Different plasmonic biosensing policies for viral detection

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CERTIFICATE-I

This is to certify that the review article entitled "**Different plasmonic biosensing policies for viral detection**" submitted for the award of the degree of **Bachelor of Technology in Biotechnology** to Shoolini University of Biotechnology and Management Sciences, Solan (H.P) is original research work carried out by **Suraj Singh (1714303006), Gautam Saklani (1714303007), Nitin Patial (1714303026) and Neeraj Jaswal (1714303036)** under my guidance and supervision. No part of this review article has been submitted for any other degree or diploma to this or any other university.

The assistance and help received during the course of investigation has been duly acknowledged.

Dr. Rupak Nagraik

Major Research Guide

Date: 22.05.2021

Place: Solan

DECLARATION BY THE CANDIDATE

I hereby declare that the review article entitled "**Different plasmonic biosensing policies for viral detection**" submitted for the award of degree of **Bachelor of Technology in Biotechnology** to Shoolini University of Biotechnology and Management Sciences, Solan (H.P) is original research article carried out by us, under the guidance and supervision of **Dr. Rupak Nagraik**. No part of this review article has been submitted for any other degree or diploma to this or any other university.

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ABSTRACT

Viruses has posed a serious concern and has been a threat to the biosecurity of world as epitomized by the current COVID-19 pandemic scenario. Pre diagnosis of viral infection and disease control have always been useful for future prospective. Presently COVID-19 virus has been a serious threat to healthcare system and global economy.[1,3] This has laid down the stress and the need for rapid and simple diagnostic methods. This can be achieved based on various plasmonic phenomena, including propagating surface plasmon resonance (SPR), localized SPR, surface-enhanced Raman scattering, surface-enhanced fluorescence and surface-enhanced infrared absorption spectroscopy. Plasmonic-based biosensing can manage the threat of infectious diseases by providing timely virus monitoring. Recently, many plasmonic platforms have embraced the challenge of offering on-site strategies to complement traditional diagnostic methods relying on the polymerase chain reaction (PCR) and enzyme-linked immunosorbent assays (ELISA). Quantification of different viruses (e.g., hepatitis virus ,influenza virus, norovirus, dengue virus, Ebola virus, Zika virus) with particular attention to Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) was reviewed from the perspective of the biomarker and the biological receptor immobilized on the sensor chip. Plasmon has an interesting property that occurs as an electron cloud on the surface of metallic nanomaterials. When metallic nanoparticles (MNP) interact with incident light, the electron cloud in the MNP oscillates, and in this case, the collective excitation of electrons is regarded as plasmon. In some cases, plasmonic properties can be tuned by interactions between plasmonic nanomaterials (P-NM) and shape control, thus controlling their optical properties to exhibit various colours. [2,3-4]

INTRODUCTION

The whole world has been facing the consequences of rapid airborne transmission of diseases caused by viruses again and again and are a cause of great concern since the global pandemic of coronavirus disease (COVID-19) has surpassed the number of cases and economic impact of recent virus disease outbreaks [e.g., H1N1/H5N1 flu, Ebola, MERS-CoV (Middle East Respiratory Syndrome Coronavirus), and SARS-CoV-1(Severe Acute Respiratory Syndrome Coronavirus. Besides human health these has posed a threat to substantial global economic and social platforms.[2] The need for effective management of current and future epidemics or pandemics has urged the development of rapid and sensitive screening tools. Therefore, early viral diagnosis has become a primary need to control the spread of viral diseases. The spread of COVID-19 and its consequences which are faced all over the world presently has been a great threat to humans. To minimize the damage from this pandemic and increase preparedness for future reemergence of COVID-19 and other pandemics, fast and well-timed diagnostic systems are urgently needed.[2,4] Conventional viral detection methods generally require a particular methodology, such as gene sequencing, cell culturing, polymerase chain reaction (PCR), virus isolation, hemagglutination assay, enzyme-linked immunosorbent assay (ELISA), immunoperoxidase, etc. Generally, these techniques are expensive, involve sophisticated instrumentation requiring expert handling, possess a high response time, etc. Moreover, their pre-developed protocols are typically limited to specific strings or types of viruses. Here, plasmonic-based biosensing offers an alternative tool that has

already caught the scientific community's attention as a highly sensitive and promising novel technique for the rapid diagnosis of viruses. This technique also comes with the advantages of easy operation, minimal sample pretreatment and simple non-expensive instrumentation.[2,3] Consequently, the requirement for fast and cost-effective viral diagnostic methods has led to putting the focus on the development of real-time biosensing platforms. Among the variety of biosensor technologies that have arisen in the last decades for virus detection, plasmonic applications have gained significant attention, owing to their versatility, label-free monitoring, and low time of response. The potential for multiplexing and system miniaturization are additional benefits for the point-of-care testing.[3]

1. Plasmonic Biosensing Approaches :-

The functioning of plasmonic biosensors is based upon the theory of propagation of surface plasmons along the interface of a thin metallic layer (such as gold or silver) and a dielectric aqueous medium. The binding events of molecular interactions between the target analyte and the immobilized receptor due to refractive index changes in the transducer surface is counted as major advantage of the plasmonic biosensing.[5-7]
Binding events occurring on the surface of thin metallic layers can be monitored in two different ways: first by, Surface Plasmon Resonance (SPR) and second by, Localized Surface Plasmon Resonance (LSPR). However, the difference between SPR and LSPR is determined by the dimension of the plasmonic nanomaterial used respectively.

