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Review

Recent progress on developing of plasmon biosensing of tumor biomarkers: Efficient method towards early stage recognition of cancer

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ABSTRACT

Cancer is the second most extended disease with an improved death rate over the past several time. Due to the restrictions of cancer analysis methods, the patient's real survival rate is unknown. Therefore, early stage diagnosis of cancer is crucial for its strong detection. Bio-analysis based on biomarkers may help to overcome the problem Biosensors with high sensitivity and specificity, low-cost, high analysis speed and minimum limit of detection are practical alternatives for laboratory tests. Surface plasmon resonance (SPR) is reaching a maturity level sufficient for their application in detection and determination cancer biomarkers in clinical samples. This review discusses main concepts and performance characteristics of SPR biosensor. Mainly, it focuses on newly emerged enhanced SPR biosensors towards high-throughput and ultrasensitive screening of cancer biomarkers such as PSA, α-fetoprotein, CEA, CA125, CA 15-3, HER2, ctDNA, ALCAM, hCG, VEGF, TNF, Interleukin, IFN-γ, CD24, CD44, Ferritin, COLIV using labeling processes with focusing on the future application in biomedical research and clinical diagnosis. This article reviews current status of the field, showcasing a series of early successes in the application of SPR for clinical bioanalysis of cancer related biomolecules and detailing a series of considerations regarding sensing schemes, exposing issues with analysis in biofluids, while providing an outlook of the challenges currently associated with plasmonic materials, bioreceptor selection, microfluidics, and validation of a clinical bioassay for applying SPR biosensors to clinical samples. Research opportunities are proposed to further advance the field and transition SPR biosensors from research proof-of-concept stage to actual clinical usage.

1. Introduction

As the second leading cause of death in the world, cancer has become one of widespread and important health problems. According to World Health Organization's annual statistics last year, cancerous patients and cancer-related deaths are estimated at 18.1 million and 9.6 million, respectively. One out of every six women and one out of every five men develop cancer throughout their lives; also one out of every eleven women and one out of eight men pass away from this malady. The number of patients who survived within 5 years of cancer diagnosis was reported to be 43.8 million. In the Asian and African regions, the prevalence of cancer and high mortality rates have been reported higher than the other areas. WHO identifies poor prognosis and limitations as critical factors on well-timed access to therapeutic and diagnostic agents in most countries [1].

To put an end to the rapid progress of global burden of cancer and declining mortality rate, early detection of cancer is essential [2]. Now, methods which detect cancer include imaging-based methods (MRI, PET, SPECT, CT) [3], biopsy-based methods (IHC, FISH) [4], and endoscopic examinations (gastroscopy, laparoscopy) [5]. Methods which are based on imaging and histology have limitations on providing information for prognosis [6]. There are some drawbacks of endoscopic screening including bleeding, adverse reaction, infection, overdiagnosis, and false-positive results. It is important to note that achieved results through endoscopic assays are descriptive [7]. Whereas, analytical molecular biological techniques have been able to satisfactorily resolve

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mentioned limitation such as Enzyme-linked immunosorbent (ELISA) [8], real-time immuno-PCR assay [9], Fluorescence Polarization Immuno Assay (FPIA) [10], and Immuno Radiometric Assay (IRMA) [11]. Moreover, complex detection protocols and labeling steps make these approaches time consuming and intricate [12].

Biomarkers have a special place in biomedical applications and clinical diagnosis notably when it comes to cancer. Tumor markers provides great opportunities to enhance monitoring the condition of cancerous patients by improving the effectiveness of diagnosis, treatment, and post-treatment [13]. Expanding the role of biomarkers in all aspects of cancer is a logical reason to widely use them in diagnostic assays and researches [14]. There is a growing demand for diagnostic tools and analytical technologies and biosensors are at the forefront of analytical methods. Ideally, the sensor should have the following features; it must be (1) able to identify markers in the undiluted biological samples, (2) responded as quickly as possible, (3) transportable for point of care applications, (4) user friendly, (5) economical [15]. A biosensor typically is composed of a biological recognition element (BRE), an electronic equipment (processor, signal booster, and display), and a transducer. Transducers convert the occurrence of binding the target molecule to the BRE into a measurable physical phenomenon. Biosensors can be classified according to their transducers namely electrochemical, piezoelectric, and optical sensors [16]. Electrochemical transducers are divided into three categories: voltammetric, potentiometric, and conductmetric transducer. Oxidation and reduction reactions and electronic displacements form a basis for these sensors [17]. Piezoelectric crystals are sensitive to the mass changes and mechanical pressure. Binding of the target molecule changes oscillating frequencies of a piezoelectric crystal which used to determine the mass of the target molecule [18]. The functional mechanisms of optical biosensors are based on the application of the optical principles, i.e. the rules describing the nature and mechanisms of radiation, absorption, reflection, light scattering, and phenomena observed as a consequence of the interaction of light with a substance [19]. Emergences and speedy progression of nanotechnology make designing and implementing sensors possible in nanometer dimensions. These nanometer dimensions sensors were called nano-biosensor because of their sizes and applications in biological environments. Gold nanoparticles (GNP) have been of interest to scientists due to their unique optical properties which are related to Surface Plasmon Resonance (SPR) [20]. GNPs have been used in a variety of forms such as spherical golds [21], gold nanorods (GNRs) [22], gold nanostars (GNS) [23], and hollow gold nanostructures [24]. Plasmonic sensors are powerful tools for the evaluation of label-free and real-time molecular interactions analyses such as detection of biomarkers [25], pathogens [26], drugs [27], toxins [28], and hepatitis B virus [29]. Also, it has been extensively used in the studies of kinetic, affinity, and specificity of interaction in various macromolecules like protein-protein [30], protein-carbohydrate [31], protein-cell [32], protein-DNA [33], lipid membrane-protein [34], carbohydrate-carbohydrate [35], DNA-DNA [36], and virus-host interaction [37].

In spite of the abundant ongoing research, cancer diagnosis and treatment have become a global challenge. This article is organized in two parts; the former deals with the concept of plasmon and its application in the construction of sensors and the latter is dedicated to present cancer markers and advances made in identifying these markers by SPR-based sensors.

1.1. Plasmon's background

For the first time, the term of plasmon was introduced by David Pines in 1956 [38]. He attributed the reason for the rapid drop in the energy of electrons passing through metals to collective oscillations of delocalized electrons on the surface of metals and called them plasmon. The reason for this naming was the resemblance of oscillations of electrons with that of the particles in plasma. In 1957, Rufus Ritchie published a theory that the location of a plasmon could be around the surface of metals; this was the first description of a surface plasmon. About 11 years later, Erich Kretschmann, Heinz Raether and Andreas Otto presented methods for optical excitation of surface plasmons on thin metal layer, a remarkable development occurred in the field of surface plasmon. This great advancement made it easy for researchers to perform experiments on surface plasmons [39].

Plasmonic biosensors are divided into two subcategories. Those that sensing platforms includes a metallic films and the other group includes individual plasmon resonant nanostructures. This section gives a brief overview of the applications of surface plasmon in designed film-based SPR sensing and single NP.

1.2. Surface plasmon resonance (SPR)

The most common structure of film-based SPR sensing is Kretschmann configuration that the light coupled into the gold thin film layer by a glass prism. As the incident light travels through a dense medium 1 (high refractive index) to a diluent medium 2 (low refractive index) it deviates from the line perpendicular to the surface. The incident light at a certain angle is propagated tangentially to the interface knowing as the Critical Angle. When the angle exceeds the critical angle, Total Internal Reflection (TIR) occurs inside medium 1 that forms the basis for SPR-based sensors. The propagation range of surface plasmon is limited to metal and dielectric interface and its magnitude is dependent on the dielectric constants of the medium 2. The refractive index of media 2 changes by binding on the gold surface resulting in the excitation angle (θ_{SPR}) changes; thus θ_{SPR} variations monitoring can be used to analyze molecular interactions [40,41].

1.3. Localized surface plasmon resonance (LSPR)

In addition to film-based SPR sensing, there are the other types of plasmonic sensing entitled to localized surface plasmon resonances (LSPRs). When the size of noble metal particles (Au, Ag, Pt, and Pd) are significantly smaller than the wavelength of incident light applied for excitation, they exhibit plasmonic properties. Given that nanoscale objects have a high miniaturization and multiplexing potential, they are an ideal choice for integration into lab-on-a-chip or point-of-care diagnostic devices [42]. The inherent optical characteristics of NPs are greatly affected by diameter, shape, size, and composition [43]. In the following subdivisions, numerous applications of LSPRs will be described.

1.4. Single nanoparticle LSPR sensors

They are the result of incorporation of a dark field microscopy into spectrophotometry. Considering the size and shape of single NPs, the incident light upon them is divided into two parts: absorbed light and scattered light. The scattered light is collected by dark field microscopy to identify single plasmon resonant NPs. As is the case in film SPR sensors, LSPR sensors are very sensitive to changes in the refractive index of the surrounding medium and these changes are monitored by the spectrophotometry. Contrary to SPR sensors, LSPRs sensors have improved the limit of detection by reducing the sensing extends from a few hundred nanometers to tens of nanometers [44,45].

1.5. Ensemble LSPR sensors

Transmission LSPR spectroscopy (T-LSPR) are undoubtedly one of the most powerful modes of LSPR sensing. In these sensors, similar to the previous two cases mentioned, the changes in SPR spectrum can be assessed by changing the refractive index [46]. T-LSPR sensor includes a high density of different nanostructures forms such as colloidal NPs immobilized onto the transparent substrate like glass slide [47], island-like patterns annealed thin gold films [48], or structures that are provided by patterning methods [49]. T-LSPR sensors with a probe of

thousands of nanostructures simultaneously outperform other modes of LSPR sensing in improving output sensing platform [46].

1.6. Plasmonic nanoparticles as labels

Plasmon resonant NPs give much notice to be used as visual labels in sensing assays due to production of large scattering cross-sections. Signal stability with prolonged illumination time has made them superior to conventional fluorophore [50]. As already stated in the single NP LSPR part, scattered light from single NP creates very bright spots that can be seen by dark field microscopy. By using this feature, Plasmon-Resonant Immunosorbent Assay (PRISA) has been established and, dissimilar to NP LSPR, changes in RI are not the basis for measurement in these sensors. In the detection process, conjugated NPs with antibodies, as unbleachable optical labels, confirm target binding events by displaying NPs immobilized to a sensor chip [51].

1.7. Plasmonic optical nanopore

Extraordinary Optical Transmission (EOT) is the phenomenon of extremely strengthened transmission of light through a subwavelength slit arrays in either a flat or a corrugated metal film which has been patterned with a periodically repeating structure [52]. EOT can be exploited as a means of plasmonic nanopore sensor by some actions like measuring a change in the local dielectric constant [53], monitoring the intensity changes [54], and monitoring shifts in the spectrum of the light passing through nanopore arrays [53].

1.8. Plasmonic coupling

Plasmon coupling is a reaction referring to two or more plasmonic particles that are in close proximity to together (distance below 50 nm). Following occurrence of plasmon coupling, the surface plasmons of particles can coupled and the resonance spectrum will be greatly affected. Coupled NP-dimers and NP-film coupling are major branches of plasmonic sensors [55]. Coupled NP-dimers consist of two nanoparticles that are generally linked to each other by a single stranded or hairpin DNA that demonstrates significant redshift spectra compared to individual NP LSPRs. The ssDNA-linked NP dimers are utilized to identify a DNA target complementary the distance between the nanoparticles increases by the hybridization of the DNA strands and it can be detected through blue shift from an individual NP [56]. Film-coupled nanoparticle is composed of metal film, spacer layer of dielectric, and nanoparticles deposited on the spacer layer. The metal film is responsible for creating an image (similar to a mirror reflection) of the nanoparticle that interacts with its own image. Film-coupled nanoparticles are thought to have the same properties as nanoparticle dimers [57].

1.9. Bio-recognition elements

Bioreceptors are important components of biosensors, which basically determine the specificity of a sensor to a particular analyte. The capacity to detect a target in complex compounds is a crucial factor achieved by bio-receptors. Bio-receptors are classified into two broad groups based on the following bio-recognition principles: (**1**) catalytic biosensor and (**2**) affinity biosensor. Enzymes are one of the most common bio-recognition elements used in catalytic sensors. The performance of affinity based sensors is based on the special binding proteins of bio-recognition elements including antibodies, peptides, aptamers and etc [58]. Biological elements are mainly divided into five groups, which are discussed in the following sections.

1.10. Aptamer

Aptamers are short single-stranded oligonucleotides that are the result of a in-vitro selection procedures known as Systematic Evolution of Ligands by Exponential Enrichment (SELEX) [59]. Aptamers have always been considered seriously as recognition elements because of their characteristics like high selectivity and affinity, high scale production, and simplicity of chemical modification. Aptamers have the capability to bind to a wide range of target molecules including proteins, ions, and small molecules [60]. Aptamers are well utilized in a variety of fields including therapeutics [61], diagnostics [62], imaging [63], and gen-regulatory [64]. Nonetheless, there are serious objections that put limits on their practical applications like cross-reactivity, elimination by renal filtration, and rapid degradation of non-modified aptamers by nucleases (especially RNA aptamers) [65].

1.11. Enzymes

Enzymes are vital biomolecules that are widely used in the design of biosensors based on their specific binding affinity and catalytic properties [66]. So far, many sensors have been designed based on enzymes which function according to the enzymatic reactions such as detection of glucose via glucose oxidase [67] and penicillin via penicillinase [68]. Nevertheless, the use of enzymes as a biological element in biosensors has also following disadvantages: (1). High extraction cost and purification of enzymes, (2) Instability; enzymes usually lose some of their functions when immobilized [66].

