Characterization and Testing of LAS: A Prototype 'Large Area Sensor' With Performance Characteristics Suitable for Medical Imaging Applications

S. E. Bohndiek, A. Blue, J. Cabello, A. T. Clark, N. Guerrini, P. M. Evans, E. J. Harris, A. Konstantinidis, D. Maneuski, J. Osmond, V. O'Shea, R. D. Speller, R. Turchetta, *Member, IEEE*, K. Wells, H. Zin, and N. M. Allinson

Abstract—The Large Area Sensor (LAS) is a 1350×1350 array of active pixels on a $40\mu\text{m}$ pitch fabricated in a $0.35\mu\text{m}$ CMOS process. Stitching technology is employed to achieve an area of $5.4\text{ cm} \times 5.4\text{ cm}$. The sensor includes 'regions of reset', whereby three different integration times can be set on the array to achieve a large imaging range for static scenes. Characterization of the noise performance included temporal and fixed pattern sources. LAS was found to have a read noise of 62 e^- , a full well capacity of $61 \times 10^3\text{ e}^-$ and a conversion gain of 5 e^- per digital number (DN). The fixed pattern noise (FPN) was evaluated at half saturation; within a single stitched section of the array, column-to-column FPN was found to be 0.6% , while the pixel-to-pixel FPN was 3% . Both FPN sources were found to be gain related and could be corrected via flat fielding. Based on the results of characterization, LAS was coupled to a structured CsI:Tl scintillator and included in an X-ray diffraction system developed for the analysis of breast biopsy samples. Data acquired with plastic test objects agrees with that acquired by a previous prototype sensor. It is demonstrated that an imaging output range of 140 dB can be achieved using integration times of 0.1 ms to record the transmitted X-ray beam and 2.3 s to record the lower intensity scattered radiation.

Index Terms—CMOS, image sensors, semiconductor devices.

I. INTRODUCTION

ACTIVE Pixel Sensors (APSs) have emerged in the last two decades as a valuable alternative to the CCD in many scientific imaging applications. Fabricated in complementary metal oxide semiconductor (CMOS) technology, the APS can include complex circuits, and in turn functionality, at the pixel level. CMOS processes also confer other advantages, such as low power consumption, potential for low cost and fast-scaling technology [1].

Compared to the CCD, the APS provides high frame rates and the potential for true random access via column parallel readout. Recent developments in APS design and fabrication technology have helped to reduce read noise, improve quantum efficiency and achieve wafer size sensors via "stitching". These developments, together with the ability to tailor image sensor functionality, have stimulated the uptake of the APS among the scientific community.

Particular interest has arisen in "stitching" technology, which enables an APS design to be seamlessly scaled up to $12\text{ cm} \times 12\text{ cm}$ (standard wafer limits) without loss of performance [2]. This could be of great benefit in medical imaging, where large pixels, high noise, low frame rates and artefacts such as image lag limit conventional flat panel imagers. Improved tumour detection could be achieved with pixel sizes as small as $50\mu\text{m}$, as well through advanced digital mammography techniques such as dual energy contrast enhanced kinetics, or tomosynthesis, which require: fast image acquisition without image lag, full field coverage of the breast, good conversion gain and high detective quantum efficiency [3].

A number of commercial large area Active Pixel Sensors are available. For example, the Hamamatsu C9732 DK [4] measures 120 mm by 120 mm with $50\mu\text{m}$ pixels and has 75 dB dynamic range despite 1250e^- read noise. The RadIcon RadEye 100 [5] has dimensions of 98 mm by 49 mm with $96\mu\text{m}$ pixels and has been designed to be '3-sides' buttable, so it can reach much greater areas when tiled. This design has a much lower read noise of 250e^- but suffers poor conversion gain of $0.2\mu\text{V}/\text{e}^-$. Although these provide the large area required by medical imagers, they suffer relatively high read noise, poor conversion gain and limited dynamic range.

The development of the present APS has been primarily driven by the need for a sensor to perform X-ray diffraction studies of biological tissue, in particular for breast cancer

S. E. Bohndiek was with the Department of Medical Physics and Bioengineering, University College London, London WC1E 6BT, U.K. (e-mail: sbohndiek@googlemail.com).

A. Blue, D. Maneuski, and V. O'Shea are with the Physics and Astronomy Department, University of Glasgow, Glasgow G12 8QQ, U.K. (e-mail: v.oshea@physics.gla.ac.uk).

J. Cabello and K. Wells are with the Centre for Vision, Speech and Signal Processing, University of Surrey, Guildford GU2 7XH, U.K. (e-mail: K.Wells@eim.surrey.ac.uk).

A. T. Clark, N. Guerrini, and R. Turchetta are with the CMOS Sensor Design Group, Rutherford Appleton Laboratory, Didcot OX11 0QX, U.K. (e-mail: r.turchetta@rl.ac.uk).

P. M. Evans, E. J. Harris, J. Osmond, and H. Zin are with the Joint Physics Department, Institute of Cancer Research and Royal Marsden NHS Foundation Trust, Surrey SM2 5NG, U.K. (e-mail: phil.evans@icr.ac.uk).

