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Review

Chemical surface modifications for the development of silicon-based label-free integrated optical (IO) biosensors: A review

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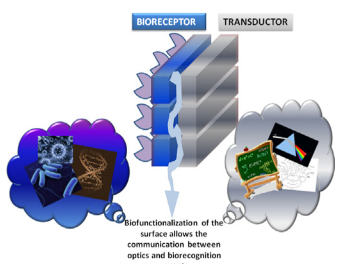
HIGHLIGHTS

- IO devices made with silicon based technologies are at the core of biosensors development.
- Surface biofunctionalization is crucial to reach competitive performance.
- Main achievements reached in real sample biosensing are critically discussed.

GRAPHICAL ABSTRACT



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ABSTRACT

Increasing interest has been paid to label-free biosensors in recent years. Among them, refractive index (RI) optical biosensors enable high density and the chip-scale integration of optical components. This makes them more appealing to help develop lab-on-a-chip devices. Today, many RI integrated optical (IO) devices are made using silicon-based materials. A key issue in their development is the biofunctionalization of sensing surfaces because they provide a specific, sensitive response to the analyte of interest. This review critically discusses the biofunctionalization procedures, assay formats and characterization techniques employed in setting up IO biosensors. In addition, it provides the most relevant results obtained from using these devices for real sample biosensing. Finally, an overview of the most promising future developments in the fields of chemical surface modification and capture agent attachment for IO biosensors follows.

Contents

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1. Introduction: approach to refractive index optical biosensors

Nowadays, biosensing is a scientific and technological hot topic given its potential in fields such as medical diagnosis, healthcare, environment, defense and food security. In these realms, the specific and sensitive detection of targets in short-time analyses plays a primordial role.

Traditionally, labeled formats have been used, where targets or reporter molecules carry fluorescent, enzymatic or radioactive tags. These techniques present high sensitivity, and even achieve single molecule detection [1], and are currently the standard techniques for many determinations. However, the development of label-free techniques has attracted the interest of many researchers over the last decade [2–6]. They offer advantages such as direct detection, real-time monitoring, kinetic information, fewer reagent costs, and the native molecular conformation of the protein is not altered by a tag. Thus, label-free biosensors based on optical [7], electrical [8–13] and mechanical principles [14–18] can be found. Optical sensors are more versatile than others because they can be made from different materials, such as silicon, glass, metals or polymers, and they offer different detection modes and architectures that can be combined [19]. They also offer other advantages; mass-scale fabrication, excellent physical properties, good selectivity and sensitivity; and can accomplish multiplexed detection in a single device [20,21]. Label-free optical biosensors have received increasing attention and many reviews can be found that provide a general overview of the state of the art [22–25]. In label-free optical detection, the transduction mode may be based on the refractive index (RI), optical absorption or Raman spectroscopy [26–30]. In past two decades, optical sensors based on refractive index (RI) changes feature among the most studied (Fig. 1).

In ordinary dielectric material, the refractive index (RI) directly relates to the polarizability of molecules at optical wavelengths. Biological molecules have a higher RI than air or water, and they lower the propagation speed of the electromagnetic fields passing through them. Optical biosensors are designed to translate changes in the propagation velocity of light through a medium that contains biological material into a quantifiable signal proportional to the amount of material present on the sensor surface. For this reason, the electromagnetic field bound to an optical device that couples some energy to an external medium (called an evanescent field) penetrates a few hundred nanometers into the optically rarer environment from the optically denser guiding medium.

Different optical phenomena have been employed to design RI optical biosensors. Representative methods include: Surface Plasmon Resonance [31,32], Reflectometric Interference Spectroscopy [33,34], Dual polarization Interferometry [35,36], Photonic Crystal Technology [37,38], and Whispering Gallery Mode Resonators

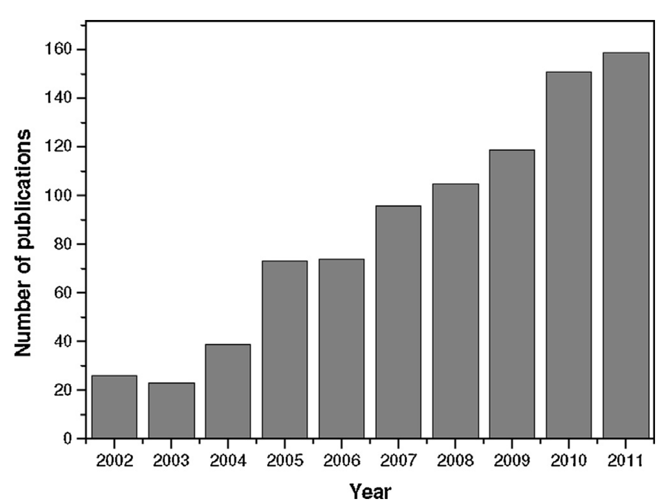

Fig. 1. Number of publications per year on the Refractive Index Optical BioSensing topic during the last decade.