# Surface Plasmon Resonance Sensor for Covid-19 Detection: A Review on Plasmonic Materials


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***Abstract*— This review aims to investigate the potential of various types of plasmonic materials for Covid-19 detection in terms of the performance, limitation and future prospects. Few parameters have been reviewed such as sensitivity, the limit of detection, time response, and thickness of materials. In this review, we analyze plasmonic materials that is used to excite SPR effect such as gold-based material, silver-based material, copper-based materials, and metal nanoparticles. In addition, the additional or hybrid material are reviewed as well. Gold-based SPR sensors portray an excellent performance in detecting various viruses including Covid-19. The implementation of gold-based materials includes gold nanomaterial as well which has different shapes for instance, nanospheres, nanorod, and nanoisland. Obviously, the deployment of gold nanomaterials resulted in the best sensitivity and according to the analysis, about 50% of recent research chose gold nanomaterials as plasmonic materials for sensing applications concerning their outstanding properties such as high stability, oxidation resistance and simple fabrication. Other than gold nanomaterials, hybrid-based gold material such as graphene-gold based sensor exhibits a good sensitivity which is about 183.3 °/RIU, in which 25% of current studies utilized this type of plasmonic material for virus detection. In conclusion, gold nanomaterials-based plasmonic sensors have a bright potential to be implemented for Covid-19 detection and the addition of another material like graphene can enhance the performance. We believe that the output of this study will contribute to developing biosensors for detecting Covid-19.**



***Keywords—SPR sensor, Covid-19, optical sensor, biosensor, plasmonic materials***


## I. Introduction

The Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) or known as Coronavirus Disease 2019 (COVID-19) cases were first reported in Wuhan, China in December 2019. According to World Health Organization (WHO), as of 6 April 2023, the reported cases of Covid-19 infection have reached more than 76 billion cases and 6,893,190 deaths around the world. This highly contagious disease is similar to the influenza virus which affects the respiratory system and causes one to have symptoms like coughing, shortness of breath, exhaustion, fatigue, fever, and exhaustion [1]. In 2020, due to the rapid spread of this air bone virus, WHO declared that Covid-19 can be characterized as a pandemic. This deadly infected virus needs can be avoided by detecting the infection early and currently, in clinical settings, reverse-transcriptase polymerase chain reaction (RT-PCR)-based molecular diagnostic methods and computed tomography (CT)-based medical imaging technologies are now employed to diagnose COVID-19 infection and pathological condition [2].

Covid-19 has been detected as a member of the coronavirus family's β-CoV genera, which normally get their gene origins from bats and rodents [1]. The diagnosis of coronavirus is by using the RT-PCR method [3] and this is also applied to Covid-19. Instead of using the RT-PCR method, other sensors have been introduced including the distinguished sensor nowadays which is the optical sensor. Optical sensors are mostly been chosen to use in many applications due to their tremendous advantages. Due to their safe, simple-to-use, and cost-effective technology, optical sensors offer an alternate technique for viral detection, avoiding the requirement for nucleic acid amplification [4]. There are a few optical sensors for biological application, for instance, surface-enhanced Raman scattering (SERS), visible-light laser diodes, fluorescence, infrared analytical arrays, narrowband optical filters, surface plasmon resonance (SPR), and other laser techniques [5]. Previous studies reported the uses of these optical sensors such as a paper-based multiplex SERS sensor based on silver nanodots substrate and a double-labeled probe used for the detection of multiple fluorescent dyes for the use of pathogens detection [6]. Light scattering and fluorescence measurement can be used to detect and classify individual viruses by quantitative analysis and sorting of viruses and other particles in the micron and nanoparticle size ranges [5], [7]. These works prove that the optical sensor proves can be used in biomedical applications including viruses such as coronavirus.

The application of sensing material for optical is vital to enhance sensor performance. There are a few types of sensing materials that were used in previous works such as polymers, composites, and nanomaterials [8]. Polymer has been used as a sensing material due to its reasonable value that may be placed on a variety of substrates with varying forms and sizes. Nanomaterials include metal and noble metals nanomaterials (gold nanoparticles (AuNPs) and silver nanoparticles (AgNPs), metal oxide nanoparticles like zinc oxide (ZnO), tin oxide ($SnO_2$), and titanium oxide ($TiO_2$), carbon-based nanomaterials (graphene and carbon nanotubes), polymer and bio-nanomaterials (polymer and bio nanomaterials). These nanomaterials have been remarkable in optical sensing due to their characteristics such as being small in size, chemically stable, easy to fabricate, and have a high surface-to-volume ratio which is better than the use of bulk films [9].

There are two alternative methods for detecting viral infection: the first one is a serological investigation for the measurement of biomarker levels such as immunoglobin M (IgM) and immunoglobin G (IgG). This method has limitations because of the concentration and half-life of the marker (host antibodies). The second method is the detection of viruses through cell surface protein. The current technique in detecting Covid-19, RT-PCR is a reliable method compared to other techniques, nevertheless, it is time consuming which takes a few hours for analysis and might provide false negative or positive cases [10], [11]. According to a recent study [11], 5 (3%) out of 167 COVID-19 infected patients confirm to have a positive result by CT scanning but false-negative RT-PCR testing results. The repeated swab test revealed that these five patients were infected with COVID-19. Besides, it also requires a lot of manpower [10] which may not suitable to use when there are many suspected cases at a time. It may cause a delay in time and exhaustion to the persons in charge. Alternatively, the optical sensor is one of the candidates to overcome those issues due to its minimal size [12], insensitive to electrical interference, and not needing a second reference sensor [13]. Direct and label-free analyte detection by optical sensors provides various advantages, including mobility, tolerance to electrostatic and electromagnetic interferences, ultrasensitive detection limits, and resilience [14]. The RT-PCR is a gold standard is detecting Covid-19 as it provides high sensitivity and specificity [15]. Nonetheless, RT-PCR method is time consuming and might cause false negative or positive cases [10], [11]. CT imaging can be used in detecting Covid-19 by giving detail visualization of the lung condition of the infected patients. It is claimed to be more sensitive than RT-PCR method. Nevertheless, it can cause confusion with different medical condition like influenza, SARS-CoV, and H1N1[15]. Immunoassay which can provide faster result and cost-effective is said to be suitable only to post-symptomatic patients. Moreover, it is less sensitive compared to the nucleic acid base method known as the RT-PCR method [15]. SPR sensor is considered to be a suitable sensor for biomedical sensing applications as mentioned by Sakib et al. since it has been highly recommended in bioengineering, gas detection, virus detection, medical diagnosis, environmental observation, and antigen-antibody collaboration [16]. SPR sensor is a sensor that excites surface plasmon polaritons (SPP) when incident light strikes the surface of the noble metal which leads to the existence of an evanescent field due to the SPR phenomenon [17]. It has high sensitivity [18], in-situ dynamic monitoring [19], and fast response [20]. In order to design an efficient SPR sensor with high sensitivity, it must include sensing material such as dielectric layers such as reduced graphene oxide (rGO) and metal nanoparticles [21].

Covid-19 had leave very bad impacts on the world and even now people who have been infected with this virus still experience the post-Covid-19 symptoms like dyspnea, fatigue, cough, tightness of the chest, muscle or body aches, and brain fog [22]. Besides, Han et al. demonstrated a research by collecting data about longer-term persistent symptoms of COVID-19 and found out that the multiple symptoms including physical, mental, and cognitive health persist for at least one year in sizeable proportions of Covid-19 infected patients [23]. This scenario gives us a strong signal about the need for efficient and sensitive biosensors. By considering the extraordinary features of plasmonic materials in sensing applications, we believe that SPR sensor has a bright future in sensing Covid-19 effectively. The plasmonic materials need to be analyzed as the spike protein for Covid-19 gives good interaction with certain materials and there is a need for using suitable plasmonic material as it can affect the sensing performance. This review study is carried out to evaluate the potential of various types of plasmonic materials in SPR sensors for Covid-19 detection. At the end of this study, it can be concluded that Au nanomaterial is the most suitable material to be deployed. We believe that the output of this work will contribute to the development of biosensing technology in addressing the Covid-19 issues.

## II. COVID-19

### A. *Background and the Structure of SARS-CoV-2*

Covid-19 is named SARS-CoV-2 due to its sequence identity which has high sequence similarity to SARS-CoV. According to Kabir et al., SARS-CoV-2 has 29,891 nucleotides in its genome, comprising 9860 amino acids, with 79 percent pairwise genomic level identical to human SARS-CoV and 50% identity to human Middle East Respiratory Syndrome Coronavirus (MERS-CoV) [2]. SARS-CoV is considered as human coronavirus that affects the respiratory system. The sources of human coronavirus including SARS-CoV are generally from mammals like bats, mice, or rodents that is transmitted through other animals such as bird as intermediate sources [24]. The transmission of this virus can be done in different ways. As mentioned by Lotfi et al., Covid-19 is transmitted by direct contact (droplet and human-to-human transmission) or indirect contact (airbone contagion and contaminated surface) [25]. Coronavirus is divided into four types based on its genetic structure: alpha, beta, gamma, and delta. Only mammals are infected by alpha and beta coronaviruses, which mainly cause respiratory symptoms in humans and gastroenteritis in other animals [24].

According to Shi et al., the common structure of coronavirus is round or multi-shaped. They are measured to have a diameter of 120-160 nm and consist of a petal-shaped projection which is S protein [26]. Covid-19 contains four structural proteins including spike glycoprotein (S), membrane (M), nucleocapsid (N), and envelope (E) [2]. The spike glycoprotein (S) is made up of two subunits which are S1 and S2. The subunit S1 functioned in binding to the host cell receptor meanwhile S2 is used for the fusion of the viral and cellular membranes [27]. The N protein binds with the Ribonucleic acid (RNA) genome to make up nucleocapsid, meanwhile, M protein which has three trans-membrane domains, serves as a primary organizer for the virions, determining their morphologies and binding to the nucleocapsid. Finally, by interacting with the M protein, the E protein aids in the formation of the virus's envelope membrane [2]. According to Kabir et al., S and N proteins are among the most valuable antigen indicators for identifying coronavirus disease in 2019, much as S and N proteins are used in numerous detection methods for detecting SARS [2].

### *B. Various techniques to detect the Covid-19 virus*

Due to the rapid transmission of Covid-19, a suitable detection method is vital to control the transmission. There are a few techniques for detecting Covid-19 that have been studied in previous studies such as [15]:

- Nucleic Acid Base Method
- CT Imaging
- Immunoassays

The RT-PCR is a nucleic acid amplification assay and it has been implemented in detecting RNA viruses [15]. According to Kabir et al., RT-PCR is currently a gold standard in detecting infectious diseases including CoVs in previous epidemics [2]. It is claimed to be highly sensitive to the DNA/RNA target because the primers bind to a specific section of the viral genome. The RNA-dependent RNA polymerase (RdRp) sequence and the open reading frame 1ab (ORF1ab) sequence, which have been chosen as gene targets for RT-PCR molecular tests by several countries, are genetically similar [10]. Kabir et al. mentioned that there are three steps in the PCR experiment; the first step is to collect and process samples from infected patients. Then, the second step is regarding the extraction of RNA followed by cDNA synthesis by using the reverse transcriptase technique. Lastly, the target-specific primers are used for amplification, and real-time quantitative PCR is used for detection [2]. The sensitivity of SARS -CoV-2 or Covid-19 is 3.7 RNA copies on detecting the RdRp sequence [10]. Though it is considered to be highly sensitive, there are few cases reported that RT-PCR has false-negative cases. Qiu et al. stated that there is a previous study that found false-negative results from RT-PCR testing [10]. According to Xie et al., out of 167 samples from Covid-19 patients, 3% of the sample tested positive by using a CT scan but was detected as negative by the RT-PCR method [28]. Thus, further study needs to be done in improving RT-PCR testing to avoid false-negative results.

