ThA2 (Invited)
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Single Photon Imaging in CMOS

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Abstract[1]– *CMOS single photon detectors enable large pixel arrays and integrated ancillary circuits. As a consequence, higher timing accuracy and reduced power consumption can be achieved at lower costs. This paper discusses applications and implementation considerations to take into account when designing single photon imagers.*

Single Photon Detection

Recent advances in neurobiology and medical imaging have put an increasing burden on conventional optical sensor technology. This trend is especially pronounced in time-correlated imaging and other high precision techniques, where timing accuracy and sensitivity is critical. Some of these methods help enable new fundamental scientific discoveries almost daily.

Alternatives to conventional CCDs and CMOS APS sensors are single photon counters (SPCs). Several types of SPCs have been known for decades. Among the most successful devices in this class are microchannel plates (MCPs) and photomultiplier tubes (PMTs) that have become the sensors of choice in many applications. Even though they have been studied since the 1960s [1], silicon avalanche photodiodes (SiAPDs) have become a serious competitor to MCPs and PMTs only recently. In SiAPDs, carriers generated by the absorption of a photon in the p-n junction, are multiplied by impact ionization thus producing an avalanche. The resulting optical gain is usually in the hundreds. The main drawback of these devices however, is a relatively complex amplification or monitoring scheme and, often, specific technological requirements.

If biased above breakdown, a p-n junction can operate in so-called Geiger mode. Such a device is known as single photon avalanche diode (SPAD). In Geiger mode of operation, SPADs exhibit a virtually infinite optical gain, however a mechanism must be provided to quench the avalanche. There exist several techniques to accomplish quenching, classified in active and passive quenching. The simplest approach is the use of a resistance along the avalanche path. The avalanche current causes the diode reverse bias voltage to drop below breakdown, thus pushing the junction to linear avalanching and even pure accumulation mode. After quenching, the device requires a certain time, known as recovery, to return to the initial state. The quenching and recovery times are collectively known as *dead time*.

Recently, SPADs have been integrated in CMOS achieving timing resolutions comparable to PMTs [2]. Current developments in more advanced CMOS technologies have demonstrated full scalability of SPAD devices, a 25μm pitch, and dead time as low as 32ns. The sensitivity, characterized in SPADs as photon detection probability (PDP), can exceed 25-40%. The noise, measured in SPADs as dark count rate (DCR), can be as low as a few Hertz [3],[4].

In this paper we explore some applications of SPCs, including potential fields of imaging where SPADs can be a compelling implementation aspect of SPCs.

Time-Correlated Applications

Thanks to their picosecond accurate accuracy, SPADs have been proposed for imaging where speed and/or event timing accuracy are critical. Such applications range from fluorescence-based imaging, such as Förster Resonance Energy Transfer (FRET), fluorescence lifetime imaging microscopy (FLIM) [5], and fluorescence correlation spectroscopy (FCS) [6], to voltage sensitive dye (VSD) based imaging [7],[8], particle image velocimetry (PIV) [9], instantaneous gas imaging [10], etc.

Among time-correlated imaging methods, time-correlated single photon counting (TCSPC) is one of the most successful in bioimaging. The method makes use of multiple exposures to reconstruct the statistical response of matter to light pulses. From the response statistics, biologists generally extract parameters that can be used to characterize the molecule under observation and/or its environment, e.g. the calcium concentration. The understanding of calcium based cellular physiology has advanced mainly thanks to the development of fluorescent Ca^{2+} indicator dyes. Examples of heavily used dyes or fluorofores are Oregon Green Bapta-1 (OGB-1), Green Fluorescent Protein (GFP) and many others. calcium concentration can be determined precisely by measuring the lifetime of the response of the corresponding fluorophore, when excited at a given wavelength.

Fig. 1 shows a simple setup where a neural cell soma is being exposed to light via, for example, a fiber. The fluorophore molecules, previously injected into the cell, thus enabling monitoring of the neuron's activity as a function of external stimulation (not shown in the figure).

