# Design of a noninvasive blood glucose Sensor

D. Nguyen[1], Janet Meiling Wang-Roveda[2],

**I.P. Brief:** MIAO Active Reset and pixel differential amplifier are needed to achieve the pixel Signal-to-Noise at $10^4$.

**Keywords:** active reset, pixel differential amplifier, Noninvasive glucose monitor, Pulsed Photoacoustic, Monte Carlo simulation, Diabetes, skin optics model.

**Primary Industry:** Biotech & Medical
Full IP Descriptions available on-site.

**Abstract**

This paper describes the design of a non-invasive blood glucose testing device. The Monte Carlo Pulsed Photoacoustic simulation of Figure 1 with the skin optic model in Figure 2 suggests we will need at least a signal to noise ratio (SNR) of $10^4$. This SNR adequate to resolve 1 mili-Mole (mM) glucose variation in a 1 mm path length aqueous solution as wanted by ISO DIS 15197 [5]. The needed pixel signal to noise ratio (SNR) is achieved with in pixel differential gain amplifier which provides the pixel conversion gain in mV/e-. The normal CMOS imager typical conversion gain is a few µV/e-. Further, we substantial reduce the pixel noise to KT / 100 Cpd (Figure 5) with MIAO active pixel reset scheme. The prior art of pixel noise are KT / 30 Cpd (Pain active reset – Figure 4 Ref 7) and KT / 18 Cpd (Fowler active reset – Figure 3 Ref 6). Where Cpd is the pixel diode capacitance, K is Boltzmann constant and T is the temperature.

## I. Introduction:

25.8 million Americans (8.3% of the U.S. population) have Diabetes Mellitus with an annual increase rate of 1.3 million cases [1]. There is 1.9 million new cases in 2010 [1]. Diabetes also results in kidney failure, lower limb amputations, blindness, heart disease and stroke [4]. The cost of material used to manage diabetes is roughly $2,500 a patient for each year. Annual sales of meter and strips are $1.2 to 1.5 billion in the USA (3 billion worldwide in 2003) and are projected to reached $10 billion worldwide by 2014 [2,3]. Noninvasive blood glucose recording has been long envisioned to serve as an invaluable tool in prevented or slowed down the debilitating and costly micro-vascular complications of diabetes. The Monte Carlo Pulsed Photoacoustic simulation of Figure 1 with the skin optic model in Figure 2 suggests we will need at least a signal to noise ratio of $10^4$. This SNR adequate to resolve 1 mili-Mole (mM) glucose variation in a 1 mm path length aqueous solution as wanted by ISO DIS 15197 [5].

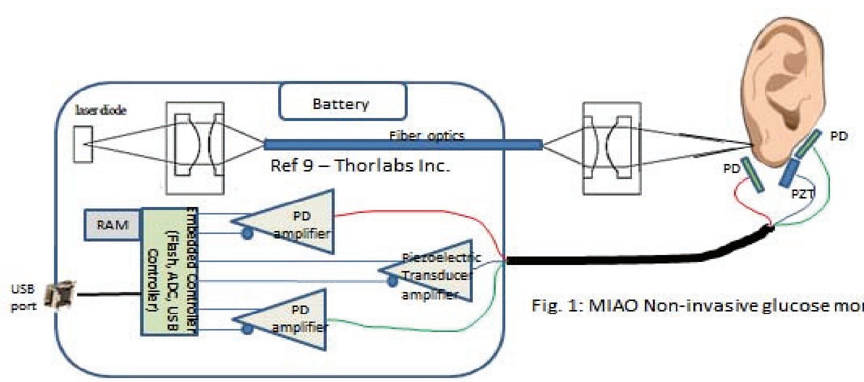
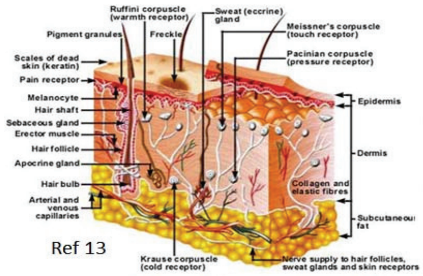



