A Minireview on The Applications of Nanobiosensors Based on Localized Surface Plasmon Resonance

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Abstract:

In this new era of nano-materials, most chemists and physicists are familiar with the phenomenon of localized surface plasmon resonance (SPR). Noble-metal nano-particles with dimensions (3–100 nm) much smaller than the wavelength of incident light (400–900 nm) exhibit this tendency. In nanostructured materials, due to their very small particle size, the electrons are restricted within the nanoparticle surface area and oscillate with a certain frequency. It is noteworthy that the phenomenon of localized surface plasmon resonance appears when the frequency of the incoming photons overlaps with the frequency of the electrons. As this oscillation of surface electrons is taking place against the restoring forces of the positive nuclei, there is a formation of plasmon resonance. This characteristic property of scattering and absorption of photons appearing in the SPR of every nano-structured material, make them excellent nanoprobes for a variety of applications such as cell imaging and detection of protein phosphorylation and many others. The performance of bio-chemical sensing devices has been greatly improved by the development of localized surface plasmon resonance (SPR) based sensors. In the present minireview, we have briefly discussed the classification of biosensors and the basics of their instrumentation. Some of these applications have been discussed here using some nano-engineered biosensors.

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Introduction:

An optical sensor is a piece of detecting equipment that, through the use of light, transforms the quantity under-measure into another variable, which is often recorded into one of a light wave's properties. At the interface of a metal film and a dielectric material (superstrate), in which alterations in refractive index are to be detected, a surface plasmon is excited in SPR sensors. The surface plasmon's propagation constant changes when the superstrate's refractive index changes. An alteration in one of the properties of the optical wave interacting with the surface plasmon can be seen as a result of this modification, which modifies the linking situation between a light wave and the surface plasmon. A potent tool for the label-free, authentic surveillance of biological molecules is the surface plasmon resonance (SPR) based sensing technique. In SPR-based biosensors, targeted molecules selectively receptors located on the sensor surface, causing changes in the sensor's refractive indices that may be monitored for label-free, real-time identification of a variety of target analytes.

Bionanomaterials are widely studied in the last 10 years. To increase applications in medical fields, novel structure and functionalities are the key factors.[1–8] Important nanomaterials used are nanofibers, nanotubes and nanowires, etc.[9–16] Optical nanosensors are new development which is suitable for intracellular applications. Their applications in the monitoring of in-vivo biological processes could greatly improve current knowledge of cellular functions. Optic nanosensors could be chemical sensors and biosensors.[17-19] Amongst all these biosensors are the most widely used. Many works are also done on gold biosensors,[20-23] titanium biosensors,[24] quantum dots biosensors,[25-29] and carbon nanotube biosensors. [30] Many nano-enabled medical products have already hit the market, and the industry is likely to boom in the next years as applications extend and pervade more complex diseases including cancer, cardiac and neurological disorders, infection, tissue engineering, and many more.

The concentration of a certain analyte or collection of analytes is related to a measured response by bio-sensors, which are analytical devices that combine a biological recognition component with a signal transducer. The kind of transducer and/or recognition molecule that biosensors use is commonly categorised. The majority of biosensors recognise and bind a

molecule of interest before catalysing a chemical conversion of that molecule into a product that is subsequently detected, such as antibodies, nucleic acids, and hormone receptors, as well as enzymes and microbial cells. By transforming the biological reaction into usable electrical signals, the transducer may detect any interactions between the affinity-pairing partners. After being transformed, the electrical signal is evaluated by a processor. The basic configuration of a biosensor is illustrated in Fig. 1.[31]

Nanoparticles, nanowires (NWs), and nanotubes (NTs) have all been widely explored and exploited in innovative biosensor devices thanks to recent advancements in fabrication processes.[32]

Classification of biosensors:

