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Integrated photonics for miniature flow cytometry

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Abstract

We present a miniature flow cytometry device based on on-chip integrated photonics and microfluidics. At its heart is a specially designed diffraction grating which delivers uniform fluorescence excitation with an extremely small footprint. This device concept allows dense parallelization and can constitute an important next step in the miniaturization of fluorescence-activated cell sorting (FACS) with a fabrication process that is fully CMOS compatible.

1. Introduction

For many applications in life sciences, the biologically relevant information is probed by means of visible light. Many of the critical optical components have unfortunately still a large footprint and heavy price tag. At telecom frequencies, on-chip silicon photonics is revolutionizing optical communication systems. A similar evolution can be anticipated for integrated photonics in the life sciences, at visible frequencies. Integrated waveguide optics –allowing for complex routing schemes of light across a chip– assumes a prominent role in the progressing miniaturization of optical devices. However, in order to have the light in the chip interrogate a distant biological entity, diffraction gratings have to be used to couple light out of the chip.

Here, we present a specially designed diffraction grating that is able to deliver a highly uniform illumination that escapes the chip in a collimated beam at a predesigned angle (illustrated in Fig. 1). Because of its integrated nature, a component like this is highly relevant for the miniaturization of, e.g., flow cytometry applications [1,2]. We therefore include microfluidic channels on top of the photonics chip and demonstrate the cytometric capabilities with fluorescent polystyrene beads.

2. Discussion

Diffraction gratings are an essential tool to couple light into and out of on-chip waveguide systems. Ideally, all the light from the waveguide would be coupled out into a beam with a predefined polarization, phase, and intensity profile. As such they should be able to produce any functional beam that is typically prepared by free space optical components. Yet, in practice, there is a design trade-off between beam quality and out-coupling efficiency. For a standard, linear grating an exponential intensity decay is observed along the grating, i.e., much more light is coupled out at the start than at the end.

For fluorescence based applications, it is often crucial to determine relative intensities, especially so in cytometry where different cell populations are distinguished based on the relative expression of different fluorescent markers. All cells passing by the detection region therefore are required to receive the same excitation intensity. Prior to passing by the detection region, the cells are focussed using, typically, hydrodynamic or acoustic focussing. The focussing accuracy is only a few tens of micrometres, so the illumination should be uniform within at least the same length scale. Standard diffraction gratings don't meet this requirement in combination with high efficiency.

We therefore developed a special grating yielding a uniform illumination as illustrated in Fig. 1. Using finite difference time domain (FDTD) simulations, we show that these gratings can efficiently couple-out light and form a well-defined light sheet. We verify this experimentally by measuring the light sheets of gratings fabricated in a silicon nitride (Si_xN_y) on SOI wafer stack. The chips were processed in a CMOS pilot line using PECVD Si_xN_y which allows for low loss waveguide propagation in the visible and near-infrared spectral range [3]. This range is ideally suited for several laser lines typically used in the life sciences. The gratings were designed for both green and red laser light, indicating the possibility for multicolour on-chip excitation.

In the same pilot line, microfluidic channels are defined in a polymer layer on top of the chip. A quartz cover slip with fluidic inlets is finally flip-chip bonded to seal the fluidic channels.

The cytometry functionality of the devices is verified by running fluorescent polystyrene beads used for cytometer calibration through the microfluidic channel and detecting their luminescence.

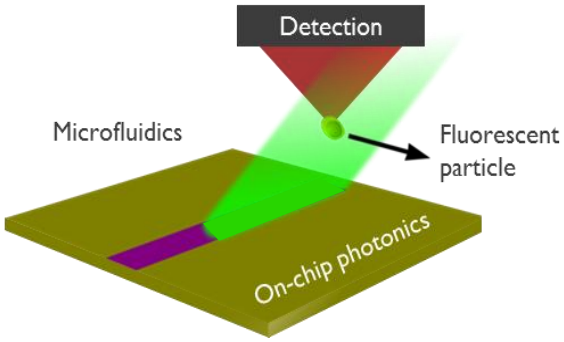

Fig. 1: Illustration of the miniature cytometry device indicating the photonics chip with specially designed grating (purple), created uniform illumination (green), fluorescent particle flowing through the microfluidic channel after being hydrodynamically focused, and its luminescence being detected (red).

3. Conclusions

We have demonstrated a proof-of-concept miniature cytometer built around an integrated photonics chip. Using integrated microfluidics, the opto-fluidic system was characterized with calibration fluorescent polystyrene beads. The compact photonics-based cytometer can be an elementary component for chip-based cytomics. Our work further demonstrates the potential of integrated visible photonics and flat optics for life science applications.

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