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Article

Monitoring biomaterials with light: Review of surface plasmon resonance biosensing using two dimensional materials

Parsa Yari [1], Homa Farmani [2,†,‡], Ali Farmani [3,‡] and Amir Mosavi [4,5*]

[1] Department of Electrical Engineering, Razi Kermanshah University, Kermanshah, Iran; parsayari99@gmail.com
[2] Department of Chemistry, Lorestan University, Lorestan, Khorramabad, Iran; hodgesdanawhs652@gmail.com
[3] Department of Electrical Engineering, Lorestan University, Lorestan, Khorramabad, Iran; farmani.a@lu.ac.ir
[4] School of Economics and Business, Norwegian University of Life Sciences, 1430 As, Norway; a.mosavi@ieee.org
[5] John von Neumann Faculty of Informatics, Obuda University, 1034 Budapest, Hungary; a.mosavi@ieee.org
* Correspondence: a.mosavi@ieee.org

Abstract: The purpose of this paper is to present advanced techniques in optical biodevices. Moreover different configurations involving the generation of fiber optical biosensors are described. To overcome some limitations of fiber optical biosensors, plasmonic phenomena proposed. In addition novel plasmonic phenomena have broaden researcher's horizons in new discovering in terms of technology and application. As regards there are many challenges to detect ultra-low concentration samples with high sensitivity in real time. Researchers have always made great efforts to discover more effective methods. Throughout the paper SPR and LSPR as a powerful analysis instrument are introduced. Finally surveys the current practical performances of plasmonic sensors in detection of bio target are provided. As a result these devices demonstrate great potential in identifying target analytic due to their unique optical biosensors.

Keywords: Optical Biosensor; Plasmonics; Plasmonics sensors; SPR biosensor

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1. Introduction

A huge number of devices introduced by biosensor such as chemical, optical, mechanical for molecular detection in medical diagnostic clinics[1–7]. Based on promising investigation optical biosensor not only has to respond direct detection but also must have ability for label free discrimination [8]. The promise of biosensor play an important role in many sector: Covid-19 detection [9], biomarker detection, monitoring, environment production, food safety [10–21]. So depend on their application can be classified in two categories include bio recognition or combined with transducer system. Examples of biomarker detection sample used in sensing technique are enzyme, antibodies, nucleic acids, oligonucleotides. Optical biosensors based on ellipsometry, reflectometry, photoluminescence and SER, fluorescence are direct and indirect respectively. Furthermore biosensors integrated with optical transducer have been used in a large verity of devices based on fluorescence, spectroscopy, interferometric. Optical methods are based on interrogating sample with a wide range of wavelengths simultaneously [22,23]. Evanescent and fiber optic biosensors are two kind of optical method. In spite of the extraordinary conventional optical biosensor advantages in direct sensing namely low consuming time, low cost, label free detection, sensitivity, compact size, fabrication simplicity, but they have some problem the main is faced with is limitation of their detection in Nano meter scale structure. To solve the abovementioned problems optimization algorithm such as deep-learning is proposed recently [16,24–33]. This is because they were not able to detection of sub wavelength images. To overcome the prevalence of studies on Nano scale size, a great deal of study have been done by researchers to propose reliable method for sub wavelength features. According to the evidence based documents surface plasmon resonance (SPR) in terms of their remarkable ability to resolve diffraction limit is considered as a powerful method. However due to increasing efficiency of plasmonics noble metal nanoparticles (NPs) of

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gold and silver proposed which exhibit significant properties in sensing. Regarding to a progress of nano materials zinc oxide as one of the most amusing metal oxide has drawn researcher's attention. Performance of SPR is based on changing of refractive index in different synthesis. It is noteworthy when plasmon is generated by incident wavelength in specific ranges and angles they can be used in different detection[34,35]. The smart detection based on surface plasmon resonance has demonstrated ultra-sensitive qualification in biomolecules sensing by converting small changes in refractive index into spectral changes. Advancement of surface plasmon resonance have gained remarkable attention to the diagnosis of disease [36–38].

