REVIEW

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# Viral Nano-Bio-Sensing and SARS-CoV-2: A Literature Review

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## Abstract

As new advancements and technologies are emerging in this world, so is the spread of new diseases. The world, as we know it, is moving very fast. With this pace, diseases are also borne. The spread of new viruses, such as coronavirus disease-2019, require new technologies faster and more precise than ever before. Countries all around the world are connected, and moving from place to place has become easy. For that reason, pandemics are an increasing threat. A disease is considered a pandemic when it has spread through a large area, possibly worldwide and has become an international threat. In order to limit the spread of diseases, or viruses in particular, the early detection and diagnosis of patients is essential to decrease the number of infections. Biosensors play an important role in the medical field, such as in viral detection. Nanotechnology has gained a lot of interest in its use in bio-sensing. Nano-biosensors have shown more advanced properties than regular biosensors and thus are able to detect diseases faster and more precisely than before. Our main focus in this literature review is to explore new technologies and advancements made with nanotechnology and bio-sensing in viral detection, especially in the detection of severe acute respiratory syndrome-coronavirus-2.

**Keywords:** COVID-19, pandemic, virus, bio-sensor, nanotechnology, nano-biosensors, SARS-CoV-2

## INTRODUCTION

Coronavirus disease-2019 (COVID-19), also known as COVID-19, is an illness caused by the severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2). COVID-19 was declared a global pandemic by the World Health Organization (WHO) on March 11th, 2020.[1] Back in 2003, a similar outbreak occurred, known as SARS, which was caused by the SARS-CoV infecting over 8,000 people and killing 774.[2] Coronaviruses are enveloped viruses which have S-proteins making them appear as crowns, thus leading to the name "corona" (Latin for crown). All CoV have a single stranded RNA genome. As many errors occur during RNA replication, CoV have a high mutation rate. The RNA genome encodes many structural proteins. From these proteins, the S-glycoprotein found on the surface of CoV binds to the receptor angiotensin-converting enzyme 2 (ACE2) found on the lower respiratory tract of human cells. SARS-CoV-2 uses the ACE2 receptor to infect humans.[3,4] Infectious diseases can arise due to many factors, some being the lifestyle of humans, their eating habits or their interaction with animals, as well as urbanization which allows the fast spread of diseases. Other causes include climate change which allows a disease to move to a different environment infecting more of the population, or mosquito borne diseases which move to many different areas. Furthermore, the mass production of animals during an outbreak readily spreads the disease further. Infectious diseases have spread causing epidemics and then pandemics all through history.[5]

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A biosensor is an analytical instrument which is used to accurately determine analytes in a living sample. This device is precise, delicate and has a particular measurement configuration. Since it is used for the detection of living samples, it consists of living elements such as microorganisms, organelles, cell receptors, enzymes, or nucleic acids. Due to the interaction with the sample, a signal is generated which can be electric, optical or thermal. Those signals are then transformed using a transducer to a parameter which can be measured. Figure 1 represents the different components of a biosensor.[6]

Nano-biosensors are bio-sensors which are based on the presence of nanomaterials. As the size of a material decreases, the surface area to volume ratio increases, which corresponds to a better signaling and transduction process and a better detection system.[7] The most promising nanomaterials in nano-bio-sensing include carbon nanotubes (CNTs), gold nanoparticles (GNPs), quantum dots (QDs) and magnetic nanoparticles (MNPs). These nanomaterials may be used in the transduction or bio-recognition process due to having smaller sizes, higher speeds, and faster electron transfer due to smaller distances, large surface area, using less power and lower voltages. Metallic nanostructures such as QDs (0D), CNTs (1D) and graphene sheets (2D) have been found to increase electronic properties such as when used as electrode components to improve transduction. CNTs are used in electrochemical sensing for various analytes such as in glucose, fructose, galactose, insulin, cancer biomarkers, cells and DNA. Graphene has been used in electrochemical biosensors as well as impedance, fluorescence and electrochemiluminescence biosensors to detect various analytes such as glucose, cholesterol and uric acid. QDs have excellent optical properties and various emission wavelengths based on their size and thus are used as fluorophores in optical biosensors to detect ions and various pharmaceutical analytes. They are also being used for the *in vivo* detection of cancer. GNPs have mainly been focused on usage in bio-sensing, drug delivery, cancer therapy etc. GNPs are non-toxic, biocompatible and have an inert core. MNPs have also been used in bio-sensing for the detection of various analytes such as proteins, enzymes, mRNA, DNA and tumor cells.[8]

The aim of our literature review was to discover basic virology, then explore nano-bio-sensing of different viruses, focusing on the applications of GNPs as they are the most frequently used NPs in viral detection, and then to include a summary of other NPs which are used as well. We then aimed to concentrate on COVID-19 detection as well as the current progress of nanotechnology in COVID-19 vaccines.