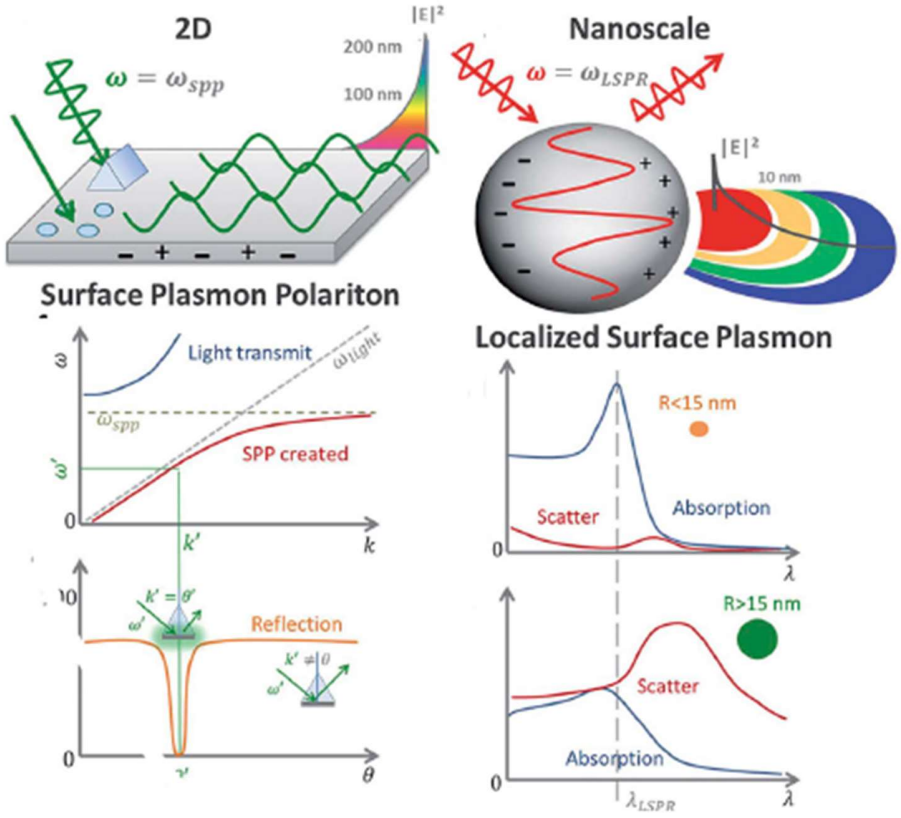

Figure 1 : Overview of Surface Plasmon Resonance (SPR) & Localized Surface Plasmon Resonance (LSPR). Showing difference in surface, volume and LSPR of Zero dimensional metallic nanoparticles and two dimensional thin metallic surfaces. Taken with the permission from Li at al.[8] Copyright (2015) Royal Society of Chemistry (RSC).

Hence, the basis for colorimetric plasmonic biosensing is based upon the enhanced spatial resolution of LSPR configuration by designing the geometry along with composition of metallic nanoparticles.[9-10] Optical processes like Raman Scattering and fluorescent which leads to SERS, obtained by local electromagnetic field. This is also applicable for plasma enhanced electrochemiluminescence (ECL) sensing strategies. The sensitivity achieved by Raman scattering and fluorescence is much greater as compare to LSPR & SPR, hence, can detect a single virus particle. Alongside, the propagation of electromagnetic radiation using optical fibres can also be applied to virus detection via miniatured platforms with SPR & LSPR configurations.[11,12] Thus, improvement in plasmonic biosensing schemes including above mentioned optical configurations as well as utilization of nanomaterials and optical aperture nanostructure for obtaining highly sensitive virus detection are explained in this section.

1. Plasmonic Nanoparticles :

Nanoparticles have characteristics like optical, electrical and magnetic properties by which it provide signal amplification to plasmonic biosensing. Alongside, the properties like chemical activation and biocompatibility of nanomaterials are also significant advantages.[13-16] There are various types of plasmonic nanoparticles ranging from metallic and quantum dots to graphene nanostructures.[17-19] Since from last decade, there has been number of nanostructured- based strategies developed out of which, some are represented below.

*** Metallic Nanoparticles :**

Plasmonic nanoparticles are classified into organic and inorganic on the basis of the nanomaterial used. Organic nanomaterial consist of fullerenes, carbon nanotubes, etc. whereas inorganic nanomaterial consist of metal, oxide-based particles and quantum dots respectively. Among the inorganic, noble-metal nanoparticles have been extensively used in biosensing polices as they have characteristic feature of strong absorption of light resulting from the oscillation of free electrons. Also, the size and shape of nanoparticles along with interparticle distance determine the amplitude of oscillation and the position of the SPR band[20]. The physiochemical properties of the metallic nanoparticles can be tuned to convert LSPR spectra and hence produce colour variations which generates signal response because variation in the chemical environment media due to the binding event between the biological receptor and the target analyte which can also effect the oscillations[21,9]. Therefore, most common use of silver and gold nanoparticles in LSPR,SERS, fluorescence enhancement and colorimetric assays represent a popular approach for detecting small analytes.

LSPR based Biosensing schemes:

LSPR Biosensors exploit gold nanoparticles (AuNP) which have been successfully applied to clinical diagnostic, environmental monitoring and food safety.

Detection of Hepatitis B Surface Antigen (HBsAg) :
Since gold nanoparticles have high light absorption and a large scattering cross-section in the SPR wavelength ranges. So, the further investigation of the HBs-antibody modified gold nanoparticles showed physical absorption and successive blocking leads to a flexible shell enveloping the nanorod which reduces the non-specific absorption and allow the assay to run in buffer, serum and plasma. LSPR biosensor can measure HBsAg concentration even at 0.01IU/mL, which is approximate 40 times lower than the limit of detection of the ELSIA method respectively. So this type of gold nanoparticle-based biosensor can be extensively used in quantitative analysis with a dose dependent response which ranges from 0.01 to 1 IU/Ml.

