Silicon photonic biosensors

Invited paper

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ABSTRACT

Silicon-based optical biosensors used for biomedical applications are described. In particular, integrated optical devices and their advantages, in terms of high performance and compactness, and also high reliability and long life term, have been reported. Since the last years, these features have been allowing to realize high-efficiency biosensing platforms with on-chip integration of several biosensors for a multi-analyte detection. Many lab-on-chip systems integrated in portable medical instruments have been proposed in literature and already commercialized in the worldwide market, so reaching extraordinary improvements in the early detection and monitoring of several diseases. Therefore, fast and accurate self-tests achievable with silicon photonic biosensors are remarkably opening new possibilities and applications in the healthcare industry.

Keywords: Biosensors, Silicon Photonics, Biophotonics

1. INTRODUCTION

In the last decades a strong effort has been observed in the healthcare industry to improve the quality of services for patients, in order to reduce the number of deaths and improve the outcomes in a shorter time. This corresponds to a better patients' life quality and also remarkably reduced costs for Health System. In particular, many advantages have been achieved by adopting electronic patient records and by developing a better organization and management of first aid centres and hospitals to reduce the average hospitalization period for each patient with a continuous monitoring at home after the hospital discharge without requiring expert users. The recent spread of point-of-care (POC) technologies is enabling such change in the worldwide Health Systems, because high performance and accuracy are guaranteed by the biosensors integrated in these biomedical systems together with high portability and ease of handling, so allowing their use also by not expert users in every place with no laboratory infrastructures [1]. Many improvements have been reached for several widespread diseases to detect viral infections and allergies, but many farther results can be also obtained for many stigmatized diseases for which the absence of fast and cheap tests still represent one of the first causes of death.

A further step for the next generation of biosensors in POC systems is to reach a stronger efficiency with a better resolution, with the aim of enabling their use also for other dangerous and deadly human diseases, such as cancer, cardiovascular diseases and genetics [2], for which the prevention at first stages represents the first reason of survival. Nowadays, similar diseases can be detected and monitored with bulky and expensive medical instruments and long and complex processes carried out by expert users are also necessary. Therefore, novel techniques and devices have been investigated to overcome such limitations in the last years.

2. STATE-OF-THE-ART OF SILICON-BASED PHOTONIC BIOSENSORS

An ultra-compact footprint and high resolution together with reliability and versatility represent the main features required to biosensors, in order to facilitate their integration in portable instruments.

The best performance in terms of resolution, compactness and reliability have been obtained with optical biosensors also due to the ease of on-chip integration with microfluidics, so opening new opportunities and applications for diseases detection and drug delivery [3].

Several configurations, technologies and materials have been proposed to realize high-efficiency optical biosensors. In particular, silicon technology is the most largely used due to the extraordinary improvements observed in nanofabrication, that makes possible to obtain high control and high reliability for the final pattern of the silicon-based optical biosensors with remarkable advantages in terms of cost-efficiency and mass production, together with a stability much better than other materials, such as polymers. Furthermore, the CMOS compatibility of silicon enables the on-chip integration of electronic components together with the optical biosensors, which is necessary to realize lab-on-chip systems for the real-time analysis and data transfer to a database of patient records or medical centres, besides low cost, low power consumption and long life term [4].

