Particle and Cell Detection using a DVD Pickup Head

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In this report we present an optical detection system for single biological cells that utilizes a standard DVD pickup head. In a feasibility study we have shown the detection for different plain and silver coated polystyrene particles and cells (yeast) suspended on a platinum mirror. For these experiments the integrated magnetic actor of the pickup was used to simulate the particle movement and we found a remarkable sensitivity. Then a flow cell with integrated mirror has been designed to be able to measure particles in a cytometric setup. First measurement results are given that show the high sensitivity and a good repeatability for polystyrene beads.

Introduction

Flow cytometry is a process where physical or biochemical characteristics of single biological cells are gained as the cells pass through the device in a fluid flow [1]. These systems are usually based on optical or impedance measurements where commercially the optical flow cytometers are the most important ones. Parameters like cell size, viability, and cytoplasm conductivity can be measured electrically by impedance changes, but more complex parameters like DNA content and the presence of certain biomolecules are only accessible by optical methods using fluorescent markers. Hereby a laser is used for excitation and the filtered fluorescent response from the cell is measured as a function of the angle (fluorescent activated cell sorting).

If one is interested in having information about the cell concentration in a suspension a less complex system is sufficient where every single cell generates a counting peak and the total number of peaks is the output of the instrument.

In this project we follow a low-cost approach using a DVD pickup head for detection of cells. Measurements with particles in a microchannel were performed to show the principle.

The Sensor System

The optical part of the system consists of a DVD pickup head (Sanyo SF-HD68V) which is explained in Fig. 1.

A laser diode is used to generate a beam that is reflected by a beam splitter to a lens and focused to a small spot of ca. 0.65 µm size. The lens position is controlled by two voice coil motors (VCMs) such that the focus of the beam can be adjusted to a reflective surface. The reflected beam propagates back to a four quadrant photodiode array. An astigmatic distortion in the optical path causes the beam profile at the photodiode array to be spherical only when the beam is reflected in the focal point. If the reflection is out of focus, the profile becomes elliptic with the principal axis depending on the sign of the focus error (Fig. 1, Beam Profiles). A focus error signal can be generated by summing up the photocurrents as follows: FE = A + D – B – C. In a typical DVD appli-

cation this signal is used to control the VCM such that the focus error becomes zero. The sum of all four photocurrents corresponds to the total reflected intensity.

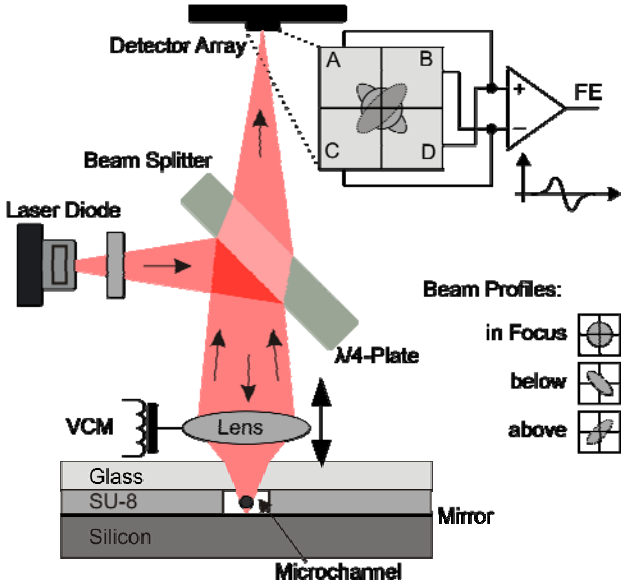

Fig. 1: The DVD pickup head in cytometric setup.

Compared to conventional optical cytometers where the light beam is coupled through the flow cell our system includes a mirror that is used to reflect the light back to the sender. The internal photodiodes of the pickup can be utilized which has several advantages: first the alignment between sender (laser diode) and receiver (photodiodes) is not critical because both are integrated in the pickup. Second, the VCM can be used to correct for alignment errors between the fluidic chip and the pickup head and third, the total cost of system is comparatively low because the whole high precision optical system is integrated in a mass product.

When a particle enters the detection region in the microchannel it influences the optical path and the reflected signal changes.

Flow Cell

The flow cell (Fig. 2) consists of a silicon glass sandwich with an intermediate layer of SU-8. The through holes for the fluidic interface were KOH-etched and the surface of the silicon is coated with titanium which acts as the mirror. The SU-8 layer defines the fluidic geometry of the microchannel and is also used to form a tight bond to the top glass wafer. At the detection region the channel has a cross section of 50 µm by 50 µm.

The chip was clamped to a device holder that provides O-rings to seal the liquid connections.

Measurements

In a first attempt different objects (spherical silver coated and plain polystyrene beads) were distributed on a platinum mirror and the reflected intensity signal was measured while a second VCM was used to simulate the movement of the cell with a speed of ca. 5 m/s. The results are shown in Fig. 3(a) and (b). The non-transparent particles (20 µm

diameter) cause an intensity drop while the transparent plain particles (15 µm diameter) cause a signal with a peak that exceeds the unperturbed reflected intensity which is labeled with 100%. In a cytometer the measuring speed would only be limited by the bandwidth of the pickup.