Chest CT scan can be used to detect Covid-19. The image obtained from the chest CT scan has characteristic features of Covid-19 which include a crazy-paving pattern, glass opacities, septal thickening, consolidative opacities, and the reverse-halo sign [15]. Pokhrel et al. as well mention that a chest CT scan is not recommended to detect Covid-19 in the US due to confusion that can happen as the result may overlap with other diseases such as influenza, SARS-CoV, and H1N1 even though this method is more sensitive than RT-PCR [15]. Chest CT imaging may cause false-positive cases as it shares similarities in features with other viruses. Immunoassay is another type of method where it is used to detect viral protein antigens or blood antibodies of an infected person. Antibody testing is crucial for recognizing previous infections [15]. Pokhrel et al. mentioned that there are few immunoassay test kits are on the market that gives faster results and cheaper. Nevertheless, the main drawback of this technique is that it is only applicable to post-symptomatic individuals who have an immunological response to SARS-CoV-2. Besides, it is less sensitive compared to the nucleic acid base method known as the RT-PCR method [15]. Besides all of these clinical techniques, research by Kabir et al. reviewed on the SPR based assay to detect Covid-19 and mentioned that a previous research proposed an SPR sensor to detect Covid-19 [2]. The proposed sensor is a photothermal biosensor based on a prism-based SPR. The plasmonic photothermal (PPT) effect and localized surface plasmon resonance (LSPR) effect are combined in this biosensing approach to producing an accurate and promising clinical diagnosis of COVID-19. This kind of sensor is a good candidate for detecting Covid-19 as it has advantages such as low cost, high sensitivity, ultra-low detection limits, and low power consumption. Further research in the optical sensor for detecting Covid-19 is vital to construct an excellent performance sensor.

## III. Surface Plasmon Resonance (SPR) Sensor

### *A. Theory*

SPR refers to the excited charge density oscillation along with the metal-dielectric interface, with the permittivity of opposing signs [29]. This phenomenon principle relates to the resonance of a strong electromagnetic field oscillation at the interface of a nanometal film and dielectric medium with p-polarized incident light resulting in a dark band profile in the light reflectivity at an incident angle and specific wavelength [30]. The specific wavelength is called resonance wavelength which is dependent on the refractive index (RI) of the dielectric material [31]. Surface plasma waves (SPW) or SPP can be created when the orientation of the electric field vector of an incident light complements the motion of free electrons in the metal. It is controlled by boundary restrictions connected with the material and structural considerations, and thus efficient coupling with large energy as guided electromagnetic waves along the interface can happen [29]. SPR sensor is known for their high sensitivity and different types of design [32]. The prism coupled sensor is the earliest type of sensor discovered by Otto and then improved by Kretschmann. According to Zhao et al., the prism-coupled SPR in Otto configuration was based on attenuated total reflection. It was then improved by Kretschmann configuration as the analytes separate the prism and plasmonic metal layer, leading to a complex design [32]. Fig. 1 (a) and Fig. 1 (b) show the Otto and Kretschmann configuration design. Otto and Kretschmann's configuration has been widely used in SPR based sensors, nevertheless, the drawback of these configurations is the large and complex design. Thus, the design of the SPR sensor has been upgraded to enhance its performance. For instance, as was mentioned by Zhao et al., a few designs are created such as prism couple sensor, grating coupled sensor, optical fiber coupled sensor, and waveguide coupled sensor [32].

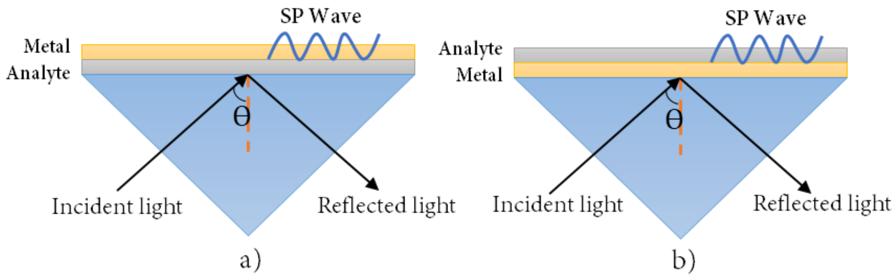


Fig. 1: (a) Otto (b) Kretschmann configuration

Compared to the SPR phenomenon that is excited by metal thin film, LSPR is regulated to smaller particle called nanoparticles which has a size range from 1 nm to 100 nm. It happens when a light wave is trapped within conductive nanoparticles smaller than the wavelength of light. The interaction of incident light with surface electrons in a conduction band causes this phenomenon [33]. It is observed in metal nanoparticles where the electromagnetic light hits the metal nanoparticles and results in the interaction between the electric field and free electrons. This causes them to distinct from the metal core. The repulsive force between electrons makes them travel in opposite directions, causing them to oscillate and excite the LSPR. Strong light absorption can be induced via LSPR excitation [34]. Few parameters can affect the resultant wavelength position of the LSPR absorption bands such as size, shape, interparticle distance or aggregation state of the nanoparticles, composition, and the dielectric constant of the surrounding medium [35], [36]. The function of LSPR is implemented to detect the RI changes in a small area as it deals with smaller volumes. When the SPP and the localized plasmon polariton (LSP) exist at the same moment, they will pair to generate a localized electromagnetic field enhancement [21]. As it enhances the electromagnetic field, it can also maximize the optical extinction of the metal nanoparticles. According to Bai et al., LSPR can increase the time for optical extinction for AuNPs more than 1000 times stronger than typical organic molecules where it can enrich the photothermal conversion efficiency, light absorption, and photochemistry conversion of AuNPs [37]. Fig. 2 shows the phenomenon of LSPR of AuNPs. LPSR sensors have been used in a few industries such as clinical uses [33], virus detection [6], food safety, and environmental monitoring [38].

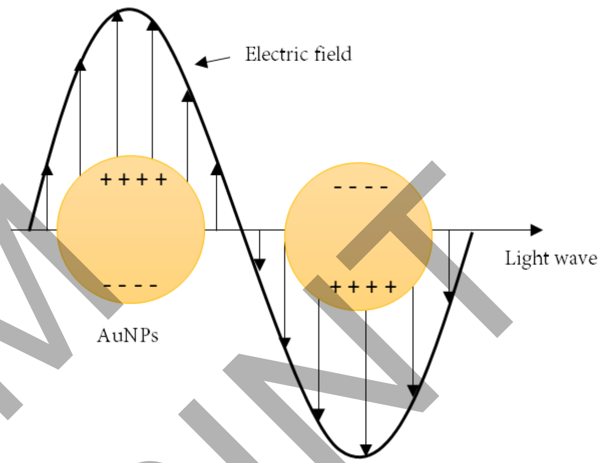


Fig. 2: Properties of LSPR of AuNP

According to Qiu et al., among other sensing techniques for biosensing, LSPR applies to different types of analytes of clinical interest. This is due to local variations, such as RI change and molecule binding detected with high sensitivity LSPR sensing systems [10]. As a result, LSPR is an excellent choice for detecting microscale and nanoscale analytes in real-time and without the need for labels. For example, Hassan et al. stated that LSPR biosensor is used for virus detection [39]. Fig. 3 shows the construction of the LSPR biosensor.

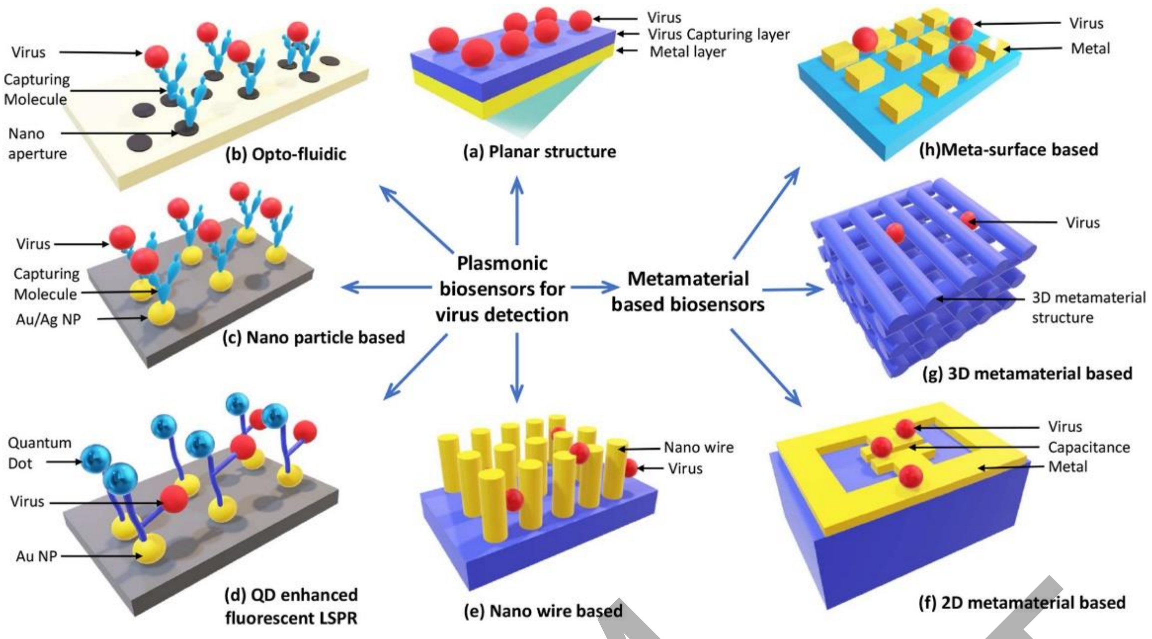


Fig. 3: The construction of LSPR biosensor [39]



*B. The mechanism of SPR*

SPR occurs when light irradiates the metal-to-medium interface. It will resonate with the SPW to induce energy transfer and causes the light intensity to rapidly decrease from resonant wave valley at a certain wavelength [12], [19], [40]. The resonance condition varies when a metal surface changes the RI, causing the resonance wavelength to move. As a result, the movement of the resonance trough produced by a change in the external medium's RI can be employed for sensing [40]. SPW can be formed between a dielectric layer and a metal layer as the evanescent wave can penetrate through the metal layer. Surface plasmon will oscillate and propagate along the boundary between a dielectric medium and a thin metal film. The wave vector ($k_{spp}$) between metal and dielectric layer can be written as [41]:

$$k_{spp} = k_0 \sqrt{\frac{\varepsilon_{metal}\varepsilon_{dielectric}}{\varepsilon_{metal}+\varepsilon_{dielectric}}} \tag{1}$$

where $\varepsilon_{metal}$ is the dielectric function for metal, $\varepsilon_{dielectric}$ is the dielectric function for dielectric medium, and $k_0$ is the wave vector for free space of the optical wave and can be calculated by using the formula [41]:

$$k_0 = \frac{2\pi}{\lambda_0}$$

The incident light's energy can be firmly linked from photons onto the surface plasmon wave, which dissipates by heat dissipation along the propagation route during SPR. The relationship between $k_x$ and the angle of incident light can be described by the equation [41]:

$$k_x = k_0 n_{glass} \sin\theta_{inc} \tag{2}$$

where $n_{glass}$ is the index of refraction of the glass prism and $\theta_{inc}$ is the incident angle. In a glass-metal-dielectric system, the requirements for surface plasmon excitation at the metal-dielectric layers interface are given by:

$$k_x = k_{spp} \tag{3}$$

Resonance is obtained by matching the projection of the incident light's wave vector in the direction of the interface with the wave vector of the surface plasmon oscillations, as shown in Eq (3). The value of $k_x$ can be calculated using a prism with a dielectric constant greater than 1 and an incidence angle greater than the critical angle. When the incident light meets the resonance requirement, the reflectance shows a significant absorption decrease. Fig. 4 shows the total internal reflection in the prism coupling SPR sensor.

