Smartphone-based Surface Plasmon Resonance Sensors: a Review

Gaurav Pal Singh1 · Neha Sardana1

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Abstract
The surface plasmon resonance (SPR) is a phenomenon based on the combination of quantum mechanics and electromagnetism, which leads to the creation of charge oscillations on a metal–dielectric interface. The SPR phenomenon creates a signal which measures refractive index change at the metal–dielectric interface. SPR-based sensors are being developed for real-time and label-free detection of water pollutants, toxins, disease biomarkers, etc., which are highly sensitive and selective. Smartphones provide hardware and software capability which can be incorporated into SPR sensors, enabling the possibility of economical and accurate on-site portable sensing. The camera, screen, and LED flashlight of the smartphone can be employed as components of the sensor. The current article explores the recent advances in smartphone-based SPR sensors by studying their principle, components, application, and signal processing. Furthermore, the general theoretical and practical aspects of SPR sensors are discussed.

Keywords Plasmonics · Surface plasmon resonance · Smartphone sensor · Portable sensor

Introduction
Surface plasmons are observed when an electromagnetic wave under suitable conditions excites the free electrons at a metal–dielectric interface leading to collective charge (electron) oscillations. The surface plasmon resonance (SPR) effect creates a dip in the reflectance spectrum or alternatively, a peak in the absorbance spectrum of the electromagnetic wave, which is shifted due to a change in the refractive index of the surrounding; this shift forms the basis of SPR-based sensing. The surface plasmons were first published in 1902 as anomalies which appeared as dark bands when light was incident on a metallic grating [1]; these anomalies were later proved to be associated with electromagnetic surface waves [2]. In 1968, Otto [3] and Kretschmann and Raether [4] independently reported techniques to excite the surface plasmons using a prism and a metallic thin film. The earliest practical application of the SPR effect was a gas sensor reported by Liedberg et al. in 1983 [5]. Since then, numerous SPR-based sensors have been developed for medical diagnostics, food safety, water pollutant detection, etc., owing to the label-free and real-time detection of these sensors. The various applications of SPR-based sensors are summarized in Table 1. SPR is able to measure changes in the refractive index of the order of \(10^{-6}\) to \(10^{-7}\) of its surrounding medium, which can be interpreted as the change in refractive index due to 0.01 to 0.001 °C variation in water temperature [6]. The advantages of SPR sensing over other conventional techniques are its sensitivity, selectivity, low background noise, lack of labeling requirement, immediate results, small sample volume requirement, reproducibility, and its ability to multiplex [7, 8]. Therefore, during the COVID-19 pandemic, SPR was explored as one of the options for quick and accurate detection of the virus SARS-CoV-2 [9–12]. SPR sensors’ ability to detect viruses can be confirmed from the examples in Table 1, particularly its extensive use in the detection of the Ebola virus [13, 14].

The SPR-based sensor technology was confined to laboratory implementation due to the sensitivity of its complex setup and bulky components, but the instantaneous output of sensor results and minimal sample preparation make SPR-based sensors ideal for on-site detection. The miniaturization of a device is challenging, but it increases its potential applications and affordability. The recent advancement of optical and electronic components have made smartphones highly adept at performing complex tasks both in terms of...
hardware and software. Hence, several smartphone-based sensors are being developed. Modern smartphones include CMOS or CCD-based cameras, LED flashlight and screen, and massive computational power, which can be integrated with other attachments to form a portable SPR-based sensor. A smartphone has the capability to replace the detector or spectrometer (using a diffraction grating) of an optical sensor, which is usually the most expensive part of the setup. Moreover, smartphones now have easy access to store and send data to the desired locations via high speed internet.

The current article studies several portable SPR-based sensors that use a smartphone to perform one or more sensing processes. The principle, working, setup, immobilization process, and signal processing of the sensors have been complied. The principle, application, and performance parameters reported by the authors have been summarized in tabular form. A comprehensive report of the processes involved in SPR-based sensors are initially discussed, which are required in all SPR-based sensors. All smartphone sensors were unique and improved the performance and practicability by incorporating new and innovative optics, housing design, sensing chip fabrication, microfluidics, and signal processing. The review is envisioned to create a complete guide of SPR sensor technology with a specific focus on smartphone-based SPR sensors. The diverse applications and portability of the SPR technology establishes its massive potential for commercialization.

**Basic Principle**

The structure of metals is generally described as positive ions surrounded by a sea of electrons. Metals are charge neutral, but the electrons surrounding the positive ions are charged mobile species; hence, metals can be considered as plasma in electromagnetic terms. The plasma frequency of a bulk material can be calculated by the following equation [15]:

$$\omega_p = \sqrt{\frac{ne^2}{\varepsilon_0 m}}$$  \(1\)

where m, n, and e are the mass, concentration, and charge of the charged mobile species, respectively, and \(\varepsilon_0\) is the relative permittivity of free space. The most frequently used metals for SPR sensors are gold, silver, and aluminum; whose bulk plasma frequency lies in the UV region. Moreover, visible light being a transverse wave, cannot directly excite the surface plasmon wave, which is longitudinal in nature. Therefore, certain conditions have to be applied so that visible light can excite the surface plasmons on the metal–dielectric interface. In plasmon-based sensors, the plasmons can be excited as the localized surface plasmon resonance (LSPR) mode or the surface plasmon polariton (SPP) mode. The excitation in SPP mode can be achieved by prism, waveguide, and grating coupling techniques; these techniques are studied in detail in the “SPP Mode” section. To improve the SPR signal, the metal dielectric interface is generally immobilized with a ligand that specifically targets the analyte species.

Depending upon the light source, coupling technique, and detector used, the analysis method is selected. The commonly used analysis methods include modulation of coupling wavelength, coupling angle, and intensity; summarized in Fig. 1. For prism and grating coupling, any of the aforementioned methods can be selected. However, for waveguide (fiber optic) coupling, angle-based modulation cannot be selected due to the lack of angle measurement capability in the fiber optic cable [46]. Theoretically, the angle-modulated sensor has the best sensitivity among the three techniques [47].

The main performance parameters of SPR sensors are limit of detection (LOD) and sensitivity. Sensitivity is the ratio of change in output of the signal to the change in the measurand, which can be calculated by the slope of the calibration curve. The sensitivity depends upon the coupling

| Field                | Detection | Species                                                                 |
|----------------------|-----------|--------------------------------------------------------------------------|
| Food safety          | Bacteria  | *E. coli* [16], *Salmonella* [17], *Listeria monocytogenes* [18], *Campylobacter jejuni* [19] |
|                      | Mycotoxin | Botulinum [20], Deoxynivalenol [21], Nivalenol [21], Zearalenone [22], Aflatoxin B1 [23] |
|                      | Exotoxin  | Staphylococal enterotoxin B [24]                                         |
| Medical diagnostics  | Cancer marker | Prostate specific antigen [25], Interleukin 6 [26], Interleukin 8 [27] |
|                      | Cardiac marker | Myoglobin [28], Troponin I [29]                                           |
|                      | Virus marker | Ebola [13], Influenza [30], Hepatitis B virus [31], DENV E-protein (Dengue) [32] |
|                      | Drug      | Morphin [33], Interferon-γ [34], Warfarin [35]                           |
| Environmental monitoring | Metal ion | Hg²⁺ [36], Pb²⁺ [37], Cu²⁺ [38], Cd²⁺ [39]                              |
|                      | Pesticide | Atrazine [40], Dichlorophenoxyacetic acid [41], Thiabendazole [42], Phenol [43] |
|                      | Explosive | RDX [44], Trinitrotoluene [45]                                           |
technique (instrumentation), the modulation parameter selected for analysis, and the binding effect of the ligand and analyte. LOD is the smallest concentration of the analyte added to a blank solution which can be observed in the output signal with reasonable confidence (99%). It is generally defined as the ratio of noise (two or three times the standard deviation) in the system to the sensitivity [48]. Other important parameters include resolution, accuracy, reproducibility, and range. Resolution of SPR sensors is the smallest change in the refractive index of the bulk solution which can be detected in the signal output. As opposed to LOD, resolution does not take into account the binding effect of the ligand and analyte; hence, it only depends upon the instrumentation of the system.