Localized surface plasmon resonance (LSPR) also is considerable biosensor for biological detection. The main principle mechanism of detection is based on interaction between incident light and analytic sample resulting in generating optical signal that record by detector [34,35,39,40]. Bio sensing application is impacted by surface parameter and physical and chemical properties (roughness, valence and conductance band, concentration of sample, functional group). Through the above result smart sensing devices have been unique candidates for detection which need highly sensitivity and selectivity especially in the early stages of diagnosis. Also, in the realm of wireless sensing abovementioned structure can be used [41,42].

2. Optical Biosensor

2.1. Fiber Optical Biosensor

In these biosensor biological detection performance occur within evanescent wave confinement in an optical fiber or waveguide. In the following figure we present some advanced applications of battery-on-chip. Optical fibers include a silica cylindrical core and cladding. To increasing the refractive index of the core, it is doped with germanium as a result propagating electromagnetic wave which is called evanescent wave produced. It is noteworthy for decreasing loss light propagation to minimal, exposing the evanescent field was proposed. Furthermore tapering was shown to increase the evanescent field magnitude and evanescent field exposing. Research shows that tapering of core fibers increase the sensitivity to 10 fold.

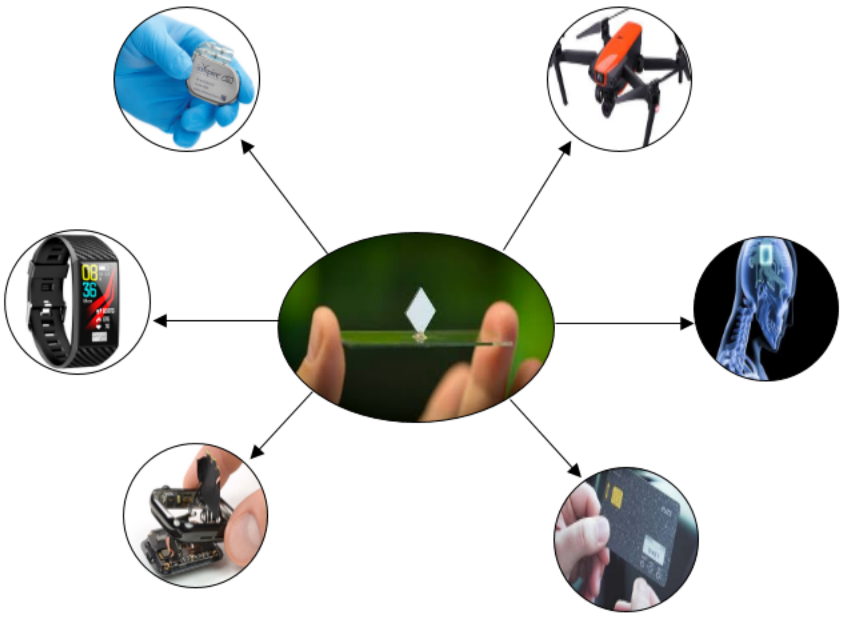

Figure 1. Advanced applications of Optical Biosensors.

Also in another studies shown using Nano sized fiber the sensitivity can increase and adiabatic tapers with a diameter of 1 μm could increase optical power intensity by at least 10 times compared to previous studies. In terms of effecting of bending it was clear that sensitivity of sensor with more than one bend increase. A wide range of studies showed U shaped probe has an exponentially sensing ability and producing large evanescent field compered to strain probe. In U shaped the evanescent wave penetration increases by decreasing in an angle of propagation. Some research has been done that wavelengths at near IR or IR range increase evanescent penetration. In some laboratory studies has been observed high sensitivity at low concentration at IR wavelengths. There are a rich diversity geometric methods to increase penetration depth of fiber optical biosensors. Thus far two kinds of tapered fiber geometrics proposed: firstly, tapered tips that are used in biochemical detection by using fluorescent. Secondly, a continuous biconical taper which is include three different section: a region of reduction diameter, fixing diameter region, increasing diameter region.