1.12. Cellular structures

Biological molecules (cells, microorganisms, specific cellular compounds) are used as recognition elements in the design of biosensors [69]. Microorganisms (bacteria and fungi) are utilized as indicators of toxicity or to measure specific factors such as cellular metabolism and cellular respiration [70]. Bilitewski and colleagues made use of microbial biosensors to monitor short-chain fatty acids in milk [71]. Numerous cellular proteins are also considered as bioreceptor for molecular detection or cellular mechanisms [72].

1.13. Antibodies

Antibodies (a member of immunoglobulin superfamily) are mainly produced by plasma cells. Antibodies work by recognizing and sticking to the specific proteins, which can be found on the surfaces of viruses and bacteria and cancer biomarkers in a highly specific way. There has been a lot of excitement about the potentiality of antibody-based biosensors to detect various cancers [73]. Regrettably, there are some drawbacks that impose a limit on the use of antibodies such as high molecular weight, limited stability and high cost of production [74]. Thanks to gene libraries and the development of recombinant DNA technology, it is now possible to provide recombinant antibodies with desired properties. Recombinant antibodies are low molecular weight and high stability and these positive points can compensate for the problems of antibodies. Recombinant antibodies have gained a lot of attention in the field of bioreceptors by overcoming common problems of antibodies [75]. Researchers have been able to benefit from single-chain variable fragment (scFv) in multiple areas of marker detection such as detection of C-reactive protein [76], medicine such as treatment of CNS diseases [77], imaging [78] and drug delivery [79].

1.14. Phage display

Phage display is based on a direct linkage between the genotype and phenotype of phage that results in appearance of large protein libraries on its surface. The method of phage display is exploited to study protein-ligand interactions and improve the affinity of proteins to their receptors [80]. So many reports have been published on the bacteriophage which has been used as a robust molecular recognition element of bacterial detection such as *Staphylococcus aureus* [81], *Listeria monocytogenes* [82] and Hepatitis B virus [83].

1.15. Plasmonic biosensing of cancer biomarkers

Biomarkers are means of describing biological status by analyzing biomolecules like proteins, DNA, RNA, and chemical modifications of biomolecules. WHO gave a more comprehensive definition "A biomarker is any substance, structure or process that can be measured in the body or its products and influence or predict the incidence of outcome or disease". A clinical and more specific definition says cancer biomarkers indicate incidence of cancer in a particular tissue and its progression and response to treatment process. Mainly, biomarkers play a key role in clinical decision. Biomarkers are divided into three categories according to their applications [84]. Predictive biomarkers predict the intervention effects such as trastuzumab against HER2 in breast cancer as complementary therapy along with chemotherapy [85]. Other sorts of biomarkers, prognostic biomarkers warn the risk cancer recurrence and its prognosis in the future. A set of genes were investigated as prognostic markers in tamoxifen -treated breast cancer patients to predict probability of distant recurrence (metastasis) [86]. The last category is diagnostic biomarkers that are used to diagnose cancer and other diseases. These types of biomarkers are best suited for designing sensors to quick identify of cancers that are effective for treatment outcomes. For example, an aptamer-based sensor was developed to identify of Mucin 1 protein (MUC-1) in MCF-7 cell line for efficient detection of breast cancer [87]. Table 1 shows a list of tumor biomarkers.

Markers' detection is not the main diagnostic tool for cancer, but they can be used as a complementary assay to support the diagnosis. This review considers a list of well-known cancer biomarkers that are widely applied to diagnose cancer in the following section.

1.16. Prostate-specific antigen (PSA)

Prostate-specific antigen (PSA) is a glycoprotein that is secreted by normal and cancerous cells of the prostate gland. PSA is a strong prognostic serum marker that applies to the diagnosis and monitor of prostate cancer. The width of the diagnostic gray zone of PSA is described 4.0–10.0 ng/ml. At the concentration of 10 ng/mL and above, the risk of developing prostate cancer increases [88]. Clinical diagnostic methods which are being used, compared with nanobiosensors, provide less sensitivity. Nearly 68 % of cases who were diagnosed had no symptoms. Therefore, a high-accuracy diagnostic method is needed [89]. Also, non-cancerous agents such as age, prostatitis, benign prostatic hyperplasia, urinary tract infection can increase the level of PSA in the blood [90]. Total PSA exists in two free PSA (fPSA) and complex PSA (cPSA) forms in the circulation. Accurate measurement of free/total prostate antigen (f/t-PSA) ratio is required to distinguish between benign and malignant prostate disease [91].

So far, various SPR and LSPR-based sensors have been developed for detection of PSA. According to researches, replacing optical fibers (FO) with a prism in the conventional structure of the SPR sensor can be a novel tool for creating low-cost, remote sensing, miniaturized, and in vivo sensors [92]. As shown in Fig. 1, immobilization of antibodies on nanodisk arrays at the end of optical fiber provided real time monitoring interaction and the possibility of combining FO LSPR with laparoscope or endoscope [93,94]. Breault-Turcot and coworkers established an innovative dual-detection immunoassay, which derived from the combination of SPR and fluorescent ELISA assay. They designed the plasmonic substrate based on microhole arrays which increase 2-fold the sensitivity of the detection [95]. According to the research results, the combination of SPR and fluorescence methods with the lowest LOD of 50 nM showed the best performance comparing to conventional SPR and fluorescent ELISA assay. The LOD of conventional SPR and fluorescent ELISA assay have been reported10 nM and 10 pM, respectively Various sensitivity-enhancement strategies have been reported and most of them are based on nanomaterials including quantum dots (QDs) [96–98], Au NPs [99–102], magnetic nanoparticles [103], and intact polyclonal antibodies [104]

Luminescent semiconducting nanocrystals known as quantum dots (QDs) have got researcher' consideration for signal amplification. Size-dependent fluorescence and stability against photobleaching of QD are strong reasons to prove that these nanomaterials are valid alternatives to organic dyes [105]. Signal boost attributed to bidirectional propagating between SPs and QDs emission and the somewhat mass-loading effect caused by SA-QDs on the SPR surface.

The plasmonic peak of gold nanoparticles is strongly influenced by three decisive factors that are size, shape, and dielectric constant. Zeng et al. have examined varioussizes (40−80 nm) to examine enhancement of SPR sensing signals. According to this study, 40 nm diameter AuNPs displayed the highest coupling effect [106]. Among various shapes of AuNPs, gold nanospheres are mostly utilized because of their isotropic structure [107]. Mustafa et al. compared the effect of three different forms of AuNPs) including nano-octahedrons, nanospheres, and nanorods) to improve the signal of SPR system. They found a direct relationship between signal amplification of nano-octahedrons and nanospheres and their size. The maximum SPR angle shift is attributed to nanorods [108]. All these unique properties enable them to serve as a good candidate for signal amplification.

Sensing community have extensively investigated magnetic nanoparticles (MNPs) for signal amplification studies. Many advantages have been mentioned for these particles including electrical and optical properties, high molecular weights, high refractive index, and cost-eff ; ective synthesis. Their high surface area allows extensive chemical modifications to conjugate variety of desired biomolecules [109].

Different strategies were mentioned in the articles, in addition to the sandwich method, to enhance signal including co-excitation both the PSP and LSP [110], NP-film coupling [57]. Simultaneous excitation PSP and LSP demonstrated 6- fold higher sensitivity as compared to LSP mode. Peptide labeled-magnetic beads were used as a recognition element instead of expensive antibodies. By PSA binding, these peptides are proteolytically broken followed by magnetic beads are released then they are absorbed by the external magnetic field. The refractive index of the magnetic beads and the enzyme environment is different which in the result, dramatically increases the sensitivity. Besides, due to the low molecular weight of the peptides compared to the antibodies, the peptides provide a high density of the functionalized surface [111]. This type of recognition element achieved LOD of 100 pg/mL. The results of their research show good agreement with Zeng et al., report [112]. Table 2 summarized all of SPR based biosensing strategies for detection of PSA.

1.17. Alpha–fetoprotein

Alpha-fetoprotein (AFP) is a fetal glycoprotein that is normally produced by embryonic yolk sac, fetus's liver as well as in trivial amounts by the gut. Its serum concentration rises to the maximum level of 1.2–4.0 mg/ml at 12–16 weeks of pregnancy and then drops rapidly at delivery and remains plateau afterwards. The standard level of adults and healthy individuals is around 2–4 μg/ml [117]. AFP considered a detection surrogate for hepatocellular carcinoma. The measurement of AFP levels is recommended as a complementary method along with

Table 1
The most widely used general biomarkers for cancer detection.

General biomarkers used for cancer detection	
BRCA1, BRCA2, CA 15-3, CA 125, CA 27.29, CEA, NY-BR-1, ING-1, HER2/NEU, ER/PR	Breast
PSA	Prostate
CA 125, HCG, p53, CEA, CA 549, CASA, CA 19-9, CA 15-3, MCA, MOV-1, TAG72	Ovarian
AFP, CEA	Liver
CEA, CA 19-9, SCC, NSE, NY-ESO-1	Lung
CEA, EGFR, p53	Colon
Tyrosinase, NY-ESO-1	Melanoma

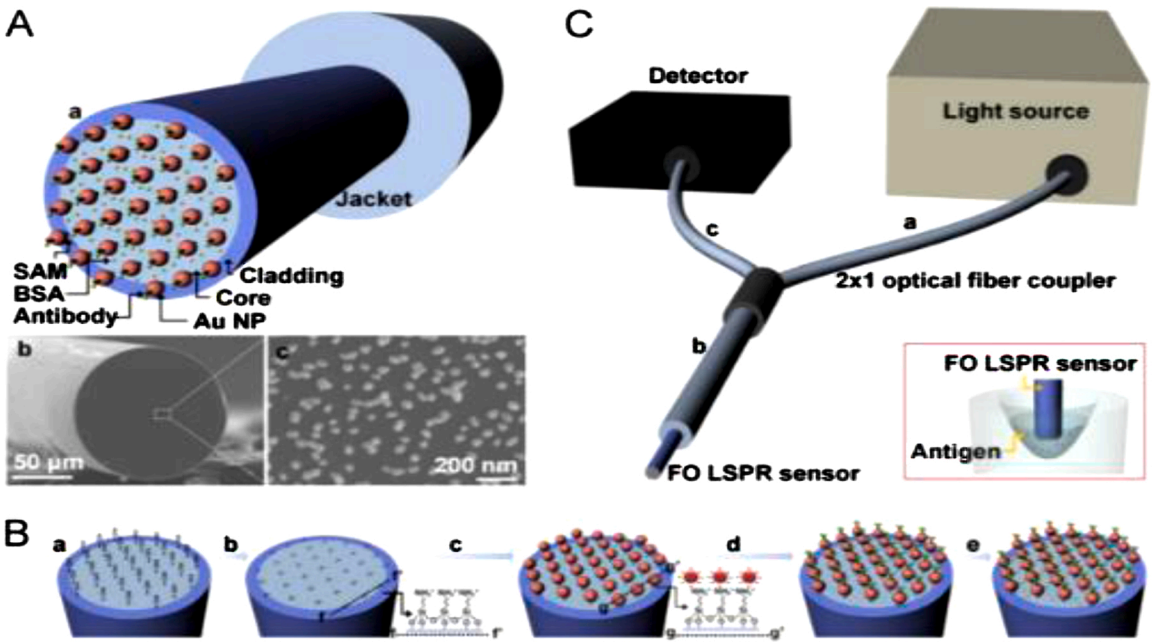

Fig. 1. (A) Schematic diagram of the FO LSPR sensor (a), FE-SEM images of the end-face for the FO LSPR sensor (b) the synthesized Au NPs on the end-face of the FO, (c) SEM image of Au NPs. (B) Preparation procedure of the FO LSPR sensor: (a) surface functionalization with hydroxyl groups, (b) creating Amine functional Groups, (c) immobilization Au NPs on the SAM, (d) antibody IFN-g and antibody PSA are captured on the Au NPs, (e) blocking by BSA. (C) illustration of the optical measurement system with the FO LSPR sensor: (a) FO connector to light source, (b) FO for receiving the reflected LSPR signals, (c) FO for transmit signals to detector [92].

imaging tools for diagnosis [118].

An important point to note is that when a cancer occurs, the level of a group of markers changes, so it is important to measure AFP, CEA and PSA simultaneously. Lee et al. functionalized individual GNPs with the related antibodies to the mentioned oncomarkers. Ag binding was supervised through blended of dark-field microscopy and spectrophotometry [119]. Despite all the advantages mentioned, MNPs have disadvantages that make their applications challenging. Firstly, these nanomaterials lose their magnetic properties in the presence of biological systems. Secondly, biomolecules cannot conjugate to these nanomaterials directly. To overcome these limitations, MNPs are constructed in core-shell form; thus, the MNPs is located at the center and it is surrounded by a coating of gold [120]. Fe_3O_4@Au–Ab_2 in the sandwich method as a booster agent had several advantages; not only it creates a high refractive index, but also it causes high molecular weight and electronic coupling between Au shell and gold thin layer [121]. The ultra-sensitive and selective biosensor proposed by Liang and co-workers was able to detect LOD of 0.65 ng/mL.

Some studies have suggested the dual signal amplification using two signal amplifier factors, in particular polyclonal antibody against the secondary [122]. Similarly, Hu and colleagues performed the double signal amplification by applying an AuNPs@DTBE-antibody. As demonstrated in Fig. 2, DTBE as an initiator of the atom transfer radical polymerization (ATRP) provided the polymer chains grow under controlled conditions on AuNPs@DTBE-antibody resulting a dual amplification of the signal. The primary signal amplification was due to the coupling of Au NPs to the interface layer as enhancer tags and the latter signal amplification was related to the ATRP polymer growth. The LOD of ATRP polymerization approach was 1 ng/mL, which was 5 orders of magnitude less than that obtained by Au NPs coupling method [123].

Table 3 summarized recent biosensors for the SPR based detection of AFP.