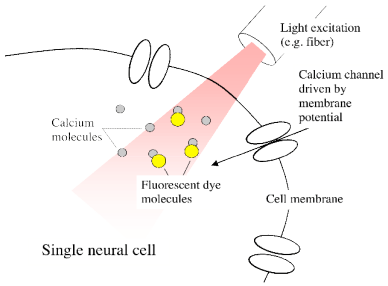

Fig. 1. Calcium environment in and around a cell membrane. Calcium moves through the membrane via so-called ion channels. A fluorophore can detect small variations of calcium concentration.

Two-photon FLIM, even though conceptually known for decades, only recently has become an essential tool for neurobiology and other disciplines. There are several advantages to two-photon FLIM. First, fundamental spatial confinement for the excitation can be achieved, thus allowing

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one to isolate a single molecule or cluster of molecules. Second, due to the reduced optical powers in play, effects such as photobleaching and photoxicity, can be mitigated, thereby enhancing the suitability of the approach. Third, a better penetration in turbid media can be achieved, due to reduced scattering. Fourth, the large spectral difference between in- and out-going radiation simplifies the separation of response from excitation [5].

A typical two-photon FLIM setup consists of a high-power femtosecond source, generally a mode-locked Ti:Sapphire laser, a SPC, time discrimination hardware, and a standard laser-scanning microscope. The latter is generally used to compensate for the fact that no multiple locations in the sample can be illuminated and analyzed simultaneously. This limitation would require the study of appropriate high efficiency optics in combination with arrays of SPCs and it is the goal of several current research projects.

An example of laser-scanner based FLIM image is shown in Fig. 2. In this experiment it was possible to detect intra-cellular chemical waves to help identify inner-workings of pathogens or the impact of certain pharmaceuticals [10]. The binding of neutrophil at the interface of two endothelial cells was monitored at high speed via calcium-triggered chemical waves propagating through the cells.

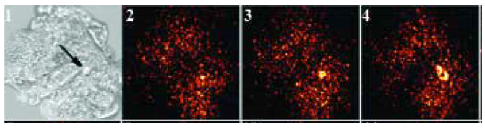

Fig. 2. High-speed image sequence of the binding of neutrophil. (Courtesy of H.R. Petty [11]).

Implementation Considerations

CMOS SPAD arrays have been demonstrated in various technologies [3],[4]. As an illustration, Fig. 3 shows the photomicrograph of the first published 32x32 CMOS SPAD array [3]. This design uses a simple random access readout mechanism, where each SPAD is addressable by a 10bit code.

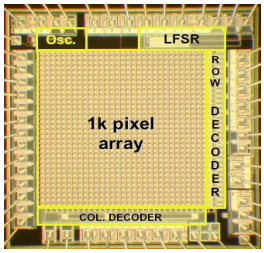

Fig. 3. Random access SPAD array realized in 0.8µm CMOS technology.

Time-correlated counting can be performed either via a fast clock or dedicated time discrimination circuit. Time-uncorrelated counting requires counters with a bandwidth greater than the inverse of the dead time of the measurement.

If counting is performed on-pixel, the operation of the sensor becomes relatively straightforward, but the silicon real estate may not be utilized efficiently. In principle, this configuration enables the best time utilization since it maximizes parallelism. If counting is performed on-column, SPDs may be implemented in a smaller area and a smaller pitch may be obtained, however a mechanism must be devised for pixels to share the column counter. As a consequence, the time utilization efficiency is reduced and the readout complexity increases. A good trade-off has been shown to be an event-driven readout system, which works best with low photon fluxes [4]. In this approach a SPAD uses the column as a bus, accessing it only when it absorbs a photon. The saturation of the device is thus determined by the bandwidth of the column divided by the number of rows.

Time-correlated counting may be implemented using fast time discrimination circuits running at lower speed, such as time-to-digital converters (TDCs), time-to-amplitude-converters (TACs), or correlators. A TAC is a device that converts a time interval into a voltage difference. A TDC converts a time interval directly into a digital code. A correlator relates a given impulse to another time-wise, determining in effect their phase difference.

It is usually infeasible to implement on-pixel TCSPC unless the pixel array is very small. On-column and on-chip approaches are currently the only alternative. Off-chip solutions are also a possibility, an example of which was proposed in [12]. In this design, two technologies are used to independently implement SPADs and time discriminators that are connected electrically using specific techniques.

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