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Optical particle detection in liquid suspensions with a hybrid integrated microsystem☆

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ABSTRACT

In this work, we present an optical microsystem for particle flow detection, based on hybrid integration and silicon micromachining. Sensing principle is light obscuration. We demonstrate the feasibility of integrating commercial components such as light sources (850 nm near infrared Vertical-Cavity-Surface-Emitting Lasers VCSELs) and optics (an array of microlenses) into a silicon fabricated structure to create an optoelectronic package of reduced dimensions (14 mm × 12 mm) and low power consumption (≈7.2 mW) that satisfies optical requirements and provides four collimated laser beams with reduced diameter spots (minimum radius of 124 μm measured as $1/e^2$ standard). Besides this microoptical system, the detection system is completed with a double linear array imaging sensor of 256 pixels, designed and fabricated in 0.35 μm CMOS technology, and a microfluidic platform. The designed set-up allows the simultaneous optical detection of singly aligned microbeads flowing in liquid suspensions through several parallel microfluidic channels, which share the pitch of the laser emitting sources, i.e. 250 μm. While the throughput of the system is increased up to 5000 particles/s thanks to the possibility of performing parallel measurements, the double array of the imaging sensor improves the detection process discarding false detected events. Experimental results prove that the system is able to detect and distinguish microparticles of several sizes in a mixed solution, with detection limit set at 10 μm diameter. In conclusion, the fabricated microsystem is presented as a miniaturized and robust alternative to current optical microflow cytometers based on the use of optical fibre, and the complete system, including fluidics and imaging sensor stages, represents a portable solution packaged in less than 5 cm^3. These features make it an interesting choice to consider in the field of point-of-care biosensing applications.

1. Introduction

During the last decades there has been an increasing interest in the field of particle detection and characterization, in part due to the growth of point-of-care biosensing applications which require cell counting as one of the phases in their assays for fast screening, diagnosis and detection of diseases (e.g. diabetes or HIV), but also thanks to the impetus of industry, where usually bulky and expensive particle counters are used to control the quality of materials and products avoiding the presence of contaminants and foreign particles in the production processes.

Particle size, shape or surface characteristics can influence, for example, the efficacy of a pain-reliever, the efficiency of a catalytic converter, or the resolution of a printer. Also concentration of particles in ambient air is a subject regulated by the legislation in Europe and North America, establishing the limits that should not be surpassed due to their detrimental effects in human health.

In the process of conception of instruments with the ability of performing this kind of operations, classical and conventional particle characterization methods have gradually been replaced by optical non-invasive methods based on light-matter interaction, more according to the new standard design criteria: integration, miniaturization, portability, low-cost, facility of use, user-friendly management, low consumption, good performance and multifunctionality are only a few of them. Besides, optical methods provide extra information about size, shape and surface characteristics of the analyzed particles, and are even able to identify targeted particles [1].

The flow cytometry technique for analyzing and counting particles suspended in fluids is a paradigmatic example. In this technique, a sheath flow encloses the particle sample stream to ensure that only singly aligned particles flow at high speed in controlled positions within a detection window, where optical

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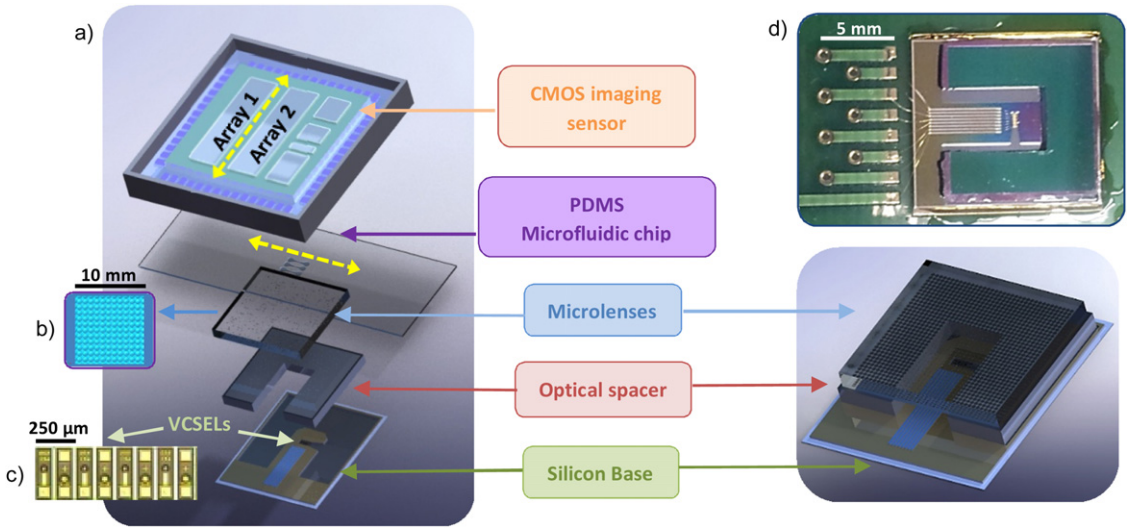