Bio-sensors can be broadly classified as (a) Direct label-free detection biosensors and (b) Indirect label-based detection biosensors. Direct label-free detection biosensors are built on biochemical interaction principles discovered through real-time analysis. Non-catalytic ligands, such as cell receptors or antibodies, are used in this approach. During these interactions, these biosensors may detect minute changes in optical, mechanical, and electrical properties, as well as any tagged moieties. Localised surface plasmon resonance sensors are a common type of ephemeral biosensor. Interferometric and grating sensors are two other types of detecting sensors. Indirect label-based detection biosensors, on the other hand, rely on auxiliary elements for identification and use labelled or catalytic elements like enzymes. Alkaline phosphatase enzymes and fluorescently labelled antibodies are examples of auxiliary elements. This approach, unlike direct label-free detection biosensors, necessitates the connection of the tagged species to the detecting site. The majority of optical indirect sensors are based on the principles to detect fluorescence, although they can also be monitored for densitometric, colorimetric, and chemiluminescence changes depending on the label employed.

Newer technology such as nanomaterials, artificial intelligence-based integrated optics (IO), graphene bioelectronics, AI-based medical portable imaging, novel fluidics and fabrication methodologies, and new cellular and molecular approaches are currently being applied in biosensors.[33]

Surface Plasmon Resonance (SPR) Biosensors Instrumentation:

An optical system, supporting electronics, and a technique for gathering and processing sensor data make up an SPR sensor instrument. In the optical system, surface plasmons are produced optically. The resulting light wave is recognised and examined to gather the required information. It carries an SPR signal that is encoded. The detector signal is processed to produce the sensor output. Along with sample handling and preparation procedures, a bio-recognition coating on SPR biosensors interacts with target molecules in a liquid sample. Even the slightest changes in the refractive index can be detected using the non-destructive optical technique known as SPR. Figure 2 depicts its components: a light source, prism, gold film, and detector.[34]

A light pulse activates surface plasmons in an SPR sensor's optical system. In the SPR sensor, surface plasmon stimulation causes a change in one of the light wave's characteristics. SPR sensors are categorised as (i) angular, (ii) wavelength, (iii) intensity, (iv) phase, or (v) polarisation modulated, depending on which property of the light wave is modified and employed as a sensor output. In today's SPR sensors, the first three types of modulation are most commonly utilized.[35]

SPR sensors based on prism couplers and wavelength modulation:

Based on wavelength modulation, Homola et al. [35] developed a functioning modular SPR sensor. The sensor consisted of a halogen lamp, SPR sensor platform, and spectrometer. White light was sent from the halogen lamp to the SPR sensor platform through a multimode optical link. A large diameter parallel beam input collimator, polarizer, and multichannel output collimator, as well as a glass prism with an attached SPR chip, were all part of the sensor platform (coated in a 50 nm thick gold coating). The output collimators, which were coupled to the spectrograph's inputs, connected the light into optical fibres.[35] By checking for a change in reflectivity in the linear region of the SPR angular or spectral response curve, one can detect the shift of the SPR dip in the intensity interrogation mode. The variation in the refractive index is inversely correlated with the variation in the SPR signal in the linear region above the metallic sheet. This necessitates changing and fine-tuning the incidence angle and wavelength of the excitation light for maximum sensitivity. An example of a prism-based intensity interrogation SPRi setup is shown in Fig. 3. On the sensor surface, the

charge-coupled device (CCD) camera continuously records a sequence of 2D intensity contrast images.[36]

Advancements in the localized surface plasmon resonance (lspr) biosensors technology:

Surface plasmon resonance at the microscale and localised surface plasmon resonance at the nanoscale sensing have proven to be very powerful next-generation probing technologies in the current Covid-19 outbreak. The maximum absorption wavelength deviation can be used by the LSPR. This is due to an increase in the intensity of fluorescent light created by near-field light, as well as a change in the local index of refraction on the surface of the Nano-material probe used as a sensing device.