Detection principle According to the previous investigation various sensing principle are proposed:

1- Intensity based sensor: it is manifested by measuring changes in output power, evanescent field are detected.
2- Evanescent absorption measurements: during the interaction between evanescent field and analytes, wavelength transmitted is absorbed by analyte. Hence, according to the sample concentration magnitude of light transmitted decreases.
3- Using fluorescence with optical fiber: evanescent wave fluorescence are used in two methods: firstly the sandwich assay. In this the primary antibody is immobilized on the surface by covalent bonding, then the target molecule that is attached to the antibody is introduced. The accuracy of the existence of biological molecules by using a secondary excited fluorescent antibody is confirmed. Secondly measurement of fluorescence quenching rate by attaching fluorescent dye on the taper surface.

Sensing Application of Fiber Optic

• Pathogen sensing: based on evanescent sensor a huge number of studies developed detection of bacterial growth by interaction between bacteria and evanescent field. Similarly coated tapered surface with poly-L-lysine in fiber biosensor used to detection of E coli population growth. Light transmitted decreased when the initial number of bacteria began to grow.

On the other hand observation indicated using tapered fiber optical via an antibody the small concentration was well detectable. These studies were followed by fluorescence resonance energy transfer (FRET) in dipole- dipole molecular interaction like detection of S.typhimurium. The results appear as an increase in fluorescence which is related to the binding of S.thphimurium to the antibody. Tapered fiber tips optimization was performed until the detection of S.thphimurium reached 1000 CFU/ml.

Nowadays fluorescent sandwich assay with a polystyrene tapered fiber have gained a great attention to detect Bacillus anthracic due to national security.

• In the clinical diagnosis there has been reported using tapered fiber optical (TFOBs) for detection of Chinese hamster ovary cells. Also some works has been under taken using a chalcogenide glass fiber in the IR absorption spectrum of mouse liver.

• Although there are many practical potential to detection of biochemical materials like Nicotinamide adenine dinucleotide (NADH) and Nicotinamide adenine dinucleotide phosphate (NADFH). It work has been done by absorbing evanescent wave in tapered fiber sensor by using flame. According to the observed results the detection limit was significantly reduced compared to the previously reported methods, which was 0.5 micro meter and 0.2 micro meter for NADPH and NADH respectively. Furthermore development of the combination of chemiluminesence with fiber optic sensors lead to the detection of enzyme alkaline phosphates and organophosphorus-based pesticides.

• In terms of diagnosis toxins many efforts have been made, take for examples: staphylococcal entero toxins was detected by measuring fluorescent in sandwich immune assay. Another researcher for detection staphylococcal entero toxins in buffer proposed an array of biosensor and used various samples of food. There also provided reports based on the detection of ricin which is very toxic and dangerous substance for human health based on

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use of fluorescence in optical fiber biosensors. Another method of detection that received much attention was based on using polymyxin B as a recognition molecule in tapered fiber optic sensor detect lipopolysaccharide which is caused sepsis.
• It is important to note that tapered optical fiber biosensors are a rapid diagnostic method in medical clinics where the results are prepared in a short time. The need to detect protein C in a short time by using inexpensive devices was a major concern. Investigators using a fluorescent fiber optic sensor to detect protein C in real time.
• Detecting of DNA hybridization: experiments were done by using fluorescent with 13-mer to examine DNA hybridization. Results indicate that fluorescent FOBS was applied for interfacial hybridization kinetics of oligonucleotides detection. by surveying extensive research it turned out TFBOS need to be further developed to detect smaller samples.it means sensitivity of this kind of biosensor are not enough due to the small size of the molecules.

2.2. Interferometric Biosensors

Evanescent field and optical phase difference measurement are combined with each other and create an optical biosensor which is called interferometric. The basis of the operation of this biosensor is changing in index of refraction of the probe (related to the analyte concentration) by probing the near surface with evanescent wave. Any changes of refractive index by interference signal that appears as a pattern detection. This biosensor has been introduced as a suitable method for detecting cellular process and cellular response and cellular contents. Also diagnosis of avian influenza virus was become possible.

