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SIGMA-DELTA ANALOG TO DIGITAL CONVERTER FOR USE IN LAB-ON-A-CHIP DEVICES FOR BIOCHEMICAL CLINICAL ANALYSES

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ABSTRACT

This paper describes a sigma-delta analog to digital converter, which was designed for use in lab-on-a-chip devices, especially in low-cost measurement of biochemical substances in biological fluids by spectrophotometric analysis. The optical sensors were integrated in the same fabrication CMOS process with the analog to digital converters, which are based on sigma-delta modulators. Signals proportional to the intensity of the transmitted light through the biological fluids, which are proportional to the biochemical substance concentration, are available at the output in the form of bit streams allowing simple computer interfacing. Although the sigma-delta converters designed for this project have a very simple architecture, they have other advantages relatively to other interfacing devices used with the same purpose, namely, the noise that is integrated with the signal and then digitally filtered, which means that, except for its small quantity in the signal band, it is eliminated by the device.

INTRODUCTION

The healthcare sector is nowadays one of the most dynamic and where the novelty is a strategic and operational imperative. For disease prevention, diagnostic and treatment patients are often subjected to biochemical analyses of their biological fluids. Usually, the analyses are carried out in clinical laboratories and the results become available after several hours, sometimes days. As a consequence a reliable diagnosis cannot be performed within the consultation time. By the other hand, the possibility of increase the quantity and quality of clinical analyses performed with instantaneous results and outside the clinical laboratories, contributes to a better quality of the health care services and also to a better efficiency of the clinical and administrative processes. These needs have led to the development of microsystems with the fluidic, the detection and the readout systems all integrated in a single chip [1]. The advantages associated with shrinking clinical analysis systems include: small sample volume, high degree of system integration, automation of measurement, short response time, improved analytical performance, laboratory safety and reduced cost [2]. The patients are the direct beneficiaries of such microsystem, once it allows more and better information and new and superior relationships and attendances by the health care personnel. Moreover, their diagnostic become easier and they will have instantaneous access to critical information for their activity and decision. The profits associated to the simple possibility of having instantaneous access to critical information are undoubted: time saving in the medical consultation, cost, time and tasks control, minimization of clinical errors, grounds

increase of clinical decision and maximization of the "clinical availability" of the health care personnel.

This paper describes a sigma-delta analog to digital converter for application in lab-on-a-chip devices for clinical analyses. Such lab-on-a-chip intended to solve the reported difficulties, especially in the spectrophotometric analysis, based on colorimetric detection, of biological fluids. It allows the measurement of the concentration of biochemical substances in those fluids. That measurement is based on colorimetric detection by the optical absorption in a part of the visible spectrum defined by the reaction of the biochemical substance with a specific reagent. When the biochemical substance reacts with the specific reagent a color is produced. The intensity of that color is directly proportional to the biochemical substance concentration [3].

Usually, lab-on-a-chip devices comprise in a MCM (Multi Chip Module) two dies: the fluid die and the detection die [4]. This paper is concerned with the detection die; however, the fluid die requires further explanation. It comprises the microfluidic cuvettes containing the fluids into analysis and it is placed above the detection die (figure 1). There are needed three cuvettes for each analysis: the first one contains the chemical reagent, in order to obtain the baseline reference; the second one contains the mixture (sample plus reagent), in order to perform the analysis of the colored mixed solution; the third one contains the calibrator, in order to calibrate the biochemical substance concentration (it contains a standard sample with a well-known concentration of the biochemical substance that is being analyzed). The detection die integrates in the same CMOS fabrication process the photodetection and the readout electronics. For the lab-on-a-chip operation, the three cuvettes are exposed to the light, and three photodetectors, placed underneath the microfluidic cuvettes, forming three optical channels, measure the transmitted light through the fluids. The readout electronics convert the analog signal that comes from the photodetectors into a digital one for further computer interfacing.

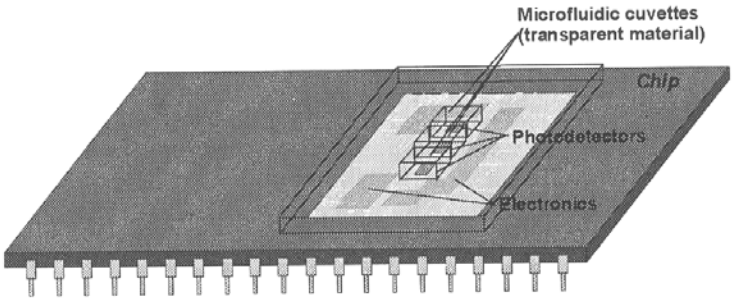

Figure 1: Lab-on-a-chip structure.

