A 5,000 fps, 4Megapixel, rad-tolerant, wafer-scale CMOS image sensors for the direct detection of electrons and photons

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Abstract — This paper presents a 4.2Mpixel, high-speed, wafer-scale CMOS image sensors (CIS) for Cryo Electron Microscopy (Cryo-EM). The sensor is sensitive to electron as well as to light. The sensor achieves 5,266 frames per second at full resolution at with 8-bit depth data. It also works with higher resolution of 9 or 10-bits, as well as with lower resolution of 4 or 6 bits. The speed varies with the bit depth, going from 3,300 fps at 10 bits, up to 7,267 fps at 4 bits.

The detailed design and characterisation of the sensor are presented in this paper.

I. Introduction

The sensor we present here was designed for the direct detection of electrons for Cryo- Electron Microscopy, but the sensor is also sensitive to light, so it can be used also for other applications, where speed and large area are required, like X-ray detection or adaptive optics. Cryo-EM is today the leading tool for the reconstruction of complex biological structures, such as the Covid-19 virus. Its importance was recognised in 2017, by awarding the Nobel Prize in Chemistry to prof. R. Henderson, MRC-LMB, Cambridge, UK, with whom we work to define the specifications of this sensor. Until now, high-resolution cryo-EM microscopes work at the relatively high volage of 300 kV [1]. In order to reduce the cost of these machines, it was proposed to reduce the voltage applied to the electrons, hence their energy to 100 keV, and it was demonstrated that, despite the reduction in energy, the image quality remains high [2].

Reducing the energy of the electrons requires new sensors because of the physics of the interaction of the electrons with the sensor [3, 4]. We already presented the detailed characterization of a prototype in [5]. Here we will present the design and characterisation of the final product, a 4Mpixel, wafer-scale sensor.

As it was already explained in the prototype paper, detection at 100keV requires pixels much larger than those used at 300 keV. The prototype had 60 µm square pixels, with the size slightly reduced to 58 µm to accommodate a greater number of pixels within a single 200 mm wafer. Consequently, the final sensor comprises 4.2 million pixels.

II. The design

The sensor was designed in a 180nm CMOS Image Sensor technology. As shown in Figure 1, the focal plane has 2052 columns and 2064 rows, and it is read at the top and at the bottom. To reduce line length while maintaining an identical design for the stitching blocks, photolithographic techniques were applied, ensuring that the readout lines run only in the top or bottom half of the sensor.

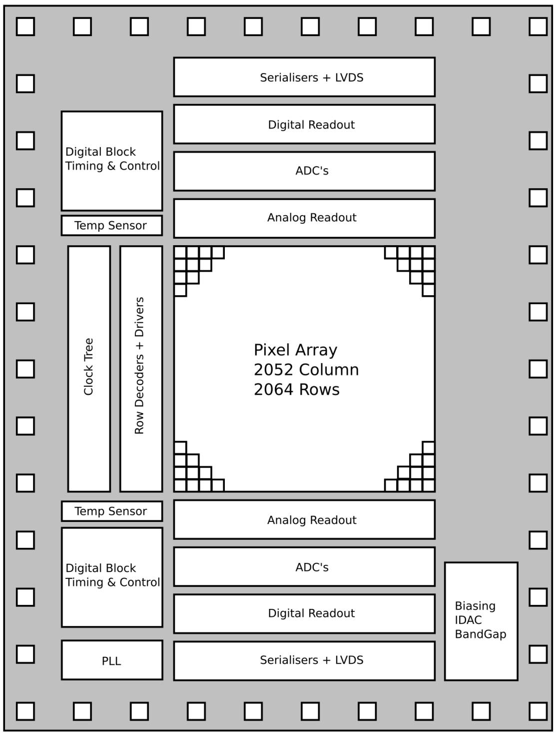

Figure 1. Floorplan of the sensor

The pixel is a 5T pixel with a PMOS reset transistor and a row-enabled active load. There is no column-shared active load. The pixel is read though column-parallel programmable gain amplifiers (PGA), where the gain can be any integer between 1 and 8. It is also possible to bypass the PGA and connect the output of the pixel directly to the sample-and-hold. The sample-and-hold has two branches that are used in turns to achieve the maximum speed. A unitary gain buffer connects to an analogue-to-digital converter ADC. The ADC architecture is 2nd order incremental sigma-delta, as described in [6]. The ADC conversion value is stored into an 11-bit register, thus having overrange for a 10-bit depth accuracy. The bit depth us user selectable and can be 4, 6, 8, 9 or 10-bit. 9-bit is the default value. The maximum clock frequency of the ADC is 35.7 MHz, thus achieving a 9-bit conversion in 1.18 µsec. Every ADC has also an 11-bit dark reference register, whose value is subtracted from the conversion value before the data are sent off-chip. The schematic of the signal path is shown in Figure 2. The sensor has a total of 24,624 ADCs.