2.3. Ellipsometric biosensor

Ellipsometric is introduced as a good candidate for detecting of influenza A virus with a piece of glycan. Generally the light reflected from the surface was used for measuring changes in the polarization. In additionally determination of the serum tumor biomarker was performed with ellipsometry and limit of detection of this work was about 18.2 units/ml which was significantly lower than normal method.

2.4. Reflectometric interference spectroscopy (RIFS)

Reflectometric interference is a simple label free biosensor. Phase changes and polarized light amplitude changes prepare the data needed to determine the refractive index and thickness of the layers that absorb the protein. A great deal of study showed diclofenac in bovine milk of about 0.12 micro gram/l.

Another author used a RIFS to detect tumor cells circulation which detection limit was less than 1000 cells/ml in the concentration range of 1000-100000 cells/ml.

2.5. Surface Enhanced Raman scattering

This biosensor is a surface sensitive technique that absorption molecules on rough metal surface or Nano particles such as silver and gold enhances Raman scattering intensity. ASER fabrication applied on the tip of optical fibers due to the high sensitivity detection of cancer proteins biomarker and mRNA [43].

A brief classification of some optical sensor mentioned above and wide had wide applications in various fields such as healthcare, bio pharmaceutical sectors, security, and food [44,45]. These optical biosensors have been developed successfully the signal-to-noise ratio and improved the detection limit. However the selectivity and reduce detection limit to a minimum and detection of very small particles (virus, protein) still remained as a major a problem. Therefore developing new optical biosensor devices has always been considered by researchers. In this regards, the heat detection is important [46,47].

Recently investigators have begun to explore alternative method that are qualitative and compatible for pattering smaller sample volumes. A number of research groups have proposed new methods for solving previous problem which we briefly explain them.

2.6. Plasmonic immune sensors

A great quantity of researches reported that such practical sensors allowing detection of very small volumes of various samples and applied to in vivo diagnosis. Label free optical biosensor with combination of dielectric and metal interfaces called surface plasmon resonance (SPR)

2.6.1. Different grating configuration used for SPR

Granting are usually made of an 8 micro meter thick core and 125 micro meter cladding which surrounding the core. Overall gratings provide a strong coupling between the core-guided incident light and cladding.
• Fiber Bragg Gratings
Fiber Bragg grating (FBG) applied as a mirror with selectivity for light propagation wavelength as a result a narrow spectral band is reflected and on Bragg wavelength centered. The Bragg wavelength is perfectly sensitive to temperature and axial strain in the range of 1.2 pm/ at 1550nm. In one hand Bragg resonance is not direct used to excite a surface plasmon. In other hand by applying chemical etching process mostly use hydro fluoric acid (HF) or side polishing process is used to excite (SP).
• Tilted Fiber Bragg Gratings (TFBG)
TFBGs are short cycle about 500 nm gratings and index of refraction angle is less than 45 degree. In every coupling that occurs for the wavelength and its effective refractive index there is a one to one relation. Also position of generated resonance spectra depends on the index of refraction of the cladding corresponded and optical properties near the surface of corresponding cladding.
• Excessively Tilted Fiber Grating
In this kind of fiber grating are manufactured with an angular slope of larger than 45. Transmitted amplitude spectrum are usually generate with a steady wave laser that used phase masks.
• Eccentric Fiber Bragg Grating
They are usually produce by highly focusing femtosecond pluses laser close to the cladding interface. Transmitted amplitude produces a dense spectrum with a very large number of mod coupling resonance with refractive index in the range between 1.45 to 1.00.
• Long Periodic Fiber Grating(LPFGs)
This fiber grating responsible for period refractive index modulated. LPFGs are usually produced by using electric arc discharge or amplitude masks. Additionally SPR generation can be achieved from optimization of grating structures surrounded by using a thin metal film mostly gold or silver [48]. Thickness of film metal was between 30 nm and 70 nm. It is noteworthy that in comparison with different sensor devices chiefly in immune sensing it is not sufficient to consider sensitives it is because of wavelength play an important role in the accuracy of measurements.

2.6.2. Plasmonic Grating based Biochemical sensors

In the case of plasminic grating structures differences in refractive index reflect by optical spectra in both form optical power changes and wavelength shift.