**Immobilization of Sensing Surface**

The immobilization of the sensing surface is a critical step of the sensing process. This section aims to provide a brief introduction to the immobilization process. Earlier, simple adsorption techniques were used to detect the targeted particles [49], but owing to their poor performance, in modern SPR sensors, the surface of the metal film is deposited with a ligand [50, 51]. A solution containing the targeted particles flows over the ligand, and the ligand creates a binding effect with the targeted particles. The binding process induces a change in refractive index of the area surrounding the metal dielectric interface; hence, the resonance condition is deviated, which can be observed as a change in signal based on the modulation technique. A proper selection of immobilization method should ensure high selectivity and sensitivity. High selectivity pertains to the phenomenon of only sensing the targeted particle, and no other particles present in the system should have a major influence on the signal. High sensitivity indicates that a large number of targeted particles bind to the ligand as the solution flows; hence, a significant response in the signal is observed. Recent advances in SPR-based sensors have instilled the practice of surface modification prior to ligand immobilization. The surface modification increases selectivity and ensures stable ligand deposition. The most popular surface modification technique is the growing of a self-assembled monolayer (SAM) [52–55]. The SAM is also helpful in creating a non-fouling effect to increase the selectivity of the process. Towards detection, the frequently used immobilization techniques can be broadly split into covalent based, non-covalent based, and other specialized methods. The most commonly used groups for direct covalent coupling are amines, thiols, aldehydes, and carboxylic groups. The specialized methods include the growth of a lipid bilayer for the study of various biomacromolecular complexes (e.g., proteins, lipids, DNA, etc.); the lipid bilayer is of several types depending upon the application. Generally, a combination of the aforementioned methods are utilized; a popular method reported combines the use of a lipid bilayer with thiol coupling [56, 57]. Another method of categorizing the immobilization techniques is based on the methodology; the immobilization can be broadly split into antibody, aptamer, and molecular imprinting. The antibody immobilization targets a specific molecule called antigen noncovalently [58]. The drawback of this technique is that in some cases, the target molecule which is bound can be too far away from the sensing surface [7]. Aptamers are DNA or RNA or short chains of amino acid molecules which can have the ability to trap the targeted molecules near the sensing surface electrostatically [59]. However, the antibody and aptamer methods are not able to detect very small molecules. One method to overcome this problem is to use molecular imprinting; in this method, the presence of the targeted molecules leads to the creation of cavities in the immobilized polymer layer [60].

The binding process in SPR sensing can be direct or indirect depending upon the molecular weight of the analyte. For analytes of high molecular weight (greater than 5000 Da),
direct binding is used; while indirect binding is used for low molecular weight analytes [61]. In a direct binding process, a ligand is immobilized on the metal surface, and when a solution containing the analyte flows over the surface, analyte particles bind to the ligand, which creates a response in the reflectance signal. However, in an indirect binding process, analyte derivative molecules are first immobilized on the metal surface; further, ligand particles are added to the solution, which bind to these analyte derivative molecules. When the solution being tested flows over the surface, the ligand particles remaining in the solution bind to the analyte particles being targeted, and the remaining are immobilized to the surface. This creates an inverse response regarding the presence of analyte particles in the solution. To increase the sensitivity of the process, multi-step technique or labeling can be used, as shown in Fig. 2. Some of the immobilization techniques allow for sensing multiple times before requiring regeneration [17]. The SPR-based platforms can be used to study the interaction of the ligand and analyte in real time. The kinetics, thermodynamics, and mass transport processes involved in the interactions have been reported extensively using SPR sensors [62, 63].

**Smartphone SPR Sensors**

A brief summary of the recent advances in smartphone-based SPR sensors is provided in Table 2, along with the critical performance parameters provided by the authors. The objective of using a smartphone is to reduce the size and cost of the sensor by utilizing the inherent features of the smartphones, which makes the sensor an attractive option for on-site and remote area applications. Modern smartphones contain a CMOS or CCD-based camera, which is used as a detector among all of the sensors mentioned. Moreover, the LED flashlight of the smartphone or the smartphone screen itself can be used as the input light for the sensor. Most smartphone-based sensors mentioned in the current article are still in the research stage at the time of publishing; hence, they are reliant on computers for the signal processing. However, the smartphone has the required processing power to perform all the back-end calculations in the form of an app.

A feature shared by many of the smartphone-based sensors is the presence of a grating in front of the detector (smartphone camera) of the sensor. The role of the grating is to disperse the incoming light wave intensity into a continuous increasing wavelength spectrum. This enables spectral analysis using the smartphone camera, which is generally more sensitive than colorimetric sensing. Colorimetric sensing only involves intensity analyses without its dispersion into the wavelength spectrum. The first order diffraction from the grating is generally used for the analysis as the smartphone camera is not capable of capturing higher order diffractions. The signal received in the camera is split into three channels, RGB (Red, Blue, and Green). The smartphone is able to provide the intensity value of RGB channels separately or in a combined form when the image is converted into black and white. Furthermore, calibration of the wavelengths corresponding to particular pixels is generally performed using a combination of monochromatic lasers as the light source of known wavelengths. Many of the authors have confirmed the refractive index sensitivity of their sensors by comparing it with commercial spectrometers. This section explores the sensors mentioned in Table 2 in detail and is organized to highlight the major excitation technique used in the sensor. If a major focus for a sensor is its signal processing, it is discussed separately. Furthermore, the theoretical and practical aspects of each technique are explained prior to the exploration of smartphone SPR sensors.

**LSPR**

The metal particles of size smaller than the wavelength of incident electromagnetic radiation are excited in the LSPR
When an electromagnetic wave strikes metallic nanoparticles in a colloidal solution, the free electrons experience a force that causes the particles to displace, which induces a dipole movement to oppose the charge created; this leads to oscillation of the free electrons. At the resonance frequency, a dip in the reflectance spectrum is observed, which is sensitive to the surrounding refractive index. The behavior of the metallic nanoparticles is predicted using the Drude model; further, Maxwell’s equations are used to calculate the extinction cross-section of a spherical nanoparticle of size much