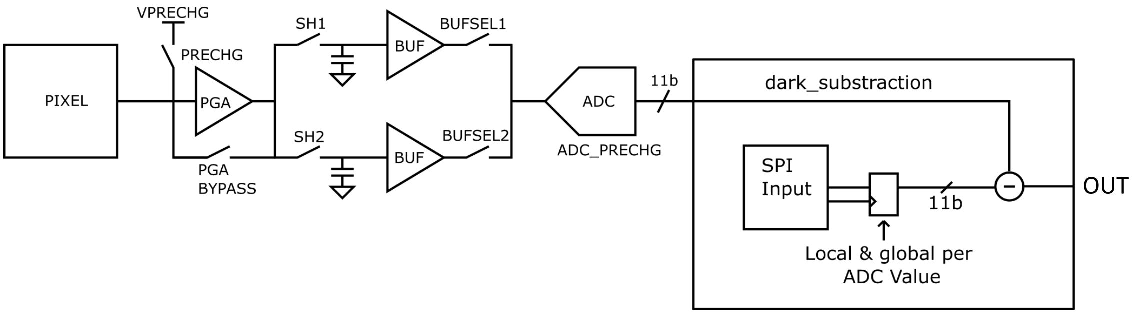

Figure 2. Schematic of the signal path.

Figure 3. Geometry of the readout block for one column in one half of the sensor.

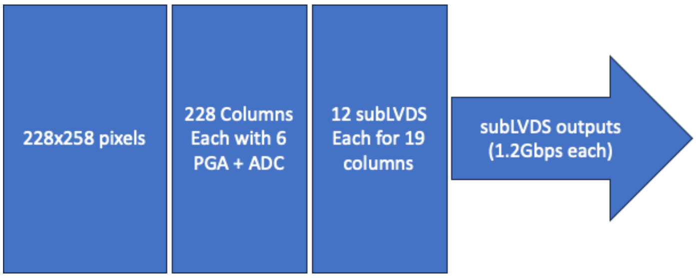

Figure 4. Organisation of one stitching block.

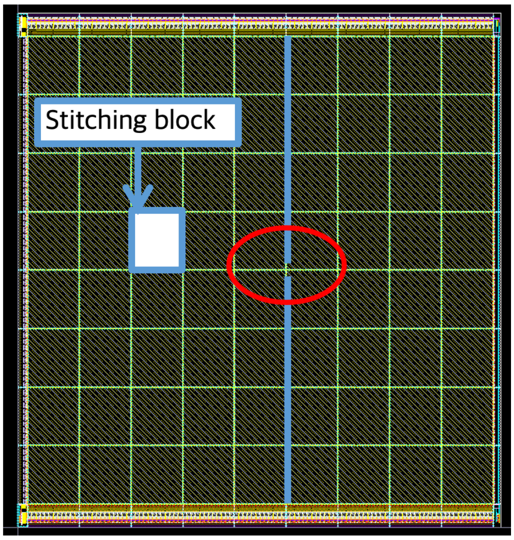

Figure 5. Organization of the sensor with 9 horizontal and 8 vertical repetitions. The output lines from the pixel are split in the middle to allow reading on both, top and bottom, sides

In each half of the sensor, 6 rows are read out in parallel, so that a total of 12 rows are read simultaneously in the sensor. The organization of the PGAs and ADCs is shown in Figure 3.

The digital data are serialized and output through sub-LVDS I/Os, which can work at a maximum speed of 1.2Gbps, at double data rate (Figure 4). There are 12 outputs in each stitching block and the readout is done on two sides, top and bottom, with 9 repetitions horizontally (Figure 5), for a total of 216 data IOs. The high-speed clock for the data serialization is generated on-chip by a PLL from a lower frequency input clock.

The sensor is fully digital, with an SPI interface, through which it can be programmed.