A great quantity of research is conducted that spectra and intensity are two important techniques Compared to conventional commercial optic equipment. In these Biochemical sensors molecular interactions occurred on the top of the outer film which bio receptors located on outer film then modified spectra are generate.
• Spectrum Analyzer Interrogation
This technique is the most widespread and the majority of FBG based on this principle that relies on the wavelength shift induced by changing in the index of refraction. This manufacture consists of broad band and optical spectrum analyzer.
• Quantization of the intensity interrogation
Intensity interrogation is another method that light with plasmon wave coupled that demonstrates the intensity variations produced.

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This technique is carried out by using tunable laser that match the wavelength of sensitive mode as a source and a photodiode applied as a detector and to obtain data we need an analog to digital converter. It noteworthy that intensity interrogation has been widely applied to propagate reduced size plasmonic optical fiber sensors.
• Other techniques
Due to integration use of polarization analysis and using polarization depended loss are two method that have exhibited good performance especially when nanoparticles were applied.

2.6.3. Application of Plasmonic Optical Fiber Grating

This section reports a summary of examples ofthese biosensors in the diagnosis of disease such as cancers and tumors. A great survey of recent investigation have been focused on grating configuration. For different detection such as biotin and glycoprotein with limit of detection about 11PM-8PM and 0.0002 g/ml. Also a lot of evidence for their use in different medical diagnosis like detection of cytokeratin for lung cancer that released from malignant cells. A group of author used a layer of gold with fibronectin in detection of cellular behavior under different stimuli. Other researcher proposed gold layer and thiol modified aptamers which is applied in thrombin detection in buffer and serum solutions with limit of detection 22 nm.

2.7. SPR Biosensors

Surface plasmon waves in kretschman configuration mostly generated by injecting light on a surface (coated by metal) through a prism at a specified angle to reflect the light. In this configuration (prism-metal-bio recognition) surface plasmon waves only occur at the external surface and inner surface cannot able to excite surface plasmon this is because of propagation constant is too small compared to external surface. Biochemical recognition localized on the thin layer metal and analyte attached to the bio receptor producing refractive index changes increase so does the surface plasmon propagation which can measurement by optical equipment like wave length modulation, angular modulation and phase modulation [49–51]. The first proposed SPR biosensor dates back to 1983.SPR biosensors development have made accessible the advancement of technology and their applications in different field such as medical diagnosis, biotechnology and drug delivery.

2.8. Localized Surface Plasmons

Other category of plasmonic sensing is localized surface plasmon resonance. LSPR signal generated when surface plasmon resonance confined by the nano scale subjects. The detection in gigahertz and terahertz is considered [47,52–58]. This platform are more miniaturization than SPR platform sensing. Ergo this plasmonic sensing convert to remarkably detection system for diagnosis and can integrated by point-of-core diagnosis devices. Interestingly this platform system use wavelengths which does not overlap with the created spectrum has received much attention specially in biological sensing such as high sensitivity detection of hemoglobin and urea in blood [28,59,60,60–64].

3. Different Effective Parameters

In the context of sensing we define several parameters related to the analyte detection in biosensors.
• Refractive index and figure of merit
Ability of plasmonic sensors depend on detecting of refractive index changing. It has also been demonstrated sensitivity can be increase by using of a low refractive index substrate. Bulk sensitivity depends on angle of incident. Furthermore sensitivity influenced by figure of merit that define as a ratio bulk sensitivity to spectral dip. It allows to compression between different Nano devices in terms of the sensitivity. In LSPR based biosensors figure of merit (FOM) depends on the resonance wavelength for example by applying gold nanoroad can show a maximum value of FOM obtained at a wavelength of roughly 700nm.

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It is noticeable that narrower spectral produced by using delocalization modes. The result is high value of FOM also improving FOM have been achieved by reducing the width of spectrum. Another extensive research shows that detecting minute changes in the bulk sensitivity can improve the FOM. Refractive resolution followed by ability of detecting small changes in refractive index. It is expressed as inversely noise of the sensor to the bulk sensitivity.