### Table 2 Recent smartphone-based SPR sensors

| No | Principle | Smartphone utilization | Signal modulation | Application/detection | Performance | Ref |
|----|-----------|------------------------|-------------------|-----------------------|-------------|-----|
| 1  | LSPR      | Camera and LED         | Wavelength and intensity | Heart disease biomarker | LOD: 50 ng/mL, Resolution: 0.386 nm/pixel | [64] |
| 2  |           | Camera                 | Wavelength and intensity | Protein *Bovine serum albumin* (BSA) | LOD: 19.2 μg/mL, Resolution: 0.336 nm/pixel | [65] |
| 3  |           | Camera                 | Intensity           | Water pollutant NH₄⁺ | LOD: 200 mg/L | [66] |
| 4  |           | Camera                 | Intensity           | Water pollutant Cr⁶⁺ | LOD: 11 μM | [67] |
| 5  |           | Camera                 | Intensity           | Water pollutant Hg²⁺ | LOD: 0.2 ppb | [68] |
| 6  |           | Camera                 | Intensity           | Water pollutant Cd²⁺ | LOD: 1.12 μg/L | [69] |
| 7  |           | Camera and LED         | Wavelength and intensity | Cancer biomarker *CA13-5* | LOD: 0.87 U/mL, Resolution: 0.71 nm, Sensitivity: 161 nm/RIU | [70] |
| 8  | Prism coupled | Camera and screen | Angle and intensity | Cancer marker *β2 microglobulin* (*β2M*) | LOD: 0.1 μg/mL, Resolution: 0.111 degree/pixel, Sensitivity: 11 × 10⁻³ RIU/degree | [71] |
| 9  |         | Camera                 | Angle and intensity | Antibiotic Doxycycline | LOD: 22.5 aM | [72] |
| 10 | Waveguide coupled | Camera and LED | Wavelength and intensity | Refractive index sensor | Sensitivity: 5.96 × 10⁻⁴ RIU/pixel | [73] |
| 11 | Polarization coupled | Camera and LED | Intensity | Antibody in blood *Immunoglobulin G* (IgG) | LOD: 47.4 nM | [74] |
| 12 | Polarization coupled | Camera and LED | Intensity | Antibody in blood *Immunoglobulin G* (IgG) | LOD: 0.02 mg/mL, Resolution: 2.3 × 10⁻⁴ RIU | [75] |
| 13 | Waveguide coupled | Camera and LED | Wavelength and intensity | Temperature sensor | Sensitivity: 0.46 pixel/°C | [76] |
| 14 | Waveguide coupled | Camera and LED | Intensity | Refractive index sensor | Resolution: 3.8 × 10⁻⁵ RIU, Sensitivity: 5.47/RIU | [77] |
| 15 | Grating coupled | Camera and Screen | Angle and intensity | Protein *Bovine serum albumin* | LOD: 32.5 ng/mL, Sensitivity 10⁻⁵ RIU/degree | [78] |
| 16 | Grating coupled | Camera and LED | Wavelength and intensity | Endotoxin *Lipopolysaccharides* | LOD: 1 ppb | [79] |
| 17 | Grating coupled | Camera                 | Intensity | Antibody in blood *Mouse IgG* | Resolution: 4.12 × 10⁻³ RIU | [80] |
| 18 | Grating coupled | Camera                 | Intensity | Refractive index sensor | Sensitivity: 282/RIU | [81] |
| 19 | Grating coupled | Camera                 | Intensity | Pesticide Imidacloprid | LOD: 1 ppb | [82] |
| 20 | Grating coupled | Camera                 | Intensity | Protein *Bovine serum albumin* (BSA) | LOD: 0.001 mg/mL | [83] |
| 21 | Grating coupled | Camera                 | Wavelength and intensity | Protein *Bovine serum albumin* (BSA) | LOD 2.43 μg/ml, Resolution: 5.88 × 10⁻⁶ RIU | [84] |
condition is satisfied when per unit area is scattered and absorbed [89]. The resonance cross-section defines the rate at which the incident energy upon it and \( \epsilon'' \) takes into account the dissipation effect on the electric field in the metal [87, 88]. The radius of the nanoparticle is \( r \), and \( N \) is the electron density, \( \lambda \) is the wavelength of the incoming radiation. The extinction cross-section defines the rate at which the incident energy per unit area is scattered and absorbed [89]. The resonance condition is satisfied when \( 2\epsilon_d = -\epsilon' \); for silver and gold nanoparticles, the resonance wavelength lies in the visible spectrum [90]. The particle size and shape also influence the resonance wavelength [91, 92]. The general configuration of a LSPR based smartphone sensor is shown in Fig. 3.

The nanoparticles used in the LSPR-based smartphone sensors mentioned in Table 2 use spherical nanoparticles (Au or Ag) with diameter in the range of 15 to 40 nm. The concentration of the nanoparticles has to be optimized; a higher concentration leads to an increased SPR signal because of the increased interaction with the target particles; hence, the signal strength is increased. However, a higher concentration can lead to agglomeration, which adds inaccuracies to the output [68].

Amirjani and Fatmehsari [66], Upadhyay et al. [67], and Gan et al. [69] have developed sensors to detect various water pollutants colorimetrically using the smartphone camera. Amirjani and Fatmehsari [66] reported a method of measuring \( \text{NH}_3 \) in water using Ag nanoparticles with a response time of 20 s. The phenomenon observed was that the yellow color of Ag nanoparticles in solution faded away as \( \text{NH}_3 \) was introduced into the solution because of the formation of \( \text{Ag(NH}_3)_2^+ \) complex. As the concentration of \( \text{NH}_3 \) was increased, the yellow-colored solution turned transparent. The LOD of \( \text{NH}_3 \) sensing was 200 mg/L, which was comparable to spectroscopic LSPR sensors available in literature [93]. However, the selectivity of the sensor was not established. Upadhyay et al. [67] used CAPLP functionalized Au nanoparticles (16 nm diameter) to detect \( \text{Cr}^{3+} \) ions in an aqueous solution. When \( \text{Cr}^{3+} \) was introduced into the solution, the wine red color turned bluish purple. A linear response was observed, and the optimal pH range of the sensor was determined to be between 4 and 12. The LOD of \( \text{Cr}^{3+} \) ions using the smartphone camera was about 11 \( \mu \)M, which does not comply with the standards required for drinking water [94]. Gan et al. [69] used aptamer functionalized Au nanoparticles (15 nm diameter) which produce a colorimetric change when \( \text{Cd}^{2+} \) ions are introduced to the aqueous solution within 10 min. It was reported that to avail the best performance of the sensing platform, the concentration of the aptamer should be 4 \( \mu \)M. The approximate behavior of the red to blue channel intensity upon increasing \( \text{Cd}^{2+} \) concentration was linear. The reported LOD of 1.12 \( \mu \)g/L was well below the suggested limit for water intended for drinking. However, the time required for functionalization and reaction of the target was the main drawback of the sensor. All three of the aforementioned sensors tested the working of the sensors in tap water to confirm the practical usability of the sensor. The selectivity of the sensors was established by both Upadhyaya et al. and Gan et al. by performing tests with various heavy metals. Although the authors have not provided the detailed working setup [66, 67, 69], the compatibility of the detection method to be used with a smartphone was validated.

