Integrated optical sensing in a lab-on-chip by femtosecond laser written waveguides

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Abstract: Integrated optical detection in a commercial microfluidic chip for capillary electrophoresis has been implemented by means of femtosecond laser written optical waveguides for excitation and a high numerical aperture optical fiber for collection.

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Lab-on-chips (LOCs) are microsystems capable of manipulating small (micro to nanoliters) amounts of fluids in microfluidic channels with dimensions of tens to hundreds of micrometers: they have a huge application potential in many diverse fields, ranging from basic science (genomics and proteomics), to chemical synthesis and drug development, point-of-care medical analysis and environmental monitoring [1]. Notwithstanding their potential, LOC commercial exploitation has been slow so far. One breakthrough that could promote LOC diffusion is an integrated on-chip optical detection system. In this work we propose the use of femtosecond lasers as a novel highly flexible tool for optical waveguide microfabrication in LOCs, for the realization of low-cost and truly portable biophotonic microsystems. Femtosecond laser processing is a direct, maskless fabrication technique enabling spatially selective three-dimensional material modification [2]. It allows to position optical waveguides inside an already made LOC without affecting the manufacturing procedure of the microfluidic part of the device, thus greatly simplifying the production process and taking advantage of the already well developed microfluidic chips.

As a first example of the potential of integrating optical waveguides in LOCs for optical sensing, we took a commercial microchip for capillary electrophoresis (LioniX bv, the Netherlands), whose layout is shown in Fig.1(a). This chip has two crossing microchannels (folded in a complex way in order to reduce the chip footprint), that are responsible for the sample injection (channel going from reservoir 1 to 3) and for the electrophoretic separation (channel going from reservoir 2 to 4).

Figure. 1(a) Schematic diagram of the commercial microfluidic chip; (b) fluorescence induced in the microchannel by the optical waveguide.

The separated species at the end of the channel 2-4 are typically detected by laser induced fluorescence (LIF) using a standard microscope. We propose the use of optical waveguides to provide a highly localized excitation for an integrated LIF measurement. Several optical waveguides have been inscribed perpendicular to the separation channel towards its end (red lines in Fig.1(a)) by means of an amplified Ti:sapphire laser delivering 4-μJ, 150-fs pulses at 1 kHz. A very precise alignment procedure has been developed in order to have the 10 μm-diameter waveguides exactly crossing the 12 μm-high microfluidic channel. The waveguides have circular cross section and

are single mode in the visible with propagation losses as low as 0.5 dB/cm in the green [3]. A compact frequency doubled Nd:YAG laser at 532 nm is coupled to the waveguide by a single mode optical fiber providing the excitation light.

In order to demonstrate the capability of the femtosecond laser written optical waveguides to excite fluorescence inside the microfluidic channel, the latter was filled with a solution of Rhodamine 6G. Figure 1(b) shows the fluorescence in the yellow excited by the green light coupled into the waveguide. The excitation is very selective in space (10 μm , as the waveguide diameter), as a further confirmation of the very low leakage out of the waveguide, which is quite important for a high resolution in the electrophoretic experiments. In addition, the excited fluorescence covers the whole width (50 μm) of the channel due to the low divergence of light coming from a waveguide with a numerical aperture below 0.1. As shown in Fig.2, the induced fluorescence is collected by an optical fiber glued to the chip in correspondence to the excited portion of the microchannel in a 90° geometry with respect to the exciting waveguide, thus giving the best signal to noise ratio (SNR). The collection fiber has an ultrahigh numerical aperture of 0.5 and a core diameter of 600 μm in order to collect as much fluorescence signal as possible. Such signal is detected by a photon counting photomultiplier tube. Notch and interference filters are used to further reject the excitation light and autofluorescence. A complete characterization of the limit of detection of this integrated detection scheme is in progress, but preliminary results showed that a fluorescence signal as low as 3.5 fW could be detected with a SNR of 10 for an excitation power of 4 nW and a rhodamine concentration of 4 μM . This should allow to detect the nM concentration level with a few μW s of excitation power.

Figure. 2 Schematic of the excitation/detection of the fluorescence in the microchannel. FIB1: optical fiber; FIB2: ultrahigh numerical aperture fiber; WG: waveguide; CHAN: microchannel; AL: aspheric lens; FIL1: notch filter; FIL2: interference filter; PMT: photomultiplier tube

Standard excitation/detection schemes for LIF in LOCs use a confocal geometry with a microscope objective, i.e. a single objective is employed for both the excitation and the collection with a dichroic beam splitter. The present integrated scheme provides several advantages, the main ones are: i) it is monolithic, thus it does not require any fine alignment to the microfluidic channel, with an increased portability; ii) it provides the same collection efficiency as that of a microscope objective, but it generates a much higher signal since the optical waveguide used for excitation has a much lower numerical aperture than the objective and is thus capable of exciting the fluorescence in the whole channel width; iii) it allows a 90° detection geometry, strongly suppressing the excitation light background.

This work demonstrates that the femtosecond laser writing of waveguides can be a very important tool to integrate optical excitation/detection in commercial LOCs without affecting their manufacturing process. The integrated scheme here discussed could strongly increase the portability and compactness of the LOCs by overcoming the present limitation where microfluidic systems are coupled to macroscopic bulk optical detection systems.

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