Fig. 1: MIAO Non-invasive glucose monitor



NSTI-Nanotech 2012, www.nsti.org, ISBN 978-1-4665-6276-9 Vol. 3, 2012




| | μa (mm$^{-1}$)[10] | μs'(mm$^{-1}$)[10] | g[12] | n | t (mm)[11] |
|---|---|---|---|---|---|
| epidermis | 0.025 | 0.9 | 0.9 | 1.5 | 0.2 |
| capillaries dermis | 0.053 | 0.93 | 0.9 | 1.4 | 0.2 |
| reticular dermis | 0.025 | 0.9 | 0.9 | 1.4 | 1.5 |
| subcutaneous fat | 0.0112 | 1.08 | 0.9 | 1.44 | 0.3 |
| muscle | 0.032 | 0.59 | 0.9 | 1.37 | 10 |

Parameters of the skin model

Fig. 2: Skin parameters for Monte Carlo Pulsed Photoacoustic (PA) simulation

## II. Low noise and high sensitive pixel design:

The needed pixel signal to noise ratio (SNR) is achieved with in pixel differential gain amplifier which provides the pixel conversion gain in mV/e-. The normal CMOS imager typical conversion gain is a few µV/e-. To achieve low read noise and some immunity to common-mode disturbances, a pseudo-differential amplifier with a pinned photo diode (P+/Nwell/Psub) is used. The high conversion gain in implemented with an ADC step size of 100e-. In order to achieve a $10^4$ SNR, the readout architecture is Correlated Multiple Sampling (CMS). A summary of current known CMOS imager sampling techniques can be found in Table 1.

Table 1: CMOS imager sampling techniques (Ref. 14)

| Technique | Offset | Reset | Flicker | Read |
|---|---|---|---|---|
| Delta-Reset | | | ✓ | 2× |
| Correlated Double Sampling | ✓ | ✓ | | 2× |
| Correlated Triple Sampling | ✓ | | ✓ | 4× |
| Multiple Correlated Sampling | ✓ | ✓ | | 2×/N |
| Correlated Multiple Sampling | ✓ | ✓ | ✓ | 4×/N |

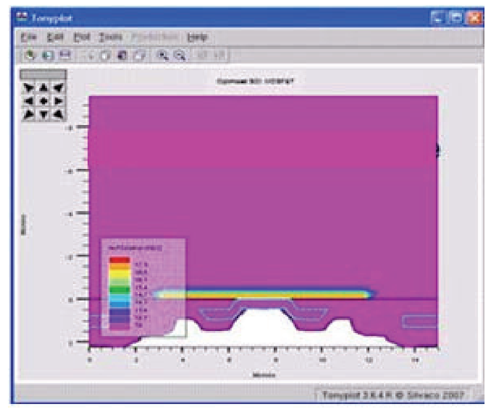


Fig. 7 Optimized pinned photodiode

The ATLAS (Silvaco TCAD) simulations of the MIAO pinned photodiode is shown in Figure 7.

The prior art of pixel noise are KT / 30 Cpd (Pain active reset – Figure 4 Ref 7) and KT / 18 Cpd (Fowler active reset – Figure 3 Ref 6). Where Cpd is the pixel diode capacitance, K is Boltzmann constant and T is the temperature.

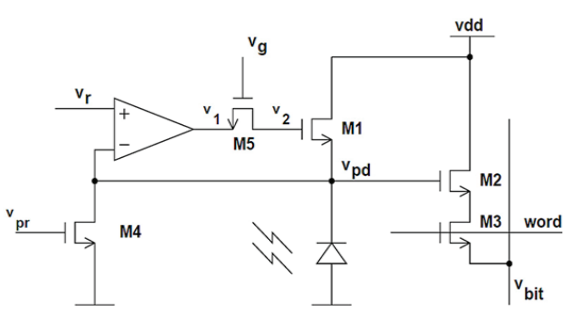



Fig. 3: Fowler active reset (6). Pixel noise KT/18 $C_{pd}$

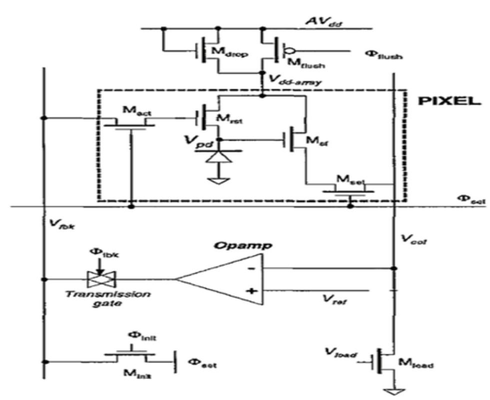



Fig. 4: Pain active reset (7). Pixel noise is KT / 30$C_{pd}$

Further, we substantial reduce the pixel noise (Figure 5) with MIAO active pixel reset scheme. The innovative active pixel reset is the combination of soft reset (for KT/C noise reduction) with the extended dynamic range (with further lower the noise floor) by clipped pixel based on the barrier stepping concept [18].