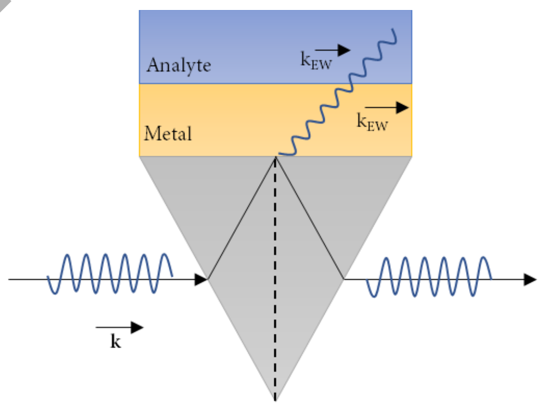


Fig. 4: Prism coupling SPR sensor

*C. Materials for SPR sensor*

The construction of the SPR sensor must be equipped with plasmonic materials to trigger SPR phenomenon and perhaps other additional materials to support sensing action and enhance performance. In an optical fiber sensor, materials are coated on the fiber to increase the sensitivity and give protection from temperature changes and extreme surroundings to the fiber. Early configuration of SPR usually uses single layer of plasmonic thin film that can excite SPR effect, nevertheless as time passes by, many research have been done which results in the uses of multilayer materials or known as hybrid material instead of a single plasmonic thin film. The commonly used materials in SPR sensors include gold (Au) [16], silver (Ag) [6], Copper (Cu) [42], and Aluminum [43]. Latest design of SPR sensor uses nanoparticle instead of thin film such as AuNPs [44] to excite SPR effect as nanoparticles result in excellent performance as well. Few improvements that were done by previous research on plasmonic materials where they combine a single plasmonic thin film layer with other materials like graphene [45], graphene oxide (GO) [6], and hydrogel [46] to enhance the performance. It is stated by Niu et al., the methods that can enhance the sensitivity of detection include two aspects: one is to add a dielectric layer on the sensor's surface to increase the load of the object to be measured, such as dopamine and rGO; the other is to use metal nanoparticles, such as AuNPs, gold nanorods (AuNR), magnetic nanoparticles, and conical nanoparticles [21]. In addition, the new form of nanoparticles was implemented to excite LSPR effect recently such as gold nanowires (AuNWs), Au nanosphere, gold nanoisland (AuNIs), and AuNR.

*1)* AU AND AG

The most commonly used plasmonic material to trigger SPR effect is Au film. It is reported by Sakib et al., these days SPR has been using Au due to its advantages such as chemical inactivity, ease of materialization, biocompatibility, and stability in the aquatic environment. They reported that the optimum thickness of material in the SPR sensor can provide better performance. It is stated that the sensitivity of the sensor enhanced with the increment of the thickness of Au film. The confinement loss peak is lower when the thickness is raised which leads to less energy transmission from the core to the metal surface. Furthermore, the difference of effective RI between the core and cladding ($n_{eff}$) of SPP mode becomes increasingly bound in the Au layer as the thickness increases. This research found optimum thickness in this performance where the maximum sensitivity obtained is 123 $RIU^{-1}$ at 40 nm [16]. Murat et al. study the optimum thickness of an Au film to enhance the sensing performance and found out that the optimum thickness for the Au thin film was 50 nm. The study uses Au and GO layer on the prism and compared the sensitivity to the layer of Ag/GO. The sensitivity of Au/GO was higher which is 19.42 °/RIU compared to Ag/GO layer which has a value of 5.45 °/RIU [47]. In 2019, Zhang et al. proposed a sensor to detect RI and temperature and found that the thickness of Au film is optimum around 40 nm as well. The maximum temperature and RI sensitivities obtained are 2933.25 nm/RIU and -0.91973 nm/°C, respectively at 40 nm. This research prefers Au to include in SPR sensor construction because it is not easily oxidized compared to Ag [48]. As reported in research by Samavati et al., the Au/GO coated Fiber Bragg Grating (FBG) sensor is said to be reliable as the fabricated probe exhibited a rapid response time to the patient's saliva even at the early stages of infection. The wavelength and intensity of detected light were regulated for 0.39 nm and 0.49 dB, respectively, after 10 seconds of exposing the probe to patients' saliva in the early stages of the disease ($1.6 \times 10^3$ copies/mL) [49]. According to Priyadarsini et al., GO is made from a highly oxidized form of graphene exposed to various strong oxidizing chemicals and chemically exfoliated from other graphene derivatives [50]. As stated by Wang & Wang, GO outperforms graphene in terms of biocompatibility, solubility, and selectivity compared to graphene [51]. Fig. 5 shows the optical image of GO coated on fiber in [51]. In 2018, Q. Wang et al. used a tilted FBG-SPR sensor to detect human IgG. The fiber is coated with Au and GO and modified with staphylococcal protein A (SPA). GO is chosen as plasmonic material in their research due to its characteristics such as can immobilize antibodies to the sensor surface. They found out that the sensitivity for the sensor is 0.096 dB/(µg/mL) and the LOD is 0.5 µg/mL. They claimed that this proposed sensor can be used in biochemistry molecular detection technology due to its excellent sensitivity, flexible design, and low cost [12]. In 2018, Kushwaha et al. studied the performance of Au, ZnO and graphene in SPR biosensors to detect pseudomonas-like bacteria. The proposed sensor provides a great sensitivity which is 187.43 °/RIU and they claimed that ZnO and Au layer in the sensor affects the performance which gives better performance with the right thickness. The thickness of the ZnO layer is fixed at 5 nm meanwhile thickness of Au is optimized. It is found that the optimum thickness of Au is 45 nm which shows the strong coupling of the light of incidence to surface plasmons [52]. Another research that proves ZnO can be used with Au film to enhance the performance is by Xu et al. where they grow ZnO nanoflowers on Au film. The structure that contains a cylindrical prism coated with Au and ZnO nanoflowers is used as an alcohol photochemical sensor. The angle test of water contact and alcohol contact between Au film and Au/ZnO nanoflower shows that the water contact angle and alcohol contact angle of Au/ZnO nanoflowers is smaller than Au film alone under the same exposure time in air which means that it has a longer lifetime. The result of SPR signals of different concentrations of alcohol for Au/ZnO nanoflowers shows that by increasing the alcohol concentration, the resonance peak is red-shifted. It shows a good linear relationship and the sensitivity improved to 127 nm/% for the concentration range from 0 vol% to 95 vol% [53].

Fig. 5: The optical image of GO coated on fiber [51]

Even though Au is more popular, Ag has been used frequently in SPR sensors as well. It has good characteristics where the resonance peak on the Au film SPR sensor was very sharp, and the detection accuracy was excellent [51]. Ag-based SPR sensors have a higher sensitivity and a more defined reflectivity spectrum than Au-based SPR sensors. When an Ag film is used as the excitation film, the limit of detection (LOD) or resolution is improved. Research by Chen & Lin proved that Ag has the highest sensitivity when they investigate the performance of the SPR biosensor with Au, Ag, and Cu with monolayer graphene in the visible region. The work investigated the reflectance curve for these three materials at their optimum wavelength and thickness. It is found that the material with excellent sensitivity is Ag compared to Au and Cu where the maximum sensitivity of monolayer graphene with Ag layer is 300.26 °/RIU which is the highest compared to Au (137.02 °/RIU) and Cu (136.24 °/RIU). However, at 633 nm wavelength, the sensitivity of Au, Cu, and Ag is 90.96 °/RIU, 93.88 °/RIU, and 68.16 °/RIU respectively. Thus, this proves that the sensitivity of Ag-based biosensor is great as it has higher sensitivity and compatible to be used with graphene but occasionally the connection between Au-based, Ag-based, and Cu-based SPR biosensors will change with different wavelength and thickness. As a result, the sensitivity of the biosensor can be enhanced by adjusting the metal and wavelength used [42]. Another performance comparison of Au and Ag is done by Rahman et al. where the work uses Ag and Au coated on Platinum diselenide ($PtSe_2$) and Tungsten disulfide ($WS_2$). The work found that by using Ag, the maximum sensitivity is much higher than Au which is 194 °/RIU [54]. Kanmani et al. studied the effect of $TiO_2$ and Ag in SPR sensors for alcohol sensing applications. $TiO_2$ was coated on the Ag thin layer to sense isopropanol at numerous concentrations. It is proved that the combination of a 30 nm thickness of Ag layer with a dielectric TiO2 improves the sensor performance where the sensitivity reading is 268 nm/RIU with a detection limit of 0.012 [55]. Besides, W. Wang et al. used modified chitosan film (MCS) along with Ag and Au in SPR sensor to trace $Cu^{2+}$. They found out that MCS has a stand out stability before and after adsorbing $Cu^{2+}$ [56]. This work proved that hybrid material like Ag/Au/MCS can be used I ehnahnceng performacne instead of using single layer of plasmonic material only. This can be seen in the change of intensity modulation in Fig. 6. In 2018, Mukhtar et al. studied the optimum thickness of Ag film in the SPR sensor. This research used the layer of Ag/GO to detect the presence of $Pb^{2+}$ ions. They discovered that the optimum total thickness for the nanocomposites was 50 nm with the thickness of GO to be ±2 nm and the thickness for Ag film was 48 nm. The maximum sensitivity obtained was 0.452°/RIU for the combination of Ag and GO [57]. Apart from that, the material that is compatible to be used with Ag in an aqueous solution is hydrogel. This is reported by Zhao et al. who mentioned that Ag/hydrogel coated fiber SPR sensor has been used in detecting pH. They reported that hydrogel can enhance the sensing performance of SPR for measuring pH and protecting Ag film during the measurement. When the hydrogel coating is in contact with pH solution, the dissociated carboxylic ions in the hydrogel will vary according to the value of pH of the solution and it will lead to the modification of volume and RI of the hydrogel. Thus, there is a shift in transmission spectra and wavelength that is related to the principle of the SPR sensor. The maximum sensitivity for the proposed sensor in this research is 13 nm/pH from the pH range of 8 to 10 which is quite high. The hysteresis is found to have a small value and can be the factor of increasing accuracy in pH sensing. The proposed sensor was claimed to have great sensitivity and stability, as well as amazing reproducibility, and the effect of temperature in the range of 20°C to 40°C could be minimal due to the properties of hydrogel [46]. Anyhow, Ag applicability is limited due to its weak chemical stability [58]. The optical damping of Ag is lower, with a strong resonance peak and no interband transition. The use of Ag in a larger sense is limited by oxidation in an aqueous media [49]. On top of that, Ag is claimed to be easily oxidized [51]. To overcome this problem, the sensor can be coated with multilayer of materials. Wang et al. mention that bimetallic Ag/Au layers, deposition of dielectric thin films or polymers, the use of dense oxide thin films or polymers, oxide film, and the use of self-assembled monolayers (SAM) can be done for protecting Ag films from oxidation and sulfuration [58].

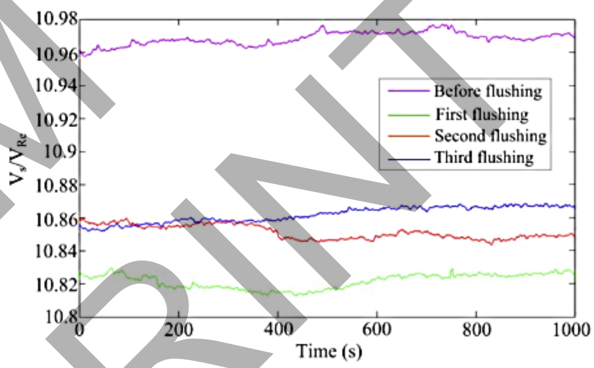


Fig. 6: Stability of the proposed sensor before and after adsorption of $Cu^{+2}$ [56]

*2)* Other Noble Metals

Antohe et al. used polyaniline (PANI)/platinum (Pt) to coat the fiber optic SPR (FO-SPR) sensor. Pt layer was used to replace Au film to excite SPR effect. The FO-SPR sensors were then used for 4-nitrophenol detection, with a shown bulk sensitivity of 1515 nm/RIU and an excellent LOD in the low picomolar range (0.34 pM) [59]. Other plasmonic material used is titanium nitride (TiN) [60] and Aluminum (Al) [43]. According to Kaur & Singh, TiN is chemically stable, has good conductivity, a low work function, and is a complementary metal-oxide semiconductor (CMOS) compatible. They proposed a photonic crystal fiber (PCF)-SPR coated with TiN and the sensitivity obtained is 10000 nm/RIU. However, the amplitude sensitivity is low due to the optical properties of TiN that depend on the substrate [60]. Ibrahim et al. proposed a grating SPR sensor and deposited Al as plasmonic material to excite plasmon waves for temperature sensing. The proposed sensor has a sensitivity of 0.387 nm/◦C with a response time of 1 ms. It's repeatability estimation is said to have good stability of sensitivity and lead to precise temperature measurement where the measurements shows that the sensitivity is varying from 0.40 nm/◦C to 0.39 nm/◦C [43].

