High sensitivity photonic configurations for biochemical detection

(Invited paper)

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ABSTRACT

In this paper, we present different approaches for the creation of high sensitivity nanophotonic-based biosensing devices that are currently being developed by our group. These approaches not only focus on the improvement of the photonic sensing structures themselves, what can have a limited effect over the sensitivity, but also on other aspects as the use of functional biomolecular receptors, the use of advanced microfluidic systems, or a proper selection of the constitutive materials of the photonic sensing structures. The aim of these approaches is being able to detect very low concentrations of biological/chemical analytes having a very reduced size and/or molecular weight, something that has a tremendous importance for many application fields as medical diagnosis, environmental control or biological/chemical threats detection, among others.

Keywords: photonic sensors, high sensitivity, PBG structures, molecular beacons, porous silicon.

1. INTRODUCTION

Photonic technology is one of the main candidates to create the core transduction elements of future high-performance analysis devices since it provides significant advantages such as high sensitivity, compactness and high integration level, short time to result, label-free detection, and use of very low sample volumes. These advantages will allow deploying compact and low cost analysis systems able to simultaneously detect hundreds/ thousands of analytes in few seconds/minutes using simply a couple of drops of the sample to be analyzed. Therefore, this type of technology will be crucial for the development of many high impact applications as for example the implementation of minimally-invasive screening programs for a higher accuracy early diagnosis of diseases as cancer or cardiovascular diseases, a better monitoring of environmental resources in order to promptly identify hazardous pollutants and to properly manage these resources, or the surveillance of public spaces in order to provide an early warning in the case of potential biological/chemical attacks.

However, despite being very high, the sensitivity provided by photonic technology is sometimes not enough to detect very low concentrations of the target analytes or to detect target analytes with a very low size and/or molecular weight. In those situations, the local variations of the refractive index that are produced by the presence of the targets analytes are almost negligible, making them practically undetectable. Unfortunately, many of the most promising applications nowadays fall in that scenario, so alternatives to further increase the sensitivity of photonic-based biosensors are required. Within this context, we present in this paper different approaches being developed in our group for increasing the sensitivity of nanophotonic-based sensing devices.

2. HIGH SENSITIVITY DETECTION APPROACHES

2.1 Use of photonic bandgap sensing structures

Our current work is specially focused on the development of photonic sensors based on 1D photonic bandgap (PBG) structures, as that shown in Fig. 1. In these structures, the periodicity in the propagation direction gives rise to the appearance of a spectral PBG region where guided modes are forbidden; the position of this PBG will be shifted when the target analytes are bound to the surface of the structure. These PBG periodic structures are also characterized by the appearance of the so-called slow-wave effect for the PBG edge modes. That slow-wave behavior translates into a higher sensitivity due to the higher interaction that is produced with the target analytes because of the group velocity reduction.

By using these 1D PBG sensing structures in combination with molecular beacon (MB) probes, we have demonstrated a very high sensitivity towards the detection of short length target oligonucleotides. Spectral shifts of the PBG edge even above 1 nm have been obtained for the detection of a 35-mer target oligonucleotide [1,2], as shown in Fig. 1. These shifts are even more than one order of magnitude higher that those typically obtained using other photonic sensing structures as ring resonators for the detection of similar targets (in the range of 50-100 pm [3]), thus demonstrating the higher sensitivity of PBG structures. Note also that a further increase of the sensitivity can be obtained by properly designing the constitutive parameters of the PBG sensing structure in order to have a better interaction with the targets to be detected.

