Ultra-compact label-free silicon-nanoantenna-based optofluidic microflow cytometer with a high signal-to-noise ratio

(Student Paper)

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ABSTRACT

Flow cytometry currently represents a fundamental source of progress in biomedical research and chemical diagnosis, opening new means in the treatment of diseases such as AIDS or cancer. Via this technique, flows of live cells or biotargets can be dynamically analysed via the use of optical- or impedance-based devices. In this work, an ultra-compact microflow cytometer enabled by on-chip silicon photonic antennas with an enhanced signal-to-noise ratio (SNR) is designed and experimentally demonstrated. The authors previously employed the design of these all-silicon integrated nanoantennas, allowing the realization of an optofluidic lab-on-a-chip sensor. Going a step further, here, we developed an enhanced version of this system, focusing our efforts on improving the SNR of a target in several angular positions. We find an optimal receiving angle with SNR figures higher than 14 dB, which not only overcomes our previous scheme by more than 10 dB, but also competes with the best state-of-the-art on-chip implementations, yielding the most compact footprint demonstrated so far.

Keywords: Lab-on-a-chip Devices, Integrated Optics, Nanoantenna, Sensing, Silicon Photonics.

1. INTRODUCTION

Flow cytometry allows the rapid and simultaneous analysis of multiple parameters of live cells in aqueous solutions as they flow in a stream via optical or electric signals. As mentioned before, this technique has become an essential tool in cell sorting and analysis with a notable impact in the biomedical and chemical fields. However, traditional top bench flow cytometers are expensive devices and require the presence of trained personnel in their use, implying additional indirect costs. Moreover, traditional flow cytometers demand large amounts of expensive reagents and solutions, with non-trivial post-processing steps, feature that entails high maintenance costs [1]. Along this line, lab-on-a-chip technology has arisen as a promising alternative for reducing both the cost and the bulky implementations of traditional biomedical equipment [2]. Most of the current approaches to on-chip microflow cytometry are based on the use of optical- or impedance-based technology [1, 3], as mentioned before. While both schemes offer valuable and complementary information [3], impedance-based systems present some disadvantages as compared to optical ones. For instance, an impedance-based multiparametric analysis can only be performed by using alternating electric currents with different frequencies, requiring external equipment [4]. In contrast, this can be achieved with optical cytometers just by scanning different angles at a single frequency. The integration of electrodes into the microfluidic channel, typical in these schemes, also increases the cost and complexity of the device as compared to optical approaches [1]. Those are the main reasons why most of the current approaches to on-chip microflow cytometry are based on optofluidic devices [1]. Within the optical approach, fluorescence-based flow cytometry has proved its suitability to identify and classify biotargets. However label-free systems -as those based on scattering biotarget analysis- are currently preferred [5], as they avoid the cost, time, and the use of fluorescent biomarkers that could potentially damage the analyte.

In this paper, we propose a novel antenna-based approach -able to radiate sharp beams thanks to its high directivity- that avoids the use of non-compact structures such as fibres or microlenses, usually in the mm-scale, to illuminate the targets and collect the scattered light, commonly used at previous lab-on-a-chip designs [1]. Thus, we get rid of the previously mentioned bulky structures enabling an ultra-compact on-chip nanoantenna-based optical subsystem ($0.64 \times 14\ \mu m^2$ for a single nanoantenna) able to yield the most compact implementation of microflow cytometers demonstrated so far. Moreover, this reduced footprint, together with the fact that the proposed structures can be fabricated using standard CMOS-compatible silicon-on-insulator (SOI) technology, shows the low-cost nature of this approach. This scheme provides a notable advance in portability, fabrication automation and cost reduction not only respect to standard top bench cytometers but also to previous integrated approaches [1]. Outstandingly, thanks to the high-directive nature of the nanoantennas, we can achieve an enhanced SNR in the target detection as passing in front of the emitting antenna regarding our previous design [6], also rendering a very low coefficient of variation (CV) for specific angular directions. All designs and experiments were carried out at the wavelength $\lambda = 1550$ nm, for the target illumination.

2. THEORY AND SIMULATIONS

The main building block of our microflow cytometer is an all-silicon highly-directive photonic nanoantenna. Specifically, we used the antennas proposed in [6], which are based on open-ended strip waveguides. The directivity of these structures was modelled via the Huygens' principle (typically used in classic antenna theory [7]) to achieve sharp radiation beams in the fluidic channel. In the final configuration of the microflow cytometer we use an antenna consisting of a transition from a standard 450-nm-width 220-nm-height strip silicon wire to a 150-nm-width silicon tip through an inverted taper, which already achieves a directivity as high as 54 (linear units), see Figure 1A. Several additional elements (the so-called directors) were placed in front of the antenna to further improve its directivity [6]. Figure 1A additionally shows the impact of the number of directors on the antenna directivity. In Figure 1B, the final configuration of the antenna and the directors is depicted.