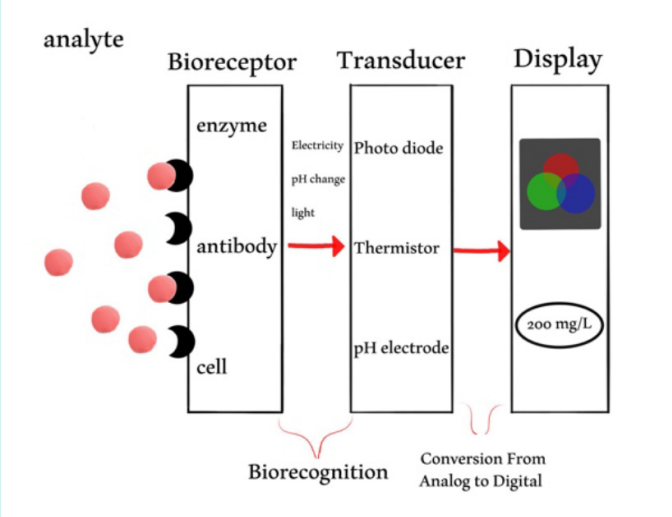


**Figure 1.** A schematic representation of a biosensor.

## Viruses

Viruses are microscopic, subcellular entities which cannot replicate outside of a host cell. In the simplest viruses, a simple virus (virion) has just one kind of nucleic acid (RNA or DNA) and a protective protein coat. The nucleic acid carries the genetic information required to instruct the host cell's synthetic machinery for viral replication. The protein coat has two purposes: First, it shields the nucleic acid from extracellular environmental insults such as nucleases; and second, it allows the virion to adhere to the host cell's membrane, the negative charge of which would reject a naked nucleic acid.[9]

Antigens are responsible for initiating an immune response in the host cell to inhibit further viral replication and kill infected host cells. Inhibiting further viral replication is done when the body is signaled by the antigens to produce antibodies to prevent the virus from entering cells and further replicating. Infected cells are killed by cytotoxic T-cells when activated by the viral antigens. Viruses that have more than one kind of antigens (having variant antigens) are more likely to attack the host cell since an antibody for a certain serotype will not protect against another serotype.

Some viruses have a viral envelope made up of a lipid bi-layer that carry the capsid as well as the genome. Other virus may lack this envelope. The viral envelope is a lipoprotein membrane which contains protein which is virus specific and which attaches to certain receptors of certain host cells. In addition to the viral envelope, the human cell is also made up of a lipid bi-layer, therefore, it is easy for the virus to fuse into the cell and release genetic material into the host cell. The envelope, therefore, aids in the attachment to host cells. However, the envelope increases the virus' sensitivity to parameters such as heat, dryness, detergents and solvents such as alcohol. It has been clinically shown that almost all viruses which are transmitted via the fecal-oral route lack an envelope and are capable of enduring certain environments more.[10-12]

## Applications of Gold Nanoparticles (AuNPs) in Virus Detection

Nanoparticles have made nanoscale bio-targets such as proteins, lipids, and viruses detectable. The size scale of nanoparticles corresponds to the size scale of biological objects, which are of importance in many medical and bioengineering applications. Despite the fact that the scales are similar, the detection of binding events at the nanoscale only results in minor perturbations on resonance, resulting in less detectable signals. This is especially problematic when it comes to identifying viruses, which might be quite infrequent in solutions. As a result, other ways for enhancing and amplifying resonance disturbances and allowing greater shifts which are observable and quantifiable are urgently needed to progress this discipline.