The fibre optic surface plasmon resonance (SPR) sensor system for cellphones, seen in Fig. 4, was first published by K. Bremer *et al.* [37] A simple silver coating procedure was used to create the sensor, and both ends of a 400 m optical fibre were polished to create 45° end-faces. The smartphone's backside flashlight and camera were used, respectively, for activating and querying the SPR sensor system. Consequently, the created sensor system does not need any external electrical components to function. A refractive index sensor was created as an initial use case. Different volume concentrations of glycerol solution were used to show how well the SPR sensor system performed.

SPR biosensors have recently drawn a lot of interest as medical diagnostic tools for a variety of reasons. They can be quickly and cheaply prepared without labels. A reusable magnetic surface plasmon resonance (SPR) sensor chip was created by Yoo et al. to repeatedly detect different target molecules in a typical SPR system. We showed that it is possible to measure the nucleoprotein (NP) of the H1N1 influenza virus solution repeatedly more than 7 times with a single reused SPR sensor chip without noticeably degrading the signal. Additionally, a single SPR chip might be used to repeatedly measure various target molecules. The cost of SPR sensing should be greatly decreased because our reusable SPR sensor chip can be used repeatedly in a traditional SPR system without the need for chemical treatments for refreshment.[38]

Differential levels of microRNA expression are found in cancer, and they have an impact on metastasis, carcinogenesis, and cellular transformation. Although dye molecule labels for

fluorescence approaches have been investigated, label-free molecular-level measurement of miRNA is incredibly difficult. For the precise label-free detection of therapeutically important biomarkers like miRNA-21 and miRNA-155, Tianyu Xue and colleagues developed a surface plasmon resonance sensor based on two-dimensional antimonene nanomaterial. Since antimonene contains more delocalized 5s/5p orbitals than graphene, which has previously been employed in DNA molecule sensing, first-principles energetic calculations show that antimonene has a significantly stronger interaction with ssDNA. The detection threshold can be raised to 10 aM, which is 2.3–10,000 times greater than that of current miRNA sensors.[39]

For an early ovarian cancer diagnosis, the discovery of the biomarker human epididymis secretory protein 4 (HE4) is essential. Y. Jialing, *et al.* [40] sought to develop a novel localised surface plasmon resonance (LSPR) biosensor for detecting HE4 using blood samples from ovarian cancer patients. The conceptual design of this biosensor is as shown in Fig. 5 and Fig. 6. [40] In experiments for the detection of HE4, the LSPR-based biosensor was discovered to have a quick detection speed, strong specificity, effective repeatability, and long-term stability. The linear range for LSPR was between 10 and 10,000 pM with a detection limit of 4 pM. The results of the enzyme-linked immunosorbent test and the LSPR have a very strong correlation in human serum. Patients with ovarian cancer were shown to have human epididymis secretory protein 4 in their serum using a label-free LSPR technique.[40]

The Summary, Future Perspectives, and Challenges:

Review of the development trend for SPR sensors based on light source technology. One of the most demanding applications for the SPR sensor's ultralow detection limit is in the realm of medicine, where early biomarker identification is one of the most common uses. Nanoelectronics manufacturing and technology are advancing quickly to reach smaller devices. The development of smartphone-based SPR sensors has amazingly served as a crucial turning point in the merging of digital technology with biosensor application technologies and lab-on-chip platforms. Internet-of-things (IoT) technology will indefinitely play a significant role in the data transmission of the SPR sensor in clinical settings.

The main challenges to the study and development of SPR sensors are the expensive platforms and components. Commercial platforms often do not cover the expense requirements of small research groups or points of care (PoC) to invest in and maintain. As a

result, it offers a feasible route for scientists and engineers working in both the academic and industrial sectors to develop a low-cost yet powerful SPR sensor platform in the future.[41]

Conclusions:

When nanomaterials or nanostructures are utilised in biosensors, their unique physicochemical properties open up a whole new world of sensing options. As a result, nano-bio-sensing is an excellent illustration of how material sciences, physics, chemistry, and biology interact at the nanoscale. Nanomaterials and nanostructures have unique physicochemical properties that cannot be obtained by normal bulk materials, which bodes well for the future of this field.