- Surface Refractive Index

The surface refractive index usually expressed as the sensitivity to changing in index of refraction

- Surface figure of merit

For optimization of plasmonic Nano structure consider not only figure of merit but also electromagnetic and size of the target analyte so it seems be a complex task to experimental and theorical determination of FOM.

- Limit Of Detection

Limit of detection is the best describe for the power of biosensor detection. It is described as smallest concentration of analyte that provide a sensor response for specific measurement detection [65,66].

4. Plasmonics Metamaterial

Metal as a substrate plays a central role. Plasmonic surface have to provide high ratio of surface–to-volume and during connection between functional groups show a good biocompatibility. Moreover in metal based substrate cost of the material considered as a significant factor [67–69]. In the following figure, some traditional plasmonics materials for biosensing is provided .

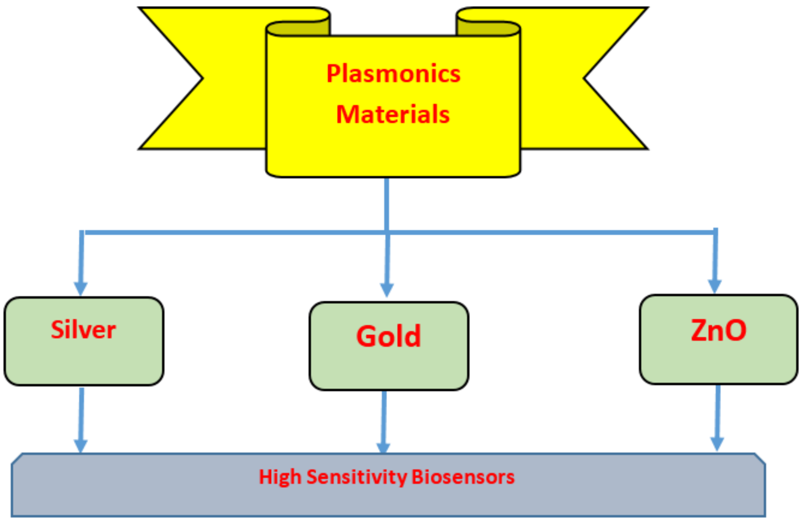

Figure 2. Traditional plasmonics materials.

Silver

In the majority cases proposed palladium but in commercial and mass production is not affordable. Another group vastly used silver as inexpensive substrate. Despite it has low toxicity and rapid oxidation but it has low sensitivity and limitations in biochemical applications. Aluminum has gained attention due to its optical properties, cost effective and high abundance. The main drawbacks is controlling of size and shape. Nitrides have shown good biocompatibility. However drawbacks of using nitrides is represent by difficulties in manipulating.

Gold

Gold is a most promising candidate for sensing applications. Gold shows good optical properties in SPR platform for wavelength above 580 nm. Additionally it is suitable to

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manipulate with Nano fabrication method. Another advantageous is stable surface of gold for long period time after biological interaction.

ZnO

Regarding to a progress of material science new method have been developed to fabricate zinc oxide ZnO nanostructures. The crucial points of advanced properties with different types of ZnO (Nano rods, quantum dots, thin film) are used in biosensors platform [70,71]. Researcher has proposed using Nano rods ZnO in detection of protein G and DNA. In some investigations ZnO Used directly for glucose detection. One of the most interesting application is indicated in diagnosis of cancer cells by using carbohydrate antigen biomarker [72]. Researchers attention has been paid to determine Rhodamine 6G by using ZnO Nano particles. Particularly the mechanism of interaction between ZnO and cholesterol oxides indicate a good potential to detection of cholesterol. Also it was proposed for lowest concentration of rabbit IgG that determination was about 16-folds lower than another biosensor detection that used Au thin film. A group of researcher observed good interaction between ZnO and nucleic acid bases. A great deal of study measured proteins (BSA, HAS) by using ZnO Nano rods as a metal substrate. In addition new approaches are obtained using ZnO to measurement 4-amino-thiophenol.