The lowest values of limit of detection (LOD) have been obtained with silicon optical devices based on Mach-Zehnder (MZI) [5], Bimodal Waveguide and Young interferometers [6]. In particular, a value of LOD up to 10^{-7} RIU has been achieved with the MZI configurations [5] and even lower (LOD < 10^{-8} RIU) with the latter ones [6]. These very-low resolution values provide an extraordinary mass sensitivity, as demonstrated in [5], where the DNA hybridization of the BRCA-1 gene has been obtained, which is involved in breast cancer development, with a detection limit of this biological element up to 0.06 pg/mm^2. The limitation of the interferometric structures is mainly related to their large footprint with a length also of 1.5 cm [5], which makes difficult their on-chip integration in particular with an array of biosensors for a multi-analyte detection. Significant improvements have been realised with integrated label-free optical biosensors in silicon technology, and particularly, with resonant cavities, because light-matter interaction is stronger in optical resonators than conventional optical waveguides and this allows higher sensitivity together with small volumes [2]. Photonic crystal (PhC) cavities and microring resonators (MRR) have demonstrated the highest values of the figure of merit *S/A*, where *S* is the device sensitivity and *A* is the device footprint. A values of LOD ~ 10^{-5} RIU has been already demonstrated with PhC cavities with ultra-compact device footprints (< 10 μm^2), up to 5 orders of magnitude smaller than interferometers. Further improvements have been attained by including a slotted waveguide in the PhC structures, because of an enhancement of the *Q/V* ratio, which is strongly related to light-matter interactions [7]. In particular, Di Falco et al. in [7] have demonstrated a LOD ~ 10^{-6} RIU with a PhC slotted cavity and such performance can provide the detection and the monitoring of low concentrations of DNA and proteins, such as BSA, streptavidin and biotin.

Higher performance have been also obtained with silicon microring resonators, with a device footprint slightly larger than that typically obtained with PhC cavities, but several orders of magnitude smaller than interferometers, so facilitating their on-chip integration with ultra-high sensitivity [3]. A resolution of 0.3 pg/mm^2 has been obtained with conventional microring resonators with $A \sim 10^3$ μm^2, enabling the detection of low concentration of proteins [8]. Dell'Olio et al. in [3] have proposed a novel configuration of a slotted microring resonator (see Fig. 1).

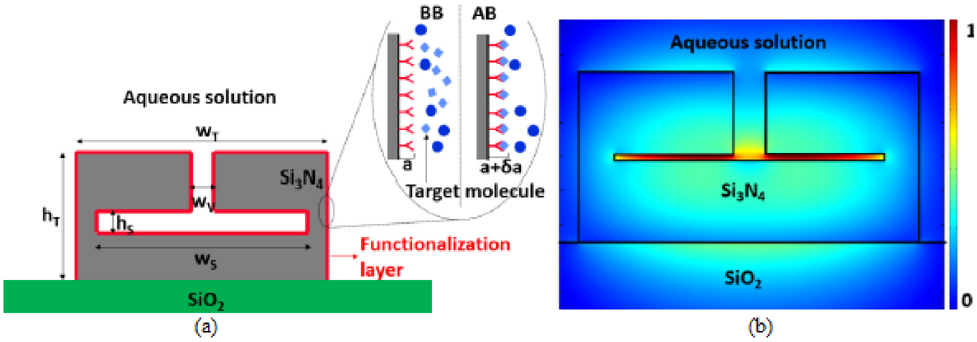

Fig. 1. (a) Cross-section of the waveguide of the slotted MRR configuration and (b) fundamental quasi-TM mode distribution.

The biosensors allows to strongly confine the optical energy at resonance in the ultra-small slot with a consequent enhancement of light-matter interaction, so obtaining an ultra-high resolution of 0.2 ng/mL, corresponding to a value of LOD up to 0.06 pg/mm^2, with an improvement of 5 times the state-of-the-art of integrated silicon optical biosensors with MRR devices. Similar performance makes microring resonators suitable to realize a high-efficiency biosensing platform with an on-chip integration of several biosensors for a multi-analyte detection. For instance, the biosensing platform proposed in [3], made by an array of different microring resonators, potentially allow the monitoring of several biomarkers for early detection of lung cancer.