III. CHARACTERISATION

The sensor has been characterized first with visible light. The transfer and photon transfer curve are shown in Figure 6 an Figure 7 respectively. The main electro-optical parameters are: noise = 86 e- rms; full well linear = 33,700e. A fully absorbed 100keV electrons would generate 27,777 e/h pairs, which is less than the full well of the sensor. A summary of the sensor characteristics is given in Table 1.

The sensor was also characterized in a cryo-EM. A measured energy loss distribution is shown in Figure 8, showing the same features as for the prototype measurements.

Example of frames recorded in the microscope are shown in Figure 9. In the zoom of this figure, the black spots correspond to single electrons recorded by the sensor.

IV. Conclusions

A high-speed, wafer-scale sensor was designed and manufactured in a 180nm CIS technology. A photo of the sensor is shown in Figure 10. The sensor is fully digital with an SPI interface and 216 LVDS data output lines. The sensor was tested with visible light as well as in an electron microscope. High-resolution structures of complex molecules were reconstructed, based on the frames recorded by the sensor.

V. Acknowledgments

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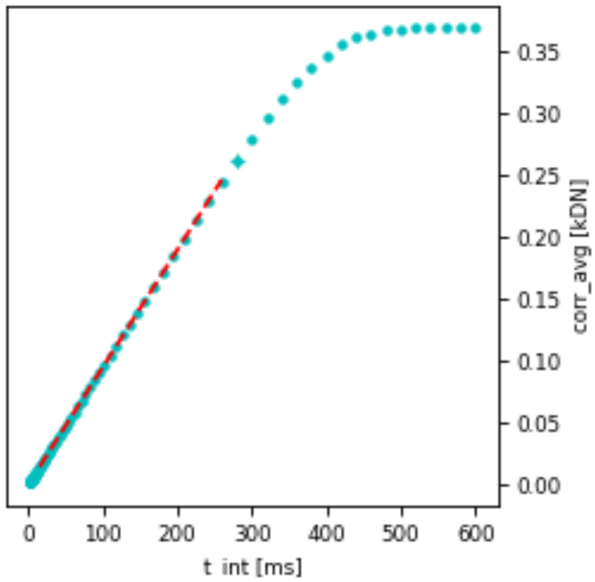

Figure 6. Transfer curve, measured with visible light.

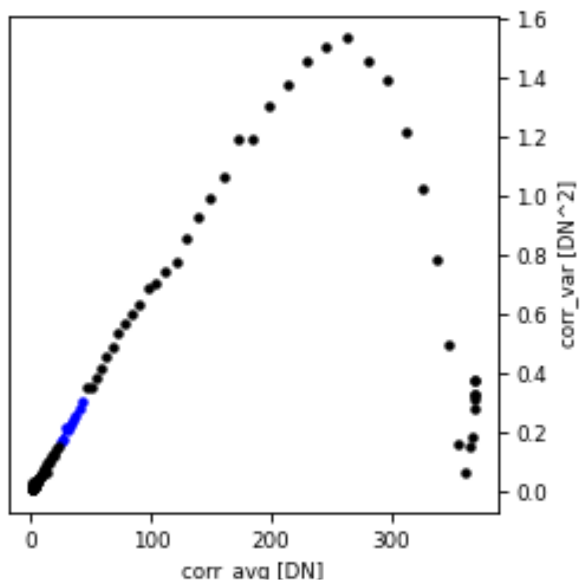

Figure 7. Photon transfer curve, with visible light.

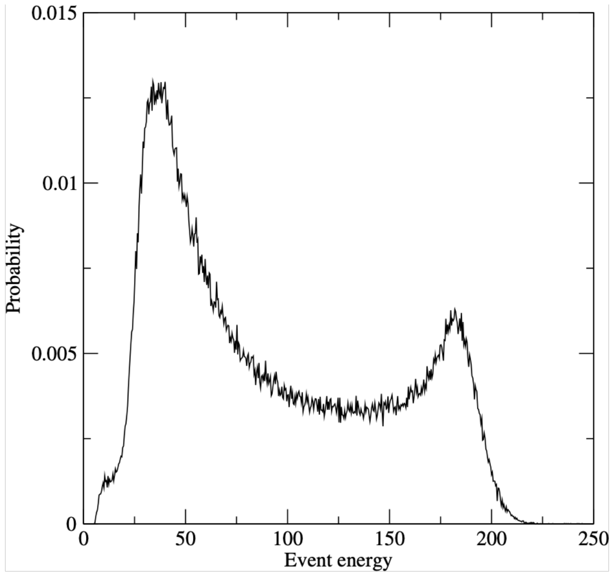

Figure 8. Energy loss distribution, i.e. measurement of the energy lost by every single electron. The measurement corresponds to what seen in the prototype, see figures 10 and 13 of [5].