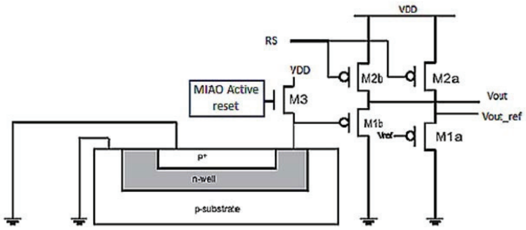



Fig. 5: MIAO active reset. Pixel noise is calculated KT / $100C_{pd}$

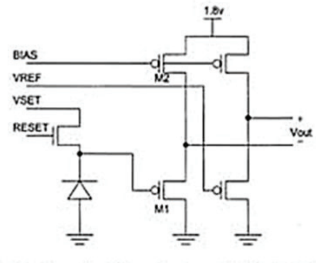
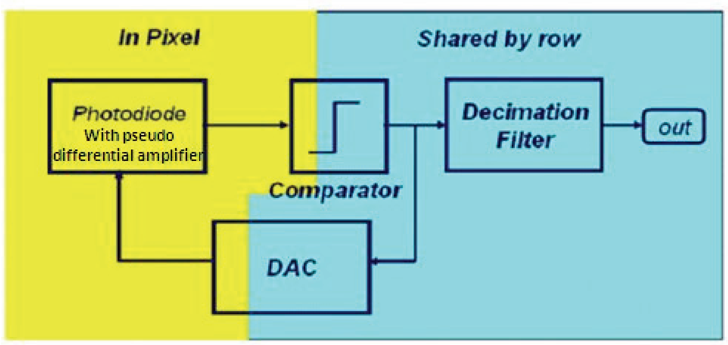



Fig. 6: Pseudo differential amplifier (8)

### III. CMOS Image Sensor (PD) Test chip:

The test structure in CRET08 and SPIE08 conference paper [15, 16] is repeated in Figure 8 for clarification purpose.



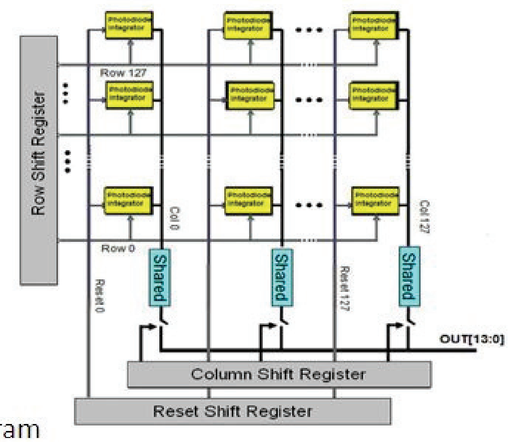




Fig. 9: Simplified Photo Diode sensor test chip block diagram

The Sigma-Delta A/D converter has been chosen because of its ability to reduce DC offset and noise in sampled-data systems. This ability is increased as the sampling rate is increased beyond the Nyquist rate (Over Sampling). Figure 10 is a block diagram of the Sigma-Delta converter [17]. The test chip layout partition is shown in Figure 9.

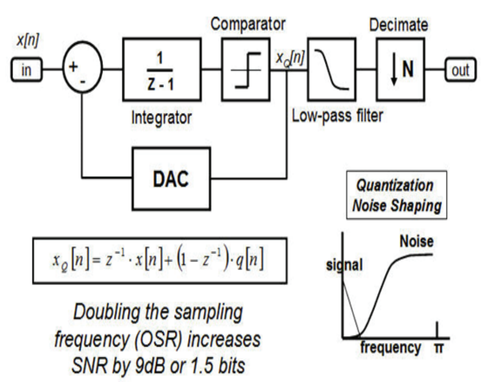



Fig. 10: Sigma-Delta ADC principle

### IV. Piezoelectric sensor

Because of the material's biocompatibility and flexibility, piezoelectric materials have been widely used in applications such as transducers, acoustic components, as well as motion and pressure sensors. In this design, we select the polyvinylidene fluoride (thin-film PVDF) as our piezoelectric sensor due to its unique piezoelectric properties, flexibility, and light weight which is one of the critical requirements for miniature biomedical applications. For the PVDF amplifier, we could use the voltage or charge amplifier configuration. In this project, we select the charge amplifier. The simplify block diagram for the charge amplifier is shown in Figure 11.