1.18. Carcinoembryonic antigen (CEA)

Carcinoembryonic antigen (CEA) is a cell membrane glycoprotein that plays a vital role in cell adhesion. CEA is expressed by normal mucosal cells and its usual concentration for healthy adult individuals is as low as 2.5 ng/mL and for smokers is as low as 5.0 ng/mL; however, its amount surpasses 100 ng/mL in presence of a tumor. Elevated serum CEA levels indicate the possibility of developing colorectal, gastric, breast, lung, and ovarian cancer [126].

GNPs are mainly used to improve the response of optical sensors. The conjugation of GNPs has been performed by various agents to form an effective binding such as secondary antibody [127] and streptavidin [128]. The achievement of these experiments testify to the profoundimpact of signal amplifiers. The LOD of CEA obtained by three strategies, namely conventional SPR, sandwich method, and signal enhancement with SA-GNPs are 13.78 ng/mL, 3.30 ng/mL, and 1 ng/mL, respectively. Furthermore, more consideration should be taken into account to prevent non-specific binding in complex media like serum sample. This goal is achieved by designing immune-sensors based on single surface referencing (SSR) approach [129] and functionalizing the gold surface with bovine serum [130]. In the case of SSR approach, an antibody-functionalized surface is divided into two distinct channels. Through the first channel, referred to by detection channel, only the sample solution passed by and a signal will recording which contains both analyte and non-specific binding. In the second channel, known as a reference channel, the mixture of sample solution and antibody were passing through. The antibody prevented the binding of the analyte, so the recorded signal containes only non-specific binding. Finally, the sensor response was obtained by subtracting the reference channel response from the detection channel response. The SSR system provided more accurate measurement of CEA [129]. Špringer and colleague reduced LOD substantially from 100 ng/mL to 0.1 ng/mL by eliminating the non-specific binding as interfering factors.

Controlling the orientation of antibodies on the sensing area has great importance. The orientation should be such that the variable parts are exposed to the analyte and the constant part is attached to the

Table 2
Examples of PSA detection by SPR biosensing.

Type of probe	Linear Range	LOD	Clinical sample	Ref.
LSPR	1−1 × 10^6 fM	10 fM	Serum	[115]
FO-LSPR	0−0.5 ng/mL	100 fg/mL	PBS	[93]
FO-LSPR	0.5−500 pg/mL	1 pg/mL	PBS	[94]
FO-SPR signal enhancement with sandwich method	0.1–10 μg/ml	4 ng/mL		[92]
SPRi signal enhancement with QD	1 ng/mL-100 pg/mL	100 pg/mL	HBS buffer	[96]
SPRi signal enhancement with pegylated CdSe/ZnS QD	100 μg/mL - 10 fg/mL	10 fg/mL	PBS	[97]
LSPR signal enhancement with SA-QDs on nanopillar arrays LSPR signal enhancement with SA-QDs on nanohole arrays	100 ng/mL -100 pg/mL 100 ng/mL - 1 ng/mL	100 pg /mL 1 ng /mL	HBS buffer	[113]
SPR signal enhancement with AuNPs 20 nm 40 nm	150- 0 ng/mL	2.3 ng/ mL 0.29 ng /mL	75 % human serum	[99]
SPR signal enhancement with Au NPs labels	3nM- 300 fM	300 fM	PBS	[100]
SPR signal enhancement with Au-pAb-HRP	0.01–100 ng/ml	0.027 ng/mL	HBS buffer	[101]
SPR direct detection SPR signal enhancement with sandwich assay SPR signal enhancement with SA-Ab	1 ng/mL- 10 μg/mL 0.07–100 ng/ml	10 ng/mL 1 ng/m 29 fM	PSA spiked in Human Serum	[102]
SPR signal enhancement with MP labels	0.01−10 ng/mL	10 fg/mL	Serum	[103]
SPR signal enhancement with pAb	1000 – 1 ng/mL	18.1 ng/mL 10.2 ng/mL	Serum HBS buffer	[104]
SPR by direct detection (t-PSA) SPR by asynchronous competitive inhibition (f-PSA)	1.0–20.0 ng/mL 0.010 to 0.40 ng/mL	NA	Serum diluted in PBS	[114]
SPR SPR signal enhancement with Ab_2 Fluorescence by modifying Ab_2-HRP combination of SPR and fluorescence	0.1 nM - 50 nM 10 pM- 5 nM	10 nM 0.1 nM 10 pM 10 pM-50 nM	PBS	[95]
LSP mode excited on Au nanohole coexcitation both LSP and PSP on Au nanohole arrays	0.3 pM to 3 nM	0.94 pM 140 fM	NA	[110]
LSPR based on Rayleigh scattering spectra of individual GNR	0.1 pg /mL	0.1 pg/mL - 1 ng /mL	PBS	[115]
LSPR based on Rayleigh scattering spectra of individual GNR	1 aM	1.11 × 10^{-1}- 1.11 × 10^9 aM	PBS	[116]
SPR signal enhancement with resonant coupling between the AuNPs and Au film	0.1 ng /mL	0.1–100 ng/ ml	NA	[57]
plasmonic responses of single AuNPs 21 nm, 43 nm 81 nm	0.1 pg/mL 1 pg/mL 10 pg/mL	10^{-4} to 10^{-1} ng/mL 10^{-3} to 10° ng/mL 10^{-2} to 10^{1} ng/mL	PBS	[112]
LSPR integrated with microfluidic	1 ng/mL	10−100 ng/mL	50 % human serum	[203]
Peptide conjugated with MP as recognition element	100 pg/mL	100 pg/mL - 1 μg/mL	NA	[111]

LOD: Limit Of Detection; NA: Not Determined; FO LSPR: Fibers Optical Localized Surface Plasmon Resonance; SA−QDs: Streptavidin− Quantum Dot; CdSe/ZnS: Cadmium selenide/ Zinc sulfide; AuNPs: Au nanoparticles; MP: Super-paramagnetic Particle; pAb: polyclonal antibody; HRP: Horseradish peroxidase; PSP: Propagating Surface Plasmon;GNR: gold nanorod.

surface. The intrinsic affinity of the protein A to the constant portion of the provided ideal conditions for Ab immobilizing. As shown in Table 4 both nitro avidin-protein a complex and biotin-labelled surface as well as proper orientation increased the surface anti-CEA antibodies density leading to increased binding efficiency [131]. In contrast, Minoru Taya and colleagues observed high resonance unit intensity for anti-CEA antibody immobilization by protein A or G. They attributed the cause to nonspecific binding of IgGs in serum, which decreased in covalent immobilizations [132].

1.19. Carbohydrate antigen

Carbohydrate Antigen 125 (CA125) or mucin16 is a member of the mucin family glycoproteins which is secreted by serosal epithelium and its normal value is 0–35 units/m [134]. CA-125 serves many purposes such as a valuable means for diagnosis, prognosis, and to monitor post-treatment of following diseases ovarian cancer [135], breast cancer [136], Non-Hodgkin's Lymphoma (NHL) [137], gastrointestinal carcinoma lymphoma [138], malignant mesothelioma B-cell lymphoma [139], uterine leiomyomas [140], uterine adenomyosis [141], Malignant Mesothelioma (MM) [142] and, Endometriosis-Associated Ovarian Cancer (EAOC) [143].

Due to the multiplicity of diseases related to CA125, the development of sensitive and specific biosensors can be useful for diagnostic tests. A few affinity-based biosensors have hitherto been reported with variety of BRE such as antibody [144] and RNA aptasensor [135]. The plasmon resonance scattering (PRS) properties GNRs have made them ultra-sensitive sensors. Individual GNRs displayed low PRS intensity. The immune reaction between GNRs-modified antibodies and CA125 caused agglomeration of GNRs which is proportional to CA125 concentration; consequently, PRS intensity increased and a shift in PRS spectra was observed [145]. The LOD of 0.4 U/mL using this approach was the fruit of their research.

Cancer Antigen 15-3 (CA 15-3) is a member of mucin family glycoproteins which is made by normal breast cells. Its normal range is below 30 U/mL, which will be increased in the case of a metastatic cancer. CA 15-3 is considered as diagnostic marker for women threatening by developing breast cancer [146]. Table 5 represents a couple of reported SPR-based biosensors for ultrasensitive measurement of CA15-3. The focus of recent research has been on the effect of the interference layer on the sensor response. Glass as a common interference layer in conventional SPR sensors has little adhesion to gold thin film. Cr is widely used to improve adhesion; however, its low optical transmission and inter-diffusion of metals to the gold thin film affects the sensitivity of the sensor. The SPR sensor based on novel Au/ZnO intermediate layer were measured against conventional Au/Cr-based SPR; consequently, the former SPR sensor showed a higher response [147,148]. Table 5 represent information about the SPR based detection of this cancer biomarker.

1.20. HER2

HER2 or ErbB2 is a tyrosine kinase receptor owned by the epidermal growth factor receptor family. Its overexpression represents the progression of breast cancer and its metastasis [149]. The standard concentration range of HER2 is 2−15 ng/mL; while, in case of breast cancers, it increase to 15–75 ng/ml [150].

Monteiro and colleagues provided a suitable platform by the combination of nanohole arrays and microfluidic system to access to HER2 from aqueous samples. These devices under extraordinary optical

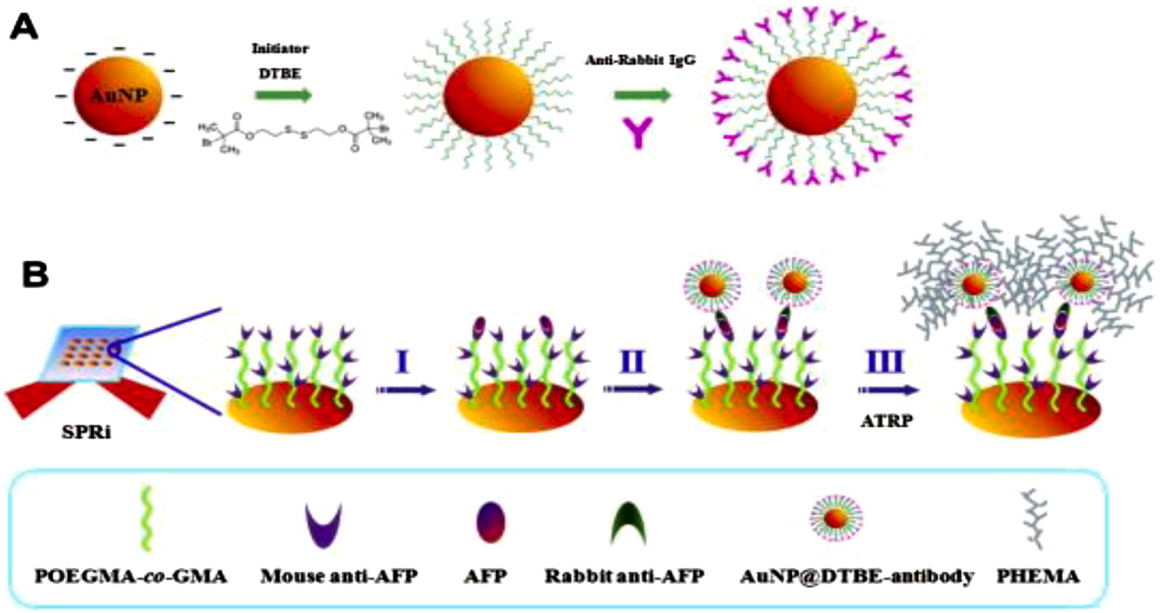

Fig. 2. (A) Preparation of AuNPs@DTBE-antibody. (B) Dual SPRi signal amplification. Sample was flowed on the SPRi chip surface to directly detect AFP target (step I), followed by AuNPs@DTBE–antibody to form immunocomplexes for the first signal amplification (step II), and on-chip ATRP was triggered to further enhance the signal (step III) [123].

Table 3
Examples of alpha-fetoprotein detection by SPR biosensing.

Type of probe	Linear Range	LOD	Clinical sample	Ref.
LSPR integrated with microfluidic	5 – 1000 ng/mL	500 pg/mL	50 % human serum	[124]
SPRi first signal amplification with AuNPs@DTBE–antibody Second signal amplification with ATRP	1–100 ng/mL	5.0 ng /ml 1.0 ng /ml	10 % human serum	[123]
SPR signal enhancement with Fe_3O_4@Au–Ab_2	1.0–200.0 ng /mL	0.65 ng /mL	NA	[121]
LSPR	1 fM -1 × 10^6 fM	91 fM	serum	[119]
LSPR based on GNMA	20–200 ng/mL	24 ng/mL	Serum	[125]

DTBE: [2- (2′-bromoisobutyryloxy)ethyl] disulfide; ATRP: Atom Transfer Radical Polymerization ; Fe3O4: Iron Oxide.

transmission (EOT) phenomenon pass the light through functionalized nanohole arrays and the intensity of the transmitted light depends on the refractive index changes [151]. The LOD of the EOT approach was determined 3 ng/mL. We face challenges to accurate measurement of biomarkers in undiluted complex media such as blood plasma, saliva, and urine or cell lysate. Fouling background associated with comprehensive proteome lead to high nonspecific interaction. Biofluid obtained from cancer cell lysate represents reliable biomarkers at high concentrations to detect cancers or any other illnesses, otherwise biofluid is confined inside the cells and is not readily available in the serum [152]. Recently, ionic liquids have attracted attentions due to simplicity in synthesis and vast applications for surface modification. $[(HS)^{12}C_{12}(COOH)^5\,C_5im]^+\,Br^-$ ionic liquid was applied to detect HER2 biomarkers in the MCF-7 cell lysate [153]. We made an inventory of synthesized polymers to achieve the antifouling surface in SPR-based sensor. Table 6 clearly shows that SPR biosensors coated with polymer were more successful in detecting the lower concentrations of biomarkers because of exclusion of the non-specific binding. As stated by clinical researchers, the combination of two SPR methods for a dynamic

Table 4
Examples of CEA detection by SPR biosensing.