Sajed et al. [68] devised a unique technique to provide a highly uniform source of light using an external LED screen placed in a housing containing the reference and target solutions; the light was detected by the smartphone camera through a hole in the housing. Citrate functionalized Au nanoparticles of 15 nm diameter were selected for the study. Upon \( \text{Hg}^{2+} \) addition, the color of the solution changes from wine red to purple, which was analyzed as RGB values through the smartphone camera. Tests were performed to observe the effect of temperature on the working of the sensor; the response of the sensor deteriorated when the temperature was increased beyond 30 °C. Therefore, the sensor cannot be used for therapeutic applications. The selectivity of the sensor was confirmed by testing with other heavy metals; moreover, its practical application was tested by performing a study in tap water. The LOD of about 1 nM was sufficient to test whether the water samples comply with the permitted amount of mercury in drinking water [95]. The rest of the sensors in the LSPR section use spectral analysis to obtain their results. Wang et al. [64] made an economical sensor completely utilizing the hardware of the smartphone and a

\[
\sigma_{\text{extinction}} = \frac{24\pi^2 r^3 \epsilon_d^{3/2} N}{\lambda \ln(10) \epsilon''^2 + (\epsilon' + 2\epsilon_d)^2} \tag{2}
\]

where \( \epsilon_d \) and \( \epsilon_m \) are dielectric constants of the surrounding medium and the bulk metal respectively, both of which are dependent on the frequency of the incoming wave. Furthermore, \( \epsilon_m = \epsilon' + i\epsilon'' \), where \( \epsilon' \) and \( \epsilon'' \) are the real and imaginary parts of the refractive index of the metal. \( \epsilon' \) describes how much a material can store or permit the electric field of Ag(NH\(_3\))\(_2^+\) complex. As the concentration of NH\(_3\) was increased, the yellow-colored solution turned transparent. The LOD of NH\(_3\) sensing was 200 mg/L, which was comparable to spectroscopic LSPR sensors available in literature [93]. However, the selectivity of the sensor was not established. Upadhyay et al. [67] used CAPLP functionalized Au nanoparticles (16 nm diameter) to detect Cr\(^{3+}\) ions in an aqueous solution. When Cr\(^{3+}\) was introduced into the solution, the wine red color turned bluish purple. A linear response was observed, and the optimal pH range of the sensor was determined to be between 4 and 12. The LOD of Cr\(^{3+}\) ions using the smartphone camera was about 11 \( \mu \)M, which does not comply with the standards required for drinking water [94]. Gan et al. [69] used aptamer functionalized Au nanoparticles (15 nm diameter) which produce a colorimetric change when Cd\(^{2+}\) ions are introduced to the aqueous solution within 10 min. It was reported that to avail the best performance of the sensing platform, the concentration of the aptamer should be 4 \( \mu \)M. The approximate behavior of the red to blue channel intensity upon increasing Cd\(^{2+}\) concentration was linear. The reported LOD of 1.12 \( \mu \)g/L was well below the suggested limit for water intended for drinking. However, the time required for functionalization and reaction of the target was the main drawback of the sensor. All three of the aforementioned sensors tested the working of the sensors in tap water to confirm the practical usability of the sensor. The selectivity of the sensors was established by both Upadhyaya et al. and Gan et al. by performing tests with various heavy metals. Although the authors have not provided the detailed working setup [66, 67, 69], the compatibility of the detection method to be used with a smartphone was validated.

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compact disk as a reflection grating (reducing the cost). This sensor has the smallest form factor among the LSPR sensors mentioned in the current article. The compact disk had 640 lines/mm and was placed at an inclination of 5°. The light from the LED of the smartphone was transmitted through the cuvette containing the solution being analyzed. The light reflected from the compact disk was detected by the smartphone camera. The setup was used to detect Cardiac human troponin I (cTnI), which is a biomarker for infarction that can lead to heart attacks. Peptide functionalized Au nanoparticles of diameter 36 nm were used in the study. A clear red shift in wavelength and intensity decrease was observed as the time of cTnI in solution increases. The setup displayed reasonable accuracy when compared to a UV/Vis spectrometer; the inaccuracy was deemed to be due to the poor linear sensitivity of the smartphone camera. Dutta et al. [65] have developed a similar setup which comprised of an external light source and a commercial transmission grating (1200 lines/mm), thus increasing the size and cost of the setup. BSA and trypsin were detected with a LOD of 19.2 and 25.7 μg/mL, respectively. The red shift and the increase in transmission intensity were observed due to increasing concentration of BSA in a solution of citrate functionalized Au nanoparticles of 20 nm diameter. The wavelength shift due to the concentration displayed an approximately linear relation. Citrate ions were added to prevent agglomeration of the Au nanoparticles in the solution. An unwanted red shift was detected when comparing the results to a commercial spectrometer; the calibration method was pointed out as a potential cause for this error. Fan et al. [70] have developed a cancer biomarker sensor that has a high potential for commercialization. The sensor was considered appropriate for home and clinical use to monitor cancer patients due to its small size, high accuracy, and minimal sample requirement (10 μL). The setup comprised of a customized microfluidics setup having 9 sensing units, with each unit containing 1 major and 8 minor sensing areas. Light from an LED passed through a microhole array onto the custom microfluidics setup. Next, the light passed through a lens and converged at a grating, and finally it was incident at the smartphone camera. The whole unit was designed to be assembled easily and modular, hence, making alterations and improving the parts a straightforward operation. The annealing method, which is considered an economical and simple method to prepare Au nanoparticles, was used to cover the microfluidic channels with Au nanoparticles. The nanoparticles were functionalized with anti-MUC1 and anti-MUC16 antibodies to detect the cancer biomarkers CA125 (LOD of 4.2 U/mL) and CA13-5 (LOD of 0.87 U/mL) respectively. The LOD was considered adequate for clinical monitoring of cancer patients. The reaction time to detect the target species was 1 h. Furthermore, the microfluidics unit after functionalization could be stored at 4 °C for a long time, hence, the users can perform a one step process at home. Additionally, it was proposed that the concentration of the biomarkers could help identify the stage of the cancer, but it was reported that a cancer specific biomarker would provide better results. LSPR based sensors require the fewest components among all the other mechanisms. However, the preparation and functionalization of nanoparticles is often a tedious process, but is critical to fabricate a sensitive and accurate sensor.

### SPP Mode

Polariton can be envisioned as quasiparticles originating due to the incident electromagnetic wave creating a collective dipole excitation. In the “LSPR” section, the metallic nanoparticles were excited as LSPRs owing to their small size as compared to the incoming radiation. The majority of the commercial SPR based sensors are SPP mode based. The excitation in the SPP mode leads to the creation of oscillating density wave of electrons which travels on the metal–dielectric interface, called SPPs. At the resonance condition, the momentum of the incoming photons matches that of the electrons present at the interface, which leads to the transfer of energy from the incoming photons to the free electrons. Thus, a dip can be observed in the reflectance spectrum at this condition, which is dependent on the refractive index surrounding the metal–dielectric interface. Maxwell’s equations are solved using appropriate boundary conditions to find the expression of the wavevector of the SPPs. Similar to LSPR calculations, the Drude model is used to model the behavior of the metal. The wavevector of the SPPs is given by [96]:

\[
k_{SPP} = k \sqrt{\frac{\varepsilon_m \varepsilon_d}{\varepsilon_m + \varepsilon_d}}
\]  

where \( k \) is the wavevector of the incoming radiation. SPR phenomenon is a combination of quantum mechanics and electromagnetism; the momentum of a quantum particle is analogous to the wavevector of a matter wave. In the above expression, the square root term is generally more than 1 and positive; hence, the wavevector or momentum of the incoming radiation has to be increased to match the wavevector of the SPPs, which is achieved via a coupling mechanism. The most popular methods of excitation of SPPs are prism, waveguide, and grating coupling. These coupling methods are explained in this section. An additional conclusion that can be drawn when solving Maxwell’s equation for SPP mode is that s-polarized (TE mode) electromagnetic wave cannot induce SPPs as there is no electric field vector in the direction of the SPP wavevector; therefore, only the p-polarized (TM mode) radiation is used for excitation of SPPs. Furthermore, while solving Maxwell’s equations to obtain the
propagation length and depth, the following conditions have to be satisfied [97]:

\[ \varepsilon_m \varepsilon_d < 0 \]  
\[ \varepsilon_m + \varepsilon_d < 0 \]

