## An All-Digital 128x128 CMOS Optical/Electrical Image Sensor

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An all-digital 128x128 CMOS optical and electrical image sensor is presented. The sensor pixels consist of a single-photon avalanche diode (SPAD), a time gating circuitry, a 1bit memory and an extended-gate, field-effect transistor (EGFET). The sensor offers on-chip time-resolved fluorescence detection and surface potential detection.

Target applications for  $\mu$ -TASs are diverse as biosensors for genetic and contagious diseases, prosthetics sensors, real time diagnostic tools, etc. Thus, a wide variety of sensors are necessary to meet the researchers' requirements. This device is based on an array of pixels capable of detecting single photons and surface potential changes. Thus, this sensor is suitable for on-chip time-resolved fluorescence detection, chemiluminescence detection [1], pH detection, charged particle detection, and a combination of these measurements. The sensor block diagram is shown in Fig. 1. The pixel consists of two concentric structures: an internal SPAD for single-photon detection mode. Time-resolved single-photon detection is achieved by sliding-time-gating techniques [2] using time gating circuitry and on-chip/off-chip delay lines. The photon detection time window is controlled by activating and deactivating the SPAD. Fig. 2b shows the surface potential detection mode. SPAD quenching time (inactive period) is controlled by the EGFET, whereby a surface potential change modulates the SPAD count rate under constant illumination conditions. Fig. 2c shows the overall pixel schematics including a 1bit memory, a memory reset control, and a readout interface.

Fig. 3 shows a microphotograph of the sensor chip with a pixel detail. The chip was fabricated in a 0.35µm high-voltage CMOS technology. At first, the optical detection performance was characterized using a conventional c-mount lens (CCTV Lens, 12VA412ASIR, TAMRON, Japan). The excess bias voltage was 3V in the experiments. Thanks to its single-photon detection capability, a high quality images were taken under very low illumination level without cooling as shown in Fig. 4. Then, the chip was subsequently tested as DNA detector to characterize optical and electrical detection performance. Three different concentrations, 36µM, 18µM, and 9µM, of Cy5 linked oligonucleotide (30bases) samples were immobilized on the sensor surface. A 637nm pulsed laser diode (Advanced Laser Diode System, GmBH, Germany) was used as an excitation light source. Fluorescence was accumulated from 3ns after the excitation laser pulse until 9.6ns. The gate window width and sliding-gate time were 3.6ns and 200ps, respectively. Fig. 5 shows a two dimensional fluorescence image. DNA spots are clearly observable without optical filter. To measure the DNA charge, the sensor was filled with a pH7 phosphate buffer solution and the electrolyte voltage was set to 3.2V via Au/AgCl reference electrode during the experiments. Fig. 6 shows an image of the DNA charge detection, whereas the count rate is inversely proportional to the DNA molecules negative charge. The DNA molecules were successfully detected optically and electrically with an estimated limit of detection (LOD) of 7.2nM and 4.5nM, respectively.

## References

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Keywords: CMOS, SPAD, TCSPC, Fluorescence, surface potential

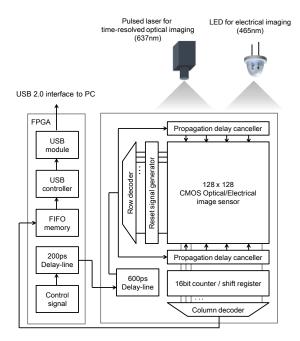


Fig. 1 Block diagram of the system. The time gating control signals are generated by a combination of an on-chip 600ps delay line and an off-chip 200ps delay line.

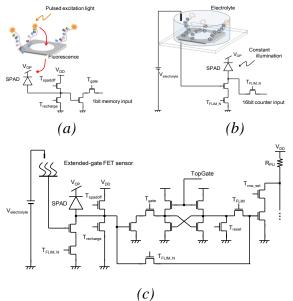


Fig. 2 Schematic diagram of the pixel. (a) Time-resolved fluorescence detection mode. The in-pixel 1bit memory holds the state of the SPAD until next readout cycle. (b) Surface potential detection mode. The digital signal is stored in a 16bit counter outside the pixel array via  $T_{FLIM_N}$  (c) Overall pixel schematic.

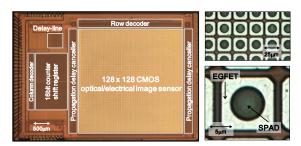


Fig. 3 Microphotograph of the chip. The pixel consists of a SPAD and a donut shaped EGFET gate. The pixel pitch is  $25 \mu m$ .

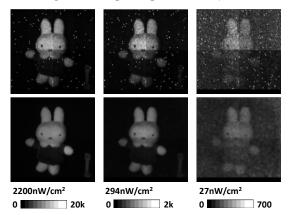


Fig. 4 Optical images under low light illumination. Top: raw image. Bottom: after sensitivity correction and median filtering.

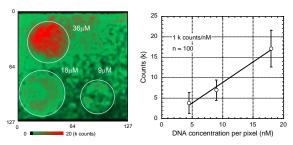


Fig. 5 Two dimensional fluorescence image. The total count rate is increased with increase of Cy5 linked DNA molecules.

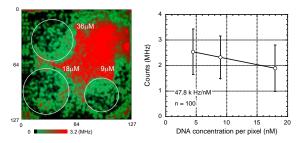


Fig. 6 DNA charge detection under 465nm LED continuous-wave illumination. The count rate was modulated due to the negative charge of DNA molecules.