A. Konstantinidis and R. D. Speller are with the Department of Medical Physics and Bioengineering, University College London, London WC1E 6BT, U.K. (e-mail: rspeller@medphys.ucl.ac.uk).

N. M. Allinson is with the Department of Electronic and Electrical Engineering, University of Sheffield, Sheffield S1 3JD, U.K. (e-mail: n.allinson@shef.ac.uk).

diagnosis. Breast biopsy tissue samples must currently be analysed by a histopathologist before a diagnosis can be made; a time consuming, qualitative and highly specialised process. If the speed and accuracy of this analysis were improved, it would reduce patient anxiety and increase throughput. X-ray transmission images of breast biopsies are already obtained to aid the histopathologist in selecting tissue slices for analysis, but scattered photons are normally rejected as they degrade image quality. The amount and direction of this scatter, however, depends on the material present; the scatter resulting from healthy breast tissue and tumour produce markedly different X-ray diffraction signatures.

Acquiring X-ray transmission information and data from the scattered photons simultaneously is a challenging task, as the intensity of transmitted X-ray beam is of the order of 10^4 times greater than the scattered X-ray beam. An imaging dynamic range of at least 80 dB is needed to visualize both in the same image. Further, X-rays scattered up to 10° from the transmitted beam provide useful information, meaning a large area detector is required. This application therefore needs a combination of low read noise, good conversion gain and wide imaging dynamic range in a large area device in order for a full biopsy analysis system to be developed [6]. A pilot study has proven APS technology for this application and shown that the present APS design should satisfy the requirements of a clinical system [6], [7].

A UK consortium (MI-3) was formed in 2004 under the RC-UK Basic Technology Programme (GR/S85733/01) to develop CMOS active pixel sensors for a broad range of scientific applications [8], [9]. One of the prototype devices, the 'Large Area Sensor' (LAS), was designed to reach an area of $5.4 \text{ cm} \times 5.4 \text{ cm}$ using stitching technology. To achieve a wide imaging range for the X-ray diffraction application, three 'regions of reset' were provided that enable different integration times to be selected in different positions on the array. This results in an extremely wide imaging range for static scenes. In Section II, a description of the sensor will be given along with details of the characterization methods used. The results of the characterization will be discussed in Section III along with an example of how LAS has been included in an X-ray diffraction system, before conclusions are drawn in Section IV.

II. MATERIALS AND METHODS

A. The Large Area Sensor

The design and fabrication of the Large Area Sensor has been described elsewhere [10] and a brief summary is given here, with specifications listed in Table I. LAS is a 1350×1350 array of pixels on a $40 \mu\text{m}$ pitch, yielding a prototype area of $5.4 \times 5.4 \text{ cm}^2$. A block diagram of the sensor is shown in Fig. 1.

Each pixel has a fill factor of 73%, with 9 transistors arranged as shown in Fig. 2. To achieve a wide imaging range, 6 transistors are added to the '3-T' APS layout, which includes the standard reset, row select and source follower transistors [1]. These extra transistors are used to define 'regions of reset' (RORs) with different integration times; appropriate for imaging a static scene with areas of differing intensity, such as an X-ray diffraction pattern. A yield in excess of 60% has been achieved (based

TABLE I
DESIGN CRITERIA FOR THE LARGE AREA SENSOR

Parameter	Value
CMOS Process (μm)	0.35
Pixel Size	$40\mu\text{m} \times 40\mu\text{m}$
Transistors per pixel	9
ADC Resolution	14-bit
Epitaxial layer (μm)	5
Maximum frame rate (fps)	20
Maximum integration time (s)	5
Read noise (e-)	50
Full well capacity (e-)	10^5

Fig. 1. Block diagram of the Large Area Sensor.

Fig. 2. Layout of the CMOS pixel for the Large Area Sensor; RST0, RST1 and RST2 refer to the three reset levels that may be applied to each pixel as the rolling shutter passes, resulting in three different integration times being available across the array.

on a sample size of 26). This is comparable to other non stitched designs, however, the circuit density is low due to the large pixels. The additional reset circuitry shows no negative effect on yield when only using a single reset.

The circuit performs a combinational AND of the column-defined "Sel1" and "Sel2" signals and the horizontal reset signals "RST1" and "RST2", which are in turn a combination of the

Fig. 3. Illustration of how integration time ratios are defined for the regions of reset. First, a row access token is clocked into the row read shift register. On the following cycle, a reset token is clocked in the "Reset 0" shift register. These propagate down the array with the reset one row behind the read as in a standard rolling shutter sensor. A number of rows later additional tokens are provided to the "Reset 1" and "Reset 2" shift registers. The relative integration times are defined in the ratio $L:M:N$ (see diagram). Dummy rows increase the maximum ratio between L and N beyond 1350:1.

rolling reset token (the row enable for a given reset), declaring this row should respond to this reset, and an external reset signal which allows for fine adjustment of reset and relative integration times. The extra transistors are all of the NMOS type in order to minimize charge collection losses by the addition of further N-wells, therefore a fifth additional signal, "RstClr" is included to return the reset transistor gate to ground and terminate the reset. By default, all pixels in a row are reset to the same level, via RST0, when the rolling shutter first passes. The longest available integration time, used to record the low intensity signals, is 2.3 s, while the shortest is 37 μ s and this records the most intense regions of the image.