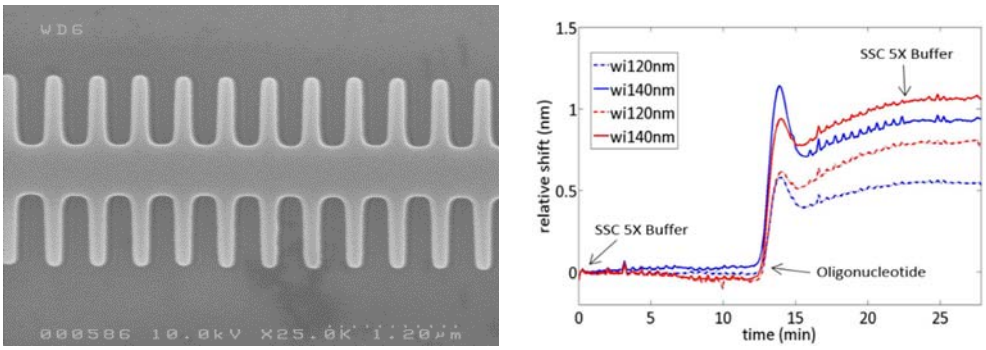

Figure 1. (Left) Scanning electron microscope (SEM) image of a 1D PBG sensing structure. (Right) Evolution of the PBG edge position for four 1D PBG sensing structures with different parameter wi (≡width of the transversal elements) being biofunctionalized with specific MB probes. The 1D PBG sensing structures respond to the presence of the target oligonucleotide when it is flowed over them.

2.2 Use of nanoparticle-labelled molecular beacon receptor probes

A molecular beacon (MB) is a special type of probe for nucleic acids detection. Its working principle is based on the conformational change that the MB probe suffers upon the recognition of its target nucleic acid: the MB probe is initially in a closed stem-loop configuration and it will open into a straight configuration when the target nucleic acid is recognized. Typical use implementations of MB probes are based on attaching a fluorophore and a quencher to their 3' and 5' terminations in order to switch on the fluorescence when the target nucleic acid is recognized (the fluorophore and the quencher are moved away when the MB changes to the straight configuration).

In our group, we are working on the use of MB probes for the biofunctionalization of photonic sensing structures. Besides using them as specific recognition elements, as for the results shown in the previous subsection, we are working on the use of nanoparticle-labelled MB probes with the objective of having additional sensing effects determined by the conformational change suffered by the MB. As it is schematically explained in Fig. 2, the conformational change of the MB can be used to move a nanoparticle away from the surface of the photonic sensing structure when the target nucleic acid is recognized. This displacement of the nanoparticle will produce an additional negative shift on the sensor response, leading to a net sensing response being combination of that negative shift and of the positive shift produced by the direct detection of the target nucleic acid. We have already demonstrated how these two effects determine the sensing response of the photonic structure by using streptavidin-labelled MB probes [2]. By properly designing the photonic sensing structure, the MB probe and the attached nanoparticle, it might be possible to have a net shift being higher than that provided for the direct detection of the target analytes, thus leading to an amplification of the photonic sensing response.

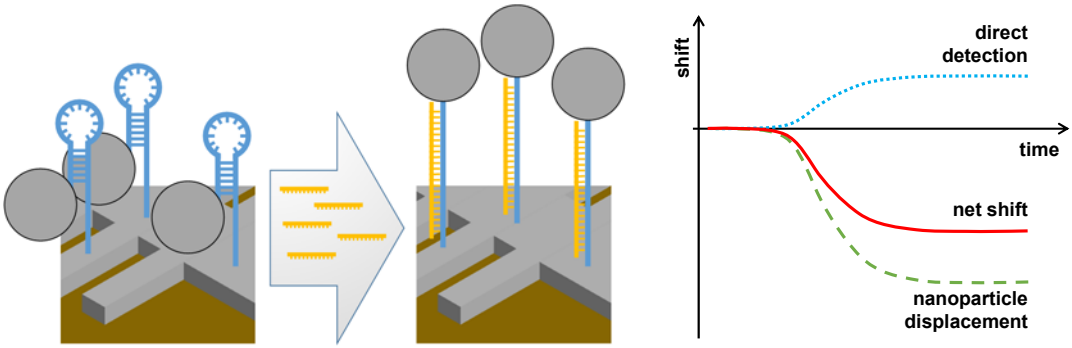

Figure 2. (Left) The nanoparticle-labelled MB probes immobilized on the surface of the photonic sensor change their shape when the target nucleic acid is recognized, leading to the displacement of the nanoparticle from the sensor surface. (Right) The measured sensing response (net shift – red solid line) will be given by the combination of the positive shift produced by the direct detection of the target analyte (blue dotted line) and the negative shift produced by the displacement of the nanoparticle from the surface (green dashed line).