### 3) Nanoparticles

A study by Niu et al. uses metal nanoparticles which are AuNPs along with Au thin film to coat the optical fiber [21]. AuNPs are widely implemented nowadays due to their good sensing characteristics. It is used to generate localized plasmon resonance [14]. Fig. 7 shows the electron images of Au thin film with AuNPs in [21]. Niu et al. mentions that metal nanoparticles are used to improve the sensitivity and the electromagnetic field strength of SPR sensors. They proved this in their study by experimenting with the SPR sensor coated with AuNPs and Au. It is found that the electric field strength produced by the coupling of AuNPs and Au film is substantially stronger than the electric field strength produced by the Au film alone. The AuNPs modification sensor has a sensitivity of 760 nm/RIU higher than the SPR sensor without AuNPs and the response time with AuNPs is faster compared to Au film alone. In addition, the study found that the sensitivity of the AuNPs-modified sensing region is significantly higher than the SPR sensor without AuNPs, indicating that the coupling effect between the Au film and the AuNPs is key in increasing the sensor's sensitivity [21]. As mentioned before, one of the improvements for SPR sensor is by combining materials. In 2022, Zhao and Wang developed AuNPs and GO heterostructure with Au film-coated SPR fiber sensor in order to enhance the sensitivity of the sensor. This research claimed that the employment of GO as an additional layer in their work is to improve the stability of the sensor and increase the strength of SPR effect as GO is known as a material that has a large surface area of an atomic monolayer. This research used AuNPs and Au as well to trigger SPR/LSPR reaction and claimed that the sensitivity has improved by 37.92% for Au with monolayer AuNPs/GO and 63.46% for Au with bilayer Au/AuNPs/GO compared to Au film alone [61]. In recent years, many research uses new structure of nanoparticle like nanowires, nanorods, and nanoisland. The uses of these materials provide a better performance as nanoparticles can excite LSPR effect which is suitable to use in biosensing. W. Li et al designed a D-shaped photonic crystal fiber SPR sensor with Au nanowires to excite the SPR effect. The simulated sensitivity 19,600 nm/RIU with maximum amplitude sensitivity 2300 $RIU^{-1}$ [62]. Xia et al. demonstrated an SPR sensor that uses AuNPs in form of Au nanosphere and Au nanorod. The work simulated an SPR sensor coated with Au film and Au nanorods to find out that the oscillation of free electron on Au nanorod is more intense compared to Au nanosphere. They constructed photonic crystal fiber SPR sensor coated with Au film and Au nanosphere for RI detection. The sensitivity obtained is 15,747 nm/RIU and LOD is 10 ng/ml. Compared to Au nanorod, the sensitivity is lower which the sensitivity of simulated sensor with Au nanorod is 25,642 nm/RIU and LOD 4.6 ng/m [63].

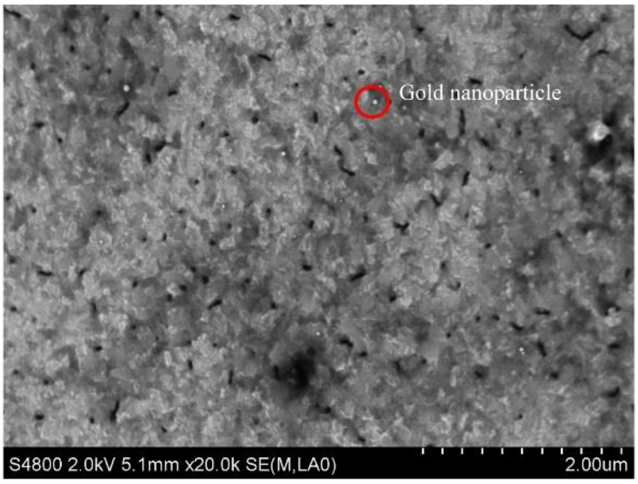


Fig. 7: The electron microscope image of Au thin film modified surface with AuNPs [21]

Plasmonic materials such as Au, Ag, Cu, and nanoparticles have been used to create the plasmonic effect in the SPR mechanism. Besides, other materials such as GO can be used in enhancing the sensitivity and giving protection to the film. Fig. 8 shows the percentage of application of plasmonic material in the SPR sensor. Among them, this study found that Au-based materials are the most used material which is 48%. Previous research used Au and doped it with other materials such as graphene, GO, and AuNPs. The properties of Au make it became more preferable compared to Ag as it is not easily oxidized and more stable. Nanoparticles have been used in SPR currently due to the plasmonic characteristic of AuNPs which are strong adsorption capacity, big specific surface area, superior conductivity, and biocompatibility [64]. Moreover, it is resistant to surface oxidation and chemically stable [65]. Graphene doped with Au enhanced the performance in terms of adsorption because it contains a large surface area for adsorption [57]. Meanwhile, GO provides good nucleation and binding sites for the probe surface [49]. Then, the percentage for Ag-based material is 32% which is the second-highest after Au-based materials. The use of Ag in the SPR sensor is one of the decent choices. However, it is easily oxidized making the performance of the sensor inconsistent and it does not suitable to use in aqueous media. Other materials such as TiN, Al, Pt, and Cu have the same percentage (5%). These materials show good conductivity but compared to Au and Ag, the value of sensitivity is lower. Table 1 shows the summary of the review of materials used in the SPR sensor.

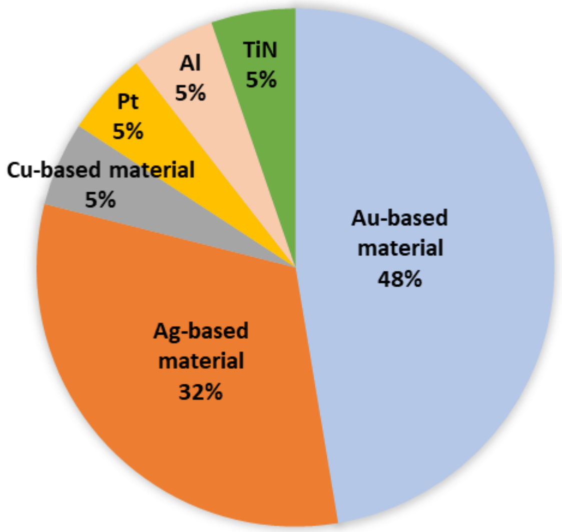


Fig. 8: Types of plasmonic materials used in SPR sensor

TABLE I. SUMMARY OF MATERIALS USED IN SPR SENSOR

| **Configuration of sensor** | **Material** | **Thickness** | **Sensitivity** | **Application** | **Reference** |
|---|---|---|---|---|---|
| OC-DC-PCF plasmonic sensor | Au | 40 nm | 38000 nm/RIU | Biosensing | [16] |
| SPR sensor | Au/GO<br>Ag/GO | Au: 50 nm<br>GO: 0.68 nm | Au/GO: 19.42 °/RIU<br>Ag/GO: 5.45 °/RIU | RI changes detection | [47] |
| MMF-NCF-MMF SPR sensor | Au | 41.487 nm | 2933.25 nm/RIU | RI sensor and temperaure detection | [48] |
| FBG- SPR sensor | GO/Au | Au: 30 nm | 0.4250 nm/virus number | Covid-19 detection | [49] |
| TFBG-SPR sensor | Au/GO/SPA | Au: 50 nm | 0.096 dB/(µg/mL) | Human IgG detection | [12] |
| SPR sensor | ZnO/Au/graphene | Au: 45 nm<br>ZnO: 5 nm<br>Graphene: 0.34 nm | 187.43 °/RIU | Pseudomonas-like bacteria detection | [52] |
| SPR sensor | Au/ZnO | 50 nm | 2825 nm/RIU | Alcohol detection | [53] |
| SPR sensor | Au/graphene<br>Ag/graphene<br>Cu/graphene | Au: 50 nm<br>Ag: 50 nm<br>Cu: 50 nm | Au/Graphene: 137.02 °/RIU<br>Ag/Graphene: 300.26 °/RIU<br>Cu/Graphene: 136.24 °/RIU | Biosensing | [42] |
| SPR sensor | Au/PtSe2/WS2<br>Ag/PtSe2/WS2 | Au: 50 nm<br>Ag:50 nm | Ag: 194 °/RIU<br>Au: 187 °/RIU | - | [54] |
| SPR sensor | $TiO_2$/Ag | Ag: 30 nm | 268 nm/RIU | Alcohol detection | [55] |
| SPR sensor | Ag/Au/Chitosan | Ag: 30 nm<br>Au: 15 nm | 0.7271 $ppm^{-1}$ | $Cu^{2+}$ ion detection | [56] |
| SPR sensor | Ag/GO | Ag: 48 nm<br>GO: ±2 nm<br>Total thickness: 50 nm | 0.452°/RIU | $Pb^{2+}$ ion detection | [57] |
| SPR sensor | Ag/Hydrogel | - | 13 nm/pH | pH sensing | [46] |
| FO-SPR sensor | PANI/Pt | PANI: ±95 nm<br>Pt: 40 nm | 1515 nm/RIU | 4-nitrophenol detection | [59] |
| PCF-SPR sensor | TiN | 50 nm | 10000 nm/RIU | Liquid sensing | [60] |
| SPR sensor | Al | 50 nm | 0.387 nm/°C | Temperature variation detection | [43] |
| SPR sensor | AuNPs/Au | Au: 50 nm | 3074 nm/RIU | - | [21] |

| Configuration of sensor | Material | Thickness | Sensitivity | Application | Reference |
|---|---|---|---|---|---|
| FO-SPR sensor | Au/GO/AuNPs | Au: 55 nm | 5174.7 nm/RIU | RI sensor | [61] |
| PCF-SPR sensor | AuNWs | Au: 60 nm | 19,600 nm/RIU | RI sensor | [62] |
| FO-SPR sensor | Au/Au nanosphere<br>Au/AuNR | Au: 50 nm | Au/Au nanosphere: 15,747 nm/RIU<br>Au/AuNR: 25,642 nm/RIU | Human IgG detection | [62] |

*D. SPR sensor for detection of various types of viruses*

The optical biosensor has been used in biological and chemical applications due to its benefits. Detection strategies for optical biosensors can be accomplished in two ways: indirect and direct optical biosensors. For the detection procedure and signal amplification, indirect optical biosensors rely on binding with fluorophores or chromophores as labels. The indirect method produces a lot of signals, but it has a lot of non-specific binding. The direct optical biosensor approach, like the SPR biosensor, is based on the analyte interacting with the optical characteristics of the sensing environment and measuring the change in RI at the analyte-sensor interface [66]. Optical techniques such as surface plasmon resonance, fluorescence, and SERS have been used to detect norovirus, Dengue Virus (DENV), and influenza virus.