Fig. 3 explains how integration time ratios are defined for the regions of reset. Each cycle of the row shift register clock represents one row access period, during which a row is sampled via the column output to capacitors at the bottom of the array. At the same time the samples for the previous row are read out from a complementary set of capacitors. The readout proceeds as follows: First, a row access token is clocked into the row read shift register. On the following cycle a reset token is clocked in the "Reset 0" shift register. These propagate down the array with the reset one row behind the read as in a standard rolling shutter sensor. A number of rows later additional tokens are provided to the "Reset 1" and "Reset 2" shift registers. The relative integration times are coarsely defined by the number of row cycles L , M and N before the following read token is injected, they define the integration times for RST0, RST1 and RST2 responsive pixels respectively. Integration times are therefore defined in the ratio $L:M:N$. Dummy row accesses are included to increase the maximum ratio between L and N beyond 1350:1, the total number of real rows, although this will reduce the overall maximum frame rate.

The reticle used to produce the stitched sensor is shown in Fig. 4. A standard CMOS reticle, the glass mask containing the design patterns, is limited in size to approximately 2×2 cm². To scale the sensor area up to full wafer size using stitching technology, the reticle is subdivided into 4 parts that are stepped repeatedly across the wafer. With reference to the left of Fig. 4,

Fig. 4. Illustration of how a CMOS reticle may be subdivided into side (A), sensor (B), corner (C) and top or bottom (D) then tiled to create a seamlessly stitched array.

each sensor stitch block (B) contains 270 rows and columns, so a 5 by 5 arrangement of stitch blocks compose the full array. Each top stitch block contains the reset circuitry, while each bottom stitch block contains the readout shift registers and there is a dedicated differential analogue output for every section of 135 columns (D). The output connects to a 14-bit pipelined ADC (Analog Devices AD9252) external to the sensor; a total of 10 analogue outputs are thus available. Side stitch blocks (A) contain row logic. Combining a set of stitch blocks, an example of which is shown on the right of Fig. 4, creates a sensor. The maximum full frame rate achievable with parallel analogue readout is 20 fps.

Data acquisition is achieved via a PC connected to either a Xilinx FPGA Development board, or an Aspect Systems test bench [11]. The former uses a compiled C executable to interface with the sensor via the FPGA. Reset, integration and readout can be determined by stimulus vector playback. Image data is transferred to the PC over Gigabit ethernet. This data

acquisition option is used for release to end users of the device so is referred to as the user readout system, while initial characterization and device benchmarking is performed on the Aspect Systems test bench, which communicates via a Camera Link frame grabber and a National Instruments Labview 8.2 interface. Characterization data was acquired on both systems for comparison.

B. Characterization Methods

Accurate characterization of device performance is critical in scientific imaging, particularly for medical applications, where it is paramount to ensure a device is suitable for the application. Device characterization is also a prerequisite for optimization of system performance. Characterization methods have been extensively described in previous works [6], [12], [13]; a brief summary of the methods used in this work is given below.

1) *Noise Characterization:* Noise sources in an APS can be classified into three main types: read noise, from transistors in the readout chain; shot noise, due to the Poisson statistics of interacting photons; and fixed pattern noise, the spatial variation in the output image due to the different gains and offsets of the in-pixel transistors, as well as the column amplifiers. To assess the suitability of a particular sensor for a given application, its properties should be expressed in physical terms (e^-), rather than the digital number (DN) output from the analogue-to-digital converter. Evaluating the number of electrons represented by each digital number, denoted by the conversion gain $K(e^-/DN)$, is necessary to achieve this. $K(e^-/DN)$ encompasses two fundamental gain stages in an APS: the charge-to-voltage conversion (V/e^-) and analogue-to-digital conversion (DN/V).

Camera characterization has traditionally been performed using the 'gold standard' photon transfer technique [13], with the conversion gain evaluated from

$$K \left(\frac{e^-}{DN} \right) = \frac{\overline{S(DN)}}{\sigma_S^2(DN) - \sigma_R^2(DN)} \quad (2.1)$$

where $\overline{S(DN)}$ is the mean output signal. $\sigma_S^2(DN)$ is the illumination dependent noise, calculated from the difference of two consecutive frames to remove the fixed pattern noise contribution. $\sigma_R^2(DN)$ is the illumination independent noise (read noise). $\sigma_S^2(DN) - \sigma_R^2(DN)$ is thus the signal shot noise. A photon transfer curve plots logarithmically the signal shot noise as a function of the mean output signal, meaning the conversion gain $K(e^-/DN)$ may be calculated from the linear fit to this curve.

