Planar Integrated Free-Space Optical Fluorescence Detector for Micro Fluidic Applications

M. Amberg*, A. Grewe*, J. Cao**, M. Köhler** and S. Sinzinger**

Technische Universität Ilmenau, Institut für Mikro- und Nanotechnologien,

**Fachgebiet Technische Optik, **Fachgebiet Mikroreaktionstechnik, Germany*

mailto:martin.amberg@tu-ilmenau.de

Based on the planar integrated free space optical systems approach the design and manufacturing results of a fluorescence detector are presented. The system is fabricated by micro milling on a KUGLER microgantry® 5x milling machine. The fluorescence detector is designed for the integration into the segmented flow environment for pH-sensing in fluid segments[1].

1 Introduction

Fluorescence detectors are useful for various applications in biomedicine e.g. for pH-sensing or single-cell detection. Commonly conventional macroscopic optical systems are used for such applications. Planar integrated free space optical systems (PIFSO)[2] offer the advantages of compact efficiently integrated systems and good accuracy in the terms of alignment and fabrication. Segmented flow systems enable the generation of thousands of fluid segments with reaction volumes in the pico-liter range in off-the shelf tubes. Within this paper we demonstrate the potential of combining the segmented flow environment and the PIFSO concept. An integrated PIFSO system manufactured by ultra precision micro milling machine in a thermoplastic material like PMMA is presented.

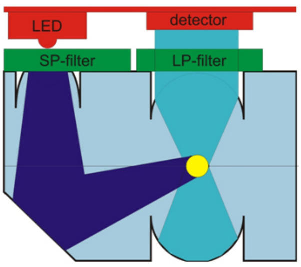

Fig. 1 *Principle Set-up of the integrated fluorescence detector.*

2 Systems Layout

Based on the PIFSO concept the goal is to build up a system which can be combined with a planar electronic layer, carrying the LED light source, the electronics and the detector. Fig. 1 shows the principle set-up. The LED source is collimated and redirected by the mirror coated surface to illuminate the tube with the fluid segments being pumped through. Within the fluid segments fluorescence markers are excited and emit light of a wavelength longer than the excitation wavelength due to the so called Raman shift. Using a short and a long-pass filter it is possible to reduce the amount of radiation from the LED's source reaching the detector. Thus the detector signal almost exclusively results from the fluorescence of the marked cells in the fluid segments. The fluorescence light from the fluid segments is collected by a lens and focused onto the detector. An additional mirror on the opposite side of the lens reflects this proportion of light back into the system and onto the detector.

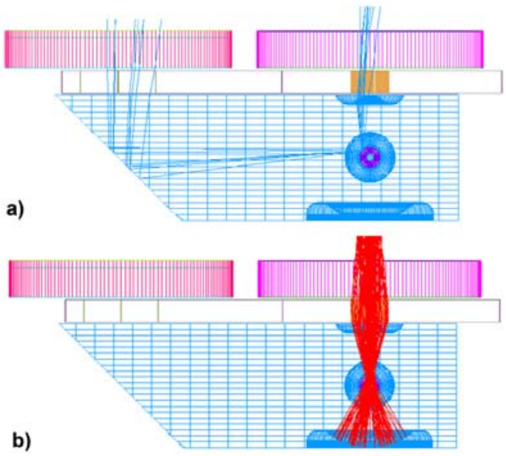

Fig. 2 *a) Analysis of light coming from the LED and going directly to the detector and b) analysis of fluorescence signal both done with ASAP™.*

3 Optical Layout

For the optical layout the optical design and simulation software tools ASAP™ and ZEMAX™ are a versatile tool. Both programs were used for the optical design of the integrated fluorescence detector. For the demonstrator system the lens as well as the mirror are implemented as spherical elements and the mirror in the illumination path is planar. From the result of the optical design process a detailed model of the system, including the needed clearance for the cutter tool is generated using a 3D-CAD-software tool. This model is simulated optically with ASAP for further analysis of the performance as it is displayed in Fig. 2a and b. An important criterion for our system is the signal to noise ratio (SNR) of the detector signal. For the presented set-up is the simulations yield an SNR=1.65. Further on, the illumination and its angular distribution on the detector is simulated to ensure that the beam remains within the acceptance angle (±20° to the normal) of the LP-filter to guarantee the blocking of the short wavelength parts of the light.