The study by Sakib et al. mentioned that the SPR sensor is a very recommended sensor to use in biosensing applications [16]. In medical sensing, SPR sensor is used to detect diseases such detecting DENV [67], Respiratory Syncytial Virus (RSV) [68], and Avian influenza virus [69], and there is even a previous study that used SPR sensor in detecting Covid-19 [34]. It is reported by Das et al., the design for SPR sensor that can be used for detecting Covid-19 is based on BK7 prism which detects small RI changes and lowers the concentration of protein antigen of SARS-CoV-2. The material used in this proposed sensor is AuNR which can effectively increase the electric field. Thus, the evanescent field improvement that was observed increased to 376.33% as compared to the basic Au nanosheet-based Kretschmann model. The maximum sensitivity obtained is 111.11 °/RIU with AuNR (diameter=10nm) coating in the sensor. Moreover, by using SPR sensor, the LOD will be low [34]. It is reported by Omar et al., the LOD achieved is as low as 0.08 pM with good linearity ($R^2$= 0.92) when the SPR sensor was used to detect the DENV-2 E-proteins within 8 minutes. The SPR sensor was designed with a gold surface with dithiobis (succinimidyl undecanoate) (DSU) for the immobilization of the $NH_2$rGO-PAMAM nanocomposite. The Au/DSU/$NH_2$rGO-PAMAM/IgM thin film-integrated SPR sensor in this study shows a good reaction towards DENV-2 E-proteins where the value of sensitivity gained is 0.2576° $pM^{-1}$ [67]. Fig. 9 shows the result of the FTIR analysis of Au/DSU/$NH_2$rGO-PAMAM/IgM sensor film before and after the DENV-2-E proteins were inserted. The peaks show the functional groups interact with the coating materials.

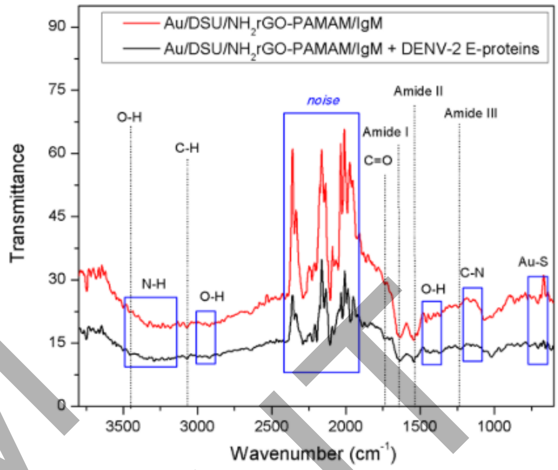


Fig. 9: FTIR analysis of Au/DSU/$NH_2$rGO-PAMAM/IgM sensor film before and after the DENV-2-E proteins were inserted [67]

SPR sensor offers excellent performance when using different types of fiber. A proposed sensor by Samavati et al. used FBG. The wavelength sensitivity of the sensor is 0.4250 nm/virus number with instant response to the patient's saliva. The advantages of this proposed Au/GO-FBG SPR sensor can become a potential device in sensing and bio-sensing applications due to its tolerance to high sensitivity, capacity for portable use, and electromagnetic interferences [49]. Besides, research by Murugan et al. used a U-bent optical fiber sensor system to detect SARS-CoV-2 virus particles and found that the response time is within 15 minutes. The plasmonic material used is AuNPs as it amplifies the interaction signal. The LOD of this sensor to the particle obtains is as small as $10^6$ particles/mL, which is enough to cause infection [11]. Fig. 10 shows the structure of the plasmonic fiber-optic absorbance biosensor (P-FAB) sensor. In addition, an SPR sensor has reportedly been used in detecting the virus that is circulating in humans and birds, avian influenza A H7N9. They found out that the biosensor proposed has a fast response time which is about 10 minutes for detecting the H7N9-RG virus, which has surface features that are similar to avian influenza A H7N9 virus. They claimed that the sensor is far superior to handmade target-captured Enzyme-linked immunosorbent assay (ELISA), commercial Rapid influenza diagnostic test (RIDT), and even Quantitative reverse transcription PCR (qRT-PCR) due to the detection limit in the mimic solution obtained is 402 copies/mL [69].


Fig. 10: P-FAB device and integrated U-bent fiber probe cartridge [11]

Currently, nanoparticles have been used in the SPR technique, thus LSPR is triggered during the sensing mechanism. Local variations, such as RI change and molecule binding, are detected with high sensitivity by LSPR sensing systems [10]. The research by Qiu et al. uses the BK7 prism in SPR sensor construction to couple the incident light into plasmonic material which is gold nano island (AuNI). The plasmonic resonances of PPT and LSPR can be induced at two different wavelengths by using two separate angles of incidence, considerably improving sensitivity, sensing stability, and reliability. The LSPR sensing unit achieved real-time and label-free detection of viral sequences, including RdRp-COVID, ORF1ab-COVID, and E genes from SARS-Cov-2, with this arrangement. Moreover, the AuNI chips in situ PPT augmentation significantly increased hybridization kinetics and nucleic acid detection selectivity [10]. Research by Zhan et al. uses AuNPs and graphene as plasmonic materials to enhance the performance of RSV detection. They found out that the combination of AuNPs and graphene results in ultrahigh detection sensitivity and the sensor requires no enzyme label, ensuring the robustness of the immunoassay. In addition, the research found that AuNPs provide stability after the removal of enhancement of the solution. The result from this research is the detection limit was discovered to be 1.7 fg/mL, which was 100 times greater than the AuNPs-based approach. The ultra-high sensitivity was due to a huge number of well-dispersed AuNPs placed on the graphene surface, which had a very large relative surface area [68]. Liu et al. proposed an SPR chip sensor with GO layer to detect Porcine Reproductive and Respiratory Syndrome Virus (PRRSV). This research employed an Au SPR chip and coated it with GO. The Fourier-transform SPR (FT-SPR) frequency shows that there were no significant changes when using fixed papain concentration which means that the surface content of GO was reproducible from one preparation to the next preparation. Besides, the SPR sensitivity was improved approximately 2.9-fold by the GO-modified sensor compared to the sensor without GO-modified [70].

Kang et al. proposed a sensor to detect Covid-19 by using a multiplex SERS platform based on a plasmonic paper substrate along with a double-labeled probe to detect several fluorescent dyes in a single-wavelength light source system with high sensitivity. SERS is a potential approach for detecting several fluorescent dyes with excellent sensitivity. The LSPR of noble metal nanostructures impacted by surrounding molecules, interparticle gap spacing, or shape results in SERS, which provides a highly defined vibrational fingerprint. The plasmonic substrate used is Ag nanodots paper that provides high sensitivity to SERS biosensing based on LSPR. Fig. 11 shows the structure of the proposed sensor and the method of fabricating it. The suggested approach can identify and quantify a wide range of fluorescent dyes with concentrations ranging from picomolar to millimolar. This experiment shows that PCR-based SERS may identify many targets using existing PCR settings without altering primer and probe sequences. The cellulose fiber matrixes' unique hierarchical ultrastructures enable highly sensitive SERS detection, even at low concentrations. The assay detection limit of SERS-PCR was lower than that of real-time PCR in this investigation. These findings shed light on how extremely sensitive SERS can be used to reduce PCR cycles [6]. Fig. 12 shows the relationships between the fluorescence intensity of the two-plex real-time PCR assay and the cycle number to prove the low detection limit of the proposed sensor. The fittings of SERS intensity that is dependent on the cycle number for 0.01 (blue line) and 0.01 ng/μL (red line) are obtained to be $R^2 > 0.99$. They mentioned that by using real-time PCR, it is not possible to detect the sample concentration under 1 pg/μL (13.64 pM for the E gene and 13.4 pM for the RdRP gene) before it reached 20 cycles. Besides, by using SERS-PCR, the detection can be done only in 10 cycles. The sensor is a good initiative to detect Covid-19 as it combines the SPR with the SERS mechanism. The SPR sensor provides high sensitivity, fast time response, and low LOD. Thus, we found that SPR sensors have a good potential to be used to detect viruses including SARS-CoV-2, or known as Covid-19. There are previous articles that use SPR sensors to detect viruses. Table 2 shows the data from the studies of the performance of different types of optical sensors in various applications in order to support that SPR can be a good candidate in detecting Covid-19 that ha similarity as SAR-CoV gene which causes respiratory virus disease.

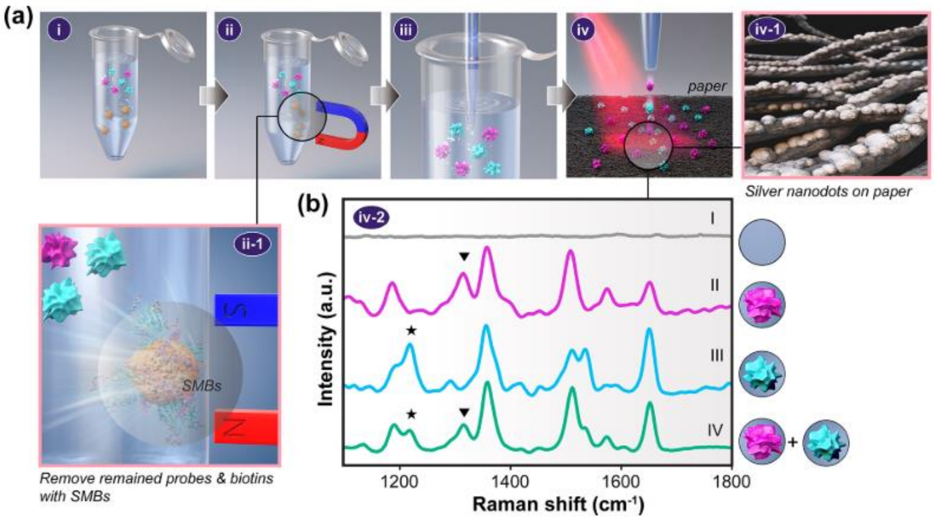


Fig. 11: Schematic diagram of SERS detection on plasmonic paper [6]

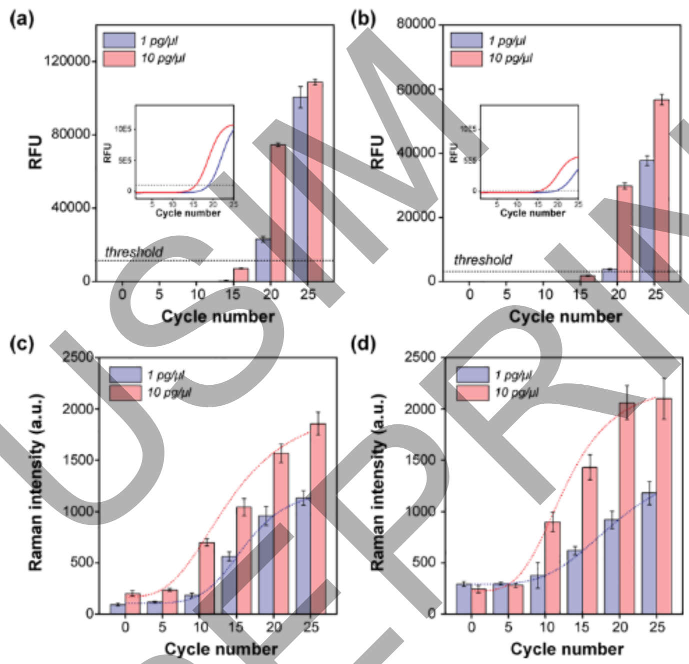


Fig. 12: Comparison between (a,b) real-time PCR and (c,d) SERS-PCR [6]