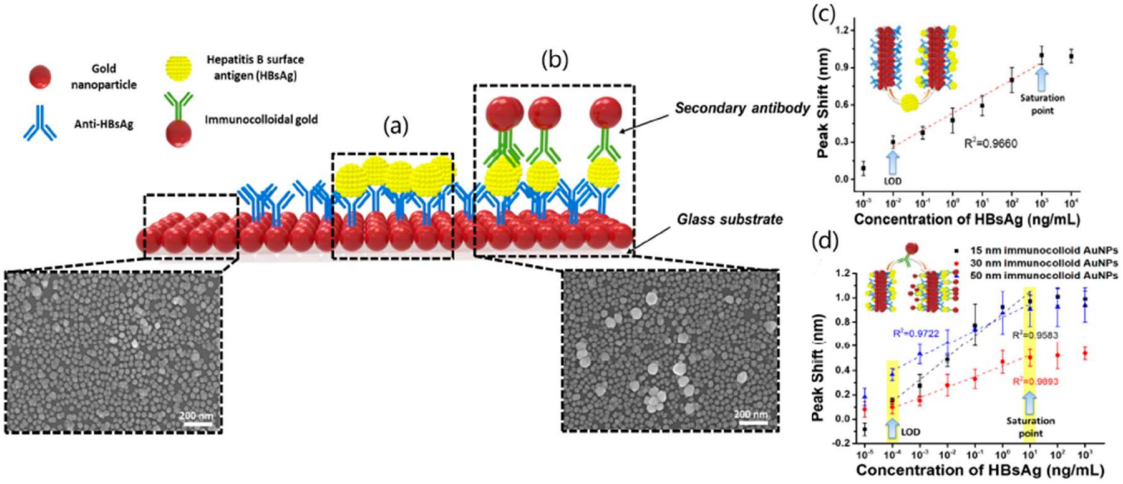

Figure 2 : Detection of Hepatitis B surface antigen by single assay LSPR chip format. Taken with permission from Kim et al.[22] Copyright (2018) Elsevier.

Detection of Avian Influenza Virus (AIV H5N1) :
In detection of Avian Influenza Virus (AIV H5N1), LSPR scheme take advantage of Au spike-like nanoparticles (hAuSN), using multi-functional DNA three way junction[22]. In this scheme, each fragment of nucleotide 3WI was joined to a hemagglutinin (HA) binding aptamer, fluorescence dye (FAM), along with thiol group. The immobilization of spiked-like gold nanoparticles onto indium trioxide (ITO) substrates and the subsequent functionalization with the DNA for detecting hemagglutinin protein at 1pM levels.

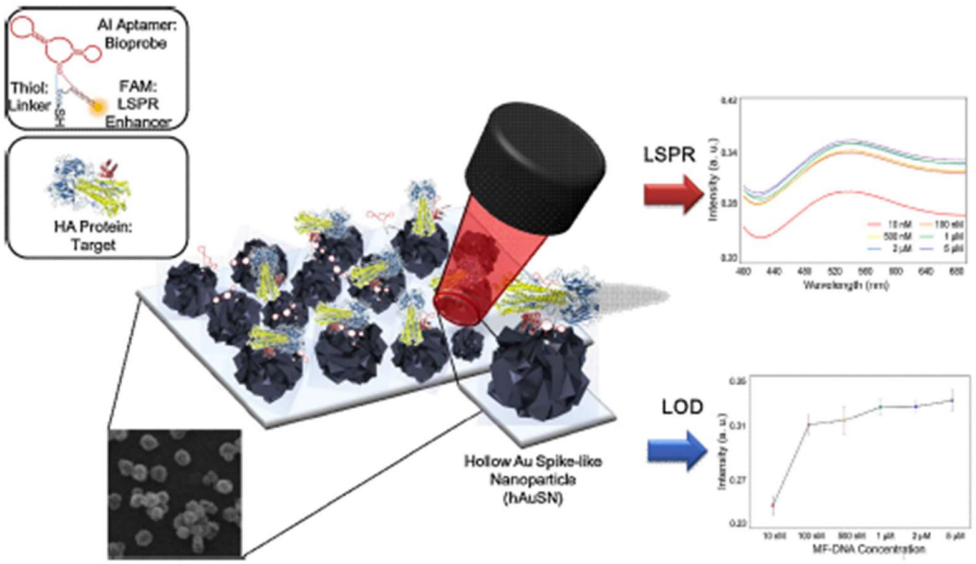

Figure 3 : Detection of Avian influenza virus (AIV H5N1) by LSPR biosensor. Shown absorption spectra was taken at 400-700 nm wavelength range. Taken with permission from Lee et al.[22] Copyright (2019) Elsevier.

SERS based Biosensors :-

Plasmonic nanoparticles are also been rapidly used in SERS Biosensors. The benefits of using SERS strategies came from using enhancement of Raman Scattering by providing the modulation of surface plasmon polaritons at a greater distance from the metallic nanoparticle surface, which offer high sensitivity as compare to SPR & LSPR.

SERS based strategy for detection of hepatitis B surface Antigen (HBsAg) :
In this, the biosensor uses active tag which consist of a composite of graphene oxide (GO) coated with gold nanoparticles. Each composite carried the SERS probe 2-mercaptopyridine in which the antibody against HbsAg was immobilized. The immunoassay took edge as the captured antibody and the detection antibody attached to the GO-GNR's composite by measuring the SERS signal provided via the 2-Mpy bound to the GNR's surface. The signal response to the interaction of the HB's Ag was measured in the 1-100pg/mL with a limit of detection of 0.05pg/mL[23-24]

1.1. Some other Plasmonic Nanoparticles :-

Quantum Dots :
Since quantum dots have characteristic feature of their broad absorption along with narrow emission band represent them as a good semiconductor nanomaterials and they have gained prominence in recent years of multiplex detection of virus. They also have an advantage of wide range of wavelength spectra and resistivity to external physio-chemical conditions. [24] Most unique optical properties are seen in fluorescent quantum dots (QD), which in they are in combination with surface plasmonic properties of metallic nanoparticles which can thereby increase the sensitivity of plasmonic bio-detection systems.[25-27,28]

In current scenario, most of QD's applications have been extensively used in LSPR-based biosensors because the distance and dimensions of the adjacent gold nanoparticles can affect the fluorescence signal. Hence, various LSPR based technologies have made use of fluorescence enhancement to detect samples like viruses which are summarized briefly in table given below.

Plasmonic configuration	**Target Virus/Protein**	**Detection technique**	**Media/Biological sample used**
LSPR-induced fluorescence	Influenza virus H1N1 antigens	CdSeTeS QD functionalized with anti-neuraminidase antibody and AuNP conjugated to anti-hemagglutinin antibody-immunofluorescence assay	0.03 pg/mL (deionized water) and 0.4 pg/mL (human serum)
LSPR-induced fluorescence	Norovirus	Composite of cysteine capped CdSeTeS QDs and AuNPs-fluorescence quenching immunofluorescence assay	12100 pg/mL (10% diluted human serum)
LSPR-induced fluorescence	Zika RNA virus	Nanohybrids of NPs bound to CdSeS alloyed QDs-hybridization	2.4-7.6 copies/mL (assay buffer)

Table 1: Analytical features of quantum dots based LSPR-induced fluorescence biosensor configuration.[25-27,28]

Carbon based Nanoparticles :

Carbonic nanomaterials are majorly Graphene structures that can attain different shapes and sizes, ranging from planar nanosheets to rod-shaped nanotubes. Graphene based nanostructures provide much benefits for plasmonic applications as they have high surface area as well as biocompatible area that facilitate surface functionalization.[29,30] Use of carbon-based nanoparticles in SERS along with fluorescence strategies are summarized briefly in the table given below, which is used for the detection of virus related diseases respectively.

