Abstract—A high resolution Time Correlated Single Photon Counting (TCSPC) image sensor based on sample and hold Time to Amplitude Converter (TAC) pixels and a global ramp voltage is presented. The $256 \times 256$ array achieves an 8 $\mu$m Pixel Pitch (PP), 19.63% Fill Factor (FF), output voltage range ($0.7 \text{ V}$) and time jitter of 368 ps at 10 fps employing an off-chip 14-bit differential Analogue to Digital Converter (ADC). A column-parallel flash ADCs also implemented, allowing coarse 3-bin TCSPC histogramming at 4 kfps for video rate fluorescence lifetime imaging.


I. INTRODUCTION

Fluorescence Lifetime Imaging Microscopy (FLIM) provides absolute measurements of the environment and interaction of specific probes in living cells. Time Correlated Single Photon Counting (TCSPC) [1] is the preferred approach for FLIM due to its high photon efficiency as well as clearly defined Poissonian statistics and easy visualization of fluorescence decays [1]. TCSPC is however generally implemented in a laser scanning system using a single instrumentation channel which severely limits image acquisition rates. In recent years, Single Photon Avalanche Diodes (SPADs) sensors offer solid-state, multi-channel implementations of TCSPC hardware [1]. Two different approaches are employed to obtain the time of arrival of each photon, Time to Digital Converters (TDCs) and Time to Amplitude Converters (TACs). Arrays of a few thousand SPAD-based TCSPC pixels have been reported at relatively low Fill Factor (FF) and large Pixel Pitch (PP) [2]–[7]. Improvements in these parameters have been obtained through simple analogue SPAD pixels, primarily through less photon efficient, time-gated approaches [7]. We present the first high resolution TCSPC image sensor based on sample and hold TAC pixels and a global ramp voltage [7]. The $256 \times 256$ array achieves an 8 $\mu$m PP, 19.63% FF, output voltage range ($0.7 \text{ V}$) and a time jitter of 368 ps. An analogue readout and an off-chip 14-bit differential ADC allows per-pixel TCSPC histograms to be constructed at 10 photons/pixel/s. To allow a trade-off between lifetime accuracy and image acquisition rate, a fast column parallel ADC is also implemented, allowing coarse, 3-bin TCSPC histograms to be accumulated at 4 k photons/pixel/s.
differential sampling technique is employed during readout of VC to cancel pixel source follower (M7) Vt offsets by resetting the pixels after readout and switching the row voltage to a reference VREF.

At the top of the pixel array a 2 bit column-parallel Flash ADC was designed (Fig. 4). This allows a trade-off between the slow but precise analogue readout with a fast but coarse operating mode of the sensor allowing video rate fluorescence lifetime imaging. Fig. 4 shows the overall concept of a histogramming time to analogue converter obviating the read-modify-write sequence of conventional TCSPC hardware implemented in the analogue domain [8]. The technique is only partially implemented on chip here due to limitations on silicon area. Each column comprises 4 comparators sampling 4 globally distributed voltage references generated by a single resistive ladder. The thermometer code output of the comparators can be decoded by combinational logic (series of XORs) to increment one of a bank of ripple counters representing the TCSPC histogram. A pixel voltage lying outside the range set by the reference voltages $V_+$ and $V_-$ representing the no-photon case can be easily discarded. In our specific implementation the comparator output bits are serialised and sent off-chip to an FPGA at 40 MHz over a 16-bit parallel I/O bus.

An additional feature of this scheme is that the two reference voltages are fully adjustable via off-chip DACs to allow zooming in to a time region of interest. This allows the TCSPC time bin range to be matched to the typical average lifetime range in a given image. Although the digital readout does not at present implement correlated double sampling, this technique would be readily applicable towards precise time-zooming once comparator

and pixel source follower offsets are cancelled.

At the bottom of the sensor a single channel differential analogue readout is designed capable of Correlated Double Sampling (CDS). The output is converted by an external 14 bit ADC.

III. RESULTS

A 1 V 10 MHz sine-wave input on VRAMP (Agilent 33220A and LeCroy WaveStation 3082) was used to characterise the array. VRAMP is synchronised to a pulsed laser (Hamamatsu PLP-10-044) and an Opal Kelly XEM6310-LX150 FPGA card. Fig. 5 shows the 600 mV improvement in DC output range, with and without, the Boost voltage [7]. A second experiment was performed in order to characterise the sampling performance and impulse response function (IRF) of the sensor. A laser was directed at the sensor with a lens spreading the laser beam over the whole array sampling a 10 MHz sine wave in each pixel. A single frame of pixel analogue time-stamps was then readout through the analogue readout and displayed as an image (Fig. 6). A histogram of the time stamps in this image is shown in Fig. 7 for a 20 ns laser pulse delay with respect to sine wave minimum. The histogram shows two clear distributions showing (1) no photon capture at 0V and (2) photon capture from the laser pulse at 0.3 V. The IRF jitter is due to pixel leakage currents, residual offsets and noise from the readout and signal generator. The laser pulse delay was then swept using a delay generator (SRS DG645) through the maximum of the sine-wave to its minimum to characterise the time
response, linearity and the noise contribution. Fig. 8 shows the peak position obtained by stepping the laser pulse in 1 ns intervals showing an excellent match to the ideal sine-wave.

Fig. 9 shows the image histogram due to uncorrelated light from a blue LED showing the expected “cusp-shaped” probability distribution expected as the code-density plot of a sine-wave. The low dark rate of the SPADs (median 50 Hz at 2 V excess bias) show very few dark count related events. A clear separation of the ‘no photon’ case from the signal range is observed.

Fig. 10 shows a CCD fluorescence intensity image of Culshaw root Xylem cells measuring around 120 µm diameter obtained after 1 s exposure with a 20 MHz, 483 nm pulsed laser. Fig. 11 shows a coarse fluorescence lifetime image taken using 50 ms total exposure using the digital readout. The image is composed of 3-bin histograms per pixel formed by accumulating 5000 x 10 µs exposure frames generating around 100 photons/pixel. At a maximum frame rate of 4 kfps, the image would be acquired in 1.25 s. With a brighter sample, a FLIM video frame rate approaching 10 fps is attainable with the same number of photons/pixel allowing live cell behaviour to be studied. Two lifetimes of 1 ns and 5 ns were measured in the image by application of the Megaframe camera from [3] with 50 ps time resolution. The 1 ns lifetime is present in the cell boundaries while the 5 ns is present in the interior and periphery of the cells. The fluorescence lifetime is estimated using the rapid lifetime determination (RLD) technique between bin 1 and bin 2 of the flash ADC output [9]. A threshold of 1.5 ns is then applied, showing clearly two lifetime populations consistent with the values obtained with the Megaframe camera [3]. The noisy pixels and no photon cases have been rendered in black. The image shows column vertical and pixel fixed pattern noise which can be improved by application of noise cancelling circuit techniques. The horizontal artefacts are due to unequal distribution of the ramp voltage through a balanced metal tree.

Table I shows a comparison between the specifications and performance of multi-channel time resolved converter arrays suited to TCSPC fluorescence imaging. The imager achieves the highest image resolution, smallest pixel pitch and highest fill-factor of SPAD-based pixel arrays. Although the time resolution is not the lowest, the imager offers a practical tradeoff of frame rate and imaging resolution for typical FLIM time constant ranges.
parallel readout whilst an slower analogue readout allows high temporal resolution, low frame rate but precise lifetime determination.

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**REFERENCES**