DESIGN AND SIMULATIONS

As explained before, the device consists in three cuvettes (for the reagent, for the calibrator and for the mixture in analysis). Each cuvette has its own photodiode underneath and its own readout electronic circuit. This scheme of having parallel measurement of the optical absorption of the three cuvettes fluids avoids the errors that can be introduced due to the light source fluctuations when it is measured one optical channel at a time. Figure 2 shows a block diagram of the photodiode and the readout electronics of each fluid cuvette.

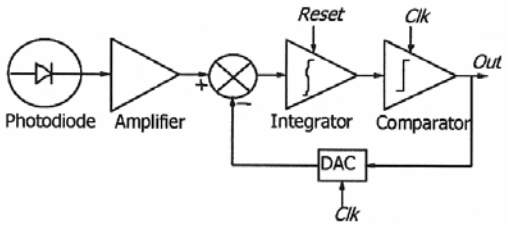

Figure 2: Detail of the channel block of the detection and readout circuit.

The readout electronics consists basically in a current amplifier and in a sigma-delta analog to digital converter. After the light reaches the photodiodes, the three analog to digital converters start the conversion and their output signal is placed in three separated lines. Further computer processing perform additional calculations of these three output signals to achieve a concentration value of the biochemical substance in analysis. The oversample frequency of the sigma-delta converters is determined by the desired number of output bits (signal to noise ratio). In this concrete application, a first order one-bit sigma-delta analog to digital converter is a good choice since the input signal has no time variations, allowing a high oversample ratio with a not so high clock frequency. The following paragraphs will describe in detail each one of the circuit components.

The amplifier and the integrator circuits are based in a single current mirror, as it is shown in figure 3.

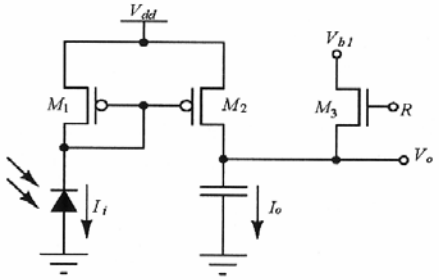

Figure 3: Amplifier and integrator based on a current mirror.

The current of the photodiode travels through M_1. Once the voltage difference between the gates and the sources of M_1 and M_2 is the same, ideally the current that travel through M_2 is proportional to I_i, being only necessary that the two transistors operate in the saturation region. Neglecting the channel width modulation, the current at the drain of M_1 is given by:

$$I_{D1} = I_i = \frac{1}{2} k_p' \frac{W_1}{L_1} \left(V_{GS1} - V_{tp}\right)^2, \qquad [1]$$

while the output current, considering that M_2 is operating at the saturation region, is given by

$$I_{D2} = I_o = \frac{1}{2} k_p' \frac{W_2}{L_2} \left(V_{GS2} - V_{tp}\right)^2, \qquad [2]$$

where I_{D1} and I_{D2} are the drain currents of M_1 and M_2 respectively, V_{GS1} and V_{GS2} are their voltages between gate and source, k'_p is the transcondutance parameter of the p-channel transistor and V_{tp} is its threshold voltage. Once $V_{GS1} = V_{GS2}$, the relationship between the two currents is given by:

$$\frac{I_{D2}}{I_{D1}} = \frac{W_2 / L_2}{W_1 / L_1}. \qquad [3]$$

Equation 3 shows that by changing the widths (W) ant lengths (L) of the transistor channels, it is possible to amplify the current of the photodiode. The amplified current will then charge the capacitor. Since the voltage at the capacitor terminals is proportional to the current integral, the circuit also works as integrator.

The maximum output voltage is limited by the fact that M_2 must remain at saturation, that is:

$$V_{o\max} = V_{DD} - V_{DSat} = V_{DD} - \left(V_{GS2} - V_{tp}\right) \qquad [4]$$

The output impedance of the current mirror is given by the output resistance of M_2, i. e.,

$$r_o = \frac{1}{\lambda I_o}, \qquad [5]$$

where λ is the channel length modulation parameter.