Plasmonic configuration	**Target Virus/Protein**	**Detection technique**	**Media/Biological sample used**

Surface Plasmon Resonance (SPR)	Dengue virus (E proteins)	Composite of reduce graphene oxide and polyamidoamine self-assembled to dithiobis (succinimidyl undecanoate) amine-activated layers-immunoassay antibody immobilization	4.24 pg/mL, PBS Solution
SERS magneto fluorometric	Influenza virus H1N1 hemagglutinin protein	Binary AuNP-graphene hybrids and QD through antibody conjugated immunoassay a sandwich structure	7.02 fg/mL (deionized water) 6.07 pg/mL (human serum)
SERS magneto fluorometric	Norovirus like particles	Binary metallic and magnetic nanoparticles decorated with graphene immunoassay	1.16 pg/mL (2% BSA solution)

Table 2: Analytical features of Carbon based nanomaterials used in SPR & SERS magneto-fluorescence biosensor configuration.[31-33]

Other Plasmonic Nanomaterial-Based Strategies :-

Nanopatterning, Nanostructures:

The invention of plasmonic structures also relies on lithographic approaches, which enable the design of ordered arrays of metallic nanoapertures, such as nanoholes, nano-antennas, nano-slits, or nano-disks. The interaction of light with periodic arrays of nanoholes exhibits astonishing optical transmission (EOT) effects, thus enhancing the transmission efficiency of light at certain wavelength[34].

For example, Zang et al. An interesting single-molecule method to recognize Ebola virus antigens. The biosensor is composed of a series of three-dimensional plasmonic nano-antennas, using a sandwich immunoassay format, with increased fluorescence concentration . The nano-antenna configuration includes silica nano-pills coated with nano-plates and gold nano-dots. Due to the formation of a nano-cavity, the nano-pills amplify the fluorescent signal. Functionalization of the surface of the nano-pill using thiol-gold bond and protein A/G layer as spacers, the best detection method and antibody detection method can be selected, while avoiding the loss of fluorescence signal when irradiated on the gold surface. The soluble Ebola virus glycoprotein (EBOV-sGP) was found under optimized conditions. The plasma concentration in plasma is 220 fg/ml, which greatly improves the recommended best immunoassay method for detecting Ebola antigen. Arrangement

of nano-scale pores functionalized with methoxy polyethylene (ethylene glycol) terminated with sulfhydryl groups[35-36].

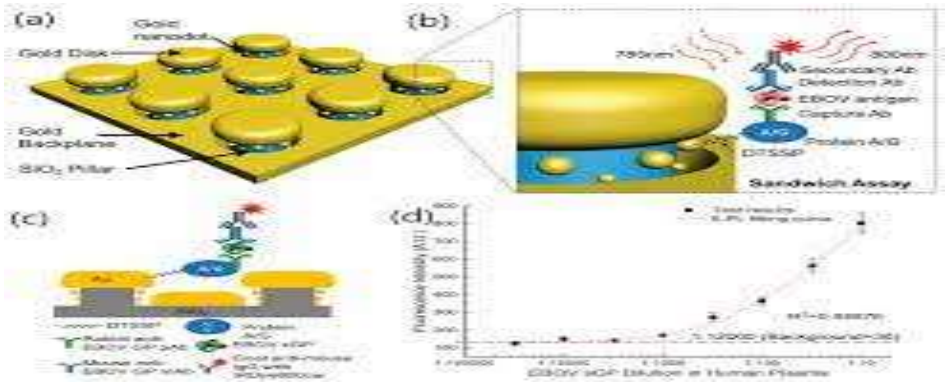

Figure 4: Systematic diagrammatic representation of nanoantenna array for detection of Ebola virus. The shown representation is based upon nanostructure and fluorescence sensing methods. Taken with permission from Zang et al.[35] Copyright (2020) Wiley.

Fibre Optics :-

SPR and LSPR biosensors combine optical fibres to couple the light excitation of surface plasmons, providing an interesting alternative to classic prism-based configurations. The ability to control the propagation of electromagnetic field radiation through fibre optic systems has enabled improvements in wavelength modulation and development. Many SPR/LSPR fibre optic platforms have provided micro-detection methods for the definition of clinical biomes. In particular, a fibre optic SPR system for analysing the H6 subtype of avian influenza virus has been described. In order to optimize the immobilization of the self-assembled monolayer (SAM) and subsequent antibody functionalization, the optical fibre was plasma-modified. The LSPR optical platform enables the development of immunosensors to determine the non-clinical uses of plant viruses: large flower orchid leaf virus (CymMV) and gum round spot virus (ORSV) . Detection limit of viral antigens on functionalized antibodies on gold nano rods. It is at the level of picograms per litre. Compared with ELISA, the increase in sensitivity is related to the higher sensitivity of nanorods, which can also prevent similarly sized nanospheres from producing colour interference. The surface fibre grid (Ex-GFR) with gold nanospheres enables the development of immunosensors for the detection of Newcastle disease virus (NDV). Compared with the reference Ex-GFR, the modified fibre coating with gold nanospheres (AuN) improved the effect of LSPR, and the activation of gold nanospheres with staphylococcal protein A (SPA) increased the biological activity of monoclonal anti-NDV antibodies Times. Without AuN treatment, it can be increased by -10- times. Monitoring the red shift of the resonance wavelength shows that the minimum detectable amount of NDV is ~5 pg, which is slightly better than RT-PCR (10 pg). The specificity of the immunoassay against avian influenza virus was also proved, and the clinical validity was confirmed by comparing the results. NVD in allantoic fluid and solutions.[37].