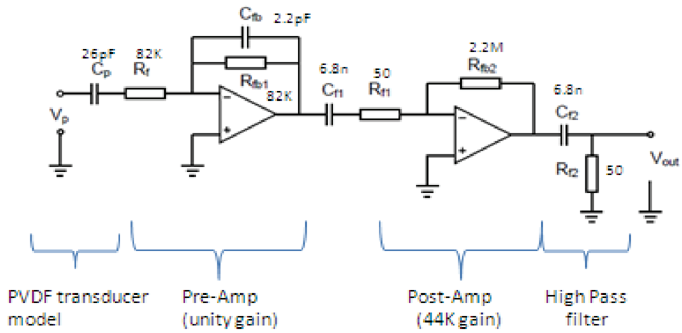



Fig. 11: PVDF Charge amplifier

**References:**


1) http://www.cdc.gov/diabetes/consumer/research.htm
2) http://www.frost.com/prod/servlet/report-brochure.pag?id=D04D-01-00-00-00
3) http://www.researchandmarkets.com/research/c84659/global_glucose_mon
4) Skyler, J., *Chronic Complications of Diabetes,* Endocrinology Metabolism Clinics of North America, Vol 25, 2, 243-254 (1996).
5) ISO DIS 15197, http://www.iso.org/iso/iso_catalogue/catalogue_tc/catalogue_detail.htm?csnumber=54976
6) B. A. Fowler, M. Godfrey, J. Balicki, and J. Canfield, "Low-noise readout using active reset for CMOSAPS," *Proc. SPIE,* vol. 3965, pp. 126-135, 2000
7) B. Pain, T. Cunningham, B. Hancock, G. Yang, S. Seshadri, and M. Ortiz, "Reset noise suppression in two-dimensional CMOS photodiode pixels through column-based feedback-reset," in Proc. IEEE IEDM, 2002, pp. 809-812.
8) Khaled Salama, "CMOS LUMINESCENCE DETECTION LAB-ON-CHIP MODELING, DESIGN, AND CHARACTERIZATION," PhD dissertation, Stanford University, 2005
9) Thorlabs Inc. http://www.thorlabs.us/Navigation.cfm?section=4
10) Jacques SL (1996) Origins of tissue optical properties in the UVA, visible and NIR regions. OSA TOPS on advances in optical imaging and photon migration 2: 364-371.
11) Goldsmith LA (1991) Physiology, Biochemistry and Molecular Biology of the Skin. 2nd edition, Oxford University Press
12) Van Gemert MJC, Jacques SL, Sterenborg HJCM and Star WM (1989) Skin optics. IEEE Transactions on Biomedical Engineering 36: 11461154
13) Primal Interactive Human Anatomy www.primalpictures.com/Complete_Human_Anatomy_Series.aspx
14) "CMOS Biotechnology," ISBN 978-0-387-36836-8, 2007 Springer Science Business Media, LLC
15) D. Nguyen, H. Cormican, C. Wiswall, J.M. Wang, D. Ma, "A mammography imaging hybrid pixel sensor test chip with low noise CMOS readout IC on fully depleted Silicon-On-Insulator Design Trade-Off Study," 9th International Conference on Applications of Nuclear Techniques, June 8-14, 2008, Crete, Greece.
16) D. Nguyen, J.M. Wang et al, "A mammography imaging hybrid pixel sensor test chip with low noise CMOS readout IC on fully depleted silicon-on-insulator design," 7080-8, SPIE2008
17) Candy, J. C. Temes, G. C., "Oversampling Delta-Sigma Data Converters : Theory, Design, and Simulation" Wiley-IEEE Press, ISBN: 0879422858
18) S. Decker, D. McGrath, K. Brehmer and C. Sodini, \A 256 _ 256 CMOS Imaging Array with Wide Dynamic Range Pixels and Column{parallel Digital Output," IEEE J. Solid-State Circuits, vol. 33, no. 12, pp. 2081{2091, Dec. 1998.