Type of probe	Linear Range	LOD	Clinical sample	Ref.
LSPR	1–1 × 10^6 fM	94 fM	serum	[119]
SPR direct assay	100–400 ng/ml	100 ng /ml		
SPR sandwich assay	3–400 ng /mL	3 ng /mL	buffer	[133]
RAM-capture assay	3–400 ng /mL	3 ng /mL		
SPR with direct detection	10–1000 ng/mL	8 ng/mL	buffer 50 % plasma	[127]
SPR signal enhancement with Ab-AuNPs	0.1–100 ng/mL	30 ng/mL 12 pg/mL 40 pg/mL	buffer 50 % plasma	
SPR with direct detection	8–1000 ng/mL	8 ng/mL	buffer	[130]
SPR signal enhancement with Ab-BSA-AuNP	0 .1–100 ng/ml	100 ng/mL 0.1 ng/mL	plasma plasma	
SSR	200 and 500 ng/mL	More accurate	plasma	[129]
DSR	200 and 500 ng/mL			
SPR direct format	50–500 ng/mL	13.78 ng/mL		
SPR signal enhancement with sandwich format	5–80 ng/mL	3.30 ng/mL	Human serum	[128]
SPR signal enhancement with SA–GNPs	1–60 ng/mL	1.0 ng/mL		
Ab immomilization by NeutrAvidin–protein A	NA	30 ng/mL	NA	[131]
Ab immomilization on bare gold surface		36 ng/mL		
SPR signal enhancement with second and third Ab	25–800 ng/mL	6.2 ng /mL 25 ng/ m	Buffer spiked human serum	[132]

RAM: Rabbit Anti-Mouse apture; BSA: Bovine Serum Albumin; SSR: single surface referencing; DSR: dual surface referencing; SA–GNPs: streptavidin– gold nanoparticles.

Table 5
Examples of carbohydrate antigens detection by SPR biosensing.

Type of biomarker	Type of probe	Linear Range	LOD	Clinical sample	Ref.
CA 125	SPR capacitive system	0.1–40 U/ml 0.05–40 U/mL	0.1 U /mL 0.05 U/ml	human serum	[144]
	PRS	1.0–80 U/ml	0.4 U /mL	PBS	[145]
CA 15.3	SPR based on Au/Cr thin film	1−40 U/mL	0.1 U/mL	diluted pleural fluid samples	[147]
	SPR based on Au/ZnO thin film	1−40 U/mL	0.025 U/mL		
	SPR based on CM5	40−300 U/mL			
	SPR based on Au/ZnO thin film	2.5–20 U/mL	NA	saliva	[148]

Au/Cr: gold/chromium; Au/ZnO: gold/zinc oxide.

Table 6
Antifouling surface for SPR based biosensing methods.

Type of polymer	LOD	Findings	Clinical sample	Ref.
pCBAA pHEMA AT-SAM surface	6×10^4 cells/mL 8×10^5 cells/mL 6×10^5 cells/mL	*E. coli* O157:H7	milk	[155]
pCBAA	NA	Ab immobilization	blood plasma	[156]
poly(HPMA-co-CBMAA)	NA	Hepatitis B	Saliva	[157]
PEG-b-PAMA and N6-PEG	800 fM	factor IX	human plasma	[158]
HA	15−700 nM	BSA	PBS	[159]
pHPMA	600- 6000 ng/ mL	peptidoglycan-polysaccharide	Blood Plasma	[160]
pCBAA	0.5 pM	miRNAs	erythrocyte lysate	[161]
pCB	1 ng/mL	ALCAM	undiluted human plasma	[162]
[(HS)12C12 (COOH)5 C5im]+ Br−	NA	HER2	cancer cell lysates	[153]
CMD	250 ng/mL	Interferon-γ	Spiked plasma	[163]
CMD	8 pg/mL	MMP-9	saliva	[164]

pCBAA: poly(carboxybetaine acrylamide) ; pHEMA: poly(2−hydroxyethyl methacrylate) ; AT-SAM: alkanethiolate self-assembled monolayer poly(HPMA-co-CBMAA): poly[(N-(2-hydroxypropyl) methacrylamide)-co-(carboxybetaine methacrylamide)] ; PEG-b-PAMA: poly(ethylene glycol)-b-poly[2-(*N,N*-dimethylamino)ethyl methacrylate] ; HA: hyaluronic acid; pCB: carboxybetaine polymer; [(HS)12C12(COOH)5 C5im]+ Br− 1-(carboxyethyl)-3-(12-mercaptododecyl)- 1H-imidazolium bromide; CMD: carboxymethyldextran; MMP: matrix metalloproteinases-9.

study and electrochemical to measure high sensitivity can be considered a perfect single sensing platform. In this way, antibody- functionalized Au–GO nano spots were served as a working electrode and Ag/AgCl reference electrodes were inserted on both sides of the nano spots [154]. In accordance with collected data, the electrochemical portion with LOD of 0.001 pM was extremely sensitive as compared to its counterpart with LOD of 10 pM. Table 7 shows the obtained data by SPR methodology for this cancer biomarker.

1.21. Circulating tumor DNA (ctDNA)

Circulating tumor DNA (ctDNA) is a fragment of DNA originates from cancerous cells and circulates in bloodstream. Following tumor growth,

Table 7
Examples of HER2 detection by SPR biosensing.

Type of probe	Linear Range	LOD	Clinical sample	Ref.
SPR based on EOT	NA	3.0 ng /ml	human serum	[151]
SPR direct method SPR signal enhancement with SAv-GNP	NA	3.8 ng/mL 180 pg /mL	Human serum	[165]
SPRi direct method SPRi signal enhancement with SA-QD	1−200 ng/mL 1−200 pg/mL	2.06 ng/mL 25 pg/mL	buffer	[166]
Electrochemical mode SPR mode	0.001–1 × 10^5 pM 10–1 × 10^3 pM	0.001 pM 10 pM	–	[154]

cells die and replaces with new cells. The membrane of dead cells is destroyed and its content, including DNA, is released into the bloodstream [167]. The introduction of the concept of biologic fluid analysis for the diagnosis of cancer attracts attention for liquid biopsy rather than the conventional biopsy whereby the quantification of circulating cancer biomarkers, such as ctDNA, CTCs, miRNA, and exosomes [168]. There is an overlap between normal ranges of 0–100 ng/ml in healthy individuals and 0−1000 ng/mL in cancerous patients, the use of ctDNA concentrations alone is not recommended for cancer diagnosis [169].

ctDNA is a favourable cancer biomarker exhibits both the genetic and epigenetic changes ongoing in the tumor. A plasmonics-based sensor has been developed to evaluate point mutations in KRAS-gene related to pancreatic ductal adenocarcinoma. GNRs conjugated with mutant-specific peptide nucleic acid (PNA) probe were hybridized with complementary ctDNA in patient sample [170]. Along with identification of the two distinct point mutations at E542 K and E545 K of the PIK3CA-gene by using PNA as described above, epigenetic alterations were also detected by immunogold colloids. Simultaneous detection of genetic changes and mCpG sites by colorimetric detection assay increased sensitivity up to 4-fold [171].

1.22. ALCAM

Activated leukocyte cell adhesion molecule (ALCAM) is a glycoprotein belonging to superfamily immunoglobulin that takes a role in cell-cell interactions, intracellular signal transduction pathways, hematopoiesis, neutrophil transendothelial migration, T-cell activation, and inflammation [172]. ALCAM /CD166 was known as a potential biomarker breast [173], thyroid [174] and colorectal cancer [175].

Scientists attempted to produce high-throughput sensors to monitor multiple biomarkers ALCAM, hCG, and TAGLN2 simultaneously. Surface functionalization with various antibodies by conventional microfluidic methods is relatively complex. Micro spotting of thiolated oligonucleotide performed antibody immobilization and ethylene glycol terminated alkanethiol on the surface followed by hybridization to the conjugated antibodies with complementary sequence. The LODs of the SPR sensors for Ab-DNA array in the plasma sample came 45 ng/mL and Ab-OEG array in the identical setting were 6 ng/mL; obviously, the latter has the greatest sensitivity [176,177]. Eskandari and collaborators proposed detecting colorimetric ALCAM-gene that does not require expensive equipment. In the MgCL2 solution, the DNA-Au NPs probes are agglomerated in the absence of complementary sequences and the color changes from red to purple. In the presence of complementary sequences with the nanoprobes, hybridization occurred which prevents agglomeration and no color change occurred. The LOD of ALCAM was estimated 300 fM which was extremely accurate and sensitive as compared to the other diagnostic methods [178]. Table 8 illustrated the archived data by SPR methodology for ALCAM cancer biomarker.

Table 8
Examples of ALCAM detection by SPR biosensing.

Type of probe	Linear Range	LOD	Clinical sample	Ref.
SPR based on Ab-DNA conjugate array	10−1000 ng/mL	7 ng/mL 45 ng/mL	Buffer 10 % blood plasma	[176]
SPRi based on Ab-OEG array	NA	10 ng/mL 6 ng/mL	Buffer 10 % human serum	[177]
LSPR based on DNA-functionalized AuNPs	NA	300 fmol/μL	NA	[178]
LSPR based on GNR functionalized by PEG	NA	15 pM	PBS	[179]
ELISA SPR direct detection SPR signal enhancement with pAb	1–128 ng/mL 0.5–4 ng/mL	0.1 ng/mL 1 ng/mL 0.5 ng/mL	Buffer	[180]

OEG: oligo(ethylene glycol) ; ELISA: enzyme−linked immunosorbent assay.

1.23. Human chorionic gonadotropin (hCG)

Human chorionic gonadotropin (hCG) or pregnancy hormone is a hormone secreted by the cells that encircle the growing embryo; finally, the placenta will be formed of these cells [181]. The levels of hCG in premenopausal (nonpregnant) and postmenopausal women are less than 1.0 IU/L and 7.0 IU/L, respectively [182]. Increased levels of hCG can be causes of ectopic pregnancy, abortion, and some cancers. Therefore, the presence of this hormone in the blood of people who are not pregnant can be considered a symptom of cancer and might be worth exploring [181].

Hyperglycosylated hCG is an over-glycosylated isoform of hCG which is associated with a group of pregnancy-related tumors like choriocarcinoma, invasive mole *i.e,* gestational trophoblastic disease, and germ cell malignancies. Furthermore, hyperglycosylated hCG can be elevated in the serum of patients with colon, lung, cervical, ovarian, and bladder cancer. Therefore, the distinction between hyperglycosylated hCG variant associated with gestational trophoblastic disease and malignant germ cell tumors and the type produced during pregnancy can be essential in diagnosis. The ability of several lectins to bind to carbohydrate components of the hCG was investigated by a lectin-based sandwich method. In the urine sample of patients suffering from cancer as comparing to normal pregnant women, less than fifty percent of lectins presented different binding in the former group [183]. Table 9 supports the conclusion that MNP as signal amplifiers reduce the LOD of hCG. The LODs attained by different detection strategies including SPR direct detection, enhanced signals with MNP-Ab_2 without an external magnetic field, and enhanced signals with an external magnetic field were 6 nM, 4.5 pM, and 0.45 pM, respectively. By analyzing acquired data, simultaneous application of MNPs with an external magnetic field significantly reduced the LOD value [184]. Špringer and teammates also achieved an incredibly sensitive approach to detect hCG whose biggest advantage is preventing nonspecific binding. In the sampling method, which involves a combination of microfluidic, system and SPR-based sensor the system has two independent inputs for sequential injections of sample and washing buffer. To eliminate interfering factors, the wash step is performed after each injection of the sample and sensor response is recorded at the end of each wash step. They were able to reduce the LOD from 50 ng/mL to 10 ng/mL by replacing the sampling method with the conventional referencing [185]. Studies show that DNA sequence diversity and specificity in base pairs can be used as a binding agent in the multichannel sensors' manufacturing. Researchers have made it possible to detect multiple markers hCG, FSH, and hLh in a mixed sample simultaneously by immobilizing the ssDNA-conjugated antibody [186]. The reported LODs about this method were13 ng/mL in the buffer sample and 100 ng/mL in the plasma sample. Chiu and colleagues have

Table 9
Examples of hCG detection by SPR biosensing.

Type of probe	Linear Range	LOD	Clinical sample	References
SPR based on Ab-DNA conjugate array	10−100 ng/mL	13 ng/mL 100 ng/mL	Buffer 10 % plasma	[176]
SPR based on ssDNA/OEG SAMs	1 μg/mL	NA	NA	[186]
SPR signal enhancement with Ab_2	46 - 415mIU/ml	46.4 mIU/mL	Urine	[190]
SPR with direct detection	0.5 pM - 0.5 μM	6 nM	PBS	[184]
SPR signal enhancement with Ab_2		45 pM		
SPR signal enhancement with MNP-dAb without external magnetic field		4.5 pM		
βhCG was incubated with MNP-dAb with external magnetic field		0.9 pM		
SPR signal enhancement with MNP-dAb with external magnetic field		0.45 pM		
SPRF	NA	80 mIU/mL	Serum	[191]
SPR baesd GO-peptide chips	0.065-250nM	0.065 nM	PBS	[187]
conventional referencing sampling method	50–500 ng/mL	50 ng/mL 10 ng/mL	50 % blood plasm	[185]
Combining SPRi with polarization contrast	0.5−10 μg/mL	500 ng/mL	PBS	[192]

ssDNA/OEG SAMs: single strand/oligo(ethylene glycol) self-assembled monolayer.

shown the potentiality of graphene oxide sheets to improve surface plasmon properties. They have created a GO-peptide-based chip with the LOD less than 0.065 ng/mL. [187]. Carbon-based nanomaterials have been utilized to enhanced SPR sensing applications such as carbon nanotubes and graphene. Creating a thin film of Au coated by graphene in a conventional SPR device was at first proposed by Wu et al. who intended to improve sensitivity in 2010. They reviewed the effect of the number of graphene layers on the SPR sensitive and and demonstrated that the sensitivity of the sensor enhances as the number of graphene layers increases. They demonstrated the sensitivity of the sensor enhanced as the number of graphene layers increased [188]. The main reason was attributed to the charge transfer from the graphene surface to the Au layer surface. Plasmonic properties of graphite sheets can be regulated by oxygen functional groups [189].