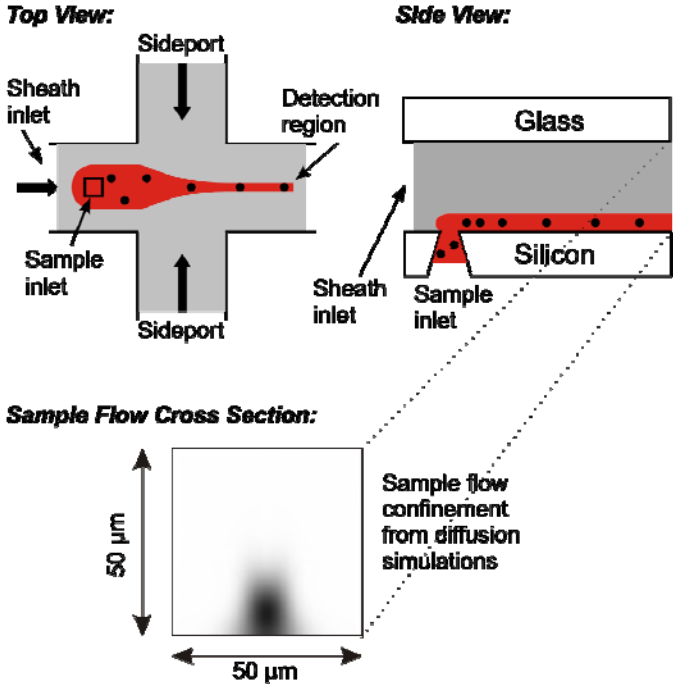

Fig. 2: Flow cell for non-coaxial sheath flow.

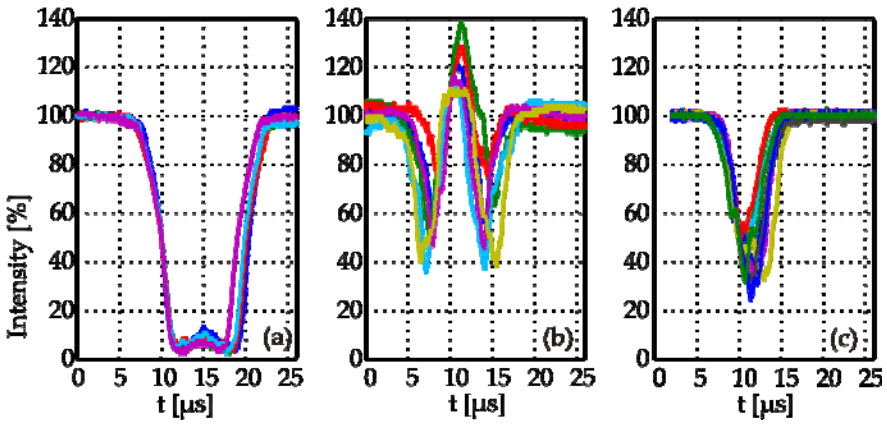

Fig. 3: Sensor response for three different particle types suspended on a platinum mirror: 20 µm silver coated polystyrene (a), 15 µm plain polystyrene particles (b), yeast cells (c). Note that the plain particles cause an intensity rise to more than 100% which is a higher response than produced by a mirror in the focal point.

To estimate the potential of the system for detection of other particles, also yeast cells have been tested. The cells were taken from a suspension and distributed on the mirror. The results (Fig. 3(c)) show a signal drop of between 50% and 70% which is a remarkably high sensitivity. This indicates that even smaller cell types can be measured in the system.

In the next step a flow cell has been used to generate a non-coaxial sheath flow to move the particles through a microchannel. To obtain a high sensitivity the sample flow has to be very close to the mirror. Syringe pumps have been used to apply the necessary flow rates.

First measurement results using plain polystyrene beads (8 µm diameter) are given in Fig. 4. The graph shows 10 consecutive measurements and demonstrates the good repeatability of the process. The intensity drops to less than 40% when a particle passes by. The variation of the amplitude of the signal is within a range of ± 4.3 %.

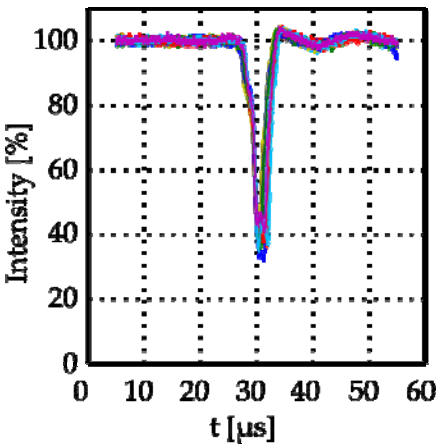

Fig. 4: Sensor response from measurements in the flow. Plain 8 µm particles (Micromer). The intensity drops to less than 40% due to the presence of a particle. The variation in amplitude is in a range of ± 4.3 %.

Conclusions

We have successfully shown the principle of a low cost cell detection system that utilizes a DVD pickup head. First measurements using a mirror instead of microfluidic channel indicate the ability to detect yeast cells from their optical reflection pattern. We have also performed measurements with polystyrene particles in a microfluidic channel that showed a good repeatability and a remarkably high sensitivity.

We conclude that our system will allow for detection of biological cells with different optical properties (fast viability tests, stained cells).

References

[1] H..M. Shapiro, “Practical Flow Cytometry”, 4th ed., 2003, Wiley & Sons

[2] J.H. Nieuwenhuis, J. Bastemeijer, P.M. Sarro, and M.J. Vellekoop, “Integrated Flow-Cells for Novel Adjustable Sheath flows”, Lab on a Chip, vol. 3, pp.56-61, 2003