AuNPs have been the most frequently used NPs in the detection of viruses. A mechanism known as "size and distance dependent nanoparticle surface energy transfer" was used to detect the presence of RNA of hepatitis C virus (HCV). In this mechanism, firstly, a single strand RNA is labelled with fluorophores and absorbed on the surface of AuNPs, such that when the complementary RNA is detected, they bind together forming a double strand RNA complex (dsRNA) by a process

known as hybridization. When dsRNA is formed and released in the solution, fluorescence emission takes place. The use of AuNPs in this mechanism is as a colorimetric signal indicating the presence of the RNA of HCV by the aggregation of AuNPs which results in a color change from red to blue. It is also important to note that fluorescence intensity is directly related to the concentration of the target RNA present in the solution.[13]

Another method which is used to detect avian influenza virus (AIV) is based on AuNPs and MNPs. MNPs are combined with "AIV-specific penta-body (pVHH3B)" to detect AIV. AuNPs are labelled with "anti-AIV monoclonal antibody (mAb3C8) forming AuNPs-mAb3C8". This configuration of AuNPs is used as a detector. In this method, when the target is present, the pVHH3B reinforce the AIV on the MNPs, and then the AuNPs-mAb3C8 bind to the MNPs forming a complex. AuNPs present in this complex stimulate the oxidation of hydroquinone to quinone. Finally, the optical density of quinone is measured. This density is used to determine the amount of AIV in the sample. In other words, this density measures the amount of yellow color produced, which is directly related to the concentration of AIV present in the sample.[14]

Moreover, a system known as "fluorescence resonance energy transfer (FRET) system" was used for the detection of the DNA of the hepatitis B virus (HBV). The general concept of this system is that an atom in the higher energy state transfers its electrons to the closest atoms in a non-radiative way.[15] In this study,[6] the FRET system is composed of gold nano-rods (AuNRs) and fluorescein (FAM). Firstly, the AuNR's surface is covered with cetyl-trimethylammonium bromide (CTAB). The CTAB is used to generate positive charges on the nano-rods. Then, a single strand DNA (ssDNA) labelled with FAM forming FAM-ssDNA was added to the AuNRs solution. FAM-ssDNA was adsorbed onto the surface of the positive charges of the AuNRs and formed a ternary complex (FAM-ssDNA-CTAB-AuNRs). This configuration resulted in the FRET process to take place from FAM to AuNRs. The fluorescence intensity of FAM was reduced. The fluorescence intensity further decreased when the complementary target DNA was added to the ternary solution. This is because of an increased FRET efficiency.

The surface enhanced Raman scattering (SERS) method is used to detect the rift valley fever virus antigen based on AuNPs. Firstly, AuNPs and MNPs are combined with a polyclonal Ab specific for the target virus antigen, forming AuNPs-Ab and MNPs-Ab, respectively. The polyclonal Ab is a group of antibodies from different cells which determine various epitopes on the same antigen. Then, when the specific antigen is held by the AuNPs-Ab and MNPs-Ab, they form a three-component immunocomplex. A laser beam is then directed towards this complex and excites it. The presence of the target antigen yields a reduction in the intensity of Raman spectrum peaks, thereby providing an estimation of its concentration. This method resulted in direct and fast detection of the virus with prominent sensitivity down to 5 fg/mL even in complex samples which is achieved by magnetic particles supporting the application.[16]

In another study, a three-dimensional plasmonic nanocomposite was established, creating a SERS detector chip for the detection of several viruses and bacteria.

In this study, the hydrothermal technique was used to allow Zinc nano-rods (ZnONRs) to grow vertically on a cellulose paper containing pores (C). Then, successive ionic layer adsorption and reaction technique is used to enhance AuNPs on the ZnONR/C, forming the three-dimensional plasmonic nanocomposite. As a result of this nanocomposite, the Raman signal showed improvement and highly specific detection.[17]

For the detection of the influenza A virus, a mixture of H3N2 IAV (antigen) with AuNPs-monoclonal anti-HA antibody (AuNPs-mAb) is added to phosphate-buffered saline. The mixture is prepared with various dilutions of H3N2 IAV added to a five-fold concentrated mAb-AuNP suspension (a diluted 1/5" ratio meaning that the ratio of H3N2 IAV to mAb-AuNP is 1:5). It then undergoes incubation at 37 °C for 30 mins. As a result, H3N2 IAV can be seen by the naked eye and a color change from red to blue of the mixture is observed, this is shown in Figure 2. Finally, in order to be able to determine the concentration of the virus, a UV-vis spectrophotometer can be used. This method is not only low cost, simple and convenient, but also it is a single step detection method, accurate and specific. In addition, it does not require further amplification.[18]