1.24. Vascular endothelial growth factor (VEGF)

Vascular endothelial growth factors (VEGFs) are known as principal drivers of angiogenesis. They encourage the growth of new blood tumor vessels. Also, they are contributing factors to their permeability. Because of the correlation between VEGF levels and tumor growth, VEGF levels are often evaluated [193].

There are many biomarkers in biological samples with very low concentrations; VEGF with a near picomolar concentration is a member of this group. Enzymatic amplification is often required to measure proteins' concentrations who has less sub-picomolar level. HRP-conjugated antibodies were introduced on the RNA microarray-VEGF surface to set up a sandwich structure; because of the reaction of TMB to HRP, a colored precipitate was formed on the surface. In comparison with direct detection, using HRP-Ab_2 resulted in 100-folds progress sensitivity. The minimal achievable LOD was 1 pM [194].

In addition, available antibody-based approaches for cancer detection are multi-stage and require a high sample volume. An aptasensor was designed to detect and signal amplification in one-step. As illustrated in Fig. 3, the fluorophore-conjugated aptamer has been previously immobilized on GNPs through an electrostatic force. In the absence of VEGF165, electrostatic force overcame spontaneous folding energy, and aptamer remained attached to the surface. In the presence of the target molecule, conformational changes were induced to aptamers, aptamer-VEGF165 complex were separated, and subsequently fluorophore radiation diminished. The decay rate of fluorescence radiation depends on the distance between it and the plasmonic nanoparticle; as fluorophore approaches the nanoplasmonic, radiation increases. Since fluorophore absorption maximum wavelength was matched up with the LSPR peak wavelength, extra signal amplification was done [195].

Enhanced signals by fluorophore seems to be more sensitive in comparison with ELISA. There has always been an effort to minimize and comfortably use the biosensor for consumers. Aptamers and optical fibers are two important components of optical sensors that make this goal close to reality. Immobilization of aptamers onto the optical fibers surface formed a user-friendly and low-cost sensor to identify the VEGF with high sensitivity. Aptamer immobilization was carried out by means of two different ways; the first method contained only aptamer (Apt) and the second one included aptamer along with mercaptoethanol (passivation agent) (Apt–MPET). The MPET took on a role in the proper orientation of aptamer. The reported LODs were 3 nM for Apt and 0.8 nM for Apt–MPET. All the data pointed to the conclusion that Apt–MPET had an impressive achievement. These compact devices which are facilitating analyses are promising point-of-care method for diagnostic and prognostic purposes [196]. Table 10 gives details for studies by SPR methodology for VEGF cancer biomarker.

1.25. Tumor necrosis factor (TNF)

Tumor necrosis factor (TNF) is a group of pro-inflammatory cytokines predominantly which are secreted by macrophages and monocytes as well as tumor cells. They contribute to the various range of signaling route inflammation, viral replication, apoptosis, tumorigenesis, angiogenesis, cell proliferation, and differentiation [197]. In addition, one of their biological activities can be a driver of progression in colorectal [198], breast cancer [199], and predictive marker to determine septic complications after burn [200]. Some signal enhancers, namely GNRs GNPs, have been employed to detect the TNF. The achieved LODs used by SPR direct detection and enhanced signals by SAv-GNP were 1.2 ng/mL and 11.6 pg/mL, respectively. Experimental results led to the conclusion, SAv-GNP has significantly boosted sensitivity. To draw a parallel between the other two studies which used SAv-GNP and SAv-GNR for signal enhancement, to detect TNF, shows that the latter boosted signals more and produced less LOD [201,202].

Table 10
Examples of VEGF detection by SPR biosensing.

Type of probe	Linear Range	LOD	Clinical sample	Ref.
POF-SPR Apt POF-SPR Apt–MPET	0–200 nM	3 nM 0.8 nM	NA	[196]
SPRi based on RNA aptamer signal enhancement with HRP	NA	10 nM 1 pM	NA	[194]
LSPR based on the fluorophore-conjugated aptamer	1.25 pM -1.25 μM	NA	diluted serum and saliva	[195]
ELISA	5 pg/mL - 2 ng/mL			

Apt–MPET: aptamer –mercaptoethanol.

1.26. Interleukin

Interleukins are subsets of the populated family of cytokines that take in various processes including immunoregulatory, inflammation, modulate cell growth, migration, maturation, proliferation, adhesion as well as activation and differentiation of immune cells. IL-1, IL-4, IL-6 contribute to cancer progression, despite IL-2 regarded as anti-inflammatory cytokines that were applied to improve the host immunity versus tumor [203]. IL-5 exerts both pro- and anticancer influence on the tumor through eosinophilia [204] and IL-3 is responsible for inducing angiogenesis [205]. IL-8 as a motogenic and mitogenic agent plays an important role in tumor growth. Investigators of UCLA found increased IL-8 concentrations in salivary of patients suffering from oropharyngeal squamous cell carcinoma (OSCC). Results indicate that IL-8 has the capability to diagnose of OSCC. The saliva sample is superior to serum or urine due to its high volume and non-invasive method of sample collection. Due to the complex composition of saliva, the carboxymethyl dextran sodium salt was added to the sample in order to minimize non-specific interaction; this salt competed for binding with the dextran layer and immobilized antibody on it. The researchers announced LODs of 2.5 pM in the buffer sample and 184 pM in the saliva sample [206]. IL-1, IL-6 and TNF-α are involved in the healing process of chronic ulcers. The researchers developed a fiberoptic-based-SPR sensor with a coating of NHS-MHA to a reliable analysis in complex environments. This SPR biosensing strategy has achieved a great deal of sensitivity, which was reported as follows: 0.45 ng/mL for IL-6, 0.29 ng/mL for IL-1, and 1.3 ng/mL for TNF-α. Fiberoptic-based biosensors eliminate old time-consuming methods and greatly facilitate the clinical studies. The bedside analysis of cytokines assist to make real-time treatment decisions for patients suffering from chronic ulcers [207].

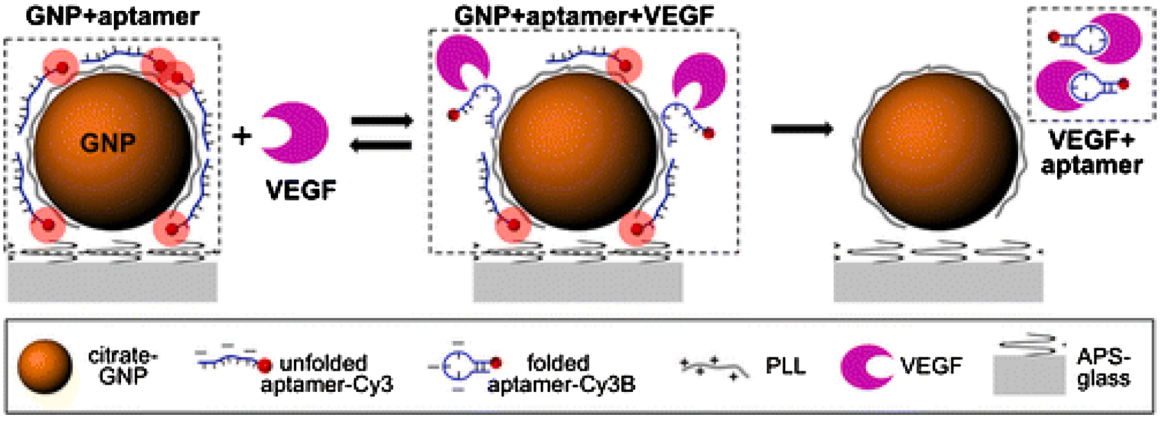

Fig. 3. Scheme of detection mechanism of the aptasensor for VEGF165 based on SEF [171].

1.27. Interferon-γ (IFN-γ)

As a key character cellular immunity, IFN-γ is capable of organizing various defensive functions to augment immune responses during infectious diseases and cancers. Researches prove that interferons exhibit dual behaviors against tumors; not only they suppresses the tumor, but also accelerate its growth with features of the immunoevasive [208, 209].

To date, diverse types of affinity biosensors have been described based on various bioreceptors such as antibodies, aptamers, and phages. As depicted in Fig. 4, the aptamer probe consists of a combination of two structural motifs; an INF-ɤ recognition site and a streptavidin binding site in the form of a hairpin. As long as INF-ɤ was absent, the probe kept inactive and the complementary sequences of the two aptamers are hybridized together. The target molecule induced conformational changes for SA binding, following that SA binding signal was improved [210].

Microfluidic-based SPR technology has been expanded with the same signal amplification approach. In a nutshell, this biosensor has promoted 3.3-fold the sensitivity as compared to the other SPR biosensor [179]. Tsai et al. have found an 8-fold increase in sensitivity to anti-IFN-γ immobilization by bithiophene-based biolinker compared to dextran. The main reason for this amplification of signal attributed to the bithiophene biolinker thickness reduction. In addition, the bithiophene-based biolinker sensor exhibited good regeneration capability [211]. Given the fact that multiple cell subpopulation of leukocytes release identical cytokines, the attribution of the cytokine released to a particular subpopulation of leukocytes is challenging. Stybayeva et al. merged two strategies of cell separation and SPR sensor to determine $CD4^+$ T-cells-secreted interferon. They exposed the blood to a chamber that was functionalized by anti-CD4 antibodies leading to $CD4^+$ T-cells being separated from other cells. Subsequently, they applied mitogenic stimulation to the cells; cell culture media transferred to the chip surface which functionalized with IFN-Abs [212]. Table 11 summarize examples of Immune cells detection by SPR based biosensing methods.

1.28. CD24 and CD44 as cancer stem cell marker

Cancer Stem Cells (CSCs) are a small subset of cancerous cells located in depth of tumors and they are involved in the onset and relapse of them. CSCs behave like normal stem cells and they have self-renewal and differentiation properties. Findings offer that CSCs can be a good target in the treatment and prevention of tumor invasion which is the result of a poor diagnosis [218]. Lee and coworkers could identify the CD24 and CD44 cell surface of breast cancer cells by designing an innovative LSPR biosensor. The DNA-Au NPs probes comprised of a pointer particles modified by anti-CD44 antibody (or anti-CD24 antibody) and ssDNA as well as an enhancer particles modified by Raman tages and complementary ssDNA. Pointer particles targeted the surface marker sites and enhancer particles hybridized ssDNA sequence of pointer particles. Au NPs' networks grew as a result of the accumulation of enhancer particles surrounding pointer particle which is detectable with SPR and SERS [219]. Another research team under strict supervision of Yu and colleagues used individual GNRs to provide multiple detection capabilities for CD24, CD44, and CD49f surface marker by spectral imaging systems (PARISS). Dark field images of GNR attached to the surface markers were obtained through collection of scattered light; consequently, GNR emerges as the light spots on the black background [220].

1.29. Ferritin

Ferritin is a versatile protein whose role in the storage and metabolism of iron is well known. However, recent studies have shown ferritin participates in cancer signaling pathways. Elevated ferritin in serum cancer patients is associated with cancer progression, angiogenesis, therapeutic resistance, and poor prognosis [221]. The typical range of ferritin concentration for healthy adult men and women is under 200 ng/mL and 300 ng/mL, respectively [222]. Ferritin as a nonspecific marker was measured by a variety of self-assembled monolayer including carboxymethyl dextran [223] and cystamine-glutaraldehyde [222]. The investigators made a comparison between cysteamine–glutaraldehyde and carboxymethyl dextran and suggested that, considering the LOD, the former is a superior linker.

1.30. Serum collagen type IV(COLIV)

COLIV is an important constituent of basement membranes that encloses tumors' vasculature. COLIV is synthesized during angiogenesis and degenerates into the bloodstream when metastasis occurs. COLIV changes during treatment can be followed as an indicator of response to anti-angiogenic treatment [224]. SPRi biosensors were developed for COLIV concentration measurements in the blood plasma of burn patients and breast cancer patients. In this study, the LOD was 2.4 ng/mL within a dynamic range of 10−300 ng/mL. Earlier than SPR technique, the corresponding COLIV concentrations were mainly obtained by ELISA technique which, from the view point of authors, SPR biosensors demonstrate more potential reproducibility and rapid response versus ELISA [225,226].

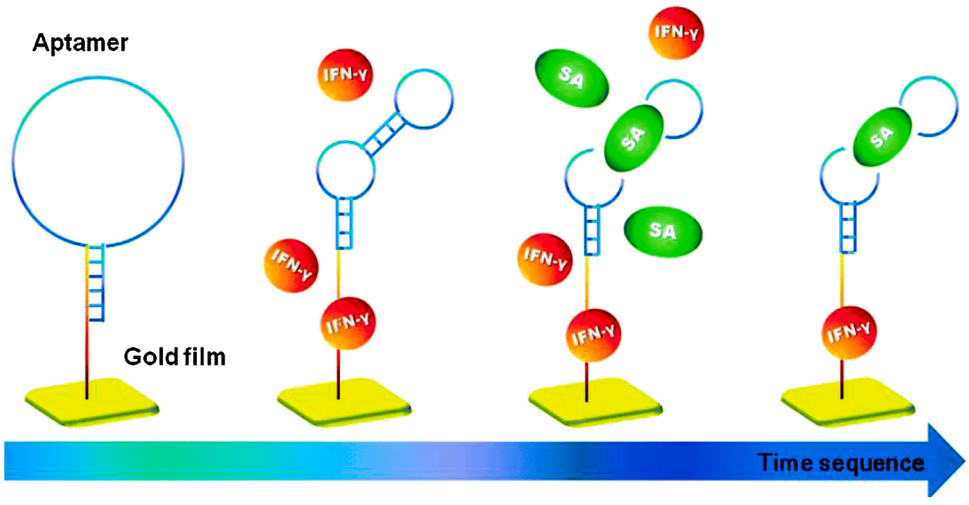

Fig. 4. Schematic representations of the process for enhancement IFN-ɤ detection [186].