3.3. Colorimetric:-

A colorimetric plasma sensor based on colloidal nanoparticle aggregation has been described for the detection of influenza virus. The application uses the interaction between hemagglutinin and sialic acid in the virus envelope to reduce and stabilize the aggregation of gold nanoparticles. Since it is not shown, it is reported that there is a good correlation between the optical density change and the influenza B virus dilution, resulting in a virus dilution of 0. 156% by volume (hemagglutination titre.(512), which causes a colorimetric change. The concentration of H5N1 virus antigen detected by sandwich immunoassay was 1 pg/ml. Compared with other methods, the sensitivity is improved. Compared with gold nanorods, the facet ratio of the gold nano-bipyramid end is higher. A plasma platform consisting of silver deposits in gold nanoparticles bound to antibodies is used to monitor hepatitis E virus (HEV).Nanozyme-based immunoassays capture HEV-like particles (HEV-LP) by binding to bound gold nanoparticles[38-39]

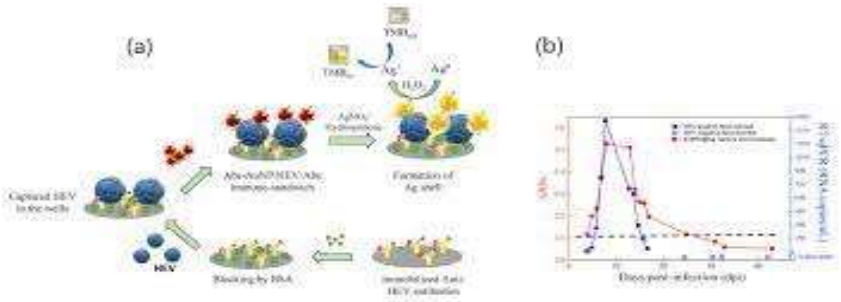

Figure 5: Diagrammatic representation of silver-deposited, gold nanozyme based capture immunoassay for detection of Hepatitis E virus like particle. Take with permission from Khoris et al.[38-39] Copyright (2020) Elsevier.

4. Electrochemiluminescence:-

As shown by the detection of LSPR, the influence of the collective vibration of free electrons on the surface of metal nanostructures can improve the optical signal of the phosphor near the nanoparticles made of precious metals. Improvement of the electromagnetic field from incident light. The distance between the plasma nanoparticles and the phosphor determines the process of electrochemiluminescence, because when the plasma nanoparticles, which act as energy or electron acceptors, are very close to the phosphor, the signal can be turned off. Energy transfer can be controlled by DNA or adaptors to remotely extinguish and amplify electrochemiluminescence Signal.

Due to the simplicity of the optical scheme, the high sensitivity and low background noise of 20 of the sensors 2020, 20, 4745, and 27 produce plasma-enhanced electrochemiluminescence.

Another ECL strategy based on plasmons is to use non-metallic MoS2 nano-films firmly bound to plasmons on the surface to amplify the ECL signal of QD doped with sulphur and boron nitrogen (S-BN QD) [40]The app uses DNA strands of different lengths to examine the effect of the distance between phosphors and nanoparticles. An increase in the distance between MoS2 and S-BNQD nanosheets will reduce energy transfer and increase the surface plasmon coupling effect. In particular, this assay is used to detect hepatitis C virus (HCV) genes. The so-called hybrid chain reaction is used as a DNA amplification method without isothermal enzymes for quantitative determination of DNA.HCV detection limit (LOD) 0.17 pmol/L.

4. Plasmonic Advancements in COVID-19 Diagnosis:-

SARS-CoV-2 is an enveloped non-segmental β-coronavirus that can cause new severe acute respiratory syndrome and new coronavirus disease (COVID-19). As the SARS-CoV-2 genome is a single-stranded RNA virus with positive significance (about 30 kb, about 9860 amino acids), it is the most important biomarker for the diagnosis of COVID-19 protein. Structural and additive or even complete SARS-CoV-2 viruses can be used as antigens for surveillance of coronavirus diseases (see Figure 14). In addition, determining the response of immunoglobulin M (IgM) and immunoglobulin G (IgG) five days after the onset of the disease can also be used as an indicator of COVID-19.Therefore, reverse transcription polymerase chain reaction (RT-PCR), gene sequencing, ELISA and lateral flow immunoassay are the most important diagnostic methods today.

