Optical biosensors: a quick overview

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This work aims to provide a brief overview of the latest trends in the domain of optical biosensors. Biosensors are devices developed to obtain precise information from human body fluids, such as plasma, blood or urine, among others. Their main elements are the bioreceptor, that binds the biomarker (the target molecule); and the transducer, which is intimately linked to the bioreceptor and provides a measurable response. The main bioreceptors comprise antibodies, enzymes, nucleic acids and molecularly imprinted polymers. Previously mentioned bioreceptors can be immobilized on the sensor surface using different techniques including physical adsorption, covalent binding, physical entrapment in a hydrogel or chemical cross-linking[1].

Regarding optical transducers, interrogation techniques primarily consist of light-intensity, phase, and frequency or polarization modulations caused by the bioreceptor in the presence of the biomarker. Optical biosensors possess increasing relevance as a result of their advantages, including their capability of a direct, real-time and sometimes label-free detection, as well as their high specificity, sensitivity, compact size and good cost-performance ratio[2]. The most widely used optical biosensors are those based on surface plasmons, fluorescence, interferometry, whispering gallery modes and photonic crystals.

Surface plasmons are electromagnetic excitations that propagate along the interface between a dielectric medium and a metal. In the presence of the biomarker, the refractive index in the region adjacent to the biosensor surface changes, therefore varying the resonant wavelength, the intensity and/or the phase of the light coupled to the surface plasmons. By monitoring one of these variables, such as the resonant wavelength in surface plasmon resonance (SPR) based biosensors, the concentration of the analyte can be obtained[3]. SPR stands out for having high sensitivity and enabling direct and real-time monitoring of the analyte binding[4]. Similar to SPRs, lossy mode resonances (LMRs) are generated when a metal oxide or polymer is used instead of a metal. LMRs have a higher sensitivity than SPRs, making them ideal for the development of biosensors.

SPR imaging (SPRi) differs from conventional SPR in incorporating a CCD (charge-coupled device) camera that enables sensorgrams and SPR images to be recorded at the same time; while SPR microscopy (SPRM) adds a high numerical aperture lens for light coupling, allowing single molecule detection. Finally, long range SPR (LRSPR), with thin films 20-25 nm thick, possess an increased sensitivity thanks to the low propagation loss and deeper field penetration[5]. In the case of localized surface plasmon resonances (LSPR), the plasmons oscillate locally to a nanostructure (such as nanoparticles) instead of along the dielectric-metal interface. The high electromagnetic fields around the nanostructure induce an increase in sentitivity[6].

Fluorescence sensors consist basically of using a light source at an excitation wavelength to excite a fluorophore or label and measuring the fluorescent response at the peak wavelength[7]. In the case of biosensors, the sensing mechanism links the analyte concentration with the fluorophore concentration. Fluorescence biosensors are characterized by a high sensitivity and specificity while their drawbacks are those associated with the use of fluorophores, including photobleaching or self-quenching. In general, fluorescence biosensors operation is based on sandwich immunoassays where the second antibody is labeled with a fluorophore.

Waveguide interferometric sensors are based on the light travelling through two different paths. Here, one path is used as reference, where the light propagates without suffering any alteration. Then, the sample is placed along the other path inducing a phase shift. The interference of the modes that travel through both paths produces a signal that is related to the analyte concentration[8]. The most commonly used interferometers in biosensing applications are the Mach-Zehnder (MZI) and the Young (YI) interferometers[5].

In the case of the MZI, the incident monochromatic light is split into two arms by a Y-junction and both beams are then recombined with another one. Modifications of the MZI basic structure include the use of slot waveguides in the sensing arm to increase the sensitivity and the integration in compact devices of several MZIs for multisensing[5]. The YI differs from the MZI in lacking the second Y-junction. In this interferometer, the light from the reference and the sensing arms diffracts and interferes on an image sensor such as a CCD camera.

Whispering-gallery modes (WGM) are electromagnetic waves that circulate and are strongly confined in a dielectric structure with circular symmetry, producing resonances through internal interference. This structure is resonantly stimulated by evanescent coupling to a waveguide. The obtained resonances have a narrow full-width at half maximum (FWHM), thus obtaining a high resolution.[9] The most widely employed WGM resonators in biosensing are microsphere resonators, which are easy to fabricate but difficult to integrate; and planar microring resonators, which are robust, compact and suitable for multiplexing and integration but have lower sensitivities[5].

Photonic crystal (PC) structures consist of spatially arranged periodic dielectric materials in which light is highly reflected at specific wavelengths. PC structures can be manufactured in one (1-D), two (2-D) or three (3-D) dimensions,

incorporating microcavities, waveguides, slabs, multilayered thin films or porous geometries, and employing materials such as silicon, glass, polymers, colloids or silk. They are fabricated through various techniques such as self-assembly or lithography and their advantages include compact size, flexible configuration, high sensitivity and the possibility of monolithic integration.[10]

In conclusion, different types of biosensors have been described focusing on the optical sensing techniques. Nevertheless, most of these configurations have been developed only for their use in the laboratory and further developments are required in order to obtain reliable, high-sensitive and low cost point of care devices for disease monitoring and diagnosis.

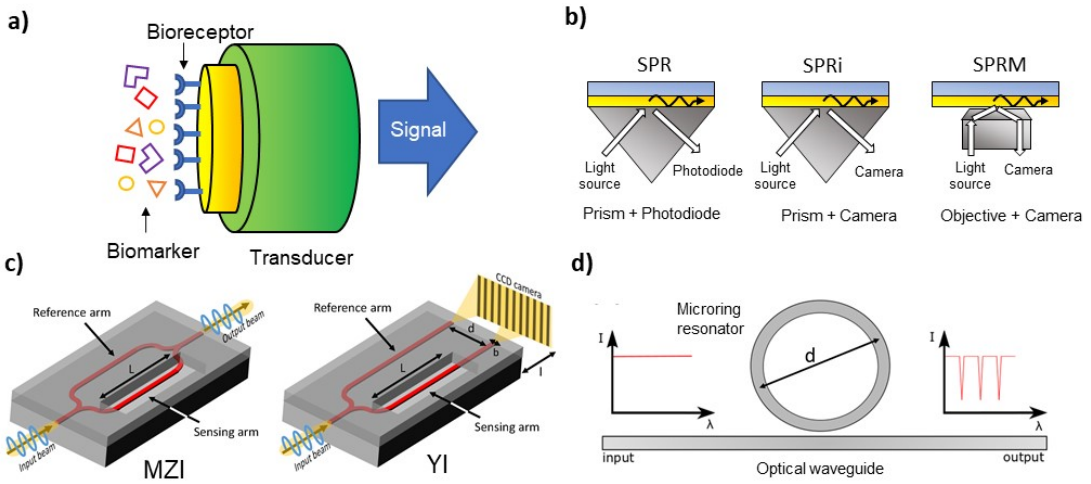

Figure 1. a) Schematic of a biosensor. b) Three types of SPR configuration. c) Schematic of MZI and YI configurations, adapted.[11] Reproduced under the terms of the Creative Commons Attribution license d) Schematic of a microring resonator, adapted.[12] Reproduced under the terms and conditions of the Creative Commons Attribution license.

Acknowledgements

We want to thank the funding from Ministerio de Ciencia, Innovación y Universidades (FPU18/03087) and Agencia Estatal de Investigación (PID2019-106231RB-I00 TEC).

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