Photon transfer analysis, however, assumes linearity of sensor response thus breaks down when this is nonlinear. Two factors contribute to APS nonlinearity: ' V/V ' (gain) nonlinearity comes from the source follower and other amplifiers in the sensor readout chain; ' V/e^- ' (sensitivity) nonlinearity arises because the APS photodiode is an element of the sense node so the sense node capacitance varies with the signal level [13]. The charge-to-voltage relationship is thus nonlinear, causing a reduction in both the signal and noise recorded at

high illumination levels as compared to the case of constant capacitance. The use of a single, constant, conversion gain $K(e^-/DN)$ therefore gives false estimates of the number of electrons generated in the pixel in response to incident illumination.

To overcome this issue, $K(e^-/DN)$ is decomposed into a signal gain, $S(e^-/DN)$, used to calculate the signal in electrons and full well capacity, and noise gain, $N(e^-/DN)$, used to calculate the read noise. The method is briefly summarized as follows; readers are referred to [13] for a full description of this analysis. At low illumination levels (less than 10^4 signal electrons), nonlinearity is not significant so we can assume that $K(e^-/DN) = S(e^-/DN) = N(e^-/DN)$ and thus determine the signal conversion gain at low illumination.

Provided we have accurate knowledge of the illumination input at higher signal levels ' n ' (e.g., light intensity or exposure time), $S_n(e^-)$ can be calculated in proportion to $S_1(e^-)$, the first signal intensity, given in electrons. $S_n(e^-)$ is an accurate estimate of the number of signal electrons in the pixel at illumination level ' n '. Dividing this by the sensor output $S_n(DN)$ at that level determines the signal gain $S(e^-/DN)$ as a function of illumination. The noise conversion gain can then be found as a function of illumination using

$$N \left(\frac{e^-}{DN} \right) = \frac{\sqrt{S(e^-)}}{\sigma_{shot}(DN)} \quad (2.2)$$

where σ_{shot} is the shot noise measured in digital numbers. As with standard photon transfer methods, the data set required to perform a complete noise characterization using the method above is a series of images taken under flat field illumination between the dark and saturation levels of the sensor.

In this work, six different 'Large Area Sensors' were characterized to test for compatibility of results between the Xilinx FPGA and Aspect Systems data acquisition options, as well as repeatability of results between sensors. Those devices read out via the Xilinx FPGA were illuminated by an array of LEDs at 546 nm (LumiLED) coupled with a diffuser (Lee Filters), while the Aspect Systems test bench combined an LED array producing illumination centred at 520 nm (bandwidth 35 nm) with a lens to achieve uniform illumination and a single neutral density filter. Both setups followed the standard protocol for producing flat field illumination as described in [12] and the illumination intensity was independently verified using calibrated photodiodes. Data was acquired both by varying the LED brightness and the integration time of the sensor and results from multiple acquisitions were averaged. Calculations were made within a single sub-stitch section (of the 5×5 stitch blocks described in Section II-A.) to avoid any stitching-related fixed pattern noise effects.

APSs may be operated in one of two different reset modes: in soft reset, the gate-to-drain voltage of the reset transistor is less than its threshold voltage; in hard reset, the gate-to-drain voltage exceeds the threshold voltage. Under soft reset, the transistor never reaches thermal equilibrium; the reset level is determined by the initial voltage on the diode and the reset time resulting in both image lag and low-illumination nonlinearity. Conversely,

hard reset yields steady-state operation so achieves superior linearity and does not suffer from image lag [12]. The sensors were therefore operated in hard reset mode for all measurements.

2) *Fixed Pattern Noise (FPN)*: Fixed Pattern Noise (FPN) has been quantified separately from the temporal noise analysis described above. It may be decomposed into separate effects due to pixels and columns [14], expressed as

$$F_{i,j} = X_{i,j} + Y_j. \quad (2.3)$$

$X_{i,j}$ is pixel-to-pixel fixed pattern noise (P-P FPN) that occurs due to differences in the offset and gain of transistors in each pixel, as well as differences in charge collection efficiency. Y_j is column-to-column pattern noise (CC-FPN), which is due to differences in the column amplifiers and manifests as vertical streaks in an image. The magnitude of these two contributions may be calculated from the overall FPN of the flat field illumination data using the difference of the mean of each pixel signal $\overline{S_{i,j}}$ over all frames, N , and the overall average signal given by

$$\overline{S}(DN) = \frac{\sum_{i,j,k} S_{i,j,k}(DN)}{LMN} \quad (2.4)$$

where L , M and N represent the number of rows, columns and frames respectively and i , j and k index over these. The fixed pattern noise at a given illumination level (usually half saturation) is then

$$F_{i,j} = \overline{S_{i,j}}(DN) - \overline{S}(DN). \quad (2.5)$$

From this definition of $F_{i,j}$, the pixel and column FPN components and their variances are given by

$$\begin{aligned} \overline{Y_j} &= \frac{1}{L} \sum_{i=1}^L F_{i,j} \\ \overline{X_{i,j}} &= F_{i,j} - \overline{Y_j} \end{aligned} \quad (2.6)$$

$$\begin{aligned} \overline{\sigma_Y^2} &= \frac{1}{M-1} \sum_{j=1}^M \overline{Y_j^2} \\ \overline{\sigma_X^2} &= \frac{1}{M(L-1)} \sum_{i=1}^L \sum_{j=1}^M \overline{X_{i,j}^2}. \end{aligned} \quad (2.7)$$

$\overline{\sigma_X}$ and $\overline{\sigma_Y}$ are usually expressed as percentage of the average signal $\overline{S}(DN)$ at the given illumination level [14]. It is particularly important to assess these contributions when using a stitched sensor to ensure that no artifacts arise from the stitching process that will significantly affect sensor performance.