These equations can be satisfied when one of the dielectric constants is negative and much greater in magnitude than the other. Therefore, \( \varepsilon_d \) being positive, the metal film should have a large negative dielectric constant. The metals generally used in SPR sensors have a large and negative \( \varepsilon' \) in the visible and NIR range. While \( \varepsilon'' \) is positive and small, which leads to low decay of the SPPs. The propagation length (\( L_{\text{SPP}} \)) and depth (\( \delta_{\text{SPP}} \)) of SPP is defined as the distance at which the intensity of the polariton decays to \( 1/e \) of its initial value in the direction and perpendicular to the direction of propagation respectively, they are calculated using the following expressions [98]:

\[ L_{\text{SPP}} = \frac{\lambda}{2\pi} \left( \frac{\varepsilon' + \varepsilon_d}{\varepsilon_d} \right)^{\frac{3}{2}} \]  
\[ \delta_{\text{SPP}} = \frac{\lambda}{2\pi} \left( \frac{\varepsilon' + \varepsilon_d}{\varepsilon^2_d} \right)^{\frac{1}{2}} \]

The conclusions previously mentioned regarding \( \varepsilon' \) can be applied to obtain a large \( L_{\text{SPP}} \). To achieve a higher selectivity of detections, the \( \delta_{\text{SPP}} \) should be small. The LSPR mode works in a shorter range (15–50 nm) as compared to the SPP mode (250–500 nm) [99, 100]. Therefore, the selectivity of the LSPR mode is higher as compared to SPP mode because of the concentrated field enhancement, but the use of LSPR sensors is limited because of its much lower sensitivity [101]. However, the LSPR effect is less susceptible to inaccuracies caused by temperature variation and other minor changes in the surroundings [86]. Gold and silver are used as thin films for various coupling techniques because of their high SPR response. Silver is considered to produce the highest SPR response and sensitivity, but silver layer exposed to the surroundings is highly prone to oxidation [102, 103]. It has been reported that the SPR phenomenon can also be explained using Fano resonance and electromagnetically induced transparency [7, 104, 105]. Sensors based on the combination of LSPR and SPP modes are also being developed, which offer high selectivity along with good sensitivity due to electric field enhancement. One of the methods is the deposition of metal nanoparticles on a fiber optic cable [106, 107]. Reports of sensing using combined LSPR and SPP mode utilizing nanoarrays on metallic film are highly prevalent in literature [6, 108], which are discussed in the grating coupled sensors.

### Prism Coupled

Prism coupling is the most simple and easy to control coupling method and offers excellent sensitivity. The prism coupling can be achieved using the Otto and the Kretschmann configuration (Fig. 4a). The Otto configuration is not generally used because the air gap between the metal film and the prism is difficult to control. The basic working of the Kretschmann configuration is that a p-polarized light incident on a prism undergoes total internal reflection (TIR), creating an evanescent wave at the metal–dielectric interface. The evanescent wave is responsible for the coupling and creation of the SPPs at a critical angle. The coupling effect only takes place if the thickness of the metal film is less than 100 nm because of the exponential decay of the evanescent wave in the metallic film. But, if the thickness of the metal is too low (lower than 30 nm), the SPR signal strength will be low due to lower the lower number of charged electrons being available to absorb the incident energy [109]. Hence, the metal film thickness generally selected is between 40 and 50 nm. The coupling condition can be visualized by the dispersion relation shown in Fig. 4b; by incorporating the prism refractive index, the wavevector is increased to fulfill the resonance condition. The resonance condition of prism coupling is given by the following equation [46]:

\[ n_p \sin \theta = \text{Re} \left\{ \sqrt{\frac{\varepsilon_m \varepsilon_d}{\varepsilon_m + \varepsilon_d}} \right\} + \text{Re} \left\{ \frac{\Delta \beta \lambda}{2\pi} \right\} \]  

where \( n_p \) is the refractive index of the prism and \( \Delta \beta \) takes into account the effect of the prism and thickness of the film. The \( \Delta \beta \) term is commonly ignored while expressing the dispersion relation. At the critical angle, a dip in the reflectance spectrum is observed, which is dependent on the refractive index of the surrounding dielectric medium. The biggest drawback of the prism coupling technique is the relatively bulky nature of its components.

Preechaburana et al. [71] devised a unique evanescent wave coupled sensor which utilizes the screen of the smartphone as the light source and its front camera as the detector (Fig. 5a, b), thereby reducing the number of components.
required and reducing the form factor of the sensor. The sensor was based upon angle modulation technique. Although a prism was not directly used, the setup worked in the Kretschmann configuration using an optical coupler and TIR off an epoxy block. The intensity of the smartphone screen (300–500 nits) was deemed to be sufficient for SPR sensing. The angle resolved modulation was achieved by utilizing the phenomenon that the image (red rectangle in Fig. 5b) displayed on the screen will emit light at a particular angular distribution which is shown using the blue zone. 10° angular range was covered with a resolution of 0.111°/pixel. A customized chip was devised to incorporate the microfluidics, which enables fluid flow over the sensing surface. The constant angle intensity variation with time was used for β2 M detection, which is a marker for cancer and other diseases. The detection levels were deemed adequate for clinical use. Although the setup was small in size, the alteration of the screen size, pixels, intensity, and front camera position when operating with the various types of smartphones available in the market will need major revisions in the alignment of the light source and calibration. Surface plasmon coupled emission (SPCE) is the phenomenon of coupling the excited fluorophores with the density wave originating due to SPR; the frequency of the emission of the fluorophores matches the frequency of the density wave. This leads to a highly directional emission that can be used to detect minute concentrations of targets. Badiya and Ramamurthy [72] developed SPCE sensor for the detection of doxycycline, which used lignin decorated with Ag nanoparticles as the source of the excited fluorophores placed between graphene oxide and the Ag thin film. Furthermore, the Ag nanoparticles induce the LSPR effect, which enhances the response of the sensing platform. The Ag-lignin was functionalized with rhodamine 6G to improve the efficiency of the sensor, which enabled the detection of attomolar concentrations. A continuous wave 5 mW 560 nm laser, after passing through a filter and a polarizing sheet, was incident on a glass slide which was coated with Ag thin film (50 nm thickness). The glass slide was placed on top of a hemi-cylindrical prism via an index matching fluid on a stage which can rotate. The reflected light was detected by the phone camera colorimetrically; the variation of signal intensity and concentration of doxycycline was approximately linear. The LOD was significantly improved when Ag-lignin was used as spacer layer instead of only lignin. The SPCE presents an excellent potential of the future of portable surface plasmon based sensors. Although the fabrication of the SPCE sensors is in its embryonic stage, utilizing specialized hardware and complex chemical synthesis, the aforementioned unit displays its capability to detect attomolar concentrations using a smartphone camera. The prism coupling is the commonly used SPR excitation technique in laboratories due to its high sensitivity, simple components, and its ability to be used in both angle and wavelength modulation. However, the prism being bulky and fragile, finds limited application in smartphone based SPR sensors.