The most recent sample publications looked at the claim that combining biomolecules with nanomaterials and nanostructures can result in biosensors with improved sensitivity and selectivity, faster reaction times, decreased power consumption, and feasible miniaturisation.[42] Real-time and label-free SPR-based biosensors are widely used by the pharmaceutical industry and fundamental researchers. Biosensors can be used for a plethora of different things, from qualitative binding to high-resolution kinetic analysis. Almost every interaction involving biological systems can be studied using these methods, including those involving proteins, nucleic acids, and even lipid surface environments. SPR-based technology will unavoidably advance as platforms with greater throughput and sensitivity are created in the future.

Figures:

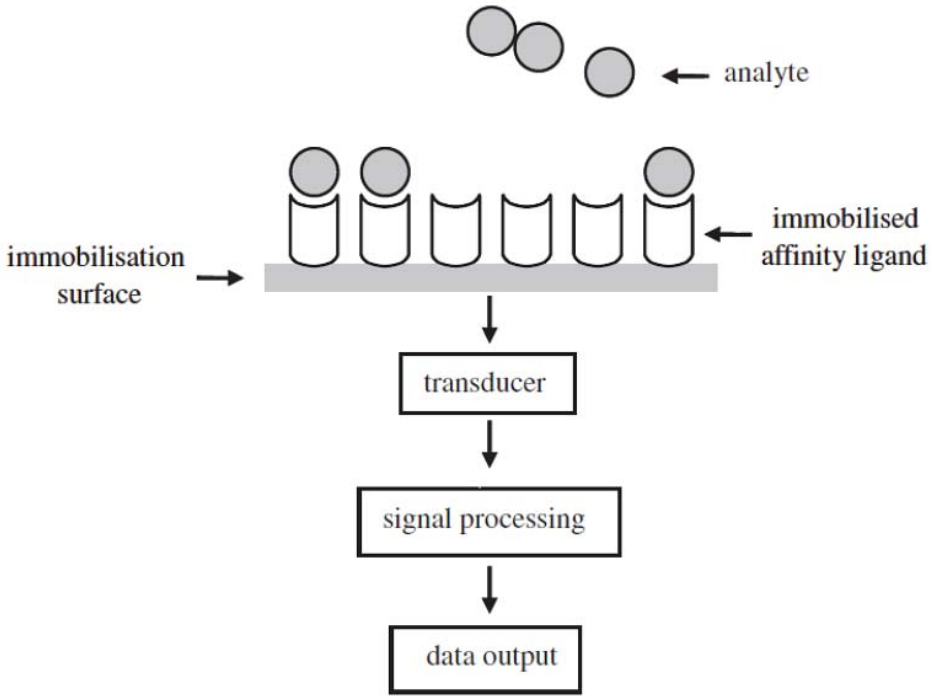

Fig. 1: General schematic of biosensors. Adapted from Mungroo, *et al.*[31]