3) *Other Performance Parameters*: Together with the noise, the sensor quantum efficiency represents the ultimate signal detection limit of any image sensor. The quantum efficiency was evaluated in 20 nm steps between 400 and 800 nm using a Hamamatsu L7893 series deuterium lamp coupled to an ISA monochromator via a UV/visible fiber optic. The output of the

monochromator was directed via another fiber optic to the surface of the sensor. The quantum efficiency may then be evaluated as the ratio of the number of electrons detected in the illuminated area, as calculated from the integrated signal and the measured conversion gain, to the number of photons incident upon the sensor, measured with an independent calibrated photodiode (Hamamatsu). The error is thus the combination of the error on the conversion gain and the error on the accumulated signal as the error in the photon measurement is negligible by comparison.

Further, a Veeco Wyko NT1100 Optical surface profiler was used to determine the physical uniformity of the sensor array. These measurements indicate whether there is any physical impact of the stitching process on the flatness of the sensor. Any contours or deviations across the sensor surface would cause problems for scintillator coupling in the application of interest so it is important to verify that the sensor surface is flat. Theoretically there should be no physical boundaries between different stitched regions, but a surface profile is necessary to ensure that this is the case. The profiler measures the roughness of the surface, the average deflection from the centre to the corners of the array and the deviation across a single pixel.

C. X-Ray Diffraction Studies

The Large Area Sensor, coupled with a scintillator to convert X-ray photons into visible light, provides an opportunity to develop a prototype 'Active Pixel X-ray Diffraction' (APXRD) system for use in breast biopsy analysis for cancer diagnosis.

The experimental setup used in this work was developed from our previous system [7] and is sketched diagrammatically in Fig. 5. LAS was coupled to a structured CsI:Tl scintillator of 150 μm thickness on a 3 mm fibre optic plate (Hamamatsu) using an index matching gel (Visilox). A tungsten anode X-ray source filtered by 0.28 g/cm² of Gadolinium was used as the X-ray source and had a mean energy of 42 keV and a spectral width of 15%. A pinhole of 1.2 mm diameter was used to restrict the area of the sample irradiated and hence to define the scattering volume. A 250 $\times$ 250 pixel region of reset was placed in the corner of the array, defined as described in Section II-A, to record the transmitted X-ray beam with an integration time of 0.1 ms. The scattered X-ray beam was measured using the global reset with an integration time of 2.3 s. LAS was placed at a distance of 22 cm from the sample, meaning that scatter up to 12° could be measured with the experimental arrangement. The ratio of the integration times was calibrated initially by imaging each X-ray beam independently; any changes in the sample-to-detector distance or attenuation properties of the sample would require the ratio chosen for this experiment to be adjusted.

X-ray diffraction profiles were recorded for four standard plastics (polytetrafluoroethylene, PTFE; polypropylene, PP; polyvinylchloride, PVC; and acetal) that had been measured with our previous prototype system. For each plastic, a set of 30 frames were recorded for averaging, both with and without the sample in place (data and background measurements) and without the X-ray source on (dark measurement). Flat fielding was then performed to correct for non-coherent background scatter present in the measurements and the dark field offset of

Fig. 5. Experimental setup for medical X-ray diffraction system [7]. The X-ray source was operated in fluoroscopy mode at 70 kV and 15 mA, with 0.28 g/cm^2 Gadolinium filtration used to narrow the spectral width to 15% with a mean energy of 42 keV. A pinhole collimator of 1.2 mm diameter restricted the area of the sample that was exposed to X-rays. An exposure time of 0.1 ms was set in a region of reset (ROR) of 250×250 pixels in the corner of the sensor exposed to the transmitted beam, while the global reset operating with an integration time of 2.3 s was used to collect scattered X-rays.

Fig. 6. Read and shot noise photon transfer curve, together with the decomposed shot noise (read noise subtracted) for a single sensor on both the user readout system (Xilinx FPGA) and the benchmarking system (Aspect system). The Large Area Sensor was operated in hard reset mode using the global reset (RST0) at 10 fps.

the sensor [6]. X-ray diffraction profiles were then calculated by radial integration in bins of 12 pixels width about the beam centre of each corrected image.

