Topic No. 7 (Detection Technology) – Poster

A ROOM TEMPERATURE CMOS SINGLE PHOTON SENSOR FOR CHEMILUMINESCENCE DETECTION

Marek Gersbach, Yuki Maruyama*, Cristiano Niclass, Kazuaki Sawada*, and Edoardo Charbon

Ecole Polytechnique Fédérale de Lausanne (EPFL), Lausanne, Switzerland
*Toyohashi University of Technology (TUT), Toyohashi, Japan

keywords: chemiluminescence, bioluminescence, molecular assay, single photon detection.

In this paper we report on a room temperature chemiluminescence sensor fully integrated in CMOS technology. The sensor is based on a single photon avalanche diode (SPAD) array fabricated in 0.8μm CMOS technology [1]. Fig. 1 shows a photomicrograph of the array. A SPAD is a p-n junction biased above breakdown, where its optical gain is virtually infinite. When a photon is absorbed, with non-zero probability, an avalanche is triggered and subsequently quenched, thus generating a pulse synchronized with the impinging photon (Geiger mode of operation). Radiation intensity can be trivially evaluated by counting pulses during the integration period and adjusting for fill factor and photon detection probability. Intensity signal-to-noise ratio (SNR) is limited in SPADs by dark count rate (DCR). This sensor exhibits one of the lowest DCR ever reported in a CMOS SPAD at room temperature. Thanks to this noise performance, chemiluminescence can be detected with an SNR comparable to that of photomultiplier tubes (PMTs) and cooled CCDs but at a fraction of the cost and power dissipation [2]. Thanks to its scalability, this sensor enables significantly higher lateral resolutions than large-area pixel solutions [3],[4]. In addition, thanks to the speed at which it is operated and its timing resolution, the sensor is indicated for fast low-emission experiments and simultaneous fluorescence-luminescence imaging.

In our experimentation the reaction platform of Fig. 2 was demonstrated. The experiment involved Enhanced Chemiliuminescence (ECL) plus Western Blotting Detection Reagents (Amersham Bioscences) and a secondary antibody, Anti-Mouse IgG (whole molecule) Peroxidase Conjugate (Sigma Aldrich) diluted in Tris Buffered Saline (20mM). The platform is a powerful tool for monitoring luminol photon emissions, occurring when a ECL Plus solution reacts with a secondary antibody. Other kinds of enzymatic activities can also be monitored with this platform. The reaction was monitored using the experimental setup described in Fig. 3. By means of a syringe pump, the reagents are forced through a Y-shaped microchannel under laminar flow conditions. The reaction takes place in the region where the two solutions are mixed through diffusion causing an anisotropic photon emission [5],[6]. A portion of this emission is collected by the optical system and concentrated over an area of 5x5 pixels. Photon counts are then evaluated independently by means of 32bit counters. Thanks to the picosecond timing resolution of each pixel, time-correlated single photon counting techniques for molecular lifetime analysis are also possible with this setup with the sole addition of a pulsed light source.

The plots of Fig. 4 and Fig. 5 show the emission decay of chemiluminescence in a 10mm tube and in a 2mm channel. The plot of Fig. 6 shows the evolution of photon emission on a section of the channel perpendicular to the flow. Fig. 7 shows a measurement of the emission intensity along the laminar flow. All the measurements were performed at room temperature. Tab. 1 summarizes the overall performance of the sensor.

REFERENCES

[1] C. Niclass A. Rochas, P.A. Besse, R. Popovic, and E. Charbon, "A 4μs Integration Time Imager Based on CMOS Single Photon Avalanche Diode Technology", to appear in *Sensors and Actuators: Physical*, 2006.

[2] K. Feather-Henigan, S. Hersey, A. Johnson, G. M. Milosevich, and K. Hines, "Immunoblot Imaging with a Cooled CCD Camera and Chemiluminescent Substrates", *American Biology Laboratory*, pp. 44-46, June 1999.

[3] H. Eltoukhy, K. Salama, and A. El Gamal, "A 0.18μm CMOS Bioluminescence Detection Lab-on-Chip", *Journal of Solid-State Circuits*, Vol. 41, N. 3, pp. 651-662, March 2006.

[4] U. Lu *et al*., "CMOS Chip as Luminescent Sensor for Biochemical Reacions", *IEEE Sensors Journal*, Vol. 3, N. 3, pp. 310-316, June 2003.

[5] C. Oda, K. Sawada, T. Tsuchiya, H. Takao. M. Ishida, "Integrated Electrochemical DNA Sensors with Microfluidic Channel Reactor", *μ-TAS'03*, Vol. 1, pp. 371-374, October 2003.

[6] K. Sawada, C. Oda, H. Takao, M. Ishida, "Smart Microfluidic Electrochemical DNA Sensors Integrated Signal Processing Circuits", *TRANSDUCERS'05*, pp. 279-282, June 2005.

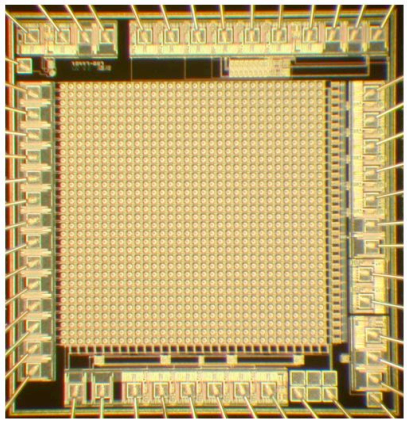

Fig. 1. Photomicrograph of the SPAD array fabricated in CMOS technology.