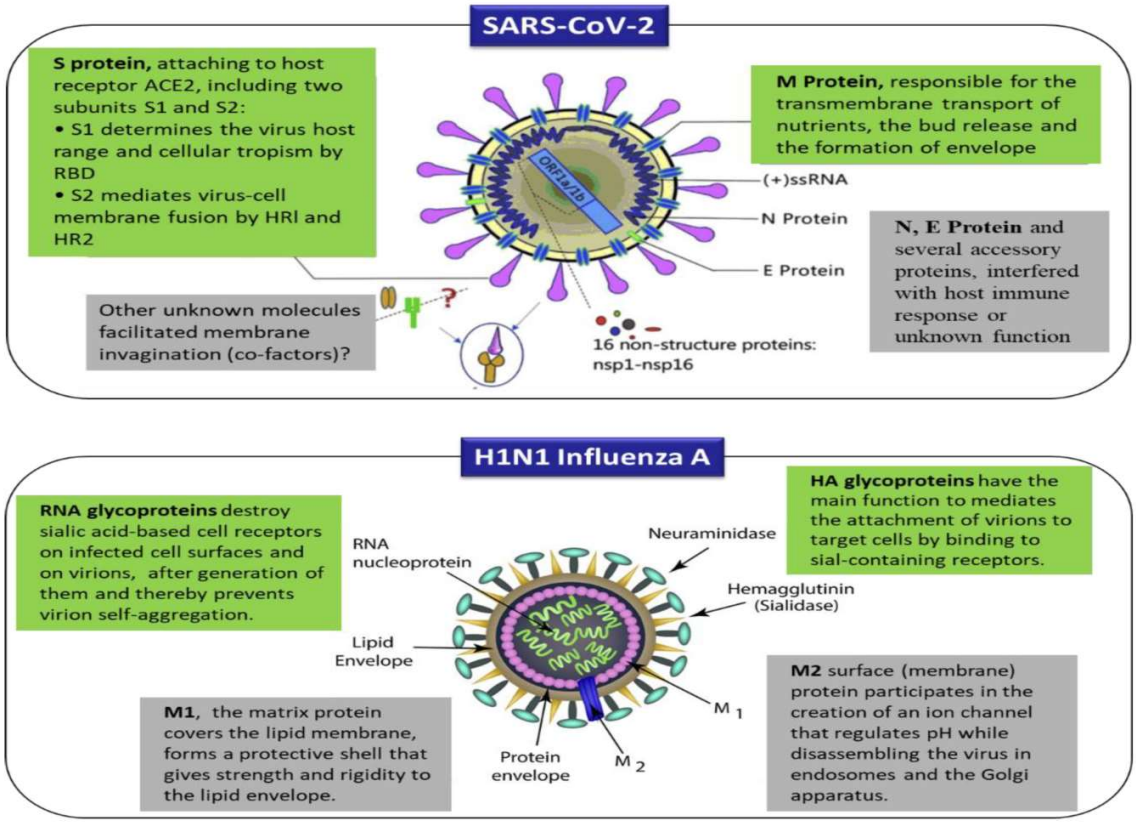

Figure 6: Systematic explaining about the structure of SARS-CoV-2. Shown structural proteins like spike glycoprotein (S), small envelope protein (E), matrix protein (M) and nucleocapsid protein (N). Taken with permission from Guo et al.[41-42] Copyright (2020) BMC Springer Nature.

However, the search for fast and reliable equipment at the time of care has led to the development of plasmon methods based on the latest technological advances. For example, the new method combines plasma photothermal effect (PPT) and LSPR detection to detect selected DNA sequences by hybridization. The DNA receptor is immobilized on the two-dimensional gold nano island (AuNI). This dual-function plasma biosensor uses the PPT heat generated on the AuNI chip to increase the hybridization temperature and distinguish two similar gene sequences (RdRp

genes), SARS-CoV and SARS-CoV-2. Detection limit is 0.A multi-gene mixture containing RdRp-COVID DNA sequence, 1ab (ORF1ab)-COVID reading frame and SARS-Cov-2E gene was used to obtain 22 pM. The incident angles of the plasmon resonance PPT and LSPR are excited at two different wavelengths. Since the proposed method is based on the method of lowering the melting temperature and uses the same nucleic acid hybridization standard as the PCR test, it is recommended to supplement the method.

Testing for COVID-19 relies heavily on RT-PCR (Reverse Transcription Polymerase Chain Reaction) technology. Although RT-PCR is currently the most sensitive method for detecting viral RNA, for example. B. Viral RNA secreted by COVID-19 virus particles, which proves that RT-PCR reagents may be overwhelmed, overwhelmed by well-trained staff, and overwhelmed by time handling. Too long. Some exposures can be absorbed by an alternative technique-local surface plasmon resonance (LSPR). Researchers from ETH Zurich stated that if LPSR is commissioned to detect COVID-19 RNA, the technology shows high accuracy, sensitivity and speed. The researchers presented a preliminary study, which was published on April 13. Plasma photothermal biosensor with dual functions can detect severe coronavirus 2 with acute respiratory syndrome with high accuracy. It describes an advanced LSPR biosensor with dual plasmon function (PPT). As a local change in refractive index. However, the ETH Explorer system is different in that it contains a DNA probe that recognizes a specific SARS-CoV-2 RNA sequence. The probe is attached to gold nanoparticles (actually two-dimensional nano islands made of gold or AuNI), and SARS-CoV-2-RNA is detected by nucleic acid hybridization. In essence, the DNA probe attaches itself to the complementary viral RNA like a closed zipper. "In order to improve the detection performance, when the AuNI crystal is irradiated with the plasmon resonance frequency, thermal plasma heat will be generated in the AuNI crystal itself." The local heating of PPT can increase the temperature of in situ hybridization and help the two similarities. Accurate distinction between gene sequences. In other words, researchers at ETH Zurich (led by Dr Jing Wang) use lasers to heat nanoparticles, which makes it difficult to maintain incomplete matching sequences and reduce false positives. For example, under these conditions, a nucleic acid "zipper" lacking a pair of teeth indicates a partial mismatch, and the nucleic acid "zipper" is decompressed. Between SARS-CoV-2 and its close relative SARS-CoV-1. According to the author of the article, "our dual-function LSPR biosensor" shows high sensitivity to SARS-CoV-2 sequence selection, and its detection limit is less than 0.22 pM, so it can detect exact specific targets. "In multigenic mix. The analysis showed that within a few minutes, the amount of viral RNA was lower than the amount present in the swab. The authors concluded: "In the context of the COVID-19 outbreak, this proposed dual-use LSPR organism Sensors can provide a reliable and easy-to-implement diagnostic platform to improve the diagnostic accuracy of clinical tests and reduce the pressure of PCR. cut back. "Technology. Testing before that, the system must be tested to check the complete viral RNA in patient samples. In addition, some practical limitations of the SPR system need to be addressed. Such restrictions are stipulated in the article ("rolling") [Tools are expensive, ranging from $50,000 to $300,000, depending on the function of the tool or the number of channels. In addition, few companies manufacture the tool. These tools are made by Provided by different companies, the supplier’s focus on research and pharmaceutical applications explains to a certain extent why clinical laboratories are not very familiar and may think that the technology is too mature, which put these companies in the queue. [41-42].