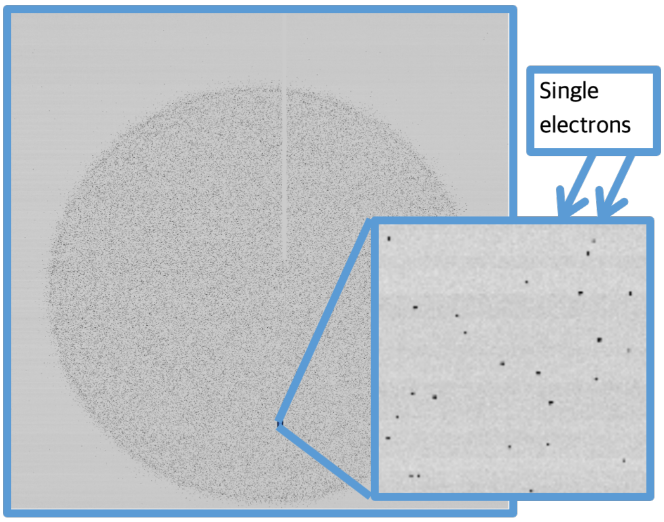

Figure 9. One of the first frames recorded in a cryo-EM showing the image of the circular beam. A zoom in the figure shows the individua electrons detected by the sensor.

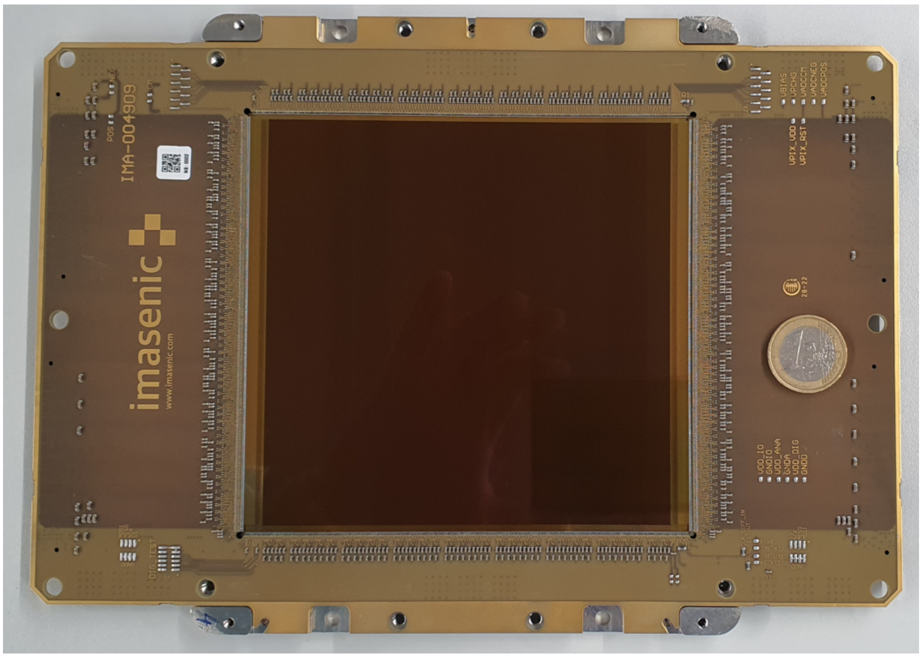

Figure 10. Photo of the sensor on its Chip-On-Board (COB). A 1-euro coin is also shown as a reference size.

Parameter	Value
Format	2052 x 2064 pixels
	4.2 Megapixels
Pixel size	58 µm
Focal plane size	119.0mm x 119.7 mm
Noise	86 e- rms
Linear full well	33,700 e-
ADC	Column-parallel
ADC resolution (User-selectable)	4, 6, 8, 9 and 10 bits
Frame rate (At full 4.2 Mpixels resolution)	7,267 @ 4 bit 5,768 @ 6 bits 5,266 @ 8 bits 4,542 @ 9 bits 3,303 @ 10 bits
Frame rate (ROI: 2052x24)	303,000 @ 8 bits 189,394 @ 10 bits
Frame rate (ROI: 2052x1056)	6,887 @ 8 bits 4,304 @ 10 bits

Table 1. Parameters of the 4Mpixel, high-speed, wafer-scale sensor

VI. References

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