In another study found in the literature, a layered complex was established creating a colorimetric medium to detect the influenza A virus (H3N2). In that study, the color change is related to the amount of hydrogen peroxide produced. First, aptamer-functionalized magnetic microparticles are needed to encapsulate the virus. Additionally, AuNPs were modified by glucose oxidase (GOx) and concanavalin A (ConA) forming a ConA-GOx-AuNPs solution which was conjugated with H3N2 virus resulting in a reaction producing hydrogen peroxide and changing the AuNPs color.[19]

In another study, an electrochemical method was used for the detection of the human immunodeficiency virus-1 (HIV-1). This method[20] is based on the direct identification of electron transfer signals from the virus. Using this method, an electrode made from indium tin oxide and coated with glass was used and AuNPs were electrodeposited on it. This configuration resulted in an improved transfer of electrons and a higher background charging current. On this modified electrode, using the self-assembly method, small pieces of antibodies were immobilized with gold-thiol bonding and various concentrations of HIV-1 virus-like particles (VLP). The VLP of HIV was successfully detected with a detection limit of 600 fg/mL-1 to 375 pg/mL-1. A summary of AuNPs in the detection of different viruses is shown in Table 1.

## Other Nanomaterials Used in Viral Detection

Apart from gold NPs which are the most frequently used nanoparticles in viral detection, other nanomaterials are summarized in their viral

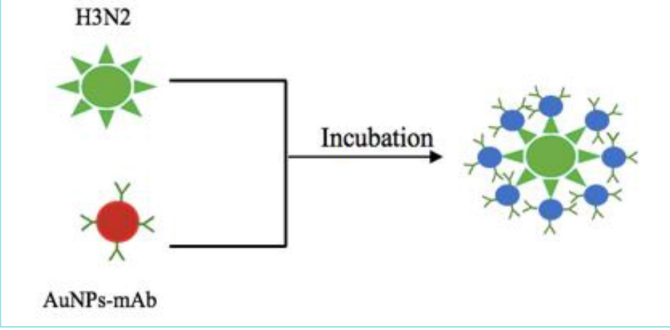


**Figure 2.** Method of influenza A virus detection.

**Table 1. Gold NPs in the detection of different viruses**

| Detected | Technique | Detection limit/sensitivity down to | References |
|---|---|---|---|
| RNA of hepatitis C | AuNPs-based assay | - | 13 |
| Avian influenza | Nanoparticle-based assay | 10 ng $mL^{-1}$ | 14 |
| DNA of hepatitis B | FRET-based assay | 15 pmol $L^{-1}$ | 6,15 |
| Antigen of RVFV | Nanoparticle-based immunoassay with surface Raman scattering | Sensitivity down to 5 fg/mL | 16 |
| Several viruses and bacteria | | - | 17 |
| Influenza A | Nanoparticle-based colorimetric assay | 7.8 HA<br>$1.1x10^7$ pg $mL^{-1}$ | 18<br>19 |
| VLP of HIV | Electrochemical assay | 600 fg/$mL^{-1}$ to 375 pg/$mL^{-1}$ | 20 |

NPs: nanoparticles, AuNPs: applications of gold nanoparticles, FRET: fluorescence resonance energy transfer, RVFV: Rift Valley Fever virus, VLP: virus-like particles, HIV: human immunodeficiency virus-1.

applications. For example, a method known as cathodic stripping voltammetry used MNPs to confirm the presence of PCR-amplified DNA of the HBV.[21] An immunosensor based on CNTs was used to identify the presence of the biomarkers of the hepatitis B surface antigen. The immunosensor consists of a glassy carbon electrode, CNTs and polypyrrole propionic acid. Moreover, for the determination of HIV, a detection system based on QDs was established.[13] Also using the QDs, another system was established which is FRET-based QDs-DNA.[6] This system is used for the fast and simple identification of the DNA of HBV. In addition, a biosensor was constructed based on graphene which contains immobilized monoclonal antibodies used to detect the presence of Zika virus.[22]

In another study, a QD was embedded inside an empty shell of iron oxide, resulting in an electrochemical/fluorescence dual probe for the detection of various viruses from clinical specimens, including the hepatitis E virus (HEV), HEV-like particles, norovirus-like particles (NoV-LPs), and norovirus. Most notably, HEV-infected monkey feces were effectively identified with a sensitivity close to the gold standard real-time quantitative reverse transcription-polymerase chain reaction (RT-qPCR). This well-defined QD@MHS NPs-based nano-platform intelligently merges dual-modality sensing with magnetic bio-separation, opening the door to efficient point-of-care viral diagnostics testing[23].