Waveguide Coupled

Similar to prism coupling, the waveguide coupling is based on the evanescent wave created by TIR, but the solution to the dispersion relation is obtained by solving hybrid modes [110]. In most practical applications, waveguide coupling is achieved by modification of a fiber optic cable. To obtain the SPP wave in a fiber optic cable, a region of the cladding has to be removed and replaced by a metal film of appropriate thickness as described in Fig. 6a. The simplified form of the dispersion relation is given as [111]:

\[
 n_w \sin \theta = Re \left\{ \frac{\varepsilon_m \varepsilon_d}{\varepsilon_m + \varepsilon_d} \right\}
\]

(9)

where \( n_w \) is the refractive index of the core of the fiber optic cable. An optimum film thickness and length can be selected to achieve the highest response in the reflectance spectrum [46]. The performance of the sensor is improved as the ratio of the sensing length to core diameter is decreased [112, 113]. The major drawback of the waveguide based coupling is the lower reflectance dip and narrow wavelength range which satisfy the coupling condition [114]. However, the compact and simple design is excellent for portable applications. Moreover, in prism based coupling, there is
measurement on only a single spot, and hence single angle assessment, which can lead to an incorrect result. But, the fiber optic–based sensors excite the entire sensing surface, leading to an accurate representation of the target area [111].

As opposed to other techniques, all the waveguide coupled smartphone SPR sensors use a similar basic setup as shown in Fig. 6b, although there are certain differences that are explored in this section. In the sensors mentioned in this section, the core diameter of the fiber optic cable selected was between 300 and 400 μm.

Bremer and Roth [73] reported the first fiber optic based smartphone SPR sensor. Glycerol solutions of various concentrations were used to establish the refractive index sensitivity of the setup. Liu et al. [74] developed a very accurate fiber optic–based sensor to detect IgG in nanomolar concentration. 50 nm thin Au film was deposited in the sensing region. A filter was used to direct red light onto the sensor, the light was collimated to improve the intensity of the signal. To improve the output extracted from the signal, three outputs were received by the camera in the form of three dots; a measuring channel received output from the sensing region which was immobilized, a reference channel which receives output directly from the filtered light, and a control channel which received the signal from a sensing region which was not immobilized. The sensing region was immobilized with Staphylococcal Protein A (SPA), the binding reaction of SPA with varying concentrations of IgG was studied. The relation between the averaged SPR signal and concentration of IgG was linear. The LOD of the smartphone sensor was comparable to a commercial sensor. Liu et al. [75] used a thin film combination of Au and Ag (15 nm Au deposited on top of 25 nm Ag); to prevent oxidation of Ag while retaining its excellent performance. The sensing surface was immobilized with SPA to detect IgG in solution. The binding of SPA and IgG was initiated after 10 min, and the intensity of the signal increased linearly with an increase in concentration of IgG. Pan et al. [76] used the SPR technique to develop a temperature sensor that detects temperature using a TiO₂ thin film deposited on a fiber optic cable. A transmission grating (1200 lines/mm) was used to disperse the signal into a wavelength spectrum. The TiO₂ film thickness and refractive index changes with variation.
in the temperature; hence, the change in temperature can be detected. A blue shift was observed as the temperature was increased from −10 to 180 °C, which was close to a linear relationship. Although temperature sensing is a new domain for SPR based sensing, the authors have not provided its comparison to the existing techniques to measure temperature to merit further exploration. Liu et al. [77] combined the LSPR and waveguide coupling principles to improve the sensitivity of the SPR based smartphone sensor. The area where the cladding of the fiber optic cable was removed, was deposited with Au nanoparticles. The light from the smartphone LED was passed through a 10 nm bandpass filter with 550 nm center, to enhance the signal. The nanoparticles placed on the fiber optic cable were expected to improve the performance owing to the combination of LSPR effect and the multiple TIRs in the sensing region of the fiber optic cable. Thereby combining the advantages of improved selectivity due to LSPR effect and sensitivity of waveguide coupling. Moreover, the sensing surface could be simply cleaned and regenerated, as opposed to conventional LSPR sensors where generally the nanoparticles cannot be reused. A linear variation of the intensity of the signal received by the smartphone camera with the refractive index of the sodium chloride solution was observed. However, the performance of the sensor was not compared with conventional fiber optic sensors. The fiber optic coupling technique is best suited to miniaturization, however, its main drawback is low sensitivity. Furthermore, all of the setups mentioned in this section use the LED and camera of the smartphone as the light source and detector respectively at a particular position which are connected via the fiber optic cable. Therefore, these prototypes can only work on the smartphones in which the LED and camera are at that particular position, hence, restricting the adaptability of the sensor. Also, the light incident on the metal film in the fiber optic coupled sensors mentioned in this section was not polarized. Although, only the p-polarized light will create the SPR effect, preserving the intended polarization is difficult in fiber optic based systems. Therefore, the sensitivity of the sensor will be reduced as a result of the additional noise in the signal due to the light in the unwanted configuration.

**Grating Coupled**

The basic principle of grating-based coupling is shown in Fig. 7a; the incoming radiation is incident on a metallic grating which leads to a diffraction wave consisting of various diffraction modes which are coupled. The different modes produce a distinctive response to the SPR signal [115]. Generally, the mode which creates the sharpest SPR response is selected for investigation. When the incident wave with a wavevector \( k \) (in the z direction) is incident on a diffraction grating with pitch of P and depth D, a diffracted wave is formed with wavevector \( k_{zm} \), which is given by [46]:

\[
k_{zm} = k_z + m \frac{2\pi}{P}
\]

where \( m \) is the order of diffraction. The coupling expression can be written as:

\[
n_d \sin\theta + \frac{\lambda}{P} = \pm \left( Re \left\{ \sqrt{\frac{\epsilon_m \epsilon_d}{\epsilon_m + \epsilon_d}} \right\} + Re \left\{ \frac{\Delta \beta_g \lambda}{2\pi} \right\} \right)
\]

where \( \Delta \beta_g \) represents the propagation constant which causes a shift in the wavevector induced by the presence of the grating, and \( n_d \) is the refractive index of the surrounding dielectric medium. The resonance condition can be visualized by the dispersion relation shown in Fig. 7b. There is an excellent potential for commercial metallic grating based sensors due to advanced manufacturing techniques, but the drawback of this method is its lower sensitivity and the noise and inaccuracies caused by the analyte molecules influencing the diffraction phenomenon [116]. A new technique that can be included in grating coupling method uses a thin metal film that is perforated with nanoscale holes or structures arranged in an array [117]. A combination of LSPR and SPP effect is observed, creating more sensitive and selective surfaces [108, 118]. The incident radiation is transmitted through the film, and because of the arrangement of the nanoholes, SPP Bloch wave (SPP-BW) is produced at Bragg’s condition. The depth of the holes play an important role in defining the sensitivity of the mechanism [119]. The resonance condition of a BW-SPP in a 2D array is given by [120]:

\[
|k \sin \theta + i G_y + j G_z| = Re \left\{ k \sqrt{\frac{\epsilon_m \epsilon_d}{\epsilon_m + \epsilon_d}} \right\}
\]

where \( G_y \) and \( G_z \) represent the periodicity in the y and z direction. Apart from the periodicity effect, transmission from the nanohole pattern creates a diffraction effect which is known as the Rayleigh-Wood anomaly. This technique provides improved sensitivity; however, the cost of fabrication is increased due to the complexity of the nanohole array.