Table 11
Examples of TNF, Interleukin and Interferon-γ detection by SPR biosensing.

Type of biomarker	Type of probe	Linear Range	LOD	Clinical sample	Ref.
TNF	SPR direct detection	1.4–333 ng/mL	1.2 ng/mL	buffer	[201]
	SPR signal enhancement with SAv-GNPs	0 −150 pg/mL	11.6 pg/mL 54.4 pg/mL	buffer spiked serum	
	SPR signal enhancement with SAv-GNRs	NA	0.03 pM	NA	[202]
	SPR signal enhancement with two kind of Ab_2 (IL-8)	1−195 pM	2.5 pM 184 pM	buffer Saliva	[206]
Interleukin	FO-SPR based with a coating of NHS-MHA IL-6 IL-1 TNF-α	1 -100 ng/mL	0.45 ng/mL 0.92 ng/mL 0.29 ng/mL 0.95 ng/mL 1.3 ng/mL 0.77 ng/mL	HBS CCM HBS CCM HBS CCM	[207]
	SPR based on SA- aptamer	0.3 - 333 nM	33 pM	buffer	[210]
	SPR based on SA- aptamer integrated with microfluidic	0.01 - 100 nM	10 pM	NA	[213]
	LSPR signal enhancement with DNA- GNRs in a competitive assay	0.1−10 nM	0.1 nM	BSA	[214]
Interferon-γ	FO- LSPR	2−500 pg/mL	1 pg/mL	PBS	[94]
	LSPR based on gold NIs chip signal enhancement with HRP	NA	2 nM 0.54 nM	PBS	[215]
	Direct immunoassay SPR signal enhancement with HRP	0.01−100 ng/mL 0.01−100 ng/mL	0.071 0.0022	PBS	[216]
	Bithiophene biolinker Dextran biolinker	2.1–66.6 nM	Enhanced signal 8-fold	NA	[211]
	SPRi signal enhancement with HRP	NA	1 ng/mL	NA	[217]

NIs: nano-island; CCM: cell culture medium.

1.31. Conclusion and outlook

The purpose of this manuscript was to introduce plasmonic sensors and express the importance of markers in the early cancer detection in oncology field. Among all sensors and methods, plasmonic sensors have a privileged position because of their characteristics such as high sensitivity and specificity, label-free, non-invasive, real-time, simpler miniaturization, portability, and multiplexing. The performance of these sensors is as good as the commercially available sensors and even better in some cases. However, the sensitivity of SPR sensors is insufficient to detect tiny amounts of all molecules that is important to the early detection of diseases, environmental protection, and food quality control. Along with the development of nanotechnology, plasmonic sensors have become powerful tools for detection. In general, there are two main strategies in signal amplification based on nanomaterials**:)** i) application of nanomaterials as amplification tags (*e.g.* metallic nanoparticles, magnetic nanoparticles),**)ii)** the SPR sensing substrate coated by nanomaterials (*e.g.* carbon-based nanostructures). Nanomaterials exert a powerful influence over desired resonance, coupling modes, and high density of chemical bindings. A combination of optical fibers, with their unique properties, with plasmonic sensors make inexpensive, portable and in vivo usable devices. In addition, the upcoming generation of these sensors will be integrated with microfluidic systems for POC applications. Although propagating film SPR platform is the most eminent plasmonic sensing device, its high-cost and high-tech equipment are challenges for users. Recent sensing platforms being developed based on LSPRs (*e.g* plasmon coupling and plasmonic nanopore) hold great promise as a sensitive and economical device. The agglomeration of nanoparticles and cross-reactivity antibodies are major constraints on this technology. In the vision of healthcare technology, the diagnosis strategy is moving toward remote diagnosis, so sensors will become ubiquitous in the coming years and plasmonic sensors will make a major contribution to the health care revolution.

Declaration of Competing Interest

The authors report no declarations of interest.

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References

[1] F. Bray, J. Ferlay, I. Soerjomataram, R.L. Siegel, L.A. Torre, A. Jemal, CA Cancer J. Clin. 68 (2018) 394.
[2] J.D. Schiffman, P.G. Fisher, P. Gibbs, Am. Soc. Clin. Oncol. Educ. Book 35 (2015) 57.
[3] J.V. Frangioni, J. Clin. Oncol. 26 (2008) 4012.
[4] M.V. Brown, J.E. McDunn, P.R. Gunst, E.M. Smith, M.V. Milburn, D.A. Troyer, K. A. Lawton, Genome Med. 4 (2012) 33.
[5] R. Lambert, World J. Gastrointest. Endosc. 4 (2012) 518.
[6] H. Horigome, T. Nomura, K. Saso, M. Itoh, T. Joh, H. Ohara, J. Gastroenterol. Hepatol. 14 (1999) 559.
[7] L.E. Moore, Clin. Tech. Small Anim. Pract. 18 (2003) 250.
[8] I. Raiko, I. Sander, D.G. Weber, M. Raulf-Heimsoth, A. Gillissen, J. Kollmeier, A. Scherpereel, T. Brüning, G. Johnen, BMC Cancer 10 (2010) 242.
[9] K. Lind, M. Kubista, J. Immunol. Methods 304 (2005) 107.
[10] J. Tian, L. Zhou, Y. Zhao, Y. Wang, Y. Peng, S. Zhao, Talanta 92 (2012) 72.
[11] J.-L. Pujol, J. Grenier, J.-P. Daurès, A. Daver, H. Pujol, F.-B. Michel, Cancer Res. 53 (1993) 61.
[12] D.L. Aisner, S.B. Sams, Diagn. Cytopathol. 40 (2012) 511.
[13] P. Maruvada, W. Wang, P.D. Wagner, S. Srivastava, Biotechniques 38 (2005) S9.
[14] P.R. Srinivas, B.S. Kramer, S. Srivastava, Lancet Oncol. 2 (2001) 698.
[15] B. Bohunicky, S.A. Mousa, Nanotechnol. Sci. Appl. 4 (2011) 1.
[16] T. Vo-Dinh, B. Cullum, Fresenius J. Anal. Chem. 366 (2000) 540.
[17] Y. Huang, J. Xu, J. Liu, X. Wang, B. Chen, Sensors 17 (2017) 2375.
[18] J. Ngeh-Ngwainbi, A.A. Suleiman, G.G. Guilbault, Biosens. Bioelectron. 5 (1990) 13.
[19] L.M. Lechuga, Compr. Anal. Chem. 44 (2005) 209.
[20] S. Zeng, D. Baillargeat, H.-P. Ho, K.-T. Yong, Chem. Soc. Rev. 43 (2014) 3426.
[21] J.P. Oliveira, A.R. Prado, W.J. Keijok, P.W.P. Antunes, E.R. Yapuchura, M.C. C. Guimarães, Sci. Rep. 9 (2019) 1.
[22] X. Wang, Y. Li, H. Wang, Q. Fu, J. Peng, Y. Wang, J. Du, Y. Zhou, L. Zhan, Biosens. Bioelectron. 26 (2010) 404.
[23] N. Cennamo, G. D'agostino, A. Donà, G. Dacarro, P. Pallavicini, M. Pesavento, L. Zeni, Sensors 13 (2013) 14676.
[24] M. Tu, T. Sun, K. Grattan, Sens. Actuators B Chem. 191 (2014) 37.
[25] A.J. Haes, L. Chang, W.L. Klein, R.P. Van Duyne, J. Am. Chem. Soc. 127 (2005) 2264.
[26] S. Shams, B. Bakhshi, T.T. Moghadam, M. Behmanesh, J. Nanobiotechnol. 17 (2019) 43.
[27] J. Khodaveisi, A.M.H. Shabani, S. Dadfarnia, D. Saberi, Spectrochim. Acta A. Mol. Biomol. Spectrosc. 179 (2017) 11.
[28] M. Zeinoddini, A. Azizi, S. Bayat, Z. Tavasoli, Plasmonics 13 (2018) 583.
[29] J. Kim, S.Y. Oh, S. Shukla, S.B. Hong, N.S. Heo, V.K. Bajpai, H.S. Chun, C.-H. Jo, B.G. Choi, Y.S. Huh, Biosens. Bioelectron. 107 (2018) 118.
[30] E. Aoyama, M. Takigawa, Evaluation of Molecular Interaction Between CCN2 Protein and Its Binding Partners by Surface Plasmon Resonance (SPR), Springer, 2017, pp. 169.

