An Integrated Projection Cytometer

J.H. Nieuwenhuis[1], J. Bastemeijer[2], P.M. Sarro[2] and M.J. Vellekoop[1]

[1] Industrial Sensor Systems, Institute of IEMW, Vienna University of Technology

[2] DIMES, Delft University of Technology, Delft, The Netherlands

Introduction

In this paper we present an integrated projection cytometer (see Fig. 1) and the first measurements results obtained. The device has a near-field optical sensor [1] capable of counting, sizing and measuring the shape of particles. Furthermore, it has a flow-cell that creates a non-coaxial sheath flow [2] that focuses the particles close over the sensor surface, thereby minimizing diffraction of the light.

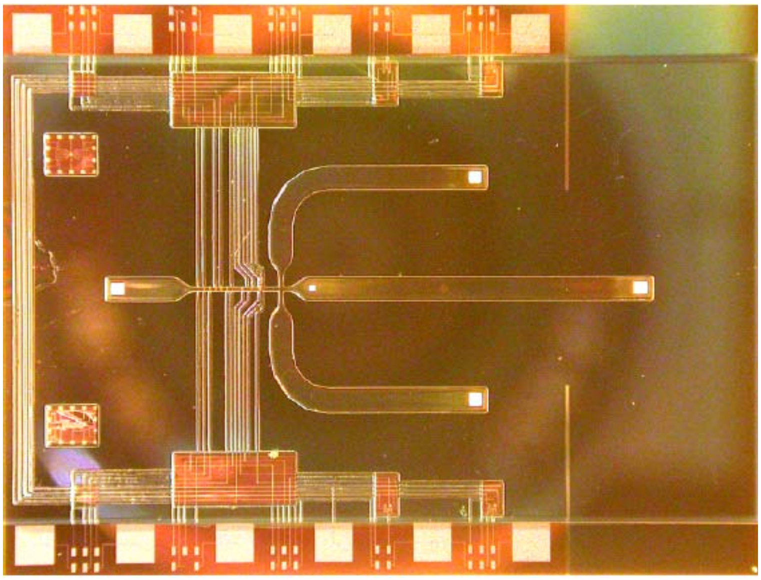

Fig. 1: The integrated projection cytometer chip (1.5 x 2 cm^2)

Operation Principle

On the bottom of the flow-channel elongated photodiodes (see Fig. 2) are defined: length 50 µm, width 1 µm. The photodiodes are illuminated from the top by a parallel beam of light, and when a particle passes it partially blocks the light, resulting in a drop in photocurrent proportional to the width of the particle. From the obtained cast shadow particle size and shape properties can be extracted.

Device Fabrication

The device consists of a two-layer glass-silicon sandwich. The silicon wafer contains the photodiode sensors, which were made in a bipolar process. As a post-processing step through-holes were etched to form the liquid inlets. In the glass wafer the channel was defined by wet-etching. Finally the wafers were bonded together using anodic bonding at 400 °C and 1 kV.

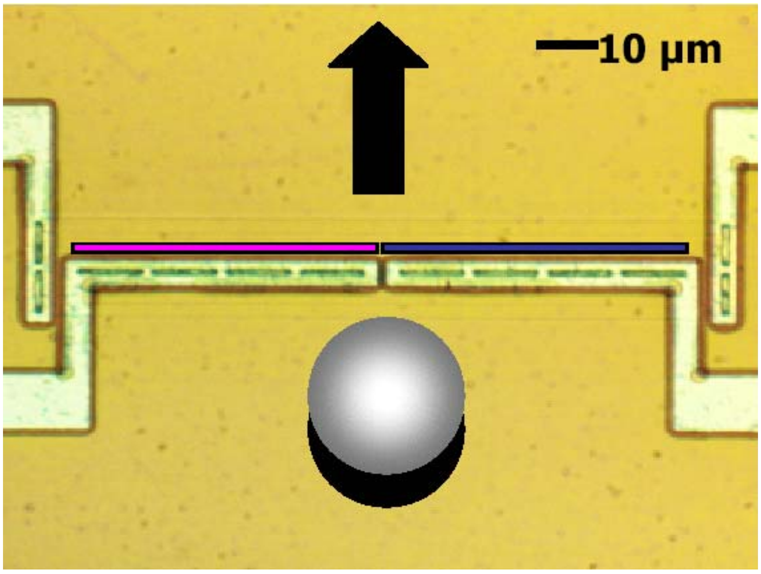

Fig. 2: The photodiodes (pink/blue squares) register the cast shadow of a passing particle

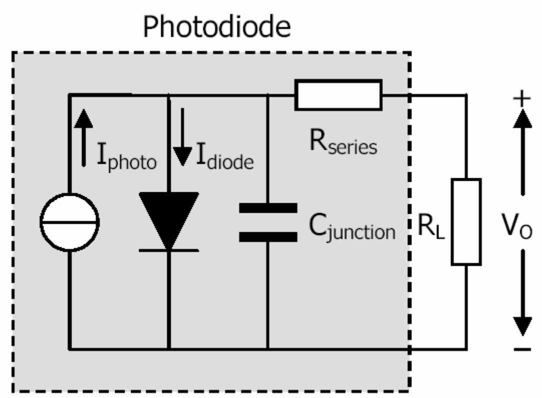

Fig. 3: A simplified equivalent circuit for the photodiode with photovoltaic readout