5. Conclusions :

The uncertain proportions of pandemic outbreaks have led to the need for robust and inexpensive protocols that can easily adapt to the changing virulence of virus strains. In recent years, plasma biosensors have been increasingly used for clinical diagnosis of viral diseases and other infectious diseases. The versatility of SPR and LSPR as a label-less detection system can track binding interactions in a short time. However, the implementation of technological advances has accelerated the development of applications based on nanomaterials to increase the sensitivity and specificity of classical configurations. The unique optical properties of plasmonic nanostructures are used in combination with SERS. Colorimetric, fluorescence or luminescence amplification can be used for virus diagnosis. Similarly, the development of methods for detecting plasmonic viruses has benefited from various viral biomarkers. Despite significant progress, the application of modern plasmon technology has not surpassed traditional laboratory immunoassay and sequencing methods. Improved detection schemes have resulted in ultra-sensitive, reliable and reproducible analysis performance. In many cases, preventing the adhesion of non-specific proteins in difficult environments remains a challenge. On the one hand, the on-site production of automated equipment is highly dependent on reliable microfluidic design and the integration of advanced software on micro platforms. With this in mind, the use of new flexible materials through a lithography method with nano-patterns can promote the inclusion of microchannels, so that samples can be delivered in micro-volumes without the need for additional equipment. Interfere with biomolecules in undiluted body fluids. From this point of view, considering the composition of the medium or the characteristics of the bioreceptor, the development of effective antifouling coatings will help bridge the gap between traditional analytical methods and plasma applications. To meet these challenges, the huge potential of individual virus detection and the efficiency and simplicity of existing plasma equipment will affect routine clinical virus surveillance during this decade.

6. References:-

1. Recent progress in plasmonic biosensing schemes for virus detection.
2. A Comprehensive review on plasmonic-based biosensors used in viral diagnostics.
3. A review on plasmonic and material based biosensing platforms for virus detection.
4. Investigation of Plasmonic Detection of Human Respiratory Virus
5. Homola, J. Surface Plasmon Resonance Sensors for Detection of Chemical and Biological Species. Chem. Rev.2008, 108, 462–493. [CrossRef]
6. Masson, J.-F. Portable and field-deployed surface plasmon resonance and plasmonic sensors. Analyst 2020,145, 3776–3800. [CrossRef] [PubMed]
7. Couture, M.; Zhao, S.S.; Masson, J.-F. Modern surface plasmon resonance for bioanalytics and biophysics.Phys. Chem. Chem. Phys. 2013, 15, 11190. [CrossRef] [PubMed]
8. Li, M.; Cushing, S.K.; Wu, N. Plasmon-enhanced optical sensors: A review. Analyst 2015, 140, 386–406.[CrossRef] [PubMed]
9. Tang, L.; Li, J. Plasmon-Based Colorimetric Nanosensors for Ultrasensitive Molecular Diagnostics. ACS Sens.2017, 2, 857–875. [CrossRef]
10. Gormley, A.J.; Chapman, R.; Stevens, M.M. Polymerization Amplified Detection for Nanoparticle-Based Biosensing. Nano Lett. 2014, 14, 6368–6373. [CrossRef]

11. Gauglitz, G. Critical assessment of relevant methods in the field of biosensors with direct optical detection Based on fibers and waveguides using plasmonic, resonance, and interference effects. Anal. Bioanal. Chem.2020, 412, 3317–3349. [CrossRef]
12. Slavík, R.; Homola, J.; Ctyrok ˇ ý, J.; Brynda, E. Novel spectral fiber optic sensor based on surface plasmon Resonance. Sens. Actuators B Chem. 2001, 74, 106–111. [CrossRef]
13. Lee, J.; Takemura, K.; Park, E. Plasmonic Nanomaterial-Based Optical Biosensing Platforms for Virus Detection. Sensors 2017, 17, 2332. [CrossRef] [PubMed]
14. Doria, G.; Conde, J.; Veigas, B.; Giestas, L.; Almeida, C.; Assunção, M.; Rosa, J.; Baptista, P.V. Noble Metal Nanoparticles for Biosensing Applications. Sensors 2012, 12, 1657–1687. [CrossRef] [PubMed]
15. Vikrant, K.; Bhardwaj, N.; Bhardwaj, S.K.; Kim, K.-H.; Deep, A. Nanomaterials as efficient platforms for Sensing DNA. Biomaterials 2019, 214, 119215. [CrossRef] [PubMed]
16. Choi, J.-H.; Lee, J.-H.; Son, J.; Choi, J.-W. Noble Metal-Assisted Surface Plasmon Resonance Immunosensors.Sensors 2020, 20, 1003. [CrossRef]
17. Tran, V.T.; Zhou, H.; Kim, S.; Lee, J.; Kim, J.; Zou, F.; Kim, J.; Park, J.Y.; Lee, J. Self-assembled magnetoplasmonic Nanochain for DNA sensing. Sens. Actuators B Chem. 2014, 203, 817–823. [CrossRef]
18. Adegoke, O.; Park, E.Y. Gold Nanoparticle-Quantum Dot Fluorescent Nanohybrid: Application for Localized Surface Plasmon Resonance-induced Molecular Beacon Ultrasensitive DNA Detection. Nanoscale Res. Lett.2016, 11, 523. [CrossRef]
19. Farzin, L.; Shamsipur, M.; Samandari, L.; Sheibani, S. HIV biosensors for early diagnosis of infection:The intertwine of nanotechnology with sensing strategies. Talanta 2020, 206, 120201. [CrossRef]
20. Link, S.; El-Sayed, M.A. Size and Temperature Dependence of the Plasmon Absorption of Colloidal Gold Nanoparticles. J. Phys. Chem. B 1999, 103, 4212–4217. [CrossRef]
21. Saha, K.; Agasti, S.S.; Kim, C.; Li, X.; Rotello, V.M. Gold Nanoparticles in Chemical and Biological Sensing.Chem. Rev. 2012, 112, 2739–2779. [CrossRef]
22. Lee, T.; Kim, G.H.; Kim, S.M.; Hong, K.; Kim, Y.; Park, C.; Sohn, H.; Min, J. Label-free localized surfacePlasmon resonance biosensor composed of multi-functional DNA 3 way junction on hollow Au spike-likeNanoparticles (HAuSN) for avian influenza virus detection. Colloids Surf. B Biointerfaces 2019, 182, 110341.[CrossRef]
23. Liu, M.; Zheng, C.; Cui, M.; Zhang, X.; Yang, D.-P.; Wang, X.; Cui, D. Graphene oxide wrapped with gold Nanorods as a tag in a SERS based immunoassay for the hepatitis B surface antigen. Microchim. Acta 2018,185, 458. [CrossRef] [PubMed]
24. Lesiak, A.; Drzozga, K.; Cabaj, J.; Ba ´nski, M.; Malecha, K.; Podhorodecki, A. Optical Sensors Based on II-VI Quantum Dots. Nanomaterials 2019, 9, 192. [CrossRef]
25. Takemura, K.; Adegoke, O.; Takahashi, N.; Kato, T.; Li, T.-C.; Kitamoto, N.; Tanaka, T.; Suzuki, T.;Park, E.Y. Versatility of a localized surface plasmon resonance-based gold nanoparticle-alloyed quantum Dot nanobiosensor for immunofluorescence detection of viruses. Biosens. Bioelectron. 2017, 89, 998–1005.[CrossRef] [PubMed]
26. Nasrin, F.; Chowdhury, A.D.; Takemura, K.; Kozaki, I.; Honda, H.; Adegoke, O.; Park, E.Y. FFluorometri Virus detection platform using quantum dots-gold nanocomposites optimizing the linker length variation.Anal. Chim. Acta 2020, 1109, 148–157. [CrossRef]
27. Nasrin, F.; Chowdhury, A.D.; Takemura, K.; Lee, J.; Adegoke, O.; Deo, V.K.; Abe, F.; Suzuki, T.; Park, E.Y.Single-step detection of norovirus tuning localized surface plasmon