## Coronaviruses (SARS-CoV, MERS-CoV, SARS-CoV-2)

Coronaviruses are a family of RNA viruses having large RNA genomes, infecting both animals and humans. Coronaviruses can infect both birds and mammals, and it has been shown that bats can act as hosts to the virus and pass it on to other species. Previous epidemics caused by the coronavirus have been recorded in history; this has been shown due to the viral protein mutations which cause them to bind to different cells, infecting more cells of different species. Back in late 2002, a novel deadly virus known as SARS emerged. There were 8,089 reported cases and 774 deaths with a fatality rate of 9.7%. In 2012, the middle east respiratory syndrome-coronavirus (MERS-CoV) immerged causing 2,494 reported cases and around 860 deaths in 27 countries with a high fatality rate of 34%. The new SARS-CoV-2, although less fatal, has a higher reproductive rate ($R_0$) of 2.5 in comparison to 2.4 and 0.69 for SARS and MERS, respectively. The reproductive rate ($R_0$) is a quantitative measure of the average number of transmissions from one infected person. Therefore, an $R_0$ greater than one means a growing epidemic. Moreover, SARS-CoV-2 has a higher incubation period (4-12 days) than SARS-CoV (2-7 days), which in turn increases its chances of transmission. The incubation period is the time of first exposure to the virus until the first symptoms start to appear.[1] Moreover, all throughout history, pandemics have wiped out populations, affected wars and societies. They have, however, also caused advancements in medicine and science. The following table (Table 2) shows several pandemics and epidemics recorded in history[24] and their estimated death tolls.

## Classification of Viral Tests and COVID-19

Viral tests are based on biotechnology, specifically analyte-based bio-sensing. Quantitative reverse transcription polymerase chain reaction (qRT-PCR) tests are necessary to decide whether a person is infected and therefore must be isolated. Since COVID-19 is generally a respiratory illness, chest X-rays, thoracic imaging and flexible bronchoscopy are also available for diagnosis and recovery. There are many drawbacks to qRT-PCR testing, such as taking from 4 hours up to 3 days to obtain results, errors in results, lengthy sample preparation and specific transportation. Moreover, the typical qRT-PCR test is inaccurate showing false results such as appearing negative to those freshly infected and positive to those who have recovered, due to it detecting dead SARS-CoV-2 in them. Therefore, alternative methods must be found to increase sensitivity and decrease time and cost.[25] Some of those alternative methods include nanofabrication and nano-science which increases effectiveness. There are 3 types of viral tests based on what they target. The first one is a genetic test targeting the viral genome. The second type is called antigenic which targets the viral proteins/antigens. Lastly, the third is called serological which targets the antibodies that are released as an immune response to a viral infection. Antigenic and serological tests are based on the antigen-antibody recognition using lateral flow assays. Antigenic tests require at least 5 days to obtain enough viral antigens to be effective and serological tests require at least 7 days for the antibodies to be produced. Antigenic test strips contain viral antibodies coated on it. Once a blood sample interacts with it, the presence of viral antigens in the blood will cause a color change due to the plasmonic resonance properties of the colloidal gold used in the strip test. Serological tests, although similar, detect the presence of antibodies instead of antigens. Those tests can detect the presence of both immunoglobulin G (IgG) and IgM which give different information on the current or past presence of the virus. After being infected with COVID-19, an immune response triggers the production of IgG and IgM in the body which fight against the virus. These antibodies

