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A Pulse Modulation CMOS Image Sensor with 120dB Dynamic Range and 1nW/cm^2 Resolution for Bioimaging Applications

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1. Introduction

Due to the high potential for miniaturization and integration to various sensors, CMOS technology has been adopted into various bioimaging and biosensing [1] applications. These involve applications ranging from detection of fluorescence for intracellular Ca^{2+} monitoring, to stimulation of nerve cells and recording its response. We propose a total optoelectronic bioimaging chip (Fig. 1) for the above mentioned purpose. We are developing a two-pronged approach to realize the chip. First, from our experience in development of the artificial retinal prosthesis chip [2], [3], [4] we are able to generate electrical stimulus current above the threshold of the human retinal ganglion cells. Next, by using pulse modulation method, low light level detection can be achieved. We have achieved a 120 dB dynamic range light detection level with resolution of 1nW/cm^2 in the lowest detection level of 20nW/cm^2.

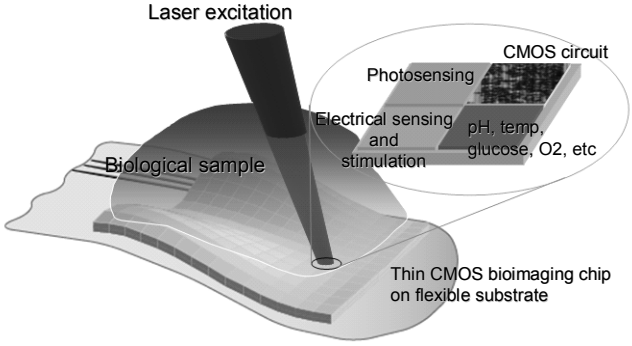


Fig. 1 Concept for total optobioelectronic bioimaging chip.

2. Low Light Photodetection

Pulse-modulation photosensing

In this work, we focus mainly on the low level detection of fluorescence emission. We have adopted the pulse modulation photosensing circuit [5] for this purpose. The advantages of this circuit are wide dynamic range detection, pulse output that enable synchronous and asynchronous operations, and noise immunity. The circuit consists of an nwell/psub photodiode, a source follower, comparator, D flip-flop and feedback logic (Fig. 2). In this photodetection method, light intensity is converted to output pulses in which the pulse period is inversely proportional to the light intensity. For extremely low light detection, the integration time and hence pulse period can be quite large, often in the millisecond- or even second-range, limited only by the dark current of the photodetector.

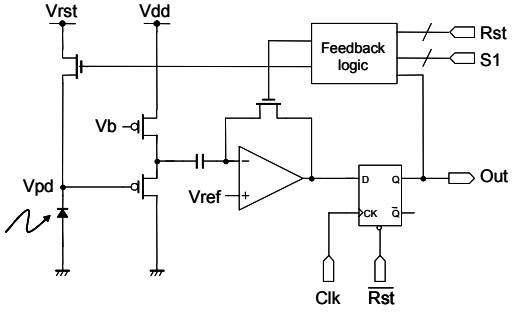
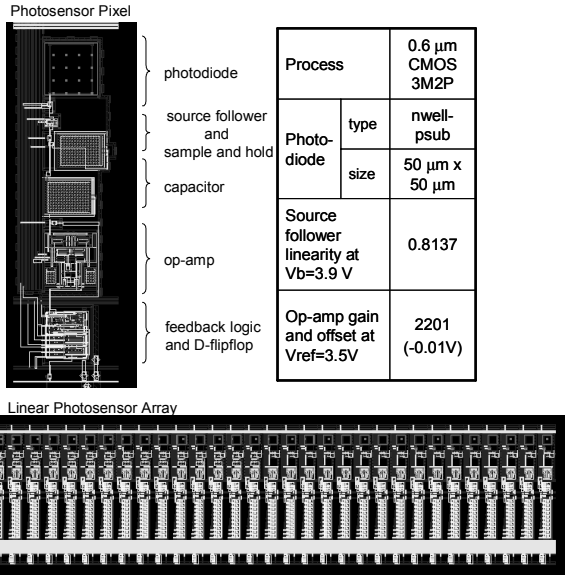


Fig. 2 Pulse modulation circuit schematic.

Fabrication

Using standard CMOS process, we have fabricated a prototype of the bio-imaging photosensor chip. It consists of a single photosenor circuit as well as a linear 32-pixel linear photosensor array. The layout of the photosensor together with circuit specifications is shown in Fig. 3.



Process		0.6 μm CMOS 3M2P
Photo-diode	type	nwell-psub
	size	50 μm x 50 μm
Source follower linearity at Vb=3.9 V		0.8137
Op-amp gain and offset at Vref=3.5V		2201 (-0.01V)

Fig. 3 Layout of the pulse modulation photosensing circuit, the linear photosensor array and specifications.