[31] M.J. Linman, J.D. Taylor, H. Yu, X. Chen, Q. Cheng, Anal. Chem. 80 (2008) 4007.
[32] A.M. Vilardell, N. Cinca, A. Jokinen, N. Garcia-Giralt, S. Dosta, I. Cano, J. Guilemany, J. Funct. Biomater. 7 (2016) 23.
[33] J. Pollet, F. Delport, K.P. Janssen, K. Jans, G. Maes, H. Pfeiffer, M. Wevers, J. Lammertyn, Biosens. Bioelectron. 25 (2009) 864.
[34] A. Šakanovič, V. Hodnik, G. Anderluh, Surface Plasmon Resonance for Measuring Interactions of Proteins With Lipids and Lipid Membranes, Springer, 2019, pp. 53.
[35] C.-H. Lai, J. Hütter, C.-W. Hsu, H. Tanaka, S. Varela-Aramburu, L. De Cola, B. Lepenies, P.H. Seeberger, Nano Lett. 16 (2016) 807.
[36] S.H. Kwon, B.J. Hong, H.Y. Park, W. Knoll, J.W. Park, J. Colloid Interface Sci. 308 (2007) 325.
[37] M. Rusnati, P. Chiodelli, A. Bugatti, C. Urbinati, Crit. Rev. Microbiol. 41 (2015) 238.
[38] C.M. Miyazaki, F.M. Shimizu, M. Ferreira, Surface Plasmon Resonance (SPR) for Sensors and Biosensors, Elsevier, 2017, pp. 183.
[39] M.L. Brongersma, P.G. Kik, Surface Plasmon Nanophotonics, Springer, 2007.
[40] H.R. Gwon, S.H. Lee, Mater. Trans. 51 (2010) 1150.
[41] Y. Tang, X. Zeng, J. Liang, J. Chem. Educ. 87 (2010) 742.
[42] J.N. Anker, W.P. Hall, O. Lyandres, N.C. Shah, J. Zhao, R.P. Van Duyne, Biosensing With Plasmonic Nanosensors, World Scientific, 2010, pp. 308.
[43] H. Malekzad, P.S. Zangabad, H. Mohammadi, M. Sadroddini, Z. Jafari, N. Mahlooji, S. Abbaspour, S. Gholami, M.G. Houshangi, R. Pashazadeh, TrAC Trends Anal. Chem. 100 (2018) 116.
[44] I. Ament, J. Prasad, A. Henkel, S. Schmachtel, C. Sonnichsen, Nano Lett. 12 (2012) 1092.
[45] L. Guo, A.R. Ferhan, K. Lee, D.-H. Kim, Anal. Chem. 83 (2011) 2605.
[46] R.T. Hill, K.M. Kozek, A. Hucknall, D.R. Smith, A. Chilkoti, ACS Photonics 1 (2014) 974.
[47] S.M. Marinakos, S. Chen, A. Chilkoti, Anal. Chem. 79 (2007) 5278.
[48] G. Kalyuzhny, A. Vaskevich, M.A. Schneeweiss, I. Rubinstein, Chem. Eur. J. 8 (2002) 3849.
[49] A.J. Haes, R.P. Van Duyne, J. Am. Chem. Soc. 124 (2002) 10596.
[50] M. Seydack, Biosens. Bioelectron. 20 (2005) 2454.
[51] S. Schultz, D.R. Smith, J.J. Mock, D.A. Schultz, Proc. Natl. Acad. Sci. 97 (2000) 996.
[52] R. Gordon, D. Sinton, K.L. Kavanagh, A.G. Brolo, Acc. Chem. Res. 41 (2008) 1049.
[53] A.G. Brolo, R. Gordon, B. Leathem, K.L. Kavanagh, Langmuir 20 (2004) 4813.
[54] Y. Wang, A. Kar, A. Paterson, K. Kourentzi, H. Le, P. Ruchhoeft, R. Willson, J. Bao, ACS Photonics 1 (2014) 241.
[55] C. Sönnichsen, B.M. Reinhard, J. Liphardt, A.P. Alivisatos, Nat. Biotechnol. 23 (2005) 741.
[56] J.I. Chen, Y. Chen, D.S. Ginger, J. Am. Chem. Soc. 132 (2010) 9600.
[57] J. Jung, K. Na, J. Lee, K.-W. Kim, J. Hyun, Anal. Chim. Acta 651 (2009) 91.
[58] K. Baryeh, S. Takalkar, M. Lund, G. Liu, Introduction to Medical Biosensors for Point of Care Applications, Elsevier, 2017, pp. 3.
[59] T. Hermann, D.J. Patel, Science 287 (2000) 820.
[60] E.J. Cho, J.-W. Lee, A.D. Ellington, Annu. Rev. Anal. Chem. 2 (2009) 241.
[61] S.M. Nimjee, R.R. White, R.C. Becker, B.A. Sullenger, Annu. Rev. Pharmacol. Toxicol. 57 (2017) 61.
[62] Q. Wu, L. Wu, Y. Wang, Z. Zhu, Y. Song, Y. Tan, X.-F. Wang, J. Li, D. Kang, C. J. Yang, Biosens. Bioelectron. 80 (2016) 1.
[63] A. Autour, S.C. Jeng, A.D. Cawte, A. Abdolahzadeh, A. Galli, S.S. Panchapakesan, D. Rueda, M. Ryckelynck, P.J. Unrau, Nat. Commun. 9 (2018) 1.
[64] S.H. Najafi-Shoushtari, M. Famulok, Blood Cells Mol. Dis. 38 (2007) 19.
[65] A. Lakhin, V. Tarantul, L. Gening, Acta Naturae 5 (2013).
[66] H.H. Nguyen, S.H. Lee, U.J. Lee, C.D. Fermin, M. Kim, Materials 12 (2019) 121.
[67] Z. Rosenzweig, R. Kopelman, Sens. Actuators B Chem. 36 (1996) 475.
[68] J. Polster, G. Prestel, M. Wollenweber, G. Kraus, G. Gauglitz, Talanta 42 (1995) 2065.
[69] O.I. Berthuy, L.J. Blum, C.A. Marquette, Biosensors 6 (2016) 2.
[70] L. Su, W. Jia, C. Hou, Y. Lei, Biosens. Bioelectron. 26 (2011) 1788.
[71] A. Schmidt, C. Standfuss-Gabisch, U. Bilitewski, Biosens. Bioelectron. 11 (1996) 1139.
[72] Y. Nakane, I. Kubo, Thin Solid Films 518 (2009) 678.
[73] T.A. Pollak, J.P. Rogers, R.G. Nagele, M. Peakman, J.M. Stone, A.S. David, P. McGuire, Schizophr. Bull. 45 (2019) 233.
[74] W. Albert, Monoclonal Antibodies: Advantages and Disadvantages in Production of Test Systems, Springer, 1985, pp. 83.
[75] X. Zeng, Z. Shen, R. Mernaugh, Anal. Bioanal. Chem. 402 (2012) 3027.
[76] E.J. O'Reilly, P.J. Conroy, S. Hearty, T.E. Keyes, R. O'Kennedy, R.J. Forster, L. Dennany, RSC Adv. 5 (2015) 67874.
[77] B. Spencer, S. Brüschweiler, M. Sealey-Cardona, E. Rockenstein, A. Adame, J. Florio, M. Mante, I. Trinh, R.A. Rissman, R. Konrat, Acta Neuropathol. 136 (2018) 69.
[78] K.L. Vigor, P.G. Kyrtatos, S. Minogue, K.T. Al-Jamal, H. Kogelberg, B. Tolner, K. Kostarelos, R.H. Begent, Q.A. Pankhurst, M.F. Lythgoe, Biomaterials 31 (2010) 1307.
[79] R.-M. Lu, Y.-L. Chang, M.-S. Chen, H.-C. Wu, Biomaterials 32 (2011) 3265.
[80] Y. Tan, T. Tian, W. Liu, Z. Zhu, C.J. Yang, Biotechnol. J. 11 (2016) 732.
[81] S. Balasubramanian, I.B. Sorokulova, V.J. Vodyanoy, A.L. Simonian, Biosens. Bioelectron. 22 (2007) 948.
[82] V. Nanduri, A.K. Bhunia, S.-I. Tu, G.C. Paoli, J.D. Brewster, Biosens. Bioelectron. 23 (2007) 248.
[83] B. Bakhshinejad, M. Sadeghizadeh, World J. Gastroenterol. WJG 20 (2014) 11671.
[84] N. Goossens, S. Nakagawa, X. Sun, Y. Hoshida, Transl. Cancer Res. 4 (2015) 256.
[85] D.J. Slamon, B. Leyland-Jones, S. Shak, H. Fuchs, V. Paton, A. Bajamonde, T. Fleming, W. Eiermann, J. Wolter, M. Pegram, N. Engl. J. Med. 344 (2001) 783.
[86] S. Paik, S. Shak, G. Tang, C. Kim, J. Baker, M. Cronin, F.L. Baehner, M.G. Walker, D. Watson, T. Park, N. Engl. J. Med. 351 (2004) 2817.
[87] Y. Li, Y. Zhang, M. Zhao, Q. Zhou, L. Wang, H. Wang, X. Wang, L. Zhan, Chem. Commun. 52 (2016) 3959.
[88] W.J. Catalona, A.W. Partin, K.M. Slawin, M.K. Brawer, R.C. Flanigan, A. Patel, J. P. Richie, J.B. DeKernion, P.C. Walsh, P.T. Scardino, JAMA 279 (1998) 1542.
[89] D. Damborska, T. Bertok, E. Dosekova, A. Holazova, L. Lorencova, P. Kasak, J. Tkac, Microchim. Ichnoanal. Acta 184 (2017) 3049.
[90] W.T. Kim, S.J. Yun, W.-J. Kim, Int. Neurourol. J. 23 (2019) 5.
[91] B. Erol, M.T. Gulpinar, G. Bozdogan, S. Ozkanli, K. Onem, G. Mungan, S. Bektas, H. Tokgoz, B. Akduman, A. Mungan, Kaohsiung J. Med. Sci. 30 (2014) 545.
[92] H.S. Jang, K.N. Park, C.D. Kang, J.P. Kim, S.J. Sim, K.S. Lee, Opt. Commun. 282 (2009) 2827.
[93] J. Wei, Z. Zeng, Y. Lin, Localized Surface Plasmon Resonance (lspr)-Coupled Fiber-Optic Nanoprobe for the Detection of Protein Biomarkers, Springer, 2017, pp. 1.
[94] H.-H. Jeong, N. Erdene, J.-H. Park, D.-H. Jeong, H.-Y. Lee, S.-K. Lee, Biosens. Bioelectron. 39 (2013) 346.
[95] J. Breault-Turcot, H.-P. Poirier-Richard, M. Couture, D. Pelechacz, J.-F. Masson, Lab Chip 15 (2015) 4433.
[96] L. Malic, M.G. Sandros, M. Tabrizian, Anal. Chem. 83 (2011) 5222.
[97] L.-H. Jin, S.-M. Li, Y.-H. Cho, Biosens. Bioelectron. 33 (2012) 284.
[98] H. Wei, D. Ratchford, X. Li, H. Xu, C.-K. Shih, Nano Lett. 9 (2009) 4168.
[99] Y. Uludag, I.E. Tothill, Anal. Chem. 84 (2012) 5898.
[100] J.-W. Choi, D.-Y. Kang, Y.-H. Jang, H.-H. Kim, J. Min, B.-K. Oh, Colloids Surf. A Physicochem. Eng. Asp. 313 (2008) 655.
[101] C. Cao, S.J. Sim, J. Microbiol. Biotechnol. 17 (2007) 1031.
[102] L. Huang, G. Reekmans, D. Saerens, J.-M. Friedt, F. Frederix, L. Francis, S. Muyldermans, A. Campitelli, C. Van Hoof, Biosens. Bioelectron. 21 (2005) 483.
[103] S. Krishnan, V. Mani, D. Wasalathanthri, C.V. Kumar, J.F. Rusling, Angew. Chemie Int. Ed. 50 (2011) 1175.
[104] C. Cao, J.P. Kim, B.W. Kim, H. Chae, H.C. Yoon, S.S. Yang, S.J. Sim, Biosens. Bioelectron. 21 (2006) 2106.
[105] M.R. Safarnejad, F. Samiee, M. Tabatabie, A. Mohsenifar, Sens. Transducers 213 (2017) 54.
[106] S. Zeng, X. Yu, W.-C. Law, Y. Zhang, R. Hu, X.-Q. Dinh, H.-P. Ho, K.-T. Yong, Sens. Actuators B Chem. 176 (2013) 1128.
[107] S. Alex, A. Tiwari, J. Nanosci. Nanotechnol. 15 (2015) 1869.
[108] D.E. Mustafa, T. Yang, Z. Xuan, S. Chen, H. Tu, A. Zhang, Plasmonics 5 (2010) 221.
[109] N. Pamme, Curr. Opin. Chem. Biol. 16 (2012) 436.
[110] Q. Zhang, L. Wu, J.Z. Ten, It Wong, X. Liu, X. Zhou, P. Bai, B. Liedberg, Y. Wang, Int. J. Nanomed. 12 (2017) 2307.
[111] C. Esseghaier, G.A. Suaifan, A. Ng, M. Zourob, J. Biomed. Nanotechnol. 10 (2014) 1123.
[112] W.S. Hwang, P.L. Truong, S.J. Sim, Anal. Biochem. 421 (2012) 213.
[113] H.Y. Song, T.I. Wong, A. Sadovoy, L. Wu, P. Bai, J. Deng, S. Guo, Y. Wang, W. Knoll, X. Zhou, Lab Chip 15 (2015) 253.
[114] Z. Jiang, Y. Qin, Z. Peng, S. Chen, S. Chen, C. Deng, J. Xiang, Biosens. Bioelectron. 62 (2014) 268.
[115] C. Cao, S.J. Sim, Lab Chip 9 (2009) 1836.
[116] P.L. Truong, B.W. Kim, S.J. Sim, Lab Chip 12 (2012) 1102.
[117] H. Schefer, S. Mattmann, R. Joss, Ann. Oncol. 9 (1998) 667.
[118] J. Lou, L. Zhang, S. Lv, C. Zhang, S. Jiang, Biomark. Cancer 9 (2017), 1179299X16684640.
[119] J.U. Lee, A.H. Nguyen, S.J. Sim, Biosens. Bioelectron. 74 (2015) 341.
[120] F. Zou, X. Wang, F. Qi, K. Koh, J. Lee, H. Zhou, H. Chen, Sens. Actuators B Chem. 250 (2017) 356.
[121] R.-P. Liang, G.-H. Yao, L.-X. Fan, J.-D. Qiu, Anal. Chim. Acta 737 (2012) 22.
[122] Y. Teramura, H. Iwata, Anal. Biochem. 365 (2007) 201.
[123] W. Hu, H. Chen, Z. Shi, L. Yu, Anal. Biochem. 453 (2014) 16.
[124] S.S. Acimovic, M.A. Ortega, V. Sanz, J. Berthelot, J.L. Garcia-Cordero, J. Renger, S.J. Maerkl, M.P. Kreuzer, R. Quidant, Nano Lett. 14 (2014) 2636.
[125] W. Li, X. Jiang, J. Xue, Z. Zhou, J. Zhou, Biosens. Bioelectron. 68 (2015) 468.
[126] P.J. Reddy, S. Sadhu, S. Ray, S. Srivastava, Clin. Lab. Med. 32 (2012) 47.
[127] T. Špringer, X.C. Song, M.L. Ermini, J. Lamačová, J. Homola, Anal. Bioanal. Chem. 409 (2017) 4087.
[128] R. Li, F. Feng, Z.-Z. Chen, Y.-F. Bai, F.-F. Guo, F.-Y. Wu, G. Zhou, Talanta 140 (2015) 143.
[129] Ts. Špringer, Mt. Bocková, J.í. Homola, Anal. Chem. 85 (2013) 5637.
[130] T. Špringer, J. Homola, Anal. Bioanal. Chem. 404 (2012) 2869.
[131] J. Chung, J. Park, R. Bernhardt, J. Pyun, J. Biotechnol. 126 (2006) 325.
[132] F. Su, C. Xu, M. Taya, K. Murayama, Y. Shinohara, S.-I. Nishimura, Sensors 8 (2008) 4282.
[133] Z. Altintas, Y. Uludag, Y. Gurbuz, I.E. Tothill, Talanta 86 (2011) 377.
[134] T. Alagoz, R.E. Buller, M. Berman, B. Anderson, A. Manetta, P. DiSaia, Gynecol. Oncol. 53 (1994) 93.
[135] I. Lamberti, S. Scarano, C.L. Esposito, A. Antoccia, G. Antonini, C. Tanzarella, V. De Franciscis, M. Minunni, Methods 97 (2016) 58.
[136] J.S. Ross, G.P. Linette, J. Stec, E. Clark, M. Ayers, N. Leschly, W.F. Symmans, G. N. Hortobagyi, L. Pusztai, Expert Rev. Mol. Diagn. 3 (2003) 573.
[137] B. Memar, A. Aledavood, S. Shahidsales, M. Ahadi, M. Farzadnia, H.R. Raziee, S. Noori, N. Tayebi-Meybodi, S. Amouian, S. Mohtashami, Iran J. Cancer Prev. 8 (2015) 42.

