PARTICLE SHADOW TRACKING – COMBINING MAGNETIC PARTICLE MANIPULATION WITH *IN-SITU* OPTICAL DETECTION IN A CMOS MICROSYSTEM

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ABSTRACT

We present a hybrid CMOS based microsystem where magnetic actuation of microparticles is combined with integrated optical detection via Single Photon Avalanche Diodes (SPADs). The system's configuration permits the manipulation and detection of single magnetic particles having diameters of 1, 3 and 5 µm. We are able to show a size sensitivity of the particle detection, with a clear distinction between different particle diameters.

Keywords: Magnetic particles, CMOS, optical detection, Single Photon Avalanche Diode

1. INTRODUCTION

Miniaturized magnetic manipulation of microparticles or cells has been gaining interest and applicability within recent years [1, 2]. A promising option is the combination of CMOS and microfluidics in hybrid systems [3], since they offer high flexibility. The system presented here, uses a CMOS chip for magnetic actuation and simultaneous optical detection. The magnetic actuation is achieved by sequential displacement of the magnetic field maximum generated by the currents in a double layer of overlapping square coils. The center of each coil is instrumented with a Single Photon Avalanche Diode (SPAD) which serves as optical sensor [4]. A glass capillary placed on top of the chip holds the magnetic microparticles suspended in an aqueous solution.

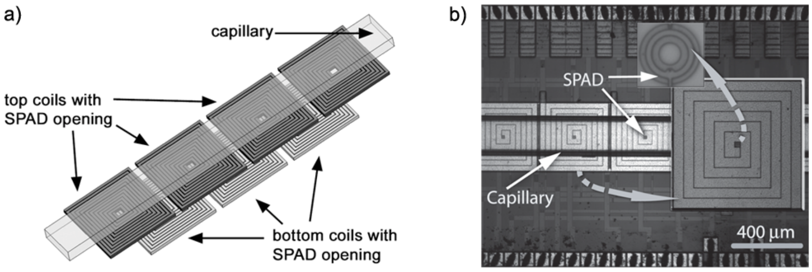

Figure 1. Representation of the CMOS system: a) Schematic explosion view showing the position of the square coils and the capillary, b) Photomicrograph of the hybrid CMOS system, with a coil and a center SPAD in detail.

2. OPTICAL DETECTION

When an object, e.g. a magnetic particle, passes over the coil center and thus the sensor it causes a temporary occlusion of the optical path, as depicted in Fig. 2. As a result the photon flux decreases and hence the photon count at the detector site. The photon count reduction is a complex function of the detector's sensitive area, the refraction indexes in the overlaying optical stack, and diffractive effects at and around the surface of the particle. Standard optics tools can predict photon count loss with reasonable precision.

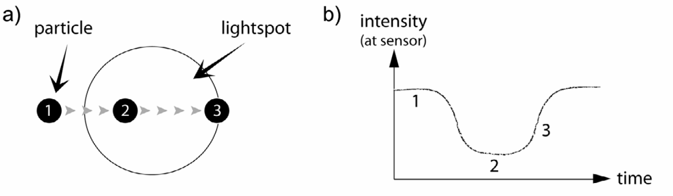

Figure 2. Illustration of the principle of the on-chip optical detection: a) Schematic passage of the particle over the illuminated SPAD, b) Stylized light intensity profile at the SPAD during the passage of a particle

The sensitive surface of the SPAD is a disc with a diameter of 8.4 μm, and its general structure is schematically depicted in Fig. 3a. The SPAD's p-n junction is reverse-biased above breakdown, which causes the optical gain to become virtually infinite. In this regime, the detector is said to operate in Geiger mode, thereby enabling single photon detection. The probability that an impinging photon results in a digital pulse, the photon detection probability (PDP), is plotted in Fig. 3b as a function of excess bias voltage and wavelength. The noise in the dark, or dark count rate, is the main limiting factor to the dynamic range.

