

Using integrated optics for advanced point-of-care diagnostic devices

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Abstract—Integrated optics is an extreme useful technology for the production of high sensitive and compact devices for biosensing purposes. Devices can be further integrated in complete lab-on-a-chip platforms for point-of-care diagnostics.

Keywords—optical biosensor; interferometer; point-of-care; microfluidics, grating couplers.

I. INTRODUCTION

Most clinical tests are based on time-consuming, expensive, and sophisticated techniques performed by specialized technicians in laboratory environments. These techniques typically require labeling of the samples or reagents with fluorescent or radioactive markers. There is an unmet need of having reliable diagnostic tools that ensure a sensitive, rapid, affordable and simple analysis, particularly in the clinical practice. Such reliable diagnostic tools could afford the decentralization of clinical diagnostics to point-of-care (POC) settings, allowing tests in primary care facilities and outpatient clinics, in hospital units, workplaces and homes, among others.

Advances in micro- and nanobiosensor technology is offering the implementation of diagnostic tools with increased sensitivity, specificity, and reliability for *in vivo* and *in vitro* applications. Such a device could contain enough hard wired intelligence and robustness to be used by the patient and deliver a multitude of data to the practitioner or the central database of a hospital. It is clear that the application of a portable, easy-to-use and highly sensitive biosensor lab-on-a-chip platform for real-time clinical diagnosis could offer significant advantages over current methods [1].

Taking into account this demand, we are seeking to develop highly-competitive label-free biosensing systems which could be integrated in a portable platform. Different photonic biosensor technologies are pursued in parallel: integrated interferometer devices (Mach-Zehnder and bimodal

waveguides), plasmonic nanostructures and waveguided microcantilevers. Our main aim is to develop a highly sensitive platform for POC analysis based on label-free biosensing detection and integrated in a microsystem instrument fabricated with low-cost technologies of polymer and silicon, and meeting the requirements of disposability and portability.

II. BIOSENSOR LAB-ON-CHIP DEVELOPMENT

The biosensor microsystem is being assembled by integrating the following parts: (i) micro/nano sensors fabricated with standard silicon technology, (ii) a polymer microfluidic cartridge monolithically integrated with the sensor and with the corresponding tube connections, (iii) novel grating coupler devices for the in and out coupling of the light in all the photonic channels for multisensing (iv) robust immobilisation and regeneration protocols for the biological receptor (iv) CMOS photodetectors, electronic & software control (v) final integration and packaging. In the following, we will show our last developments in the sensor, microfluidics and grating couplers steps and the integration between them.

A. Interferometric nanobiosensor

The key element of the microsystem is an array of photonic microsensors based on Mach-Zehnder interferometer devices of high sensitivity. The interferometer devices were fabricated on silicon technology and constructed from rib waveguides of nanometer dimensions (and wavelength in the visible range). Detection of the biomolecular interactions is done through the interaction with the evanescent wave of the light circulating in the sensor area. For the array of sensors, each sensing arm can be functionalised with a different biological receptor specific to the substance to be detected. In this way, we can obtain a device for the real-time detection of substances at the pico/femtomolar level without using fluorescent labels. The high sensitivity of the analysis is guaranteed by the design of the photonic structures in which the evanescent wave

interaction is maximized. Experimental evaluation of the devices indicate a detection limit of $\Delta n_{\min} = 1 \cdot 10^{-7}$ [2].

B. Integrated microfluidic network

One key issue is the way to bring the sample in contact with the sensing area. The volume of the sample and the flow rate are critical parameters, especially for clinical testing, where it is extremely important to reduce the sample volume as much as possible. The size of the channels in the fluidic network, their design, fabrication, connection and alignment to the sensor area are critical steps. We have performed the integration of the MZI biosensor with a microfluidic polymeric network at the wafer level [3]. The microfabrication technique is based on an adhesive bonding process and releasing steps of two photolithographic patterned SU-8 polymeric resist layers on separate wafers: the bottom substrate (the wafer containing the MZI devices) and a temporary top substrate (Kapton™ on borosilicate glass wafer). Once the two-dimensional SU-8 layers were generated, the patterned wafers were aligned and bonded together to form a three-dimensional (3D) microchannel structure between them. After the bonding, the top glass wafer and the Kapton™ film were detached from the SU-8 stack and bottom substrate.

The generated microfluidic channels have a height close to 50 μm and 100 μm width. The microchannel is homogeneous with the same height along the 15 mm length of the MZI sensor area. The successful results are showed in Figure 1 with a top overview of the microfluidic with one microfluidic channel over a sensor window with a perfectly coupled mode propagating and exposed to the channel environment.

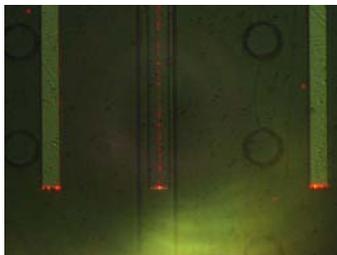


Figure 1. Light propagating in a waveguide sensor window integrated with a 56 μm microfluidic channel.

The platform can operate at pressure drops up to 1000 kPa under steady-state flow rates ranging from 1 to 1000 $\mu\text{l}/\text{min}$ in laminar flow regime.

C. Mountable diffraction grating coupler

Light coupling in/out of the waveguides can be realized by using diffraction gratings (DG) with sub-micron period. But usually the compatibility and complexity of the technologies for batch fabrication of the DG couplers and the waveguides on the same wafer is a challenge. In order to solve the known problems, we have proposed a novel approach where grating couplers were fabricated separately and then were attached to the waveguides. We used hard dielectric thin film couplers

supported by a polydimethylsiloxane (PDMS) film. We developed a technique to mount thin film dielectric grating couplers onto planar waveguides. The couplers were batch fabricated, fixed on the elastomer film, characterized and then installed on the chip containing the waveguides (see Figure 2). The property of the elastomer film to adapt or to stick to even nonplanar surfaces is employed to press the couplers against the waveguides. Similar to the prism couplers concept, the gratings can be reliably pressed against the waveguides by the elastomer and can be safely released from it. Our method has assured a good and reproducible contact of the waveguides with the thin film grating couplers, both fabricated separately. We have called this approach “mountable gratings”.

No air gaps were observed at the interface between the gratings and the waveguides, confirming that the DGC was in contact with the waveguide surface, except on defects. The out-of-plane light coupling into the rib waveguide using the proposed hybrid DGC-PDMS system was obtained focusing a He-Ne laser (632.8 nm) on the grating using a plano-convex lens. Preliminary results indicate a coupling efficiency of 5% (TE polarization). This value could be further improved.

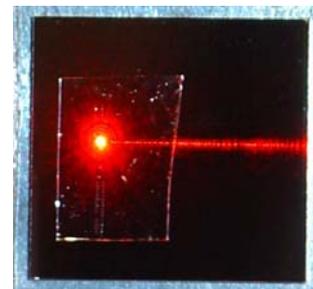


Figure 2. Out of plain coupling of light into a waveguide. Mountable DG couplers were attached to a chip with silicon nitride waveguides.

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