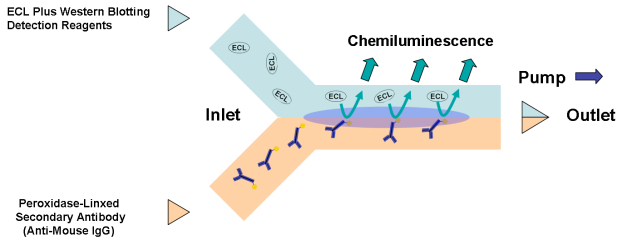

Fig. 2. Schematic diagram of the reaction. The inlet components mix in the intersection region where photons are emitted.

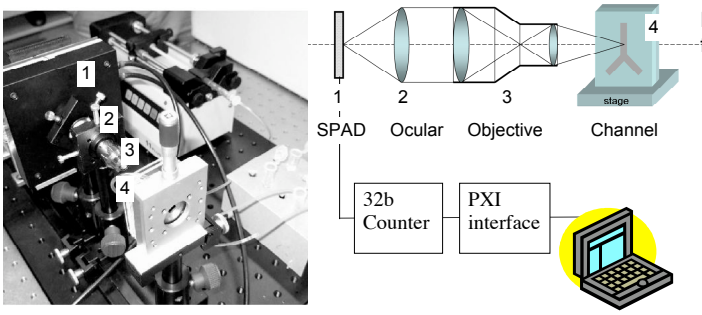

Fig. 3. Experimental setup and schematic diagram.

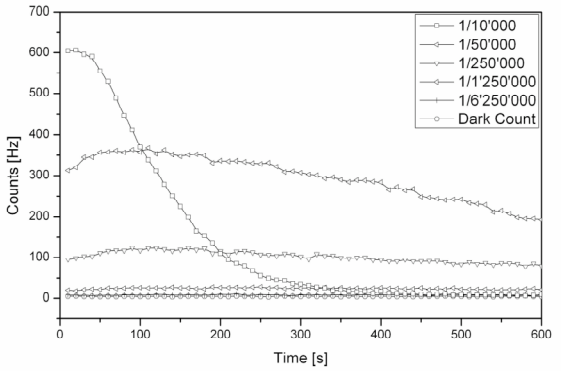

Fig. 4. Chemiluminescence emission decay in a 10mm tube as a function of concentration. Dark count rate (DCR) is also plotted.

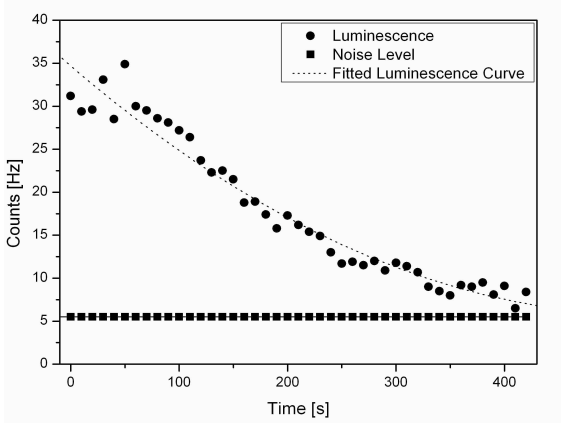

Fig. 5. Chemiluminescence decay in a 2mm channel for a 1/10,000 concentration measured using SPADs.

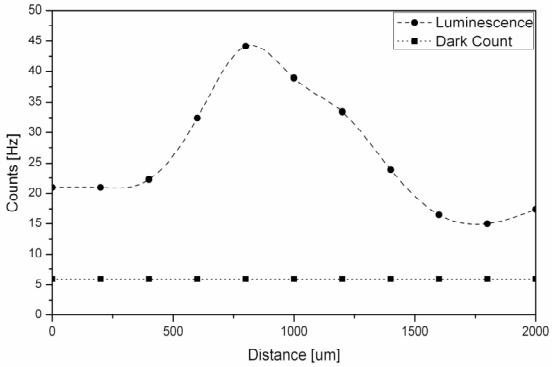

Fig. 6. Photon emission distribution in a sweep perpendicular to the flow axis in a 2mm channel as a function of the chemical flux.

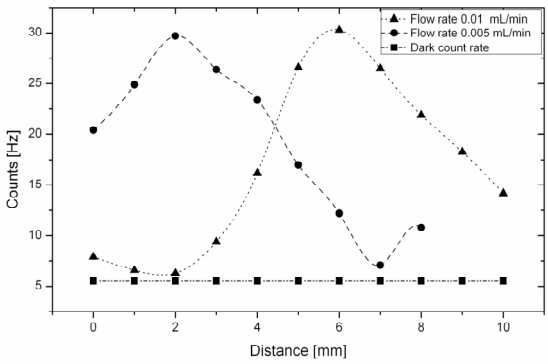

Fig. 7. Photon emission distribution ia a sweep parallel to the flow axis in a 2mm channel as a function of the chemical flux.

Performance	Min.	Typ.	Max.	Unit
Pitch		58		µm
Array size		32×32		-
Pixel Dark Count Rate (DCR)		5.5		Hz
Saturation			25	MHz
Wavelength range	350		1000	nm
Photon Detection Probability @ op. wavelength (530nm)		25		%
Power dissipation			6	mW

Tab. 1. Performance summary. All the measurements are reported at room temperature.