[138] R.C. Dolscheid-Pommerich, S. Manekeller, G. Walgenbach-Bruenagel, J.C. Kalff, G. Hartmann, B.S. Wagner, S. Holdenrieder, Anticancer Res. 37 (2017) 353.
[139] J.-Z. Wu, T. Tian, Y. Huang, J.-H. Liang, Y. Miao, L. Wang, J. Xu, X.-Y. Qu, L. Fan, J.-Y. Li, Cancer Biomark. 17 (2016) 205.
[140] A. Babacan, C. Kizilaslan, I. Gun, M. Muhcu, E. Mungen, V. Atay, Int. J. Clin. Exp. Med. 7 (2014) 1078.
[141] K. Kil, J.-E. Chung, H.J. Pak, I.-C. Jeung, J.H. Kim, H.H. Jo, M.-R. Kim, Eur. J. Obstet. Gynecol. Reprod. Biol. 185 (2015) 131.
[142] X. Cheng, H.-f. Gou, J.-y. Liu, D.-y. Luo, M. Qiu, SpringerPlus 5 (2016) 368.
[143] X.-R. Xu, X. Wang, H. Zhang, M.-Y. Liu, Q. Chen, Cancer Biomark. 21 (2018) 471.
[144] S. Suwansa-ard, P. Kanatharana, P. Asawatreratanakul, B. Wongkittisuksa, C. Limsakul, P. Thavarungkul, Biosens. Bioelectron. 24 (2009) 3436.
[145] K. Zhang, X. Shen, Analyst 138 (2013) 1828.
[146] A.F. MT, E. Darko, B.W. Addai, Pak. J. Biol. Sci. PJBS 11 (2008) 1945.
[147] C.-C. Chang, N.-F. Chiu, D.S. Lin, Y. Chu-Su, Y.-H. Liang, C.-W. Lin, Anal. Chem. 82 (2010) 1207.
[148] Y.-H. Liang, C.-C. Chang, C.-C. Chen, Y. Chu-Su, C.-W. Lin, Clin. Biochem. 45 (2012) 1689.
[149] J.L. Hsu, M.-C. Hung, Cancer Metastasis Rev. 35 (2016) 575.
[150] A. Meenakshi, R. Suresh Kumar, N. Siva Kumar, J. Immunoassay Immunochem. 23 (2002) 293.
[151] J.P. Monteiro, S.M. Predabon, E.G. Bonafé, A.F. Martins, A.G. Brolo, E. Radovanovic, E.M. Girotto, Nanotechnology 28 (2016), 045206.
[152] C. Nogues, H. Leh, J. Lautru, O. Delelis, M. Buckle, PLoS One 7 (2012), e44287.
[153] A. Aubé, S. Campbell, A.R. Schmitzer, A. Claing, J.-F. Masson, Analyst 142 (2017) 2343.
[154] M.A. Ali, S. Tabassum, Q. Wang, Y. Wang, R. Kumar, L. Dong, Lab Chip 18 (2018) 803.
[155] H. Vaisocherová, V. Ševců, P. Adam, B. Špačková, K. Hegnerová, A. de los Santos Pereira, C. Rodriguez-Emmenegger, T. Riedel, M. Houska, E. Brynda, Biosens. Bioelectron. 51 (2014) 150.
[156] H. Vaisocherová, Z. Zhang, W. Yang, Z. Cao, G. Cheng, A.D. Taylor, M. Piliarik, J. Homola, S. Jiang, Biosens. Bioelectron. 24 (2009) 1924.
[157] Ts. Riedel, S. Hageneder, Fe. Surman, O. Pop-Georgievski, C. Noehammer, M. Hofner, E. Brynda, C. Rodriguez-Emmenegger, J. Dostálek, Anal. Chem. 89 (2017) 2972.
[158] T. Lakshmipriya, Y. Horiguchi, Y. Nagasaki, Analyst 139 (2014) 3977.
[159] X. Liu, R. Huang, R. Su, W. Qi, L. Wang, Z. He, ACS Appl. Mater. Interfaces 6 (2014) 13034.
[160] C. Rodriguez-Emmenegger, E. Brynda, T. Riedel, M. Houska, V. Šubr, A.B. Alles, E. Hasan, J.E. Gautrot, W.T. Huck, Macromol. Rapid Commun. 32 (2011) 952.
[161] H. Vaisocherová, H. Šípová, I. Víšová, M. Bocková, T. Špringer, M.L. Ermini, X. Song, Z. Krejčík, L. Chrastinová, O. Pastva, Biosens. Bioelectron. 70 (2015) 226.
[162] N.D. Brault, A.D. White, A.D. Taylor, Q. Yu, S. Jiang, Anal. Chem. 85 (2013) 1447.
[163] E. Stigter, G. De Jong, W. Van Bennekom, Biosens. Bioelectron. 21 (2005) 474.
[164] S. Mohseni, T.T. Moghadam, B. Dabirmanesh, S. Jabbari, K. Khajeh, Biosens. Bioelectron. 81 (2016) 510.
[165] U. Eletxigerra, J. Martinez-Perdiguero, R. Barderas, J.M. Pingarrón, S. Campuzano, S. Merino, Anal. Chim. Acta 905 (2016) 156.
[166] A. Shabani, M. Tabrizian, Analyst 138 (2013) 6052.
[167] N. Bellassai, G. Spoto, Anal. Bioanal. Chem. 408 (2016) 7255.
[168] A.R. Ferhan, J.A. Jackman, J.H. Park, N.-J. Cho, D.-H. Kim, Adv. Drug Deliv. Rev. 125 (2018) 48.
[169] M.R. Ossandon, L. Agrawal, E.J. Bernhard, B.A. Conley, S.M. Dey, R.L. Divi, P. Guan, T.G. Lively, T.C. McKee, B.S. Sorg, JNCI 110 (2018) 929.
[170] A. Tadimety, Y. Zhang, K.M. Kready, T.J. Palinski, G.J. Tsongalis, J.X. Zhang, Biosens. Bioelectron. 130 (2019) 236.
[171] A.H. Nguyen, S.J. Sim, Biosens. Bioelectron. 67 (2015) 443.
[172] S. Chaker, I. Kak, C. MacMillan, R. Ralhan, P.G. Walfish, Thyroid 23 (2013) 201.
[173] V. Kulasingam, Y. Zheng, A. Soosaipillai, A.E. Leon, M. Gion, E.P. Diamandis, Int. J. Cancer 125 (2009) 9.
[174] F. Miccichè, L. Da Riva, M. Fabbi, S. Pilotti, P. Mondellini, S. Ferrini, S. Canevari, M.A. Pierotti, I. Bongarzone, PLoS One 6 (2011), e17141.
[175] M. Tachezy, H. Zander, F. Gebauer, A. Marx, J.T. Kaifi, J.R. Izbicki, M. Bockhorn, J. Surg. Res. 177 (2012) e15.
[176] M. Piliarik, M. Bocková, J. Homola, Biosens. Bioelectron. 26 (2010) 1656.
[177] J. Ladd, A.D. Taylor, M. Piliarik, J. Homola, S. Jiang, Anal. Bioanal. Chem. 393 (2009) 1157.
[178] L. Eskandari, A. Akbarzadeh, N. Zarghami, M. Rahmati-Yamchi, Artif. Cells Nanomed. Biotechnol. 45 (2017) 277.
[179] J.-H. Pai, C.-T. Yang, H.-Y. Hsu, A.B. Wedding, B. Thierry, Anal. Chim. Acta 974 (2017) 87.
[180] H. Vaisocherová, V.M. Faca, A.D. Taylor, S. Hanash, S. Jiang, Biosens. Bioelectron. 24 (2009) 2143.
[181] C. Theofanakis, P. Drakakis, A. Besharat, D. Loutradis, Int. J. Mol. Sci. 18 (2017) 1059.
[182] T.I. Korevaar, E.A. Steegers, Y.B. de Rijke, S. Schalekamp-Timmermans, W. E. Visser, A. Hofman, V.W. Jaddoe, H. Tiemeier, T.J. Visser, M. Medici, Eur. J. Epidemiol. 30 (2015) 1057.
[183] L.S. Kelly, S. Birken, D. Puett, Mol. Cell. Endocrinol. 260 (2007) 33.
[184] Y. Wang, J. Dostalek, W. Knoll, Anal. Chem. 83 (2011) 6202.
[185] T. Špringer, M. Piliarik, J. Homola, Anal. Bioanal. Chem. 398 (2010) 1955.
[186] C. Boozer, J. Ladd, S. Chen, S. Jiang, Anal. Chem. 78 (2006) 1515.
[187] N.-F. Chiu, C.-T. Kuo, T.-L. Lin, C.-C. Chang, C.-Y. Chen, Biosens. Bioelectron. 94 (2017) 351.
[188] L. Wu, H. Chu, W. Koh, E. Li, Opt. Express 18 (2010) 14395.
[189] K.V. Sreekanth, S. Zeng, K.-T. Yong, T. Yu, Sens. Actuators B Chem. 182 (2013) 424.
[190] J. Chung, R. Bernhardt, J.C. Pyun, J. Immunol. Methods 311 (2006) 178.
[191] J. Attridge, P. Daniels, J. Deacon, G. Robinson, G. Davidson, Biosens. Bioelectron. 6 (1991) 201.
[192] M. Piliarik, H. Vaisocherová, J. Homola, Biosens. Bioelectron. 20 (2005) 2104.
[193] M. Shibuya, Genes Cancer 2 (2011) 1097.
[194] Y. Li, H.J. Lee, R.M. Corn, Anal. Chem. 79 (2007) 1082.
[195] H. Cho, E.-C. Yeh, R. Sinha, T.A. Laurence, J.P. Bearinger, L.P. Lee, ACS Nano 6 (2012) 7607.
[196] N. Cennamo, M. Pesavento, L. Lunelli, L. Vanzetti, C. Pederzolli, L. Zeni, L. Pasquardini, Talanta 140 (2015) 88.
[197] B. Li, A. Vincent, J. Cates, D.M. Brantley-Sieders, D.B. Polk, P.P. Young, Cancer Res. 69 (2009) 338.
[198] O.A. Al Obeed, K.A. Alkhayal, A. Al Sheikh, A.M. Zubaidi, M.-A. Vaali-Mohammed, R. Boushey, J.H. Mckerrow, M.-H. Abdulla, World J. Gastroenterol. WJG 20 (2014) 18390.
[199] X. Cai, C. Cao, J. Li, F. Chen, S. Zhang, B. Liu, W. Zhang, X. Zhang, L. Ye, Oncotarget 8 (2017) 58338.
[200] A. El Ayadi, D.N. Herndon, C.C. Finnerty, Biomarkers in Burn Patient Care, Elsevier, 2018, pp. 232.
[201] J. Martinez-Perdiguero, A. Retolaza, L. Bujanda, S. Merino, Talanta 119 (2014) 492.
[202] W.-C. Law, K.-T. Yong, A. Baev, P.N. Prasad, ACS Nano 5 (2011) 4858.
[203] S. Setrerrahmane, H. Xu, Mol. Cancer 16 (2017) 1.
[204] S. Gatault, F. Legrand, M. Delbeke, S. Loiseau, M. Capron, Cancer Immunol. Immunother. 61 (2012) 1527.
[205] P. Dentelli, L. Del Sorbo, A. Rosso, A. Molinar, G. Garbarino, G. Camussi, L. Pegoraro, M.F. Brizzi, J. Immunol. 163 (1999) 2151.
[206] C.-Y. Yang, E. Brooks, Y. Li, P. Denny, C.-M. Ho, F. Qi, W. Shi, L. Wolinsky, B. Wu, D.T. Wong, Lab Chip 5 (2005) 1017.
[207] T.M. Battaglia, J.-F. Masson, M.R. Sierks, S.P. Beaudoin, J. Rogers, K.N. Foster, G. A. Holloway, K.S. Booksh, Anal. Chem. 77 (2005) 7016.
[208] M. Mandai, J. Hamanishi, K. Abiko, N. Matsumura, T. Baba, I. Konishi, Clin. Cancer Res. 22 (2016) 2329.
[209] G. Kak, M. Raza, B.K. Tiwari, Biomol. Concepts 9 (2018) 64.
[210] C.-C. Chang, S. Lin, C.-H. Lee, T.-L. Chuang, P.-R. Hsueh, H.-C. Lai, C.-W. Lin, Biosens. Bioelectron. 37 (2012) 68.
[211] P.-I. Tsai, A.S.-Y. Lee, S.-S. Lee, M.-H. Chung, M.-W. Liu, C.-K. Lee, PLoS One 11 (2016), e0160031.
[212] G. Stybayeva, M. Kairova, E. Ramanculov, A.L. Simonian, A. Revzin, Colloids Surf. B Biointerfaces 80 (2010) 251.
[213] T.-L. Chuang, C.-C. Chang, Y. Chu-Su, S.-C. Wei, X.-h. Zhao, P.-R. Hsueh, C.-W. Lin, Lab Chip 14 (2014) 2968.
[214] D.-Z. Lin, P.-C. Chuang, P.-C. Liao, J.-P. Chen, Y.-F. Chen, Biosens. Bioelectron. 81 (2016) 221.
[215] T.-H. Lee, S.-W. Lee, J. Jung, J. Ahn, M.-G. Kim, Y.-B. Shin, Sensors 10 (2010) 2045.
[216] M.-G. Kim, Y.-B. Shin, J.-M. Jung, H.-S. Ro, B.H. Chung, J. Immunol. Methods 297 (2005) 125.
[217] H.-B. Pyo, Y.-B. Shin, M.-G. Kim, H.C. Yoon, Langmuir 21 (2005) 166.
[218] Z. Yu, T.G. Pestell, M.P. Lisanti, R.G. Pestell, Int. J. Biochem. Cell Biol. 44 (2012) 2144.
[219] K. Lee, V.P. Drachev, J. Irudayaraj, ACS Nano 5 (2011) 2109.
[220] C. Yu, H. Nakshatri, J. Irudayaraj, Nano Lett. 7 (2007) 2300.
[221] A.A. Alkhateeb, J.R. Connor, Biochim. Biophys. Acta (BBA) Rev. Cancer 1836 (2013) 245.
[222] S.-F. Chou, W.-L. Hsu, J.-M. Hwang, C.-Y. Chen, Biosens. Bioelectron. 19 (2004) 999.
[223] X. Cui, F. Yang, Y. Sha, X. Yang, Talanta 60 (2003) 53.
[224] C. Mazouni, B. Arun, F. Andre, M. Ayers, S. Krishnamurthy, B. Wang, G. Hortobagyi, A.U. Buzdar, L. Pusztai, Br. J. Cancer 99 (2008) 68.
[225] A. Sankiewicz, Z. Lukaszewski, K. Trojanowska, E. Gorodkiewicz, Anal. Biochem. 515 (2016) 40.
[226] A. Weremijewicz, E. Matuszczak, A. Sankiewicz, M. Tylicka, M. Komarowska, A. Tokarzewicz, W. Debek, E. Gorodkiewicz, A. Hermanowicz, Burns 44 (2018) 931.