III. RESULTS AND DISCUSSION

A. Sensor Performance

An average of the performance parameters evaluated for each Large Area Sensor tested is given in Table II. The small standard deviation for most parameters indicates that good repeatability can be obtained between different sensors and different readout systems. The only major difference arises in the read noise, as might be expected from using two different readout systems and this is further illustrated in Fig. 6, which shows an example of the photon transfer curves obtained using each of the different readout systems. The nonlinearity of the APS is apparent from a signal level of $\sim 3000 \text{ DN}$ ($\sim 2 \times 10^4 \text{ e}^-$), justifying the use of the nonlinear compensation technique described in Section II-B-I.

The decomposed shot noise curve in Fig. 6 illustrates that both systems have the same conversion gain, as expected from the design (Section II-A.). The read and shot noise components

TABLE II
SUMMARY OF THE AVERAGE PERFORMANCE PARAMETERS EVALUATED FOR ALL SIX SENSORS TESTED UNDER HARD RESET MODE AT 10 FPS WITH THE GLOBAL RESET, RST0

Parameter	Value	Standard Deviation
Fill Factor (%)	73	-
QE at 520nm (%)	22.0	0.1
Spectral Response (mA/W)	92	-
Linear Range (% of DR)	30	-
Gain (N) (e^-/DN)	5.5	0.5
Gain (S) (e^-/DN)	5.3	0.3
Read Noise (e^-)	62.2	8.0
Full Well Capacity (10^3 e^-)	61.3	2.7
Dark Current (pAcm^{-2})	14	3.0
Power Consumption (W)	1.1	-
Dynamic Range (dB)	60.3	0.5
Imaging Range with ROR (dB)	96 (nominal)	-

Fig. 7. Quantum efficiency as a function of wavelength between 400 and 800 nm.

curve illustrates that the Aspect system achieves a lower read noise (54 e^-) on average than that of the Xilinx FPGA-based readout system (64 e^-). The read noise is somewhat higher in the Xilinx FPGA-based readout system due to electromagnetic interference (EMI) that was observed in the images. The read noise measured by the Aspect system thus represents the noise performance of the sensor in the absence of EMI. A wide variety of techniques were employed to ascertain the origin of the EMI in the Xilinx system, but unfortunately it could not be isolated in the present study. A series of potential correction techniques have been developed in order to overcome the effects of EMI for future sensor applications [15], but in this study the effect was relatively small so did not affect the results of the X-ray diffraction measurements.

The quantum efficiency of the sensor has been evaluated as a function of wavelength between 400 and 800 nm and is shown in Fig. 7. The profile of the response shows some notable peaks and troughs between 500 and 800 nm, about an average value of 16%; these are attributed to wavelength dependent reflections in the layers of oxide and nitride that exist above the epitaxial layer. LAS has a particularly complex stack of up to 10 layers and does not have anti-reflective coating, accounting for the unexpectedly low quantum efficiency measured given the good fill factor of the design. This could be overcome in future generations of the device using a different CMOS process, for example, including anti-reflective coating. It is expected that this may as much as double the quantum efficiency of the sensor.

Surface profiling of LAS indicates that, as expected, the stitching process has no effect on the physical uniformity of

the sensor. The r.m.s. roughness of the surface was measured to be $1.6 \mu\text{m}$ and the deflection from centre to corner was less than 0.5%. The peak-to-valley deviation across one pixel, which describes the difference between the maximum and minimum points on the surface, was on average just $6.0 \mu\text{m}$. The flatness of the sensor is therefore sufficient for the purpose of scintillator coupling.

Only limited information is available on the existing commercial large area Active Pixel Sensors such as the Hamamatsu and Radlcon devices mentioned in Section I. These devices have a relatively high read noise and full well capacity, rather than the low read noise and full well capacity of LAS but both achieve similar dynamic range. The latter is preferable in many low light level scientific imaging applications where low noise is a priority. LAS also has lower dark current and superior conversion gain compared to these sensors.

LAS has around half the quantum efficiency relative to fill factor compared to the only publication containing detailed characterization of a large area device [2]. It does, however, exhibit far lower dark current and half the read noise, but a factor of 10 less full well capacity leads to a dynamic range of just 61 dB compared to their 76 dB if operated without the regions of reset. With regions of reset enabled, a nominal imaging range of at least 96 dB can be achieved by combining the minimum integration time of 37 μs in RST1 with the maximum time of 2.3 s in RST0. The imaging range extension will be demonstrated in Section III-B. The Large Area Sensor can compete with existing large area Active Pixel Sensors in terms of dark current, read noise, dynamic range and conversion gain, but would benefit from the use of anti-reflective coating in future designs to match the quantum efficiency of other large area devices.

B. Fixed Pattern Noise

Fig. 8 shows an example of an output image from the sensor under uniform illumination. A region of reset of 100×100 pixels has been placed at (625,625) with an integration time of 181 μs ; the surrounding global reset has an integration time of 2.3 s and is near to saturation. Dark columns are present every 135 columns due to a defective column output; this is not an inherent fixed pattern noise and will be corrected in future devices. Differences between the 10 column outputs arise due to ADC gain and offset variations. The five evenly spaced horizontal stripes highlighted by arrows in Fig. 8 are due to fixed pattern noise introduced at the stitching boundaries.