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**Fig. 7** a Grating coupling, and b Dispersion relation for grating coupling.
Further, various studies have been performed to understand the effect of the symmetry of the array, and the shape and size of the constituents of the array through simulations and experimentation. Schade et al. [121] studied the aforementioned effect using aluminum nanoparticles of various shapes in a parodic array. It was observed that increasing the diameter of the spherical nanoparticles as well as an increase in the distance between the particles in the array caused a red shift in the transmission spectrum. Further, introducing asymmetric particles (almost quadratic and ellipse particles) created a polarization vector dependence on the SPR response. Sinibaldi et al. [122] reported that the SPP-BW based 1D photonic crystal performed better than the conventional SPP based sensors. Therefore, the periodic nanoparticle arrays have the potential to improve SPR sensing by introducing new concepts such as asymmetric shapes and novel structures [123, 124].

Filho et al. [78] developed an angle-resolved grating-coupled smartphone-SPR sensor, which uses the screen of the smartphone as the light source. The incoming wave from the AMOLED display was polarized and incident on a DOCE (Diffractive Optical Coupling Element), which was then reflected off the sensing region; the reflected light strikes the DOCE, and the dispersed signal was eventually detected by the front camera of the smartphone. The DOCE was a grating coupling element whose structure was similar to a compact disk [125]. The light received in the front camera was split into RGB values and was correlated to the pixel of the display from which it emerged, thus, creating an angle resolved sensing setup. The red channel displayed the highest SPR effect because the calculated resonance wavelength for the diffraction grating in the setup was 670 nm. BSA interaction with water and HPC (NaCl (Hypo-chlorite)) was observed; it was reported that introducing BSA into water increases the maximum energy (summation of the brightness value of all the pixels) of the red channel, and combination of water and HPC reduces the signal to the baseline, washing away the BSA. Zhang et al. [79] developed a compact and economical grating based SPR sensor using the LED of the smartphone as the light source. The light was polarized and reflected off the Au grating (period 500 nm and depth 50 nm) on which the sample holder was mounted onto a compact disk that was placed on top of the smartphone camera. The sample was placed in a sample holder above the grating; the grating was placed normal to the incident wave, while the sample holder was tilted to create an angle of incidence of 5°, which lies in the −1 order diffraction. A commercial spectrometer was used to determine that for normal incidence, the −1 order diffraction provided a sharper SPR response as compared to +1 order, owing to the presence of the natural plasma frequency of Au in the +1 order region. The surface of the grating was immobilized with KC-13 peptide to detect Lipopolysaccharides (LPS) which is an endotoxin that can cause organ failure. As the concentration of LPS was increased, a red shift was observed in the reflectance spectrum. The selectivity of the sensor was confirmed by testing with various organic compounds in solution. Furthermore, clinical studies were performed to establish the practicality and repeatability of the sensor. Guner et al. [80] developed an economical colorimetric grating coupled SPR smartphone sensor which uses a 520 nm LED as the light source, which was passed through a collimator, polarizer, and a bandpass filter; onto the camera of the smartphone. Fiber optic cables were used to connect the optical elements. The grating was fabricated using a blue ray disk with grating period 320 nm and depth 20 nm by depositing a metal film which enables plasmon coupling. The protective layering of the disk was removed, and Ag layer of 80 nm thickness was deposited on the disk using thermal evaporation. Furthermore, Au layer of 2 nm thickness was deposited on top of the Ag layer. Numerical simulation was used to determine that Ag gave excellent plasmonic response at a thickness greater than 80 nm and Ag layer of few nm thickness provides protection against oxidation. Furthermore, an economic microfluidic chamber was fabricated by laser cutting an acrylic plate and the use of adhesives. Only the green channel of the light received by the camera was used for calculations because it provided the highest SPR response for the setup. The microfluidics unit was integrated into the housing of the sensor. As BSA solution was introduced into the microfluidic chamber, the shift in resonance wavelength was observed. To detect mouse IgG, a SAM of 11-mercaptopentanecanoic acid was grown on the grating surface by using 1-ethyl-3-(3-dimethylaminopropyl)-carbodiimide (EDC) and N-hydroxysuccinimide (NHS), followed by immobilization with rabbit anti mouse IgG. Ethanolamine solution was used to ensure that only the intended target molecules bind to the immobilized surface. The smartphone sensor was used to detect nanomolar concentration of mouse IgG which was deemed comparable to commercial setups. Lertvachirapaiboon et al. [81] developed a colorimetric grating coupled transmission SPR smartphone sensor which used an external polychromatic light source and the smartphone camera as the detector. The light was incident on the transmission grating through a polarizer. The transmission grating was fabricated on a Cyclic Transparent Optical Polymer (CYTOP) substrate by pressing at appropriate temperature and pressure. 50 nm thick Au film was deposited on top of the CYTOP substrate; the substrate had a pitch of 750 nm and depth 50 nm. The grating was attached to a four channel microfluidic chamber. Liquid crystal tunable filters were used to calibrate the setup by controlling the wavelength which was allowed onto the detector. The angle of incidence of the incoming wave was optimized by observing the performance of the sensor for angles of incidence ranging from 25° to 45°. 675 nm light at 30° angle of incidence displayed the highest intensity of the SPR signal. The intensity showed a linear increase with refractive index of ethylene glycol solutions. The
 setups mentioned in this section used a conventional metallic grating, however, the sensors mentioned henceforth attempt to improve the SPR signal by using a nanopattern which creates an altered electromagnetic response.

Lee et al. [82] developed a pesticide (imidacloprid) sensor which uses a sensing chip consisting of capped nanoslits. An external optical source (white LED) was used along with a bandpass filter which converts the white light to a narrowband green light. The green light after polarization was incident normal to the sensing chip, and the transmitted signal was detected by the smartphone camera. The sensing chip was fabricated using nanoimprint lithography on a cyclic olefin polymer (COP) substrate. The slits were in a 1D array and comprised of a COP substrate on which Ag film was sputtered. The width of a slit was 80 nm, the period was varied from 487 to 525 nm, and the Ag thickness was varied from 26 to 146 nm. The optimal thickness of the Ag layer was reported to be 80 nm, which was determined by studying the transmission spectrum (not part of the smartphone sensor setup). The sensing chip was covered with a 4 nm Al2O3 film to prevent the chip from environmental harm. Moreover, the transmission spectrum informed that increasing the period of the slits from 487 to 525 nm created a red shift in the SPR transmission peak; this phenomenon was used to expand the sensitivity of the sensor over a large wavelength range by the use of sensing chips of several periods simultaneously. An indirect competitive immobilization technique was used for imidacloprid detection. The surface of the sensor was immobilized with BSA-imidacloprid and then exposed to imidacloprid antibodies and monoclonal anti-imidacloprid antibodies. The sensing chip was produced by arranging nanopatterns with periods ranging from 487 to 525 nm with a step size of 2 nm. Therefore, 20 different types of nanopatterns were arranged to enable detection of the target over a large portion of the wavelength spectrum. A shift in the bright spot was observed as the concentration of imidacloprid varies. Hence, imidacloprid was detected semi qualitatively in the ppb range by colorimetric analysis of the image, which fulfilled the requirement of the safety standards for imidacloprid (20 ppb). Although the sensor provided excellent qualitative performance, the fabrication of nanoslits of 20 different periods to produce the required sensing unit hinders its implementation. Wang et al. [83] fabricated a nanopattern known as nano Lycurcus cup array (nanoLCA) using polyethylene terephthalate as a substrate on which Au layer of 90 nm was deposited (Fig. 8a). Prior to Au deposition, Ti layer of 9 nm was deposited on the substrate. A UV cured nanoreplica process was used to develop the nanopattern on the substrate. The nanoLCA was prepared using nanocone arrays of period 350 nm, depth 500 nm, and width 200 nm. Light from a halogen lamp was transmitted through the sample, which was introduced in the setup in a glass slide that also contained the nanopattern, and was captured by the smartphone camera (Fig. 8b). The red channel was selected for performing the protein detection analysis colorimetrically, which was enabled by using the Coomassie protein assay reagent kit. Although the green channel produced the highest sensitivity, the red channel was selected to perform the study due to its higher intensity. The linear response of the sensing chip to increasing BSA concentration was observed. Four artificial urine samples were tested to confirm the practical applicability of the sample. Furthermore, it was reported that there was a 30 times upgrade in LOD of protein detection as compared to commercially available portable units. Pan et al. [84] prepared a nanoslit array by nanoimprint technique, using a mold of period 500 nm and 650 nm, and the depth and width were kept 50 nm. The nanoslits were capped using Au of thickness 50 nm and prepared on a COP substrate. Light from a tungsten light source was passed through a polarizer, and was incident on a reflective grating (1200 lines/mm). The output signal was detected by a smartphone camera. The interaction between BSA and anti-BSA was studied, and the selectivity was validated using immunoglobulin A antibody (anti-IgA). Furthermore, an advanced signal processing technique was used to improve the signal, which is discussed in the “Signal Processing” section. The grating coupling technique has a unique advantage of tunability of the shape and symmetry of sensing surface to achieve the desired results. Hence, the sensing surfaces can be fabricated to serve a particular application. Moreover, the advances in fabrication techniques and simulation enable fast and convenient optimization; and the eventual decrease in cost of manufacturing nanopatterns will permit even more portable grating coupled SPR sensors.