Measurements

The photodiodes were illuminated using a microscope light source; with an optical fiber the light was directed perpendicular to the device surface. The photodiodes were connected in photovoltaic mode (see Fig. 3) to minimize noise and dark currents using a 10 MΩ load resistor (R_L). In the first experiment the light intensity was increased in steps to verify reliable operation over a wide range of light intensities and to check the photodiode matching (see Fig. 4 (a)); the output voltage clips at 0.55V, here the PN-junction comes into forward bias. Next a suspension of spherical polystyrene particles (diameter 25 µm) was pumped through the device. The results (see Fig. 4 (b)) show that the particles can be clearly detected when they pass the sensor and the shape of the signals seems quite consistent. The difference in drop of photocurrent for both photodiodes of the sensor indicates that particles do not pass over the middle of the sensor (off-set about 6 µm). This is probably due to some small geometrical asymmetry.

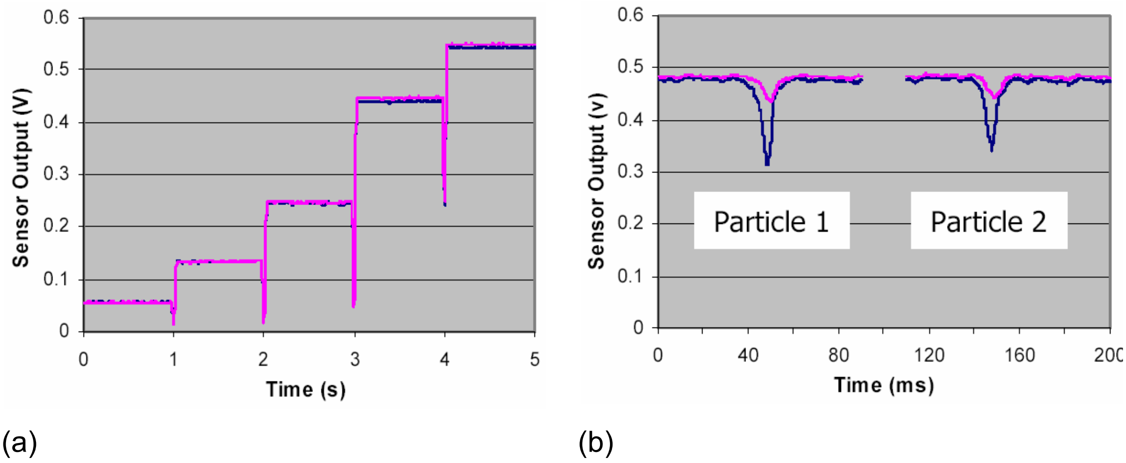

Fig. 4: (a) Sensor outputs (pink, blue) for different intensities of the light-source; (b) Measured sensor outputs (pink, blue) for two passing particles.

Discussion

The drop in photocurrent is slightly less than expected and also the height of the peaks between different particles shows some variation. This is most likely due to the non-ideal optical configuration. The rounded shape of the channel, caused by the wet etching, might cause refraction of the light rays (see Fig. 5). As a consequence, the incoming light-rays are no longer parallel and can create internal reflections which distort the projection. These effects can be reduced by carefully matching the refractive index of the liquid to that of the glass or by using a square channel, made with SU8.

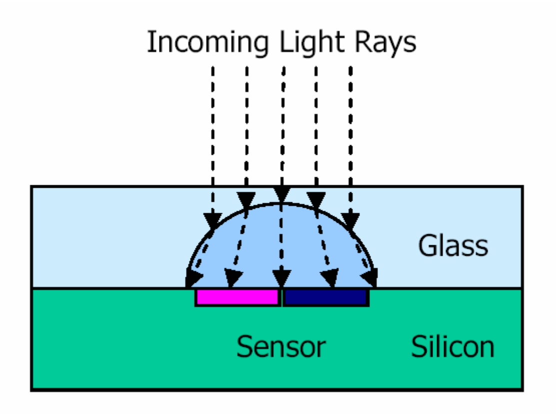

Fig. 5: A cross-sectional view of the optical setup showing possible refraction of the light

Conclusions

First measurement results were obtained with a fully integrated projection cytometer. Particles can clearly be detected, and the pulse shape is repeatable. A slight geometrical mismatch probably causes the particles not to move exactly over the middle of the sensor.

References

[1] J.H. Nieuwenhuis, J. Bastemeijer, A. Bossche, M.J. Vellekoop, "Dynamic Particle-Shape Measurements Using a Near-Field Optical Sensor", Proc. of 1st IEEE Sensors Conference, June 12-14, Orlando, USA, 2002, pp. 130–133

[2] J.H. Nieuwenhuis, J. Bastemeijer, P.M. Sarro, M.J. Vellekoop, "Integrated Flow-Cells for Novel Adjustable Sheath Flows", Lab On A Chip Journal, 2003, 3, 56–61