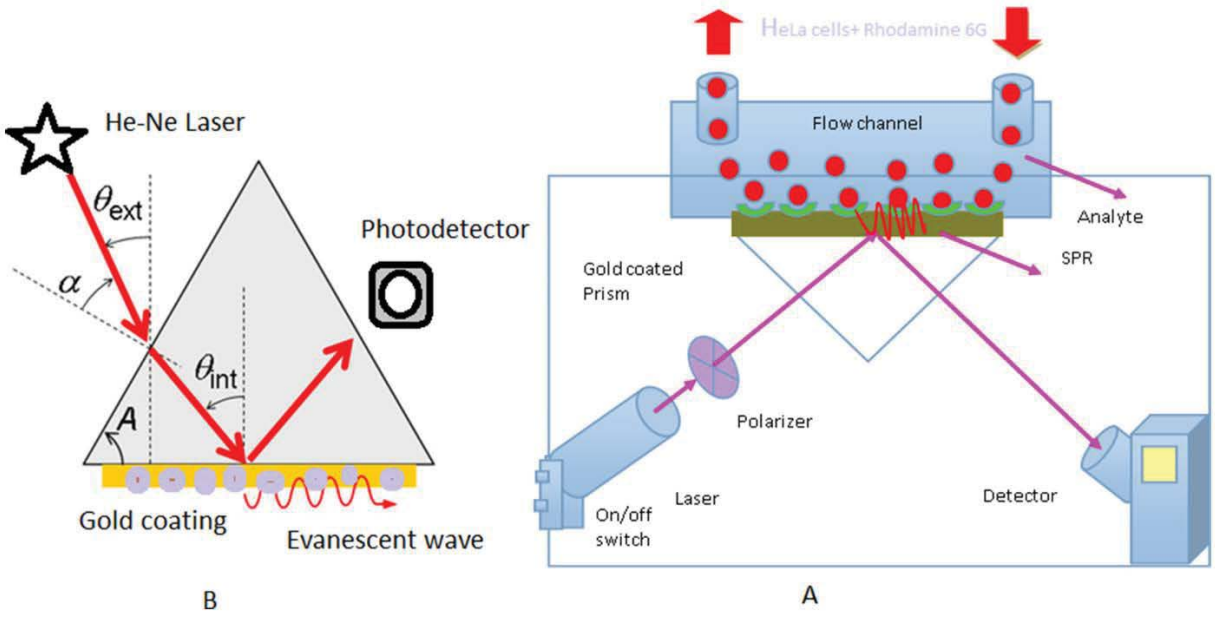

Fig. 2: Schematic of an SPR (bio)sensors. Adapted from Firdous, *et al.*[34]

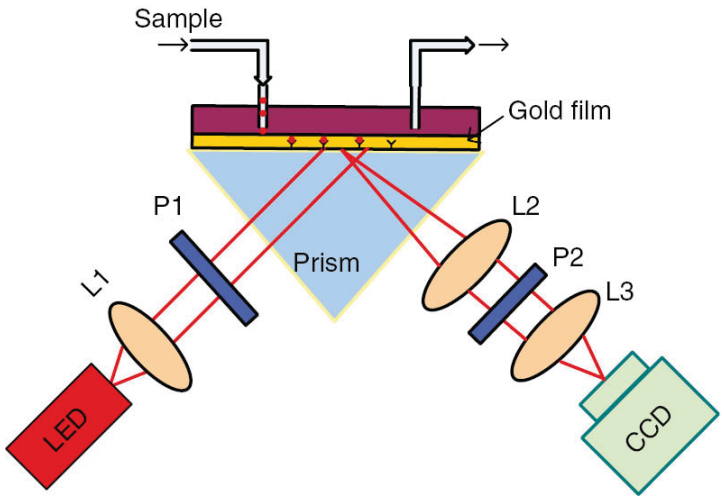

Fig. 3: Schematic illustration of a typical prism-based intensity interrogation SPRi setup. Adapted from Zeng, *et al.*[36]