TABLE II. DEPLOYMENT OF PLASMONIC MATERIALS IN DETECTING VARIOUS VIRUSES

| **Materials** | **Type of sensor** | **Sensitivity** | **Thickness/Diameter (nm)** | **LOD** | **Time-response** | **Applications** | **Reference** |
|---|---|---|---|---|---|---|---|
| Au/AuNR | SPR sensor | 111.11 °/RIU | Au: 50 nm<br>AuNR: 10 nm | 7 E-5 RIU | - | Covid-19 SARS COV-2 Spike protein detection | [34] |
| Au/DSU/$NH_2$rGO-PAMAM/IgM | SPR sensor | 0.2576° $pM^{-1}$ | Au: 48 nm | 0.08 pM | 6-8 min | Dengue Virus Type 2 E-Proteins Signals detection | [67] |
| Ag/Au | SPR sensor | - | Ag: 35nm<br>Au: 10 nm | 402 copies/mL | 10 min | Avian influenza A H7N9 virus detection | [69] |
| GO/Au | FBG- SPR sensor | 0.4250 nm/virus number | Au: 30 nm | - | 10 s | Covid-19 detection | [49] |
| Ag nanodot | SERS-LSPR | - | - | - | | COVID-19 detection | [6] |

| **Materials** | **Type of sensor** | **Sensitivity** | **Thickness/Diameter (nm)** | **LOD** | **Time-response** | **Applications** | **Reference** |
|---|---|---|---|---|---|---|---|
| AuNIs | LSPR sensor | - | 5.0 m - 5.2 nm | 0.22 ± 0.08 pM | 200 s | COVID-19 spike protein detection | [10] |
| AuNPs/graphene | Plasmonic immunoassay sensor | - | 19 nm | 1.7 fg/mL | - | RSV detection | [68] |
| AuNPs | P-FAB | - | 20 nm to 60 nm | $10^6$ particles/mL | 10-15 min | COVID-19/ antibody IgM and IgG detection | [11] |
| Au SPR chip with GO | SPR sensor | 2.9-fold | - | - | - | Porcine Reproductive and Respiratory Syndrome Virus detection | [70] |

## IV. Potential Of SPR Sensor In Detecting Covid-19

Many works have been done to study the performance of SPR sensors in detecting Covid-19. Table 3 shows the summary data of the performance of the SPR sensor in detecting Covid-19. According to Akib et al., the procedure of detecting Covid-19 starts with collecting samples by the nasopharyngeal swab test and blood. This is done to get the virus spike receptor-binding domain (RBD) or RNA and anti-spike protein respectively. Then, the sample is used in Au/ $PtSe_2$/ graphene coated SPR sensor based on different ligand-analytes which are; (i) monoclonal antibodies (MAbs) as ligand and COVID-19 viral spike RBD as analyte; (ii) specific probe as ligand and COVID-19 virus single-standard RNA as analyte; and (iii) virus spike RBD as ligand and virus anti-spike protein (IgM, IgG) as analyte. This study found that the SPR sensor has a very high sensitivity of 183.3°/RIU, compared to other conventional sensors and the performance was confirmed by the FDTD technique and TMM algorithm [20].

Dai et al. construct an SPR sensor based on laser heterodyne feedback interferometry to detect SARS-CoV-2 spike antigen. This research deployed polydimethylsiloxane (PDMS) microfluidic channel/Au film/K9 glass sandwich structure on a prism. To detect the Covid-19 spike antigen, the sensor structure was immobilized with anti-SARS-CoV-2 spike MAbs which can give better effectiveness of specific binding events on the surface of the sensor structure. As a result, the noise-limited resolution is calculated to be 0.08 pg/mL which can be termed as the concentration when the voltage change is higher than the standard deviation of the noise level which is 0.25 mV. This signifies that this biosensor can detect the antigens at low concentrations without sample labeling. However, this sensor only has one optical path which is prone to fluctuations in laser power and disturbances [71]. Another research by Das et al. reported that the SPR sensor is suitable to use in detecting Covid-19 as this sensor offers a label-free and real-time detection technique. From this study, they found that with the assistance of AuNR as sensing material, it helps to increase the sensitivity, and the optimum distance between AuNR and plasmonic Au nanosheet has improved evanescent field compared to the basic Au nanosheet-based Kretschmann model [34]. The structure of this proposed sensor is shown in Fig. 13.

A simulation done by Sudheer et al. proved that their proposed SPR sensor can be an excellent sensor to detect Covid-19 because the RI of mucus and serum falls within the suitable range for biosensing detection which for RI values of 1.388–1.422, the Al/ZnO/ $Ti_3C_2T_x$ coated fiber combination works well, as does the Al/ZnO: Pd/$Ti_3C_2T_x$ coated fiber for 1.354–1.406. This study also mentioned that better biosensors will result from the proper selection of the sandwich layer's thickness and volume fractions [72]. Another research by Moznuzzaman et al. combine six layers in their proposed sensor to detect SARS-CoV-2 antigens (S-glycoprotein). The layer consists of a layer of Ag that is inserted between a molybdenum diselenide ($MoSe_2$)/graphene composite layer and a $TiO_2$ thin sheet. The multilayer of different materials like Ag/Mose2/graphene gives improvement for the sensor as the maximum sensitivity is obtained by the multilayer compared to other plasmonic layers. It has a sensitivity of 194°/RIU, a quality factor of 54.04 $RIU^{-1}$, and a detection accuracy of about 0.2702. This study uses the CR3022 antibody for SARS-CoV-2 detection and there is some limitation such as the angle of SPR fluctuating insignificantly [45]. Research by Samavati et al. uses a different type of fiber optic which is FBG coated with Au and GO that can trigger high sensitivity during sensing performance. They claimed that the proposed sensor can be an excellent choice as it has remote sensing features and a fast-time response to the sample besides the detection accuracy is great which the standard deviation is ±0.02 dB and ±0.01 nm for wavelength and intensity. This shows that the sensitivity is constant and stable because of the low value of standard deviation [49]. Huang et al. and Qiu et al. use nanoplasmonic materials such as AuNPs and AuNI in Covid-19 detection [10], [44]. The nanoplasmonic chip in the study by Huang et al. can detect the whole SARS-CoV-2 with a quick response time [44]. Meanwhile, the proposed sensor by Qiu et al. provides high sensitivity and a low LOD, 0.22 pM [10].

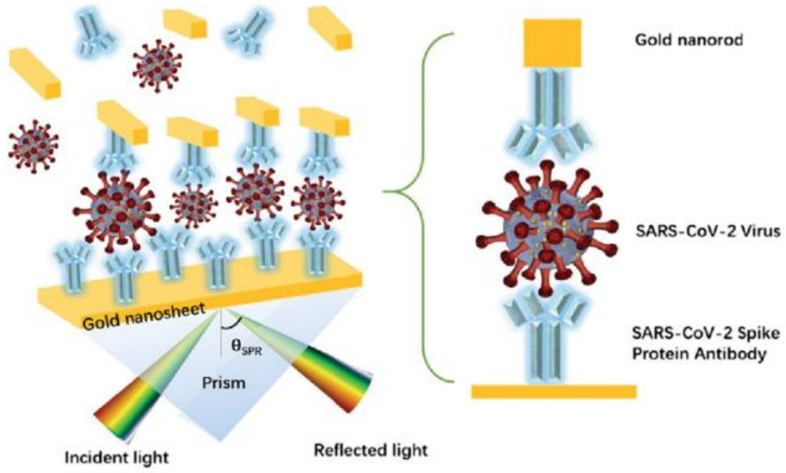


Fig. 13: The structure of Au/AuNR SPR biosensor to detect SARS-COV-2 spike protein [34]

Based on the analysis, we found that Au nanomaterial is the most preferable material which has a percentage of 50%. Au nanomaterials such as AuNR, AuNPs, and AuNI are the form of Au nanomaterials that give out the best performance. AuNR is easy to fabricate and there is a lot of chemical company can provide customized AuNRs [34]. The AuNPs enhanced the sensor which gives a low LOD [10]. Moreover, the functionalization of AuNI with complementary DNA receptors is said to be a good initiative in detecting Covid-19 as it also provides a low LOD [10]. Au doped graphene is the second preferable material (25%) because graphene has a large specific surface area for molecular adsorption and excellent conductivity properties [66]. Graphene can be used in enhancing sensitivity and gives a surface for binding [68]. The used materials to doped with Au such as $PtSe_2$/graphene and GO [20], [49]. Then, the other material which is Ag-based materials is 13% by using $TiO_2$/Ag/$MoSe_2$/graphene [45]. Finally, the least used material is Al-based material which is 12%. Fig. 14 shows the percentage of the material used in the SPR sensor to detect Covid-19. It can be seen that most research use Au-based materials to construct SPR sensor including metal film and nanomaterials.

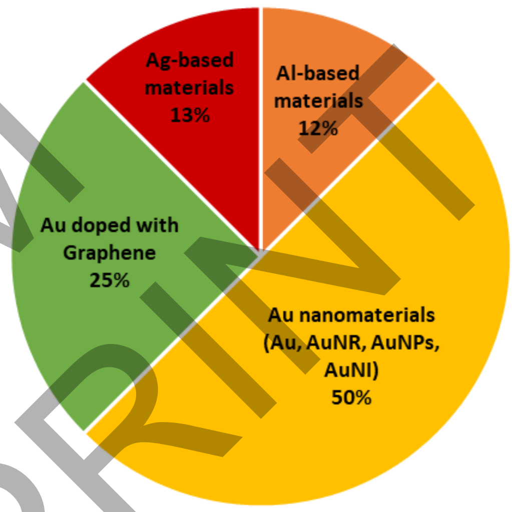


Fig. 14: Percentage of material in SPR sensor to detect Covid-19



TABLE III. THE PERFORMANCE OF SPR SENSOR IN DETECTING COVID-19

| Materials | Type of sensor | Sensitivity | Thickness/Diameter (nm) | LOD | Applications | Time-response | Reference |
|---|---|---|---|---|---|---|---|
| Au/Au NR | SPR sensor | 111.11 °/RIU | Au: 50 nm AuNR: 10 nm | 7 E-5 RIU | Covid-19 SARS COV-2 Spike protein detection | - | [34] |
| Au/$PtSe_2$/graphene | SPR sensor | 183.3 °/RIU | Au: 50 nm $PtSe_2$: 2 nm Graphene: 1.7 nm | - | COVID-19 virus spike protein, virus single-standard RNA, and antibodies against the virus spike protein | - | [20] |
| Au nanolayer/GO | FBG- SPR sensor | 0.4250 nm/virus number | Au: 30 nm | - | Covid-19 detection | 10 s | [49] |
| $TiO_2$/Ag/$MoSe_2$ graphene | SPR sensor | 194 °/RIU | Graphene: 0.34 nm $MoSe_2$: 0.97 nm Ag: 58 nm $TiO_2$: 5 nm | - | Covid-19 SARS-COV-2 detection | - | [45] |
| AuNPs | Nanoplasmonic sensor | - | 70 nm | 370 vp/mL | Covid-19 SARS-COV-2 detection | <15 min | [44] |
| AuNIs | LSPR sensor | - | 5.0 nm - 5.2 nm | 0.22 ± 0.08 pM | Covid-19 spike protein detection | 200 s | [10] |
| Au | SPR sensor | $1.07 \times 10^6$ mV/RIU | 50 nm | 0.08 pg/mL | Covid-19 spike antigen detection | <1 min | [71] |

## V. Conclusion and Future Perspective

SPR is said to be one of the best choices in Covid-19 detection as it provides a good sensitivity, accuracy, and can be designed with different types of configurations like by using prism or fiber optics or using different kind of materials that suits the virus detection. Besides, most research suggest that SPR is suitable to be used in detecting Covid-19 sensor where most of the works obtained a high sensitivity sensor, low limit of detection, and fast response time, and good repeatability. However, compared to RT-PCR, immunoassay, and CT scan imaging, SPR sensor is still on research. Thus, the implementation of SPR biosensor in detecting Covid-19 is not as reliable as other method that have been used before. Perhaps, in the future, there will be more research to improve the performance of this sensor as a biosensor. In term of sensitivity, CT imaging method provides the most sensitive detection compared to other method but it can cause confusion with other lung health condition. Therefore, it is suggested to use RT-PCR method but it is time-consuming. SPR sensor were claimed to have fast time response and is actually a bit similar to the commercialized test kit that uses immunoassay method. Nonetheless, the SPR sensor has time response less than 15 minutes which can top the immunoassay that needs 15 minutes to confirm the result. This work hopes that Covid-19 SPR-based sensor can be commercialized and designed properly for compatibleness in the future.