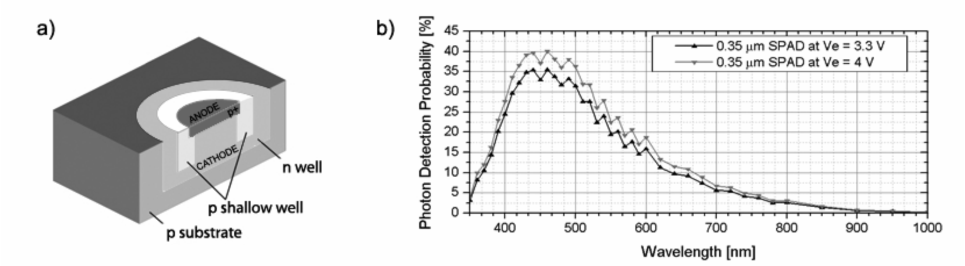

Figure 3. Schematics of the Single Photon Avalanche Diode (SPAD): a) 3D structure of the element, b) Measurement of the Photon Detection Probability (PDP) depending on the wavelength of the impinging field and the excess bias voltage

3. EXPERIMENTS AND RESULTS

In order to test the magnetic performance of our system, we introduced fluorescent magnetic particles of 5 μm diameter (COMPEL magnetic particles, BangsLabs) into the glass capillary. Fig. 4 shows a sequence of images taken during the transport of a group these particles from one coils center to the next. We see that the dispersed particles concentrate around the center of the attractive coil. The particle velocity is about 5 μm/s which is well in agreement with the forces calculated theoretically. The parallel measurement of the SPAD signal shows the expected decrease in photon count, once the particles gather over the coil's center.

For further experiments we strongly diluted the magnetic particle solution in order to obtain freely moving single particles. Figure 5a shows a single particle of 1 µm diameter sitting over a SPAD, where it induced a drop in photon count. Using single particles of 1, 3 and 5 µm in different experiments, we recorded the SPAD signals during particle transit.

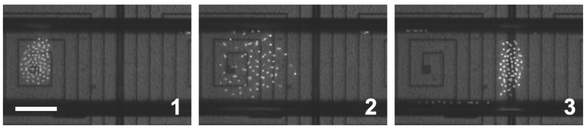

Figure 4. Photographs of a sequence of particle transport. The images of the fluorescent magnetic particles (∅ 5 µm) are overlaid with a photograph of the CMOS chip. The duration of the sequence is 20 s. (Dimension bar: 100 µm)

A comparison of the normalized photon counts, as depicted in Figure 5b, demonstrates the systems capability to distinguish between the different particle sizes with the photon count decreasing for increasing particle diameters, as predicted by theory [5]. Experiments performed using fluorescent light and fluorescent magnetic particles gave identical results indicating that the measured signal is exclusively a consequence of light occlusion.

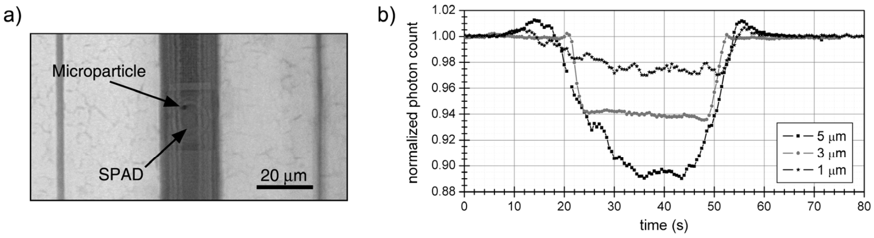

Figure 5. Optical observation and measurements: a) Photograph of a single 1 µm magnetic microparticle partially occluding a SPAD (50x objective), b) Normalized photon count of a bottom SPAD for single particles of 1, 3 and 5 µm diameter.

4. CONCLUSION

Our experiments demonstrate the capability of our hybrid CMOS microfluidic system to manipulate and detect single magnetic particles of 1 to 5 µm diameter. With the ability of the integrated optical detection to distinguish between the different particles sizes, a wide range of applications in miniaturized bioanalytical systems can be envisioned.

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