Fig. 1. (a) Scheme of the optical particle detection system. The silicon base and optical spacer create the structure where the commercial elements (microlenses array (b) and VCSELs (c)) can be assembled, resulting in an optoelectronic package. The PDMS microfluidic chip with four microchannels is placed between the optoelectronic package and the CMOS double array image sensor. Yellow arrows indicate the direction of the double array of photodetectors with respect to the direction of the microfluidic channels included in the PDMS chip. (d) Photograph of a silicon fabricated optoelectronic package. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

properties of the particles are analysed by illuminating the zone with collimated laser beams and measuring scattered light (proportional to the size and internal properties of the particles) and fluorescence (useful for cell targeting). Commercial equipment offer extremely high throughputs up to 10^5 particles/s, but the main drawback is, once more, their bulkiness. Several fabrication alternatives of miniaturized flow cytometers have been proposed by different research groups [2,3], where optics plays a prime role ensuring that the light spot illuminating the detection zone accomplishes specific requirements of shape and size.

In fact, in optical particle detection systems the goal is to obtain efficient coupling and focusing of light into the interrogation window, whether with fiber optics (off-chip approximation) [4] or with the integration of optical elements, sources and detectors as close as possible to the area of interest (on-chip approximation) [5].

Optics integration leads to the use of on-chip lenses, with benefits such as reduced cross-talk effect. In flow cytometry, these lenses can be used to improve not only interrogation, but also the sensitivity in the detection process minimizing the levels of background light collection and collecting signals of lower light intensities (e.g. with high numerical aperture lenses) [6,7].

Miniaturized and integrated optical devices result not only in a reduction of the fabrication costs, but also in the overall instrument size, improving its portability and opening the door to perform measurements near the place of interest, shortening time-to-results. Robust devices should also allow carrying out measurements in special conditions and environments where classic instrumentation fails to deliver acceptable results. Those are features pursued by point of care testing devices [8].

Unfortunately, in most cases optical detection systems still rely on the use of external elements, such as optical fibres [9,10] to transport light from an external laser source to the interrogation zone and to collect the response to the light stimulus. This results in bulky or fragile systems, difficult to miniaturize.

In other cases, those external elements are substituted by others integrated into the detection chip, such as waveguides that are usually included in systems with on-chip lenses to direct light to particular points of interest [11], but again the use of bulky external light sources represents a drawback in terms of miniaturization [12,13].

A new trend is set by devices that not only take benefit of optical detection and characterization, but also incorporate impedance analysis in order to surpass the limitations of miniaturized optical systems when dealing with the measurement of the small angle forward scattering (FSC). This parameter offers information about the volume of the particles, but it is difficult to implement in optical systems of reduced dimensions, due to the complexity in the placement of optical fibers at small angles [14,15]. Although this complementary information is indeed quite interesting, these new devices rely on the use of electronic external equipment to perform the impedance measurements, such as function generators, lock-in amplifiers or spectroscopes, resulting in non-portable systems.

Our work follows the line defined by authors who develop complete miniaturized systems [16–19] dealing with the issues of integrating optics and light sources, to obtain a robust and portable optical detection microsystem. Thus, we present the design, fabrication and testing of a miniaturized package for optical detection and characterization of microparticles flowing in liquid suspension through multiple microfluidic channels included in disposable chips. The sensing principle is based on light obscuration effect, i.e. we measure the variation of the light signal caused by the flow of particles, with a detection low limit set at 10 μm diameter particles. Practical applications in accordance with this limit could be the detection of silt, fine dust, cement dust, pulverized coal, plant spores and pollens, milled flour, protozoan cysts and even some bacteria. The device is aligned with the current tendency defined by LoC and μTAs biosensors with highlight features such as low power consumption, small sample volumes (≤μl), fast measurements and accurate results, packaged into single and portable low cost systems perfectly suitable for untrained users and point of care testing.

2. System overview

For the complete optical microsystem here presented, three subsystems were developed as an approach to a flow cytometer [20] (Fig. 1): at the top level, the double array image sensor with the embedded CMOS photodetectors, responsible for the optical detection; at the middle level, the microfluidic platform with disposable Polydimethylsiloxane (PDMS) chips containing the