High performance of optical biosensors, confirmed by the very-low values of LOD, have been also proposed with plasmonic structures [9]. In particular, Surface Plasmon Resonance (SPR) configurations based on the well-known Kretschmann configuration have demonstrated a LOD < 10^{-7} RIU [9]. Such structures are realized by a properly-functionalized thin metal film on a prism glass and they are excited by a light beam passing through the glass prism. These configurations are very sensitive to any molecular interaction in close proximity of the functionalization layer that can be monitored by the plasmon resonance shift. However, SPR instruments are bulky and their miniaturization is challenging due to the optics required to couple light into the metal film, therefore, new plasmonic technologies at the nanoscale for biosensing, e.g. those based on localized SPRs excited in metal nanoparticles or plasmonic nanopores and nanoholes in thin metal films, are currently under investigation for lab-on-chip microsystems. Among those technologies, planar resonant structures where light is confined in surface plasmon polariton (SPP) waveguides are very advantageous because a planar resonant biosensor can be easily arrayed due to a footprint of a few μm^2, and exhibits a resolution that is compliant to the requirements of many applications in the biomedical environment. A strong advantage of planar metal cavities used as biosensors is the compatibility with a silicon-based optical chip, so including the possibility to be manufactured by the standard fabrication tools and techniques widely utilized in micro and nanoelectronics. In the last years, several silicon-based biosensing platforms with the integration of plasmonic cavities have been proposed aiming at improving the sensor resolution and obtaining ultra-compact devices to carry out a multi-analyte detection with a large array of biosensors in the same platform [10]. In particular, Dell'Olio et al. have proposed in [10] a bio-multisensing platform for the selective label-free detection of protein biomarkers. Several biosensors have been included in the platform and each of them is based on a plasmonic nanocavity consisting of a periodic metal structure (see Fig. 2).

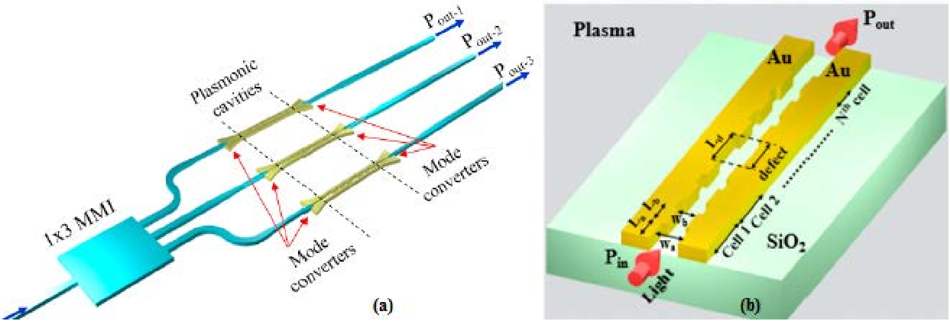

Fig. 2. (a) Silicon-based biosensing platform with (b) a zoom of the plasmonic cavity as sensing element [10]

The extreme energy confinement in an ultra-small region allows to enhance light-matter interaction, and a LOD = 0.42 μg/mL has been obtained. Such performance is not comparable to the state-of-the-art of integrated photonic biosensors, because the resolution is 128 pg/mm^2 (4 orders of magnitude lower than performance obtained with slotted MRR [3]), but very suitable for some medical applications, such as the study of coronary artery diseases, because the risky levels of the main biomarkers are at least one order of magnitude higher than the device resolution. The main advantage of the proposed biosensing platform is the high compatibility to the silicon technology. In fact, each sensor is connected to a hybrid converter that enables the conversion of the plasmonic mode in an optical one propagating in conventional low-loss silicon-based waveguides. The sensors and the converters have a very-compact device, so enabling the integration of all optical components and, potentially, also the electronic ones in the same optical chip to obtain a high-efficiency LOC system as biosensing platform.

CONCLUSIONS

A description of the state-of-the-art of silicon optical biosensors has been proposed with a focus on their features and advantages in terms of efficiency, resolution and compactness compared to the performance obtained with the commercialized biosensors with different configurations and materials. A strong improvement obtained by silicon technology is the availability to realize biosensing platforms with on-chip integration of several biosensors for a multi-analyte detection, facilitating the spread of new high-efficiency portable medical instruments that can improve the early detection and monitoring of several diseases with fast and accurate self-tests without requiring expert users or laboratory infrastructures.

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