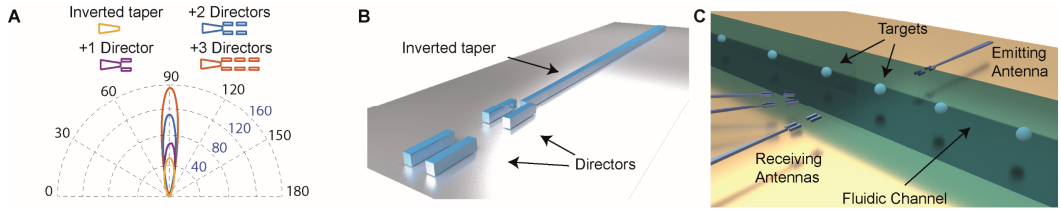

Figure 1. A) Polar directivity diagram of the designed antennas as a function of the number of directors. Blue numbers represent the directivity. B) Artwork displaying the final antenna and two directors used for the experimental microflow cytometer. A 2-µm thick layer of SiO_2 covered the antennas in the simulations and experiments. C) Scheme of the proposed microflow cytometer based on the use of the designed antennas.

A given particle scatters light differently in each direction when illuminated by a light beam, providing a traceable time-dependent pulse shape. Therefore, the power intensity detected by the receiving antenna depends on the angle at which it is placed. The goal of this work was to optimize this angle in order to maximize the SNR in the target detection. To this end, we simulated the power received in a set of antennas placed at different angular directions, which were normalised to the power received in the baseline configuration (i.e., that in which there is no particle in the channel between antennas). To design the system, we used a similar arrangement to that employed in [6], which is made up by an emitting antenna, a 10-µm-wide 4-µm-deep fluidic channel filled with an aqueous solution where the particles flow and the aforementioned set of receiving antennas, see Figure 1C. Following this previous experiment, we used the system to explore the scattered-power signature of polystyrene microspheres with a diameter of 2 µm. Polystyrene beads were placed in the middle of the microfluidic channel (x-direction), while different positions in the flowing direction (y-axis) were considered, see Figure 2A.

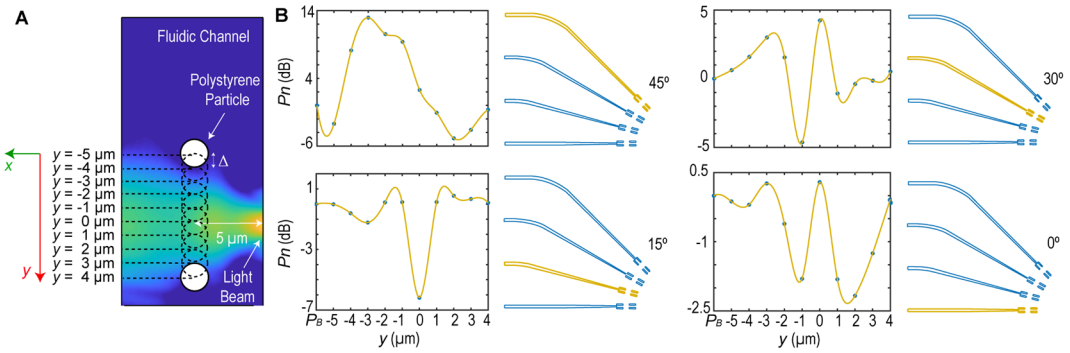

Figure 2. A) Schematic top view of a microfluidic channel where a polystyrene bead is flowing. The light beam radiated by the emitting antenna illuminates the targets (at the centre of the channel in the transverse or x-direction) for ten different longitudinal positions, from y = -5 µm to y = 4 µm, with steps of Δ = 1 µm. In an experiment, a flowing particle will be in a different position at each instant. B) The power scattered from the target at each position are retrieved for each receiving antenna. P_B accounts for the power of the baseline configuration when no targets are within the channel. $P_n = 10 \cdot \log10(P/P_B)$, where P represents the power value of a target measured in a specific position.

As can be seen in Figure 2B, there are different and characteristic pulses depending on the direction from which the scattered field of the particle is retrieved. Clearly, the better SNR was attained for the 30º and 45º directions, with an amplitude of 8 dB for the former and an outstanding 17-dB figure for the latter.