Among various advanced plasmonics materials studied for the biosensors, many research groups have been focused on the two dimensional materials [73–77]. The main advantage of 2D-material stems from their low cost fabrication process. Some advanced 2D-materials are provided in the following figure.

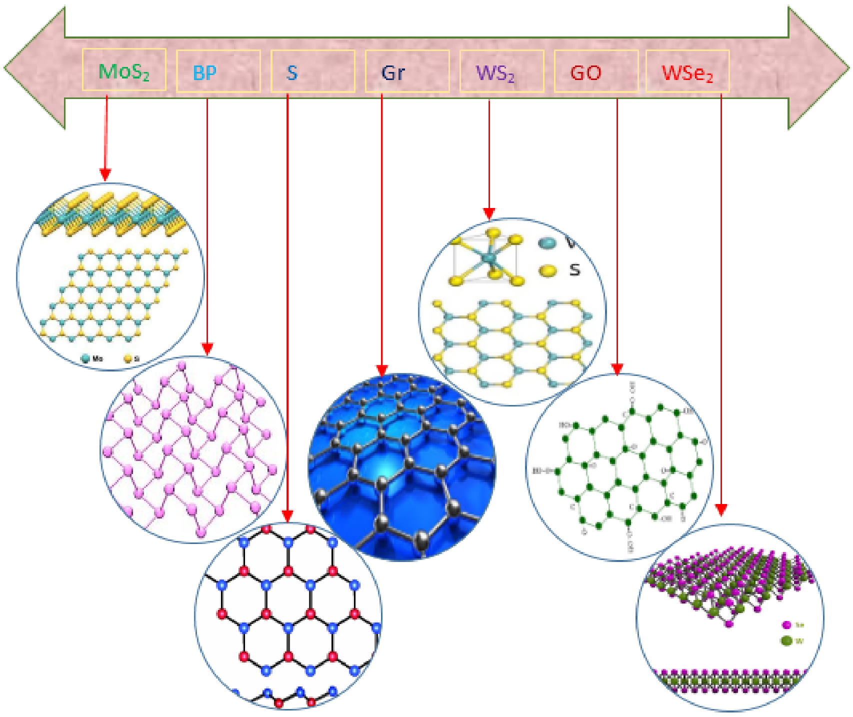

Figure 3. Advanced two dimensional plasmonics materials.

Also, it is worth to mentioning that nano and microstructure materials can be used for high sensitivity biosensing [78,79].

4.1. Advances in sensing platform

Several studies have conducted to show improvement of sensitivity by using Teflon-based LSPR with refractive index as small as 0.000003RIU. a researcher group achieved a better imagine sensitivity by using silver film as a thin film instead of gold film in terms of its lower absorption. An alternative way to prevent silver oxidation proposed using thin

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layer of graphene on the silver [80]. It has been proved graphene is impermeable for small dimension as small as He. A researcher team described electron density in graphene sheet play a crucial role in impenetrability graphene. The recent numerical study demonstrate SPR based on metallic grating. A large number of SPR biosensor most often can detect one analyte but it is necessary need to multi analyte detection because of reduced consumption time for this reason SPR based on multi-channel structure provided. At first triple multi-channel were used then it was expanded to 6 and 10 channels. One of the interesting point was deposition dielectric over a SPR surface leading to wavelength coupling to a longer wavelength. Also tilted top surface coupled with a prism can produce wavelength coupling. A lot of efforts have been done to improve sensor resolution with laser [81].

4.2. Advances in bio discriminate target

So far different types of bio recognition elements are used as biological detectors such as aptamers, peptides and antibodies. Antibodies are kind of proteins used for bacteria and viruses detection. They show high sensitivity during antibody-antibody interactions. Significant number of antibodies are applied for identification of Ebola, HIV and hepatid B AND c. to immobilize protein on the surface coated with thin layer of gold a weak attachment is sufficient to adsorb target molecules [38,82,83]. Peptides compered to antibodies have been less applied. Peptides have been used mainly for detection of small ligands. Very recently detection of heavy metal have been done. Aptamers are nucleic acid ligand and used for biosensor detection system until 2001. Additionally recognition with highly sensitive surface is a promising major for biosensor technique. For instance by self-assembled monolayers of thiols group can obtain highly immobilization on the surface made of gold but the main problem with tis was nonspecific absorption. To solve this problem a group of researcher proposed poly ethylene glycol modified and self-assembled peptides. Another way to approach was using carboxybetaine methacrylate. Also hydrogels due to their space proous are more capable in immobilization performances than planar surface. Also, silicon membarne sensors are highly considered recently by research groups [84,85].