Fig. 9 illustrates the percentage fixed pattern noise at half saturation (column-to-column C-C and pixel-to-pixel P-P) in different regions of the sensor: 'whole array' refers to the FPN calculated across the full imaging area of the sensor; 'column output' refers to the FPN calculated within 1 of the 10 column outputs, but across all of the rows in that output; 'row sub-stitch' refers to confining the FPN analysis to an area in a single column output and between two of the row stitching boundaries that are visible in Fig. 8. Using an average of 50 frames at half-saturation, the fixed pattern noise across the whole array was found to be 1.5% due to column FPN and 6% due to pixel FPN. Confining calculations to within a single column output and row sub-stitch (see Section II-A.) reduces the pixel FPN to 2.9% and column FPN to 0.6%.

Fig. 8. Illustration of the different types of fixed pattern noise (FPN) in the Large Area Sensor. Arrows point to row FPN arising from the boundaries between the 5 stitch blocks. Note the vertical columns that give zero output occur every 135 columns and are due to a defect in the prototype design rather than an inherent FPN.

Fig. 9. Level of Fixed Pattern Noise (FPN), both column-to-column (C-C) and pixel-to-pixel (P-P), in different regions of the Large Area Sensor.

A number of further calculations were made to assess the type of FPN that was introduced due to the stitching process. Firstly, the average of 50 dark frames was subtracted on a pixel-wise basis from the average frame $\bar{S}(DN)$. Following subtraction, the fixed pattern noise across the whole array is 1.5% column FPN and 4.0% pixel FPN. This indicates that dark field subtraction does not reduce column FPN and only partially compensates for pixel FPN. Secondly, two different average frames taken at the same illumination level were subtracted and the result gave 0.01% column FPN and 0.22% pixel FPN, indicating that the FPN identified in the array at half saturation is likely to be gain rather than offset related.

Flat fielding is commonly employed in the anticipated applications (e.g., medical X-ray imaging), so this could be used to remove the FPN. The origin of FPN due to stitched boundaries is at present unknown; a full investigation of this effect would require refabrication at a different foundry, which is beyond the

Fig. 10. Examples of scatter signatures acquired with LAS for Polyvinylchloride (PVC), Polytetrafluoroethylene (PTFE), Polypropylene (PP) and Acetal, compared to a previous study [6]. Error bars shown on both data series reflect the counting statistics of the experiment; these are higher for LAS due to the reduced quantum efficiency and integration time available with this array. Signatures were calculated by radial integration in bins of 12 pixels width about the beam centre of each recorded image. Data is normalized to 100 so that the peak position, shape and full width at half maximum can be compared.

scope of this work. It is, however, important that it be investigated in future.

The conversion gain calculation of Section III-A. was repeated within each of 4 column outputs and 3 row sub-stitch regions (12 ROIs total) to investigate whether the stitching related FPN would affect the measured values of the performance parameters. A variation of less than 4% was found across the array, justifying the use of a single column output and sub-stitch region for the full characterization performed above.

C. Demonstration of Functionality for X-Ray Diffraction

The X-ray diffraction profiles recorded with the present system and those from our previous prototype are shown comparatively in Fig. 10 for the four different plastics interrogated. The intensities are normalized to 100 so the peak position, height and full width at half maximum can be compared. The error bars reflect the counting statistics of each experiment: for LAS, the quantum efficiency and integration time are lower than those in our previous experiment resulting in larger errors, so representative error bars are shown on a few data points for clarity. The X-ray diffraction profiles obtained using the present system generally agree well in terms of peak position and full width at half maximum with the previous data [6] within the bounds of error.

The major benefit of using LAS, the ability to simultaneously record both transmitted and scattered X-rays, is illustrated in Fig. 11. It shows a profile taken vertically outwards from the beam centre of the signature from acetal, the intensity of which

is shown on a logarithmic scale. The global RST0 is operating with an integration time of 2.3 s, while the region of reset has an integration time of 0.1 ms yielding a minimum of 87 dB imaging range. The transmitted beam is visible up to around 1.9° and the intensity falls to zero beyond this until the scatter peak begins to emerge at 2.6° . Normalizing the signal of the scatter peak and the transmitted beam to the integration time of the given ROR, the peak 'count rates' in each region are 2×10^7 DN/s and 4 DN/s for the transmitted and scattered X-rays respectively. This illustrates that a 140 dB imaging output range has been recorded within a single image. LAS therefore represents the ideal image sensor for this application; reduced read noise and improved quantum efficiency would yield further benefits in terms of counting statistics, and enable an X-ray diffraction system to be developed for breast biopsy analysis in a clinical trial.