Considering the result from this review, the construction of Covid-19 SPR-based sensor can be improved in terms of plasmonic material selection. Based on this review, Au nanomaterials are the best plasmonic material to use in the SPR sensor to detect Covid-19 which has the highest percentage (50%) among all of the plasmonic materials used in SPR sensor. Au nanomaterials in such different forms like AuNPs, AuNWs, Au nanosphere, AuNR, and AuNI are suitable to be used in SPR sensors because they provide high sensitivity [21], low LOD [44], fast time response, high selectivity and can be doped with other materials such as Au, graphene, GO, and nanoparticles. Besides, Au nanomaterials is resistant to surface oxidation and chemically stable [65] and it provides great coating behavior as it is compatible to be used on different substrate like prism, fiber optics, and photonic crystal fiber. Apart from that, the construction of this kind of sensor is a bit costly as the gold nanomaterial is a bit pricey compared to other materials. To overcome this problem, a small amount of Au nanomaterials can be used and improve the configuration with addition of other cheaper materials like silver or use other approach which is to design different sensor configuration by using different types of fiber optics or prism or by using different method of material deposition. This research proposed Au nanomaterials to be used in SPR sensors for detecting Covid-19. Therefore, we believe that this review will help in developing an excellent sensor for Covid-19 detection.

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## References

[1] V. Chamola, V. Hassija, V. Gupta, and M. Guizani, "A Comprehensive Review of the COVID-19 Pandemic and the Role of IoT, Drones, AI, Blockchain, and 5G in Managing its Impact," *IEEE Access*, vol. 8, pp. 90225–90265, 2020, doi: 10.1109/ACCESS.2020.2992341.

[2] M. A. Kabir *et al.*, "Diagnosis for COVID-19: current status and future prospects," *Expert Rev. Mol. Diagn.*, vol. 21, no. 3, pp. 269–288, 2021, doi: 10.1080/14737159.2021.1894930.

[3] A. H. L. Bruning *et al.*, "Rapid detection and monitoring of human coronavirus infections," *New Microbes New Infect.*, vol. 24, pp. 52–55, 2018, doi: 10.1016/j.nmni.2018.04.007.

[4] H. Maddali, C. E. Miles, J. Kohn, and D. M. O'Carroll, "Optical Biosensors for Virus Detection: Prospects for SARS-CoV-2/COVID-19," *ChemBioChem*, vol. 22, no. 7, pp. 1176–1189, 2021, doi: 10.1002/cbic.202000744.

[5] B. A. Taha *et al.*, "Detection of covid-19 virus on surfaces using photonics: Challenges and perspectives," *Diagnostics*, vol. 11, no. 6, pp. 1–17, 2021, doi: 10.3390/diagnostics11061119.

[6] E. J. Kim *et al.*, "Paper-Based Multiplex Surface-Enhanced Raman Scattering Detection Using Polymerase Chain Reaction Probe Codification," *Anal. Chem.*, vol. 93, no. 8, pp. 3677–3685, Mar. 2021, doi: 10.1021/acs.analchem.0c05285.

[7] S. Buteau, J.-R. Simard, and P. Lahaie, "Joint Biological Standoff Detection System increment II : Field demonstration SINBAHD performances," no. December, pp. 1–106, 2007.

[8] N. H. Azeman, N. Arsad, and A. A. A. Bakar, "Polysaccharides as the sensing material for metal ion detection-based optical sensor applications," *Sensors (Switzerland)*, vol. 20, no. 14, pp. 1–22, 2020, doi: 10.3390/s20143924.

[9] R. Abdel-Karim, Y. Reda, and A. Abdel-Fattah, "Review—Nanostructured Materials-Based Nanosensors," *J. Electrochem. Soc.*, vol. 167, no. 3, p. 037554, 2020, doi: 10.1149/1945-7111/ab67aa.

[10] G. Qiu, Z. Gai, Y. Tao, J. Schmitt, G. A. Kullak-Ublick, and J. Wang, "Dual-Functional Plasmonic Photothermal Biosensors for Highly Accurate Severe Acute Respiratory Syndrome Coronavirus 2 Detection," *ACS Nano*, vol. 14, no. 5, pp. 5268–5277, 2020, doi: 10.1021/acsnano.0c02439.

[11] D. Murugan, H. Bhatia, V. V. R. Sai, and J. Satija, "P-FAB: A Fiber-Optic Biosensor Device for Rapid Detection of COVID-19," *Trans. Indian Natl. Acad. Eng.*, vol. 5, no. 2, pp. 211–215, Jun. 2020, doi: 10.1007/s41403-020-00122-w.

[12] Q. Wang, J.-Y. Jing, and B.-T. Wang, "Highly Sensitive SPR Biosensor Based on Graphene Oxide and Staphylococcal Protein A Co-Modified TFBG for Human IgG Detection," *IEEE Trans. Instrum. Meas.*, vol. 68, no. 9, pp. 3350–3357, Sep. 2019, doi: 10.1109/TIM.2018.2875961.

[13] D. Wencel *et al.*, "Optical Sensor for Real-Time pH Monitoring in Human Tissue," *Small*, vol. 14, no. 51, pp. 1–8, 2018, doi: 10.1002/smll.201803627.

[14] P. Nag, K. Sadani, and S. Mukherji, "Optical Fiber Sensors for Rapid Screening of COVID-19," *Trans. Indian Natl. Acad. Eng.*, vol. 5, no. 2, pp. 233–236, Jun. 2020, doi: 10.1007/s41403-020-00128-4.

[15] P. Pokhrel, C. Hu, and H. Mao, "Detecting the coronavirus (CoVID-19)," *ACS Sensors*, vol. 5, no. 8, pp. 2283–2297, 2020, doi: 10.1021/ACSSENSORS.0C01153.

[16] N. Sakib, W. Hassan, Q. M. Kamrunnahar, M. Momtaj, and T. Rahman, "Dual core four open channel circularly slotted gold coated plasmonic biosensor," *Opt. Mater. Express*, vol. 11, no. 2, p. 273, 2021, doi: 10.1364/ome.415502.

[17] W. M. Mukhtar, F. H. Ahmad, N. D. Samsuri, and N. F. Murat, "Study on plasmon absorption of hybrid Au-GO-GNP films for SPR sensing application," *AIP Conf. Proc.*, vol. 1972, no. June, 2018, doi: 10.1063/1.5041228.

[18] P. G. Prabhash, V. S. Haritha, S. S. Nair, and R. Pilankatta, "Localized surface plasmon resonance based highly sensitive room temperature pH sensor for detection and quantification of ammonia," *Sensors Actuators, B Chem.*, vol. 240, pp. 580–585, 2017, doi: 10.1016/j.snb.2016.08.159.

[19] J. Y. Jing, Q. Wang, W. M. Zhao, and B. T. Wang, "Long-range surface plasmon resonance and its sensing applications: A review,"

*Opt. Lasers Eng.*, vol. 112, no. September 2018, pp. 103–118, 2019, doi: 10.1016/j.optlaseng.2018.09.013.

[20] T. B. A. Akib *et al.*, "Design and numerical analysis of a graphene-coated spr biosensor for rapid detection of the novel coronavirus," *Sensors*, vol. 21, no. 10, pp. 1–21, 2021, doi: 10.3390/s21103491.

[21] L.-Y. Niu, Q. Wang, J.-Y. Jing, and W.-M. Zhao, "Sensitivity enhanced D-type large-core fiber SPR sensor based on Gold nanoparticle/Au film co-modification," *Opt. Commun.*, vol. 450, no. March, pp. 287–295, Nov. 2019, doi: 10.1016/j.optcom.2019.06.026.

[22] S. Long *et al.*, "Sensing absorptive fluids with backside illuminated grating coupled SPR sensor fabricated by nanoimprint technology," *Sensors Actuators A Phys.*, vol. 337, no. January, p. 113416, 2022, doi: 10.1016/j.sna.2022.113416.

[23] Q. Han, B. Zheng, L. Daines, and A. Sheikh, "Long-Term Sequelae of COVID-19: A Systematic Review and Meta-Analysis of One-Year Follow-Up Studies on Post-COVID Symptoms," *Pathogens*, vol. 11, no. 2, p. 269, Feb. 2022, doi: 10.3390/pathogens11020269.

[24] B. Alhalaili, I. N. Popescu, O. Kamoun, F. Alzubi, S. Alawadhia, and R. Vidu, "Nanobiosensors for the Detection of Novel Coronavirus 2019-nCoV and Other Pandemic/Epidemic Respiratory Viruses: A Review," *Sensors*, vol. 20, no. 22, p. 6591, Nov. 2020, doi: 10.3390/s20226591.

[25] M. Lotfi, M. R. Hamblin, and N. Rezaei, "COVID-19: Transmission, prevention, and potential therapeutic opportunities," *Clin. Chim. Acta*, vol. 508, no. April, pp. 254–266, 2020, doi: 10.1016/j.cca.2020.05.044.

[26] Y. Shi *et al.*, "An overview of COVID-19," *J. Zhejiang Univ. Sci. B*, vol. 21, no. 5, pp. 343–360, 2020, doi: 10.1631/jzus.B2000083.

[27] M. Ciotti *et al.*, "COVID-19 Outbreak: An Overview," *Chemotherapy*, vol. 64, no. 5–6, pp. 215–223, 2020, doi: 10.1159/000507423.

[28] X. Xie, Z. Zhong, W. Zhao, C. Zheng, F. Wang, and J. Liu, "Chest CT for Typical 2019-nCoV Pneumonia: Relationship to Negative RT-PCR Testing," *J. Clin. Microbiol.*, vol. 58, no. April, pp. 1–5, 2020, [Online]. Available: https://doi.org/10.1016/j.jcv.2020.104384%0Ahttp://dx.doi.org/10.1016/S2213-2600(20)30315-5%0Ahttps://doi.org/10.1016/j.rbmo.2020.06.001%0Ahttps://doi.org/10.1016/j.mayocp.2020.04.004%0Ahttps://doi.org/10.1016/j.cmi.2020.06.019%0Ahttps://doi.org/10.1080/1.

[29] A. H. P. Ho, D. Kim, and M. G. Somekh, "Handbook of photonics for biomedical engineering," *Handb. Photonics Biomed. Eng.*, pp. 1–947, 2017, doi: 10.1007/978-94-007-5052-4.

[30] B. A. Prabowo, A. Purwidyantri, and K. C. Liu, "Surface plasmon resonance optical sensor: A review on light source technology," *Biosensors*, vol. 8, no. 3. MDPI AG, 2018, doi: 10.3390/bios8030080.

[31] V. Semwal and B. D. Gupta, "Highly sensitive surface plasmon resonance based fiber optic pH sensor utilizing rGO-Pani nanocomposite prepared by in situ method," *Sensors Actuators, B Chem.*, vol. 283, pp. 632–642, 2019, doi: 10.1016/j.snb.2018.12.070.

[32] Y. Zhao, R. jie Tong, F. Xia, and Y. Peng, "Current status of optical fiber biosensor based on surface plasmon resonance," *Biosens. Bioelectron.*, vol. 142, no. June, p. 111505, 2019, doi: 10.1016/j.bios.2019.111505.

[33] T. Xu and Z. Geng, "Strategies to improve performances of LSPR biosensing: Structure, materials, and interface modification," *Biosens. Bioelectron.*, vol. 174, p. 112850, 2021, doi: 10.1016/j.bios.2020.112850.

[34] C. M. Das *et al.*, "Gold Nanorod Assisted Enhanced Plasmonic Detection Scheme of COVID-19 SARS-CoV-2 Spike Protein," *Adv. Theory Simulations*, vol. 3, no. 11, p. 2000185, Nov. 2020, doi: 10.1002/adts.202000185.