Signal Processing

Different signal processing techniques have to be applied to the output plot to extract the maximum available information. Some of the basic techniques are, subtracting the dark spectrum (the output recorded in the absence of any light source) from the raw signal received and dividing the modified spectrum by the reference (non-resonant or the s-polarized) spectrum to cancel out the unwanted instrumentation defects [126]. Several fitting techniques are usually applied to the final spectrum to enhance the readability of the resultant plot. Several authors have used signal processing techniques to improve the performance of the smartphone SPR sensors, some of which are discussed in this section. The ratio of two channels from the RGB channels was selected as the final signal for improved the SPR response [67, 69]. The concentration of Hg2+ was measured using a machine learning regression model, which was built on minimizing the root mean square error (RMSE) in the concentration by Sajed et al. [68]. Liu et al.
[74] subtracted the intensity of the control channel from the measuring channel, and the resultant was divided by the intensity of the reference channel to obtain the relative intensity, which decreased the fluctuations in the signal. Qiang Liu et al. [75] devised an innovative approach to achieve higher sensitivity; the image in the smartphone camera was in the shape of a dot. The intensity of the signal increased with the refractive index of the solution at lower wavelengths (G channel) and decreases with an increase in wavelength at higher wavelengths (R channel). It was reported that a 100% increase in sensitivity was observed by subtracting the normalized intensity of the two channels. Guner et al. [80] used s-polarization and dark region signal to normalize the reflectance spectrum. Wang et al. [83] improved the signal of the sensing response by performing two normalization steps, first used only the R channel as reference to remove the noise due to reflections and unwanted light around the sensing region, the second used the RGB channels as reference to eliminate the fluctuations in the light source. Pan et al. [84] have improved the sensitivity of nanoslit-based smartphone-SPR sensors by incorporating a position tracking algorithm for noise cancelation. The working principle of the algorithm was that the peak transmission ($T_0$) and its corresponding wavelength $\lambda_C$ were measured from the transmission spectrum as shown in Fig. 9a. The wavelength $\lambda_L$ was calculated by dividing $T_0$ by Euler’s number and measuring its corresponding wavelength. $\lambda_S$ was calculated by making the area A and B equal. Using these parameters the resonant position tracking response of the sensor was calculated. It was reported that the signal to noise ratio was much higher (17.38 times greater) by using the position tracking method than by the conventional wavelength modulation analysis. The signal due to non-specific interaction was very small and a clear response was observed when anti-BSA was introduced into the solution. Signal processing can improve performance of a sensor without requiring extensive changes to the hardware, thus, making portable sensors economical. Moreover, the advancement in artificial intelligence and machine learning will improve further improve the data analysis. The abundance of computational resources and internet connectivity of smartphones enables the smartphone based sensors to implement these advances.

Fig. 8 a Nanopattern, b Schematic, and c prototype of the smartphone SPR sensor developed by Wang et al. [83]. Reprinted with permission from Anal. Chem. 2017, 89 (1), 611–615. Copyright 2017 American Chemical Society.
Conclusions

The SPR-based sensors have the potential to be the next generation portable sensor technology incorporated in our smartphones. SPR technique enables detection and analysis of a wide range of biomolecules, gases, inorganic, and organic particles. Incorporating a smartphone leads to reduction of the parts required and the price of the sensing platform. Moreover, the portability and the span of the market covered by the sensor product drastically increase. The performance of the smartphone-based SPR sensors was comparable to their commercial alternatives. The smartphone-based sensors mentioned in the current article are SPP- and LSPR-based, and use various coupling techniques and advanced signal processing. A sensor based on a combination of LSPR and waveguide coupling phenomenon was studied [77]. Furthermore, advanced grating–coupled sensors use a nanopattern sensing surface containing holes which improve the performance by utilizing both LSPR and SPP phenomena [82–84]. A prism-coupled SPCE sensor, capable of detecting attomolar concentrations was also explored [72]. The sensors mentioned in the article have time of detection ranging from a few seconds to some minutes. The intensity of the output signal generally follows a linear trend with the concentration variation of the targeted species. The LSPR-based sensors require minimal components and show excellent selectivity, but lack the sensitivity of SPP-based sensors. Moreover, the control of the nanoparticle size and distribution, along with the concentration of functionalized particles, is critical in deciding the performance of the LSPR sensors. Among the coupling techniques for SPP-based sensors, waveguide-coupled (fiber optic based) sensors are the most compact and exploit the maximum hardware capability of the smartphone. An
innovative prism–coupled sensor was studied, whose setup
can be simply placed on a specific position on the screen,
thus, providing excellent portability in a prism-coupled
sensor which itself is a highly sensitive technique [71]. An
economic gratings-coupled sensor was developed by using a
blue ray disk as a substrate and depositing a metal film upon it [80]. Grating-coupled sensors are now becoming prevalent
due to the advantages of optimized nanopatterns fabricated
by advanced manufacturing techniques. Furthermore, vari-
ous authors have exploited advanced signal processing tech-
niques to improve the performance of the sensor.

Although all the sensors described have the ability to be
used using a smartphone, there are certain considerations
that need to be included to make the sensor a marketable
product. The housing should be adaptable to be used with
the plethora of available smartphones. The complete SPR
setup includes microfluidics; however, only a few authors
have included microfluidics in their discussion. Although
the hardware capability of the smartphone for SPR sensor
development has been extensively reported, the signal
processing is still being performed on an external computing
platform which can be easily performed on the smartphone
itself by developing a dedicated application.

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