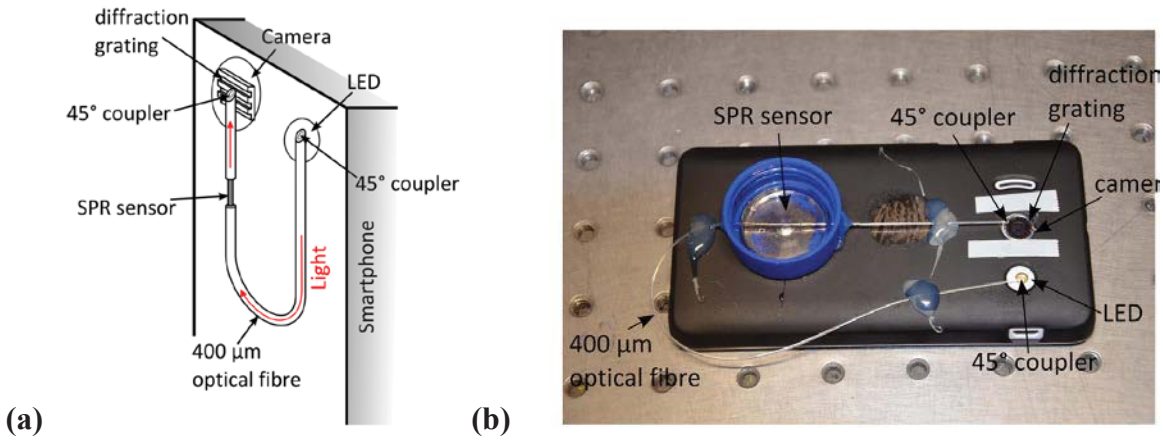

Fig. 4: (a) Schematic of the fibre optic SPR sensor system for Smartphones **(b)** Picture of the fibre optic SPR sensor system. Adapted from K. Bremer *et al.* [37]

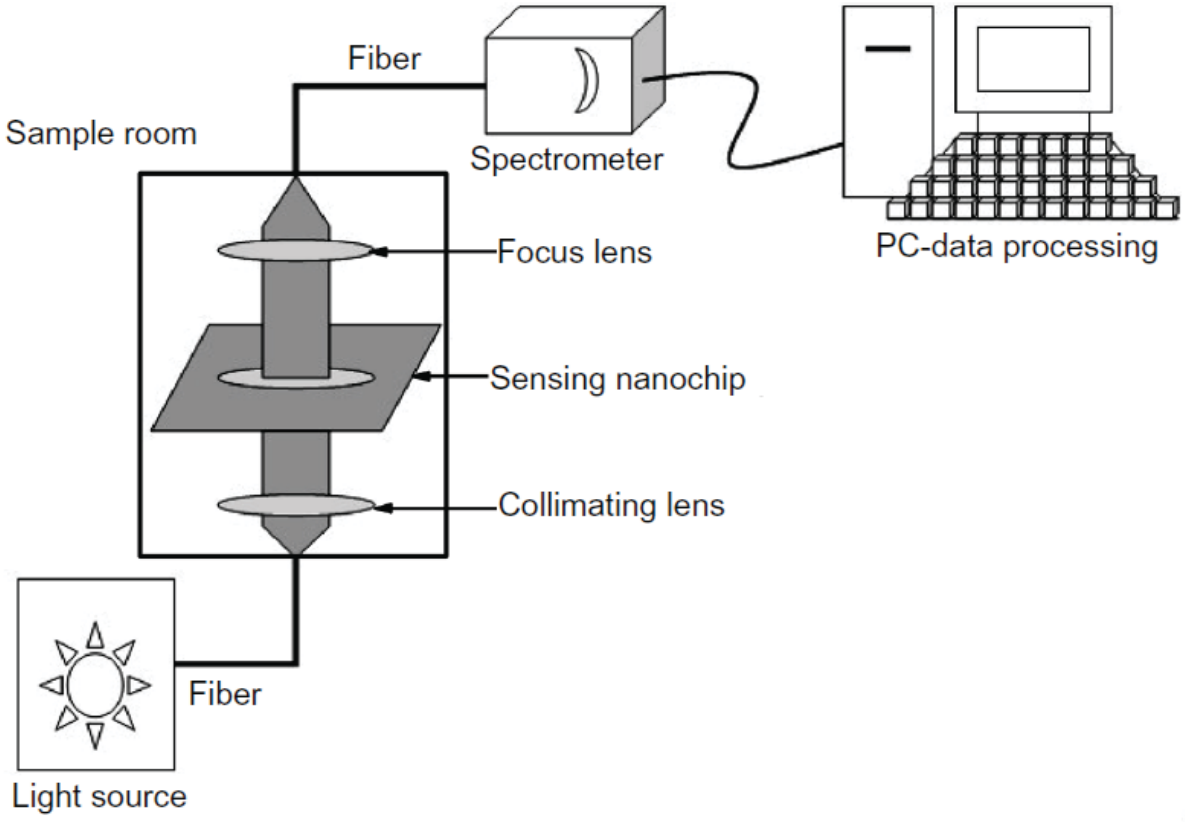

Fig. 5: Schematic representation of experimental set up of localized surface plasmon responance biosensor. Adapted from Y. Jialing, *et al.* [40]