[35] P. J. Rivero, J. Goicoechea, and F. J. Arregui, "Optical fiber sensors based on polymeric sensitive coatings," *Polymers (Basel).*, vol. 10, no. 3, pp. 1–26, 2018, doi: 10.3390/polym10030280.

[36] N. L. Razali *et al.*, "Formation of anisotropic gold nanoparticles on indium tin oxide substrates as a plasmonic sensing material," *Nanomater. Nanotechnol.*, vol. 10, pp. 1–12, 2020, doi: 10.1177/1847980420965388.

[37] X. Bai *et al.*, "The basic properties of gold nanoparticles and their applications in tumor diagnosis and treatment," *Int. J. Mol. Sci.*, vol. 21, no. 7, 2020, doi: 10.3390/ijms21072480.

[38] N. F. Fadzil and W. M. Mukhtar, "Surface Plasmon Resonance Based Fiber Bragg Grating Sensor for Food Security Applications : A Review," 2015.

[39] M. M. Hassan, F. S. Sium, F. Islam, and S. M. Choudhury, "A review on plasmonic and metamaterial based biosensing platforms for virus detection," *Sens. Bio-Sensing Res.*, vol. 33, no. May, p. 100429, Aug. 2021, doi: 10.1016/j.sbsr.2021.100429.

[40] M. Luo and Q. Wang, "A reflective optical fiber SPR sensor with surface modified hemoglobin for dissolved oxygen detection," *Alexandria Eng. J.*, vol. 60, no. 4, pp. 4115–4120, 2021, doi: 10.1016/j.aej.2020.12.041.

[41] W. M. Mukhtar, P. Susthitha Menon, S. Shaari, M. Z. A. Malek, and A. M. Abdullah, "Angle shifting in surface plasmon resonance: Experimental and theoretical verification," *J. Phys. Conf. Ser.*, vol. 431, no. 1, 2013, doi: 10.1088/1742-6596/431/1/012028.

[42] S. Chen and C. Lin, "Sensitivity comparison of graphene based surface plasmon resonance biosensor with Au, Ag and Cu in the visible region," *Mater. Res. Express*, vol. 6, no. 5, p. 056503, Feb. 2019, doi: 10.1088/2053-1591/ab009d.

[43] J. Ibrahim *et al.*, "Surface Plasmon Resonance Based Temperature Sensors in Liquid Environment," *Sensors*, vol. 19, no. 15, p. 3354, Jul. 2019, doi: 10.3390/s19153354.

[44] L. Huang *et al.*, "One-step rapid quantification of SARS-CoV-2 virus particles via low-cost nanoplasmonic sensors in generic microplate reader and point-of-care device," *Biosens. Bioelectron.*, vol. 171, no. September 2020, p. 112685, Jan. 2021, doi: 10.1016/j.bios.2020.112685.

[45] M. Moznuzzaman, I. Khan, and M. R. Islam, "Nano-layered surface plasmon resonance-based highly sensitive biosensor for virus detection: A theoretical approach to detect SARS-CoV-2," *AIP Adv.*, vol. 11, no. 6, 2021, doi: 10.1063/5.0046574.

[46] Y. Zhao, M. Lei, S. X. Liu, and Q. Zhao, "Smart hydrogel-based optical fiber SPR sensor for pH measurements," *Sensors Actuators, B Chem.*, vol. 261, pp. 226–232, 2018, doi: 10.1016/j.snb.2018.01.120.

[47] N. F. Murat, W. M. Mukhtar, A. R. A. Rashid, K. A. Dasuki, and A. A. R. A. Yussuf, "Optimization of gold thin films thicknesses in enhancing SPR response," *IEEE Int. Conf. Semicond. Electron. Proceedings, ICSE*, vol. 2016-Septe, no. 2, pp. 244–247, 2016, doi: 10.1109/SMELEC.2016.7573637.

[48] R. Zhang, S. Pu, and X. Li, "Gold-film-thickness dependent SPR refractive index and temperature sensing with hetero-core optical fiber structure," *Sensors (Switzerland)*, vol. 19, no. 19, 2019, doi: 10.3390/s19194345.

[49] A. Samavati *et al.*, "Sustainable and fast saliva-based COVID-19 virus diagnosis kit using a novel GO-decorated Au/FBG sensor," *Chem. Eng. J.*, vol. 420, no. September, p. 127655, Sep. 2021, doi: 10.1016/j.cej.2020.127655.

[50] S. Priyadarsini, S. Mohanty, S. Mukherjee, S. Basu, and M. Mishra, "Graphene and graphene oxide as nanomaterials for medicine and biology application," *J. Nanostructure Chem.*, vol. 8, no. 2, pp. 123–137, Jun. 2018, doi: 10.1007/s40097-018-0265-6.

[51] Q. Wang and B.-T. Wang, "Surface plasmon resonance biosensor based on graphene oxide/silver coated polymer cladding silica fiber," *Sensors Actuators B Chem.*, vol. 275, no. December 2017, pp. 332–338, Dec. 2018, doi: 10.1016/j.snb.2018.08.065.

[52] A. S. Kushwaha, A. Kumar, R. Kumar, M. Srivastava, and S. K. Srivastava, *Zinc oxide, gold and graphene-based surface plasmon resonance (SPR) biosensor for detection of pseudomonas like bacteria: A comparative study*, vol. 172. Elsevier GmbH., 2018.

[53] H. Xu *et al.*, "Alcohol sensor based on surface plasmon resonance of ZnO nanoflowers/Au structure," *Materials (Basel).*, vol. 15, no. 1, pp. 1–10, 2022, doi: 10.3390/ma15010189.

[54] M. M. Rahman, M. M. Rana, M. S. Rahman, M. S. Anower, M. A. Mollah, and A. K. Paul, "Sensitivity enhancement of SPR biosensors employing heterostructure of PtSe2 and 2D materials," *Opt. Mater. (Amst).*, vol. 107, no. June, p. 110123, Sep. 2020, doi: 10.1016/j.optmat.2020.110123.

[55] R. Kanmani *et al.*, "Effects of TiO2 on the performance of silver coated on side-polished optical fiber for alcohol sensing applications," *Opt. Fiber Technol.*, vol. 50, no. March, pp. 183–187, Jul. 2019, doi: 10.1016/j.yofte.2019.03.010.

[56] W. Wang *et al.*, "Reusable surface plasmon resonance sensor for rapid detection of Cu2+ based on modified-chitosan thin film as an active layer," *Sensors Actuators A Phys.*, vol. 286, pp. 59–67, Feb. 2019, doi: 10.1016/j.sna.2018.12.025.

[57] W. M. Mukhtar, R. M. Halim, K. A. Dasuki, A. R. A. Rashid, and N. A. M. Taib, "Silver-graphene oxide nanocomposite film-based SPR sensor for detection of Pb2+ ions," *IEEE Int. Conf. Semicond. Electron. Proceedings, ICSE*, vol. 2018-Augus, pp. 152–155, 2018, doi: 10.1109/SMELEC.2018.8481315.

[58] G. Wang, C. Wang, R. Yang, W. Liu, and S. Sun, "A Sensitive and Stable Surface Plasmon Resonance Sensor Based on Monolayer Protected Silver Film," *Sensors*, vol. 17, no. 12, p. 2777, Nov. 2017, doi: 10.3390/s17122777.

[59] I. Antohe, I. Iordache, V. A. Antohe, and G. Socol, "A polyaniline/platinum coated fiber optic surface plasmon resonance sensor for picomolar detection of 4-nitrophenol," *Sci. Rep.*, vol. 11, no. 1, pp. 1–10, 2021, doi: 10.1038/s41598-021-89396-w.

[60] V. Kaur and S. Singh, "Design of titanium nitride coated PCF-SPR sensor for liquid sensing applications," *Opt. Fiber Technol.*, vol. 48, no. September 2018, pp. 159–164, Mar. 2019, doi: 10.1016/j.yofte.2018.12.015.

[61] Z. Zhao and Q. Wang, "Gold nanoparticles (AuNPs) and graphene oxide heterostructures with gold film coupling for an enhanced sensitivity surface plasmon resonance (SPR) fiber sensor," *Instrum. Sci. Technol.*, vol. 50, no. 5, pp. 530–542, Sep. 2022, doi: 10.1080/10739149.2022.2044845.

[62] W. Li, Y. Chen, J. Xu, M. Jiang, and H. Zou, "A D-Shaped SPR-Based PCF Sensor with an Extremely High-Amplitude Sensitivity for Measuring the Refractive Index," *Micromachines*, vol. 14, no. 7, p. 1295, Jun. 2023, doi: 10.3390/mi14071295.

[63] F. Xia *et al.*, "Ultra-high sensitivity SPR fiber sensor based on multilayer nanoparticle and Au film coupling enhancement," *Meas. J. Int. Meas. Confed.*, vol. 164, p. 108083, 2020, doi: 10.1016/j.measurement.2020.108083.

[64] S. Akgönüllü, H. Yavuz, and A. Denizli, "SPR nanosensor based on molecularly imprinted polymer film with gold nanoparticles for sensitive detection of aflatoxin B1," *Talanta*, vol. 219, no. May, p. 121219, Nov. 2020, doi: 10.1016/j.talanta.2020.121219.

[65] S. Szunerits, J. Spadavecchia, and R. Boukherroub, "Surface plasmon resonance: signal amplification using colloidal gold nanoparticles for enhanced sensitivity," *Rev. Anal. Chem.*, vol. 33, no. 3, pp. 153–164, Jan. 2014, doi: 10.1515/revac-2014-0011.

[66] S. A. Abid *et al.*, "Biosensors as a future diagnostic approach for COVID-19," *Life Sci.*, vol. 273, no. October 2020, p. 119117, 2021, doi: 10.1016/j.lfs.2021.119117.

[67] N. A. S. Omar *et al.*, "Sensitive Detection of Dengue Virus Type 2 E-Proteins Signals Using Self-Assembled Monolayers/Reduced Graphene Oxide-PAMAM Dendrimer Thin Film-SPR Optical Sensor," *Sci. Rep.*, vol. 10, no. 1, pp. 1–15, 2020, doi: 10.1038/s41598-020-59388-3.

[68] L. Zhan, C. M. Li, P. F. Gao, and C. Z. Huang, "AuNPs/graphene Hybrids-Based Enzyme-Free Plasmonic Immunoassay for Respiratory Syncytial Virus Detection," *J. Anal. Test.*, vol. 5, no. 3, pp. 203–209, 2021, doi: 10.1007/s41664-021-00195-8.

[69] Y. F. Chang *et al.*, "Simple Strategy for Rapid and Sensitive Detection of Avian Influenza A H7N9 Virus Based on Intensity-Modulated SPR Biosensor and New Generated Antibody," *Anal. Chem.*, vol. 90, no. 3, pp. 1861–1869, 2018, doi: 10.1021/acs.analchem.7b03934.

[70] X. Liu *et al.*, "Graphene Oxide-Sensitized Surface Plasmon Resonance Biosensor of Porcine Reproductive and Respiratory Syndrome Virus," *Molecules*, vol. 27, no. 12, 2022, doi: 10.3390/molecules27123942.

[71] Z. Dai *et al.*, "Surface plasmon resonance biosensor with laser heterodyne feedback for highly-sensitive and rapid detection of COVID-19 spike antigen," *Biosens. Bioelectron.*, vol. 206, no. February, p. 114163, 2022, doi: 10.1016/j.bios.2022.114163.

[72] V. R. Sudheer, S. R. SarathKumar, and S. Sankararaman, "Nanostructured ZnO and ZnO: Pd with MXene overlayer SPR biosensors," *Opt. Quantum Electron.*, vol. 53, no. 6, pp. 1–14, 2021, doi: 10.1007/s11082-021-03042-3.