3. Measurement

Sensitivity and dark current

In order to measure the sensitivity of the pulse-modulation circuit we used a semiconductor laser with wavelength of 670 nm. The maximum incident intensity on the photodiode is 5.3 mW/cm^2. By decreasing the incident light intensity using neutral density filters we are able to measure up to 6 orders of light intensities. From Fig. 4 we can see that the pulse-modulation photosensor has

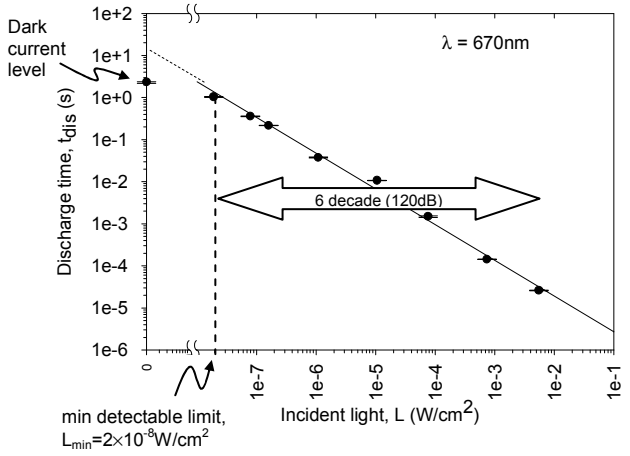


Fig. 4 Light sensitivity measurement.

excellent linearity, with dynamic range of 6 decades (120dB).

In order to determine the dark current value, measurement in absolute darkness was performed. In this condition, leakage current contributes to the discharge of the photodiode. By estimating from the discharge time (about 2.35 s in this case), we have found that, for this particular photodiode, the dark current is about 0.12 pA.

4. Discussion

From Fig. 4 it can be seen that the minimum measured detection limit is about 20 nW/cm^2 corresponding to 10^{-2} lux. This is comparable to commercially available logarithmic sensors.

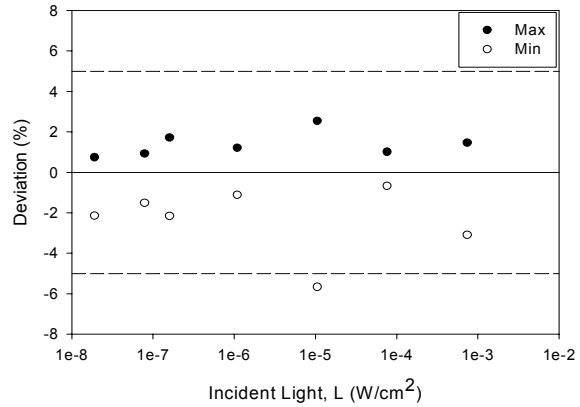


Fig. 5 Maximum and minimum deviation for measurement.

Another advantage of this photosensor is high resolution measurement over the entire measurement range. By repeated measurement for the same incident light level, the deviation of the output pulse period can be found. This is shown in Fig. 5. This graph shows that the deviation from the mean is about ± 5 % within the experimental measurement range. This represents a resolution of 1 nW/cm^2 for the minimum detectable intensity level. Furthermore, we know from circuit simulations that the deviation of the pulse width can be reduced by 1 or 2 orders of magnitude [6]. Hence, we expect to detect the intensity change of less than 0.1 nW/cm^2. Improvement in measurement results is in progress.

5. Bioimaging application (Ca^{2+} detection)

Intracellular Ca^{2+} plays an important role in cellular functions and can be studied using Ca^{2+}-binding specific flourescence probes. Ca^{2+} concentration can be measured quantitatively by using the Indo1 (Molecular Probes) fluorescent indicator. Indo1 in Ca^{2+} free and Ca^{2+} saturated environment exhibit a difference in emission wavelength and intensity. By using a HeCd laser at 325nm as the excitation light source, a change in intensity due to the introduction of Ca^{2+} into Indo1 was observed. This is made possible by continuously monitoring the pulse period. For this experiment, we are able to measure photobleaching effect in real time using the photosensor.

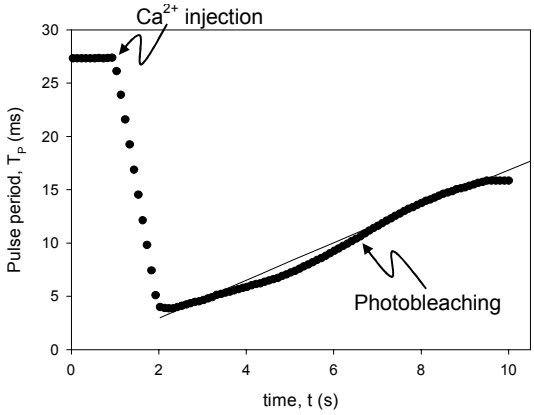


Fig. 6 Intensity measurement of Ca^{2+}-Indo1 flourescence complex.

6. Conclusion

We have developed a photodetector based on the pulse modulation photodetection scheme. By measuring over long periods of discharge time, extremely low light levels can be detected. This is useful for detection of fluorescence in many bioimaging experiments. We will combine our research in the sub-retinal implant prosthesis to fully realize the total optoelectronic bioimaging chip.

Acknowledgements

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