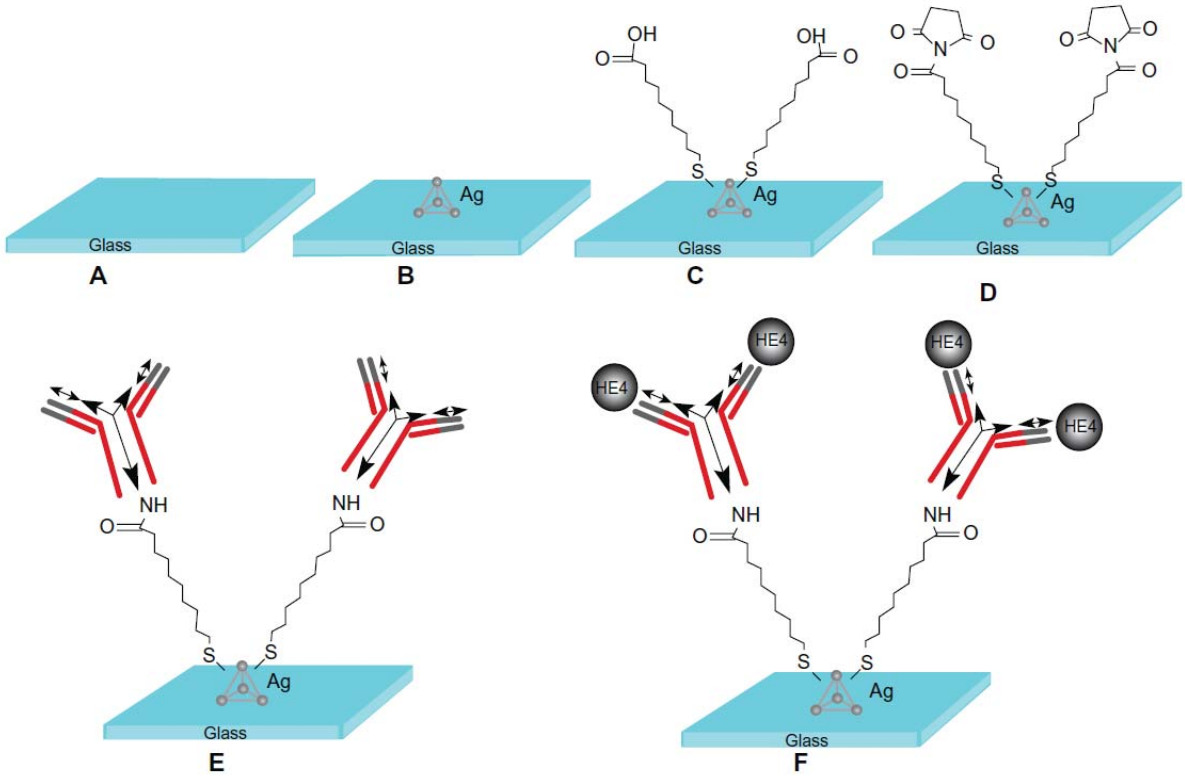

Fig. 6: Design of the localized surface plasmon resonance biosensor for HE4 detection using a direct assay format. (**A**) Glass substrate, (**B**) silver nanoparticles synthesized through NSL technology, (**C**) A self-assembled monolayer layer formed by incubation in 1 mM 11-mercaptoundecanoic acid, (**D**) incubation in 75 mM 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride/15 mM N-hydroxysuccinimide, (**E**) anti-HE4 antibody (10 µg/mL) covalently attached to the nanoparticles, and (**F**) different concentrations of the HE4 both in buffer and serum samples reacted with the anti-HE4. **Abbreviation:** HE4, human epididymis secretory protein 4. Adapted from Y. Jialing, *et al.* [40]

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