**Table 2. Pandemics and Epidemics recorded in history**

| Disease | Year | Estimated deaths |
|---|---|---|
| The Athenian plague | 430 B.C. | ~75,000-100,000 |
| The Antonine plague | 165-180 A.D. | ~5,000,000 (1/3 of the Roman population at the time) |
| The Justinian plague | 541-750 A.D. | ~50,000,000 over two centuries of recurrence |
| The black death | 1347-1351 A.D. | ~25,000,000 |
| Spanish flu | 1918-1920 A.D. | ~50,000,000 |
| HIV | 1980-present A.D. | 32,000,000 |
| SARS (SARS-CoV) | 2003 A.D. | 774 |
| "Swine Flu" or H1N1/09 | 2009 A.D. | ~150,000 |
| MERS | 2012 A.D. | 860 |
| Ebola | 2014-2016 A.D. | ~11,315 |
| Zika | 2015-2016 A.D. | ~18 |
| COVID-19 (SARS-CoV-2) | 2019-present A.D. | 5,905,481 (As of: February 20th, 2022, 22:55 GMT) |

HIV: human immunodeficiency virus-1, SARS-CoV-2: severe acute respiratory syndrome-coronavirus-2, MERS: middle east respiratory syndrome, COVID-19: coronavirus disease-2019.

can be found in the blood. IgM are the first viral antibodies produced to protect you and the IgG antibodies remain in your blood shortly after recovery to insure future immunity. Improving the sensitivity and accuracy of immunoassays has been of importance recently and it has been tackled using dyes or nanoparticles which strengthen the antibody-antigen binding signal. Various nano-materials have also been used as conjugates to the bio-receptors including carbon nanoparticles, ODs, colloidal GNPs as well as liposomes and enzymes.[26]

## Point-of-Care Biosensors

Point-of-care biosensors are those which can be used simultaneously while treating the patient and are at a close proximity with the patient thus providing immediate care. In poorer areas, typical testing may not be present and therefore a cheaper and easier point of care (POC) alternative was developed. Generally, there are two types of POC biosensors capable of detecting SARS-CoV-2. Those two tests are nucleic acid and antibody tests. Nucleic acid tests show early results even before symptoms appear by taking a sample from the saliva and/or mucus since the ACE2 enzyme is found in the lower respiratory tract where the sample is taken from. The antibody (IgG/IgM) test, however, is typically used when symptoms start to show or to confirm past diagnoses for the coronavirus. Being positive for IgG implies you have been infected with COVID-19 in the near past or are still currently infected. POC biosensors which can potentially be used to detect COVID-19 are chip-based, paper-based or other materials-based biosensors. Paper-based biosensors have become more commonly used than chip-based biosensors to detect COVID-19 due to their ease of fabrication and modification. Paper-based biosensors consist of a lateral flow test paper strip for the detection of IgM and IgG antibodies. The strip contains various pads including those with COVID-19 antigens conjugated with GNPs. Upon the presence of IgM and/or IgG antibodies, they react with the gold-COVID-19 antigen complex and form a reaction continuing along the strip.[27] A team of Korean scientists detected COVID-19 using a graphene-based biosensor. Field effect transistors (FET) use an electric field to control current flow. Using FET-based biosensors allows for instant and accurate sensing using small amounts of analytes without prior preparation. The assembly of a graphene-based FET was functionalized via the SARS-CoV-2 antibody on the surface for the detection of the viral spike protein. The sensor was able to detect the viral antigen via cultured COVID-19 viruses, patient nasopharyngeal swabs as well as SARS-CoV-2 virus lab samples and could also distinguish the viral protein from that of MERS-CoV. Graphene-based FET biosensors allow optimal sensing providing accurate results. The team used nanotechnology-based techniques such as the wet transfer method to deposit graphene onto a silica substrate followed by creating channels on the graphene layer via photolithography and etching which formed linearly ordered graphene on the substrate. Then, metal electrodes were added using thin film deposition. Finally, graphene was used to bridge the source and drain electrodes. The SARS-CoV-2 antibody on the surface of the graphene was immobilized via 1-pyrenebutyric acid N-hydroxysuccinimide ester by forming a chemical bond. Graphene was used as a COVID-19 transistor responding to the viral spike proteins, changing its electrical conductivity and, as a result, changing the amount of current flow and showing a response signal.[28]

Information on more than 240 Emergency Use Authorization-level COVID-19 diagnostic tests are available (as of 5th September 2020), and the number of commercially produced COVID-19 molecular tests and immunoassays is almost comparable. FIND has been evaluating over 800 diagnostic assays, more than 250 of which are quick tests which produce a response in less than 30 minutes. The use of immunoassays at the POC is routinely approved as part of the COVID-19 post-restriction management plans.[29]