4 Fabrication by Micro Milling

For the preparation of the fabrication process the CAD-model is imported to a CAD/CAM software tool to generate the paths of the tool during the milling process (see Fig. 3a). The fabrication is performed on a KUGLER microgantry 5x milling machine and the result can be seen in Fig. 3b.

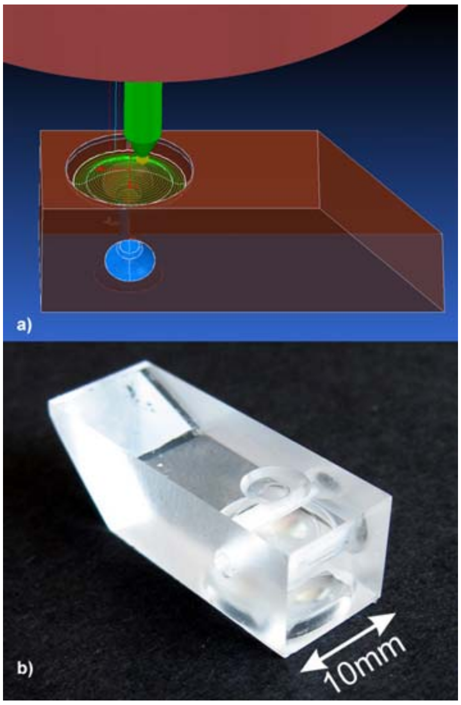

Fig. 3 *a) CAD/Cam software is used for generating the paths of the tool and b) fabricated system in PMMA by micro milling.*

This fabrication process results in surface qualities[3] with R_a=30nm and precise alignment due to the possibility to fabricate the system within a single fabrication cycle.

5 Experimental Setup

Figure Fig. 4 shows the set-up with the integrated segmented-flow tube. The fluorescence signal of the markers inside the fluid segments can be observed without an electron multiplier tube (EMT). Quantitative experiments for the characterization of the fluorescence signal are currently under progress.

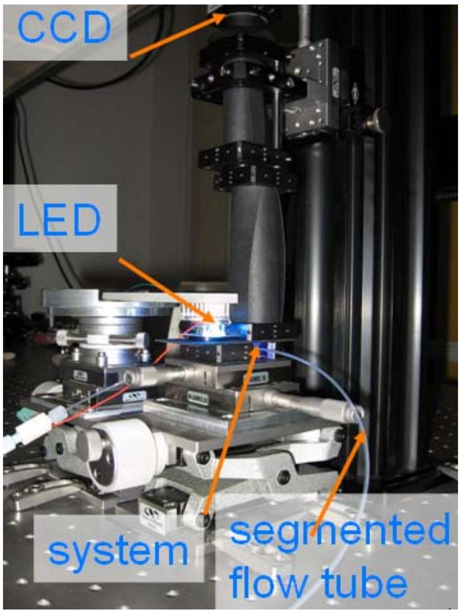

Fig. 4 *Experimental Set-up.*

6 Conclusion and Outlook

Within this paper we present the set-up, design and fabrication results of a planar integrated free-space optical fluorescence detector in a segmented-flow environment. Characterization of the fluorescence signal is currently under progress. Redesign will take aspheric optical elements into account for improved optical performance.

References

[1] A. Funfak et al., „Monitoring cell cultivation in microfluidic segments by optical pH sensing with a micro flow-through fluorometer" in Microchimica Acta, **164**(3-4), pp. 279-286 (2008)

[2] J. Jahns und B. Acklin. „Integrated planar optical imaging systems with high interconnection density", Opt. Lett., **17**(19), pp.1594-1596 (1993)

[3] S. Stoebenau, and S. Sinzinger, "Ultraprecision machining techniques for the fabrication of freeform surfaces in highly integrated optical microsystems", Proc. SPIE, Vol. 7426, 742607 (2009)

Acknowledgements

This project is supported by the "Bunderministerium für Bildung und Forschung (BMBF)" within the project "OPTIMI" as a part of "Kompetenzdreieck optische Mikrosysteme". The authors further thank S. Stoebenau for the fabrication of the system.