resonance-induced optical signal between Gold nanoparticles and quantum dots. Biosens. Bioelectron. 2018, 122, 16–24. [CrossRef]
28. Nasrin, F.; Chowdhury, A.D.; Takemura, K.; Lee, J.; Adegoke, O.; Deo, V.K.; Abe, F.; Suzuki, T.; Park, E.Y.Single-step detection of norovirus tuning localized surface plasmon resonance-induced optical signal between Gold nanoparticles and quantum dots. Biosens. Bioelectron. 2018, 122, 16–24. [CrossRef]
29. Suvarnaphaet, P.; Pechprasarn, S. Graphene-Based Materials for Biosensors: A Review. Sensors 2017, 17, 2161.[CrossRef]
30. 30.Priyadarsini, S.; Mohanty, S.; Mukherjee, S.; Basu, S.; Mishra, M. Graphene and graphene oxide as Nanomaterials for medicine and biology application. J. Nanostruct. Chem. 2018, 8, 123–137. [CrossRef]
31. Omar, N.A.S.; Fen, Y.W.; Abdullah, J.; Sadrolhosseini, A.R.; Mustapha Kamil, Y.; Fauzi, N.; 'Illya, M.;Hashim, H.S.; Mahdi, M.A. Quantitative and Selective Surface Plasmon Resonance Response Based on A Reduced Graphene Oxide–Polyamidoamine Nanocomposite for Detection of Dengue Virus E-Proteins.Nanomaterials 2020, 10, 569. [CrossRef]
32. Lee, J.; Takemura, K.; Park, E.Y. Plasmonic/magnetic graphene-based magnetofluoro-immunosensing Platform for virus detection. Sens. Actuators B Chem. 2018, 276, 254–261. [CrossRef]
33. 33.Lee, J.; Takemura, K.; Kato, C.N.; Suzuki, T.; Park, E.Y. Binary Nanoparticle Graphene Hybrid Structure-Based Highly Sensitive Biosensing Platform for Norovirus-Like Particle Detection. ACS Appl. Mater. Interfaces 2017,9, 27298–27304. [CrossRef] [PubMed]
34. Zang, F.; Su, Z.; Zhou, L.; Konduru, K.; Kaplan, G.; Chou, S.Y. Ultrasensitive Ebola Virus Antigen Sensing via 3D Nanoantenna Arrays. Adv. Mater. 2019, 1902331. [CrossRef] [PubMed]
35. Jackman, J.A.; Linardy, E.; Yoo, D.; Seo, J.; Ng, W.B.; Klemme, D.J.; Wittenberg, N.J.; Oh, S.-H.; Cho, N.-J.Plasmonic Nanohole Sensor for Capturing Single Virus-Like Particles toward Virucidal Drug Evaluation.Small 2016, 12, 1159–1166. [CrossRef] [PubMed]
36. Burkhartsmeyer, J.; Wang, Y.; Wong, K.S.; Gordon, R. Optical Trapping, Sizing, and Probing Acoustic Modes Of a Small Virus. Appl. Sci. 2020, 10, 394. [CrossRef]
37. Zhao, X.; Tsao, Y.-C.; Lee, F.-J.; Tsai, W.-H.; Wang, C.-H.; Chuang, T.-L.; Wu, M.-S.; Lin, C.-W. Optical fiber Sensor based on surface plasmon resonance for rapid detection of avian influenza virus subtype H6:Initial studies. J. Virol. Methods 2016, 233, 15–22. [CrossRef] [PubMed]
38. Xu, S.; Ouyang, W.; Xie, P.; Lin, Y.; Qiu, B.; Lin, Z.; Chen, G.; Guo, L. Highly Uniform Gold Nanobipyramids For Ultrasensitive Colorimetric Detection of Influenza Virus. Anal. Chem. 2017, 89, 1617–1623. [CrossRef]
39. Khoris, I.M.; Chowdhury, A.D.; Li, T.-C.; Suzuki, T.; Park, E.Y. Advancement of capture immunoassay for Real-time monitoring of hepatitis E virus-infected monkey. Anal. Chim. Acta 2020, 1110, 64–71. [CrossRef]
40. Zhang, Q.; Liu, Y.; Nie, Y.; Ma, Q. Magnetic-plasmonic yolk-shell nanostructure-based plasmon-enhanced Electrochemiluminescence sensor. Sens. Actuators B Chem. 2020, 319, 128245. [CrossRef]

41. Qiu, G.; Gai, Z.; Tao, Y.; Schmitt, J.; Kullak-Ublick, G.A.; Wang, J. Dual-Functional Plasmonic Photothermal Biosensors for Highly Accurate Severe Acute Respiratory Syndrome Coronavirus 2 Detection. ACS Nano 2020, 14, 5268–5277. [CrossRef] [PubMed]
42. Moitra, P.; Alafeef, M.; Dighe, K.; Frieman, M.B.; Pan, D. Selective Naked-Eye Detection of SARS-CoV-2 Mediated by N Gene Targeted Antisense Oligonucleotide Capped Plasmonic Nanoparticles. ACS Nano 2020,14, 7617–7627. [CrossRef] [PubMed]