3. EXPERIMENTAL MEASUREMENTS

Taking into account the previous discussion, we conducted an experiment to demonstrate the sensing ability of the proposed antenna-based microflow cytometer. In our final device, the wireless deployment is made up of the highly-directive emitting antenna considered above and two other identical antennas measuring the scattered field

at 30º and 45º (the angles for which a better numerical SNR was obtained), see Figure 3A. To build the fluidic subsystem, a 10-µm-wide 4-µm-deep trench was directly opened in the SiO_2 region in between the antennas. This subsystem is completed with the incorporation of two inlet and outlet reservoirs, where the solutions containing the microparticles (10 µl volume, concentration of 0.1 % solids) are drop cast with a precision micropipette. The two receiving antennas located at 30º and 45º simultaneously measured the characteristic time-dependant scattered-field pulses of these microspheres as passing in front of the emitting antenna. On the 45º direction, a well-defined pulse is displayed when the target is detected, see Figure 3B, yielding figures of SNR as high as 14 dB. Outstandingly, there is and almost qualitative and quantitative perfect agreement between the simulations (where 17-dB SNR pulses were retrieved) and the experimental results. Additionally, we calculated the experimental CV at both directions, yielding values of 28.17 % and 6.64 % in the 45º and 30º directions, respectively. This last figure (at 30º) represents a record regarding the reported CV for previous microflow cytometers where the light signal is retrieved on-chip.

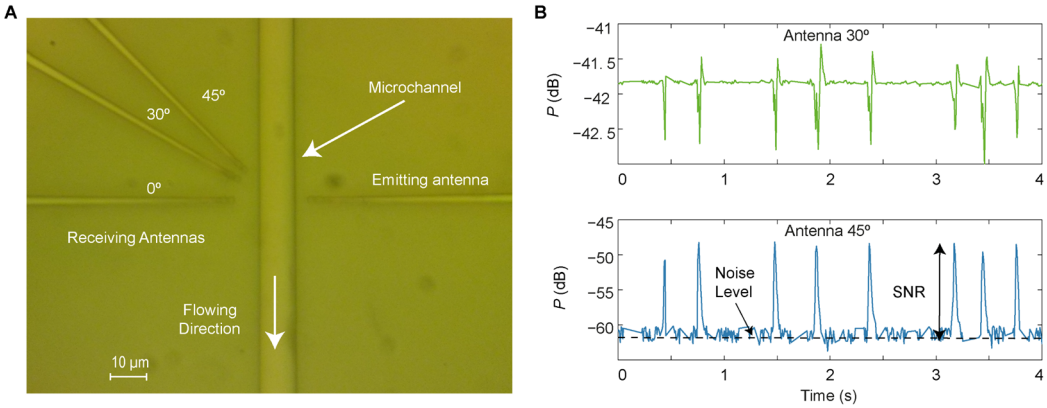

Figure 3. A) Optical microscope image of the fabricated microflow cytometer. B) Power efficiency (P) simultaneously measured at 30º and 45º during a four-second interval. In this case, P = 10·log10 (PRX/PTX), where PTX is the power injected to the emitting antenna, and PRX is the power retrieved at the receiving antennas. Very similar pulse shapes are measured if compared with those calculated numerically (Figure 2). The SNR level at the 45º configuration also matches the results anticipated by the simulations.

4. CONCLUSIONS

In this work, we have experimentally demonstrated the realization of an on-chip silicon photonic antenna-based microflow cytometer with a notably improved SNR in the target detection regarding our previous scheme [6], yielding figures as high as 14dB. Outstandingly, this design is achieved with a dramatically reduced footprint (0.64 ×14 µm^2 for a single antenna), as compared with current state-of-the-art approaches [1]. The combination of this antenna-based photonic subsystem together with integrated microfluidic deployment, paves the way towards the realization of cost-effective lab-on-a-chip flow cytometers and POC sensing devices with a direct impact for biological, chemical and medical diagnosis.

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REFERENCES

[1] Y.S. Zhang *et al.*: Optofluidic device based microflow cytometers for particle/cell detection: a review, *Micromachines*, vol. 6, 70, Apr. 2016.

[2] D. Psaltis, S.R. Quake, C. Yang: Developing optofluidic technology through the fusion of microfluidics and optics. *Nature*, vol. 442, pp. 381-386, Jul. 2006.

[3] K.C. Cheung *et al.*: Microfluidic Impedance-Based Flow Cytometry. *Cytom. Part. A*, vol. 77A, pp. 648-666, Jul. 2005.

[4] K.C. Cheung, S. Gawad, P. Renaud: Impedance Spectroscopy Flow Cytometry: On-Chip Label-Free Cell Differentiation. *Cytom. Part. A*, vol. 65A, pp. 124-132, Jun. 2005.

[5] T. Blasi *et al.*: Label-free cell cycle analysis for high-throughput imaging flow cytometry. *Nat. Comms.*, vol. 7, 10256, Jan. 2016.

[6] C. García-Meca *et al.*: On-chip wireless silicon photonics: from reconfigurable interconnects to lab-on-chip devices, *Light Sci. Appl.*, vol. 6, e17053, Sept. 2017.

[7] C.A. Balanis: Aperture Antennas, in *Antenna Theory: Analysis and Design*. 3rd Ed., New York: Wiley, 2005.