2.3 Use of micro-/nanofluidic concentration systems

Another option for increasing the sensitivity of nanophotonic-based sensing systems is acting over the delivery of the target analytes towards the sensing structure in order to have a higher interaction between the sensor and those analytes. To do so, we are working on the combination of photonic sensing structures with active micro-/nanofluidic systems able to selectively stop the target analytes over the sensing structures, as shown in Fig. 3. These micro-/nanofluidic systems are based on the depletion zone isotachophoretic (dz-ITP) effect [4], which allows controlling the velocity of analytes with a given mobility by combining electroosmotic and electrophoretic

effects. In this way, the effective concentration of the target analytes to be detected can be increased by several orders of magnitude, and thus the final sensitivity of the whole photonic-based sensing system will be increased.

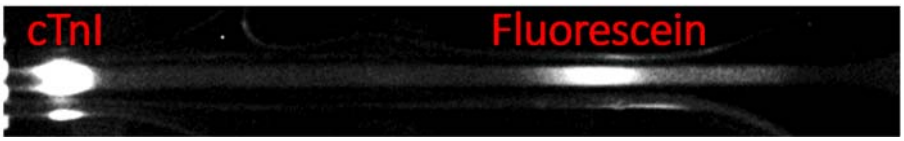

Figure 3. Fluorescence microscopy image of an experiment where cardiac troponin I (cTnI) and fluorescein are separated and concentrated. Results obtained at BIOS Lab-on-a-chip group at the University of Twente.

2.4 Use of porous silicon based sensing structures

The last approach considered to enhance the sensitivity of photonic-based sensors is changing the materials used to create the sensing structures. Typically, photonic sensors operation is based on the interaction of the evanescent field of the photonic structure with the target analytes to be detected. This fact limits the sensing performance of these sensors, since only a small amount of low intensity optical field will actually interact with the target analytes. An alternative for enhancing that interaction of the optical field with the target analytes is using porous materials for the creation of the photonic sensing structures; in that way, the target analytes can enter inside the photonic structure and thus interact with the region where the optical field is more intense. In our group, we are working on the use of porous silicon (PS) for the creation of different types of photonic sensing structures, including Fabry-Perot resonators, microcavities and ring resonators, as shown in Fig. 4. Besides the sensitivity increase produced by the infiltration of the target analytes into the photonic sensing structure, what we have experimentally confirmed by means of refractive index sensing experiments [5,6], porous silicon substrates also provide a higher surface/volume ratio, what also allows increasing the number of sensing events that can be detected, thus also improving the sensitivity.

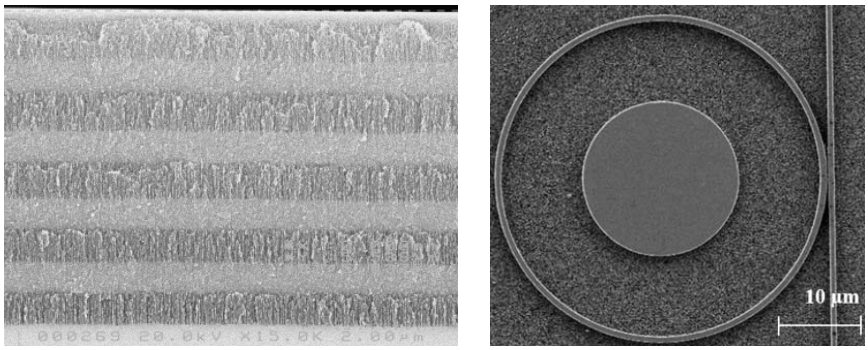

Figure 4. (Left) Cross sectional SEM image of a PS multilayer. (Right) SEM image of a PS ring resonator sensor.

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