neuraminidase and implications for drug and antibody discovery. J Mol Struct Theochem. 2004;681:137–41.

[118] Mousavizadeh L, Ghasemi S. Genotype, and phenotype of COVID-19: Their roles in pathogenesis. J Microbiol Immunol Infect. 2021;54:159–63.

[119] Vaheri A, Strandin T, Hepojoki J, Sironen T, Henttonen H, Mäkelä S, et al. Uncovering the mysteries of hantavirus infections. Nat Rev Microbiol. 2013;11:539–50.

[120] Balboni A, Gallina L, Palladini A, Prosperi S, Battilani M. A real-time PCR assay for bat SARS-like coronavirus detection and its application to Italian greater horseshoe bat faecal sample surveys. Sci World J. 2012;2012:2012.

[121] Uhlenhaut C, Cohen JI, Pavletic S, Illei G, Gea-Banacloche JC, Abu-Asab M, et al. Use of a novel virus detection assay to identify coronavirus HKU1 in the lungs of a hematopoietic stem cell transplant recipient with fatal pneumonia. Transpl Infect Dis. 2012;14:79–85.

[122] Adachi D, Johnson G, Draker R, Ayers M, Mazzulli T, Talbot PJ, et al. Comprehensive detection, and identification of human coronaviruses, including the SARS-associated coronavirus, with a single RT-PCR assay. J Virol Methods. 2004;122:29–36.

[123] Setianingsih TY, Wiyatno A, Hartono TS, Hindawati E, Dewantari AK, Myint KS, et al. Detection of multiple viral sequences in the respiratory tract samples of suspected Middle East respiratory syndrome coronavirus patients in Jakarta, Indonesia 2015–2016. Int J Infect Dis. 2019;86:102–7.

[124] Wan Z, Zhang YN, He Z, Liu J, Lan K, Hu Y, et al. A melting curve-based multiplex RT-qPCR assay for simultaneous detection of four human coronaviruses. Int J Mol Sci. 2016;17:1880.

[125] Noh JY, Yoon SW, Kim DJ, Lee MS, Kim JH, Na W, et al. Simultaneous detection of severe acute respiratory syndrome, middle east respiratory syndrome, and related bat coronaviruses by real-time reverse transcription PCR. Arch Virol. 2017;162:1617–23.