4.3. Application of SPR Biosensor

The development of plasmonic vastly has led to detection of biological analyte. The most commonly examples is identification of thrombin aptamer. In this process concentration of thrombin was roughly about 0 and 160 nm. Also the wavelength used in the calibration was about 650 nm. Moreover ELISA using SPR have been widely used for detection of prostate cancer through using prostate antigen embolization to form sandwich assay. Finally detection occurs in the peak range of 7.7 and 5.5 nm for the enzyme with a concentration of 280 Fm.

In another provided study sandwich assay formed on the cantilever surface and antibody attached on the top of the cantilever surface. To start reaction between the biomarker and captured antibody cantilever were immersed in serum then bbound to the gold nano structure to receive generated response. This Optical response biosensor leads to identification of prostate antigen and carcinoembryonic antigen with low LOD. LSPR is a lable free detection that is used for diagnosing of cervical cancer with excellent sensitivity. Plasmonic system provide a large surface area that allows to on line sensitivity with high speed sensitivity. Quantification of hepatititis B virus occur in the 700-750 nm and reduced the detection limit to 40 folds lower than ELISA test (about 0.01 IU/ml). Also LSPR was employed due to its high refractive index for detection of troponin with a limit of detection about 30 pm which 3 times lower than previous experimental performance. Furthermore high tuberculosis (TB) detection sensitivity speed followed by bounding 9 TB antigens onto the sensor chip.

Recently SPR biosensor surface fabricated by Nano hole that was coated with biotinylated antibody for Human epidermal receptor protein-2 detection which provide rapid diagnosis of the breast cancer. Some development practical method of C-Reaction protein

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(CPR) detection was employed. We review the research results briefly: CPR protein largely produced in liver-reactive protein (CPR) is considered as neurological disorders and in various damage, surgery, infection and inflammations the CPR level in blood increased. CPR levels in plod plasma in healthy people with no disorder measured about 5micro g/ml. detection of this protein is divided to three categories: firstly direct test, secondly the sandwich assay, thirdly sandwich assay improved with flat metal Nano particles or different catalysts. It has been improved drastically in different experimental based on two kinds of plasmonic biosensor, SPR based biosensors more useful in detecting than LSPR.

This is because of SPR depends on remarkably limited range of evanescent wave. Some reliable performances were used to increase immunoassay for small sized, lable free sensing such as, used artificial polymer receptor in LSPR based biosensor to identifying CPR. A Poly (2-mathacryloyloxyethyl phosphoryl choline) substrate synthesized for CPR detectionby measuring LSPR responses. A hybrid sandwich assay using Au-bound aptamer and protein C injected into aptamer is performed for detection. 4-4- dithiodibutyric acid and alpha hydroxyl acid were used for clinical detection of CPR.

5. Conclusions

Our focused investigation reveals that fiber optical biosensor and grating based SPR used in numerous application which is highly desirable for analysis spectral information to detect various sample. Further optical biosensor based on plasmonic nanostructure due to having a large surface area ratio showed extraordinary performance in medical diagnostics and a variety of analyses from proteins to bacteria. Another important point in the development of plasmoninc sensors is the selection of a suitable substrate with high biocompatibility with bimolecular analyses which provides access to high selectivity and sensitivity. Different metamaterial were applied to advancement biosensor but among them graphene is a promising candidate due to its remarkably optical properties. In some diagnosis LSPR showed lower sensitivity than SPR. However the various features of plasmonic sensor prove label-free, low cost, real-time, high miniaturization and highly efficient in detection.

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