IV. CONCLUSIONS

The performance of a Large Area Sensor designed for medical imaging applications has been presented. The 1.8 Mpixel sensor exhibits a conversion gain of $5e^-/\text{DN}$ and a read noise level of $62 e^-$. The imaging performance is limited only by the quantum efficiency of 22% at 520 nm, which could be improved in future fabrications by using a foundry that offers anti-reflective coating. Measurements show good repeatability between different sensors and measurement systems; the read noise on the Xilinx FPGA-based readout system was increased slightly due to electromagnetic interference that was not present in the Aspect system. Stitching boundaries produce a fixed pattern

Fig. 11. Demonstration of imaging range achieved for the X-ray diffraction application. Four orders of magnitude can be visualized in the same image by placing a region of reset at the beam centre with an integration time of 0.1 ms and integrating for 2.3 s in the global reset region (data shown for Acetal). Each point represents the radial average of a bin of 12 pixels width and error bars are contained within the points.

noise of around 3% at half saturation that is removed by flat field correction.

A potential application of the capabilities provided by LAS has also been demonstrated. X-ray diffraction of breast biopsy samples could provide fast, quantitative analysis that would improve the speed and accuracy of diagnosis, but has thus far been limited in clinical application by the need for a low cost sensor with large area and wide dynamic range. Scatter signatures of plastic test objects have been recorded with LAS and an extremely wide imaging range of 140 dB has been visualized using the integration time range provided by the multiple regions of reset on the detector. This capability enables both transmitted and scattered X-ray beams to be recorded in a single image. Future developments to larger area and lower noise will guarantee Active Pixel Sensors as the imaging modality of choice in X-ray diffraction of biological tissues and beyond.

More generally, there is demand for sensors like LAS in many medical X-ray imaging applications. For example, verification

imaging in external beam radiotherapy uses large sensors (typically a-Si flat panels) to verify the relationship between the patient anatomy and the collimated radiation field edge. The utility of APS technology in this application has already been demonstrated [16] and the benefits of using this technology in a large area format can now be realized.

REFERENCES

- [1] E. R. Fossum, "CMOS image sensors: Electronic camera-on-a-chip," *IEEE Trans. Electron. Devices*, vol. 40, no. 10, pp. 1689–1699, 1997.
- [2] D. Scheffer, "Wafer scale active pixels CMOS image sensor for generic x-ray radiology," *Proc. SPIE*, vol. 6510, pp. 65100–O, 2007.
- [3] C. D. Arvanitis *et al.*, "Empirical electro-optical and x-ray performance evaluation of CMOS active pixel sensors for low dose, high resolution x-ray medical imaging," *Med. Phys.*, vol. 34, pp. 4612–4625, 2007.
- [4] X-ray Flat Panel Image Sensors for Radiology, Hamamatsu, 2009 [Online]. Available: <http://sales.hamamatsu.com/en/products/solid-state-division/x-ray-flat-panel-sensor/for-radiology.php>
- [5] RadEye 100, RadIcon Imaging Corporation, 2009 [Online]. Available: <http://www.rad-icon.com/products-radeye.php>
- [6] S. E. Bohndiek, *Active Pixel Sensors for Breast Biopsy Analysis using X-ray Diffraction PhD Thesis*. London, U.K.: Univ. of London, 2008.
- [7] S. E. Bohndiek *et al.*, "A CMOS active pixel sensor system for laboratory-based X-ray diffraction of biological tissue," *Phys. Med. Biol.*, vol. 53, pp. 655–672, 2008.
- [8] Multidimensional Integrated Intelligent Imaging, 2009 [Online]. Available: <http://www.activepixels.org>
- [9] N. Allinson *et al.*, "The multidimensional integrated intelligent imaging project (M-I3)," *Nucl. Instrum. Methods Phys. Res. A*, to be published.
- [10] A. T. Clark, N. Guerrini, N. Allinson, S. E. Bohndiek, J. P. Crooks, T. Pickering, and R. Turchetta, "A 54 mm × 54 mm — 1.8 Megapixel CMOS image sensor for medical imaging," *Proc. IEEE Nuclear Science Symp.*, pp. 4540–4543, 2008.
- [11] Aspect Systems, 2009 [Online]. Available: <http://www.aspect-sys.com>
- [12] S. E. Bohndiek, A. Blue, A. T. Clark, M. L. Prydderch, R. Turchetta, G. J. Royle, and R. D. Speller, "Comparison of methods for estimating the conversion gain of CMOS active pixel sensors," *IEEE Sensors*, vol. 10, pp. 1734–1744, 2008.
- [13] J. R. Janesick, *Photon Transfer: DN*. Bellingham, WA: SPIE, 2007.
- [14] G. A. El, B. Fowler, H. Min, and X. Liu, "Modeling and estimation of FPN components in CMOS image sensors," in *Proc. SPIE*, 1998, vol. 3301, pp. 168–177.
- [15] A. Konstantinidis, S. E. Bohndiek, A. Olivo, P. Munro, and R. D. Speller, "Optical characterisation of a CMOS active pixel sensor using periodic noise reduction techniques," *IEEE Sensors*, 2009, submitted for publication.
- [16] J. P. F. Osmond, E. J. Harris, A. T. Clark, R. J. Ott, A. D. Holland, and P. M. Evans, "Image guided radiotherapy using active pixel technology," *Phys. Med. Biol.*, vol. 53, pp. 3159–3174, 2008.