## Nanotechnology-Based Vaccines

Nanotechnology has been involved in the production of messenger RNA (mRNA) vaccines for COVID-19. Those are the Pfizer-BioNTech and Moderna vaccines. They are mRNA vaccines, which unlike the other typical vaccines, do not contain an inactive or weakened virus. Instead, Pfizer-BioNTech and Moderna vaccines contain genetic information that code for the S-spike protein found on the surface of SARS-CoV-2, thus, triggering an immune response and antibody production which a typical vaccine would (such as in typical weakened/inactive vector vaccines). Moreover, these mRNA vaccines are modified with lipid nanoparticles in order to overcome the limitation of vaccine degradation by the enzymes present in the body. This is done by wrapping the mRNA of the vaccines with a nano-coating made from lipid nanoparticles.[30] These vaccines have been stated to cause allergic reactions in some, triggering anaphylaxis due to the compound polyethylene glycol (PEG). The outer lipid nanoparticles are "PEGylated" or chemically bonded to

PEG molecules which increase their performance and lifespan.[31] For that reason, as well as the search for more economical nanoparticles and easier storage requirements, alternatives have been investigated such as one which has been studied at Stanford University. The study carried out at Stanford University suggests the possible use of iron nanoparticles containing ferritin proteins which have the S-spike protein attached on its surface, thus initiating an immune response and developing antibodies.[32]

## CONCLUSION

The merging of nano-materials with their distinct properties along with biosensors results in them being more efficient, sensitive and selective (also known as nano-biosensors) as well as introducing new and easier methods of fabrication which are not present in ordinary biosensors. Furthermore, AuNPs showed the most potential to be applied in different methods for the detection of numerous different viruses. AuNPs are biocompatible with the human body, they have distinct optical properties, good catalytic activity and their surface can easily be functionalized.

Point-of-care biosensors play a huge role in fast detection, fast diagnosis and treatment. POC biosensors are also accessible in poorer areas due to them being easier to use by the individual and cheaper than typical qRT-PCR testing. Some POC biosensors include nanofabrication and nano-based materials such as AuNPs and graphene. Moreover, nanotechnology has played an important role in increasing the sensitivity of antigenic and serological tests. Specifically, this has been achieved by the use of colloidal gold NPs to increase the antigen-antibody signal, as well as by using several NPs as conjugates to bio-receptors such as colloidal gold, carbon and ODs.

From viral detection to producing a viral vaccine, nanotechnology has shown great potential and is currently being implemented. Over 12 vaccines aimed at targeting the COVID-19 virus are already in clinical trials. From which, nanofabrication has been incorporated into mRNA lipid-based nanoparticle vaccines.[33] Moreover, a team of researchers at Steinmetz Lab in UC San Diego suggest that the production of a plant-based nanoparticle vaccine, extracted specifically from black eyed peas, will be more sustainable and easier for manufacturing at a global scale in such a growing pandemic. Additionally, a team at Stanford University suggests the possible use of an iron nanoparticle-based vaccine.

Nanofabrication is a growing field with many frequent discoveries. Public, health and economic concerns must be addressed to produce globally safe and cheap nano-based vaccines as well as obtain an effective, easily accessible nano-biosensor which can serve and benefit the public and provide a faster and more precise detection method in order to reduce the spread of infections.

## MAIN POINTS

- COVID-19 is an illness caused by the SARS-CoV-2 virus which was declared a global pandemic by the WHO on March 11th, 2020.
- Nano-biosensors are biosensors based on the presence of nanomaterials which provide a better detection system.
- Nanoparticles such as AuNPs have been used to improve the antibody-antigen binding signal in viral tests based on lateral flow assays.
- Nanofabrication has been incorporated in mRNA lipid-based nanoparticle vaccines such as in the Pfizer-BioNTech and Moderna COVID-19 vaccines.

## ETHICS

**Peer-review:** Externally peer-reviewed.

### Authorship Contributions

Concept: D.K., S.A., Design: D.K., M.M., Supervision: S.A., Ş.K., Materials: D.K., M.M., Data Collection and/or Processing: D.K., M.M., Analysis and/or Interpretation: D.K., S.A., S.B., Ş.K., Literature Search: D.K., M.M., Ş.K., Writing: D.K., Critical Review: S.A., S.B.

## DISCLOSURES

**Conflict of Interest:** No conflict of interest was declared by the authors.

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