The small signal equivalent circuit of the integrator is shown in figure 4.

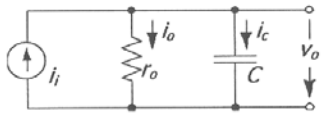

Figure 4: Small signal circuit model of the integrator.

In this circuit, $i_i = i_c + i_o$, where $i_o = v_o / r_o$ and $i_c = C dv_o / dt$. This means that:

$$\frac{dv_o}{dt} = Av_o + Bi_i,$$

where:

$$A = -\frac{1}{r_o C} \text{ and } B = \frac{1}{C}.$$

If the system is sampled with a sample period h, gives:

$$v_o(h+1) = \Phi v_o(h) + \Gamma i_i(h),$$

where

$$\Phi = \exp(Ah) \text{ and } \Gamma = \frac{B}{A}[\exp(Ah) - 1]$$

The transfer function is given by:

$$H(z) = \frac{\Gamma z^{-1}}{1 - \Phi z^{-1}},$$

and de DC gain is given by:

$$H(1) = -\frac{B}{A} = r_o. \qquad [6]$$

Equation 6 shows that the gain of the integrator is very high, so, it is finite and greater than the oversampling ratio. At these conditions, the noise in the signal band only increases 0.15 *dB* [5]. Coming back to the circuit of figure 3, the transistor M_3 is used to initialize the integrator with a known voltage level at the beginning of each conversion. This initialization allows an improvement of 3 *dB* in the signal to noise ratio of the sigma-delta modulator [6].

The circuit of figure 4 was simulated for an input current of 40 *nA*. The result is shown in figure 5. The graph shows clearly the effect of r_o in the output signal. The Pearson coefficient of the curve was calculated from 0.1 to 1 μs and its value is 0.975.

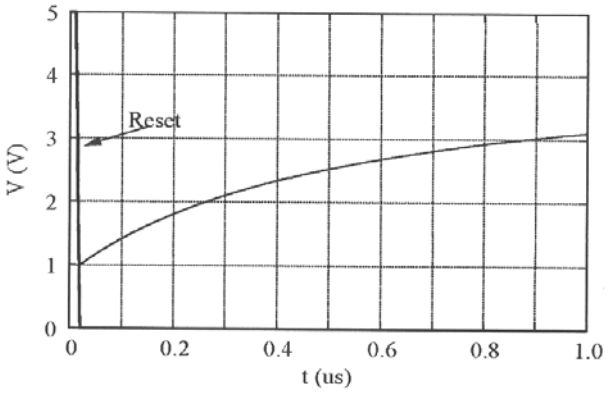

Figure 5: Time response of the integrator circuit for an input current of 40 *nA*.

However, a more important parameter, the DC gain was calculated from figure 5. Since the capacitor has a capacitance of 0.1×10^{-12} *F*, its value is 17.34×10^6, which is finite and greater than the oversampling ratio. This means that the noise in the signal band only increases a maximum of 0.15 *dB*.

Figure 6 shows the schematic of the comparator circuit.

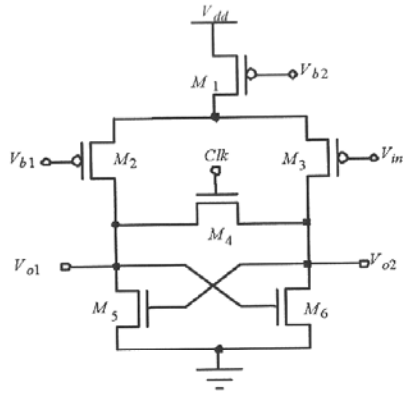

Figure 6: Comparator circuit.

Transistors M_2 and M_3 form a differential pair, which amplifies the difference between V_{in} and V_{b1}, where V_{in} is the output voltage of the integrator and V_{b1} is a reference voltage. The sign of this difference is stored in the memory formed by M_5 and M_6 in the negative transitions of the clock signal (*Clk*). The state of this memory is maintained while the *Clk* signal is at the low level. Figure 7 shows the output voltage of the comparator, for a bias voltage of 2.5 *V* and a randomly chosen input voltage. It is possible to see that for each time the clock falls down, the output of the comparator goes up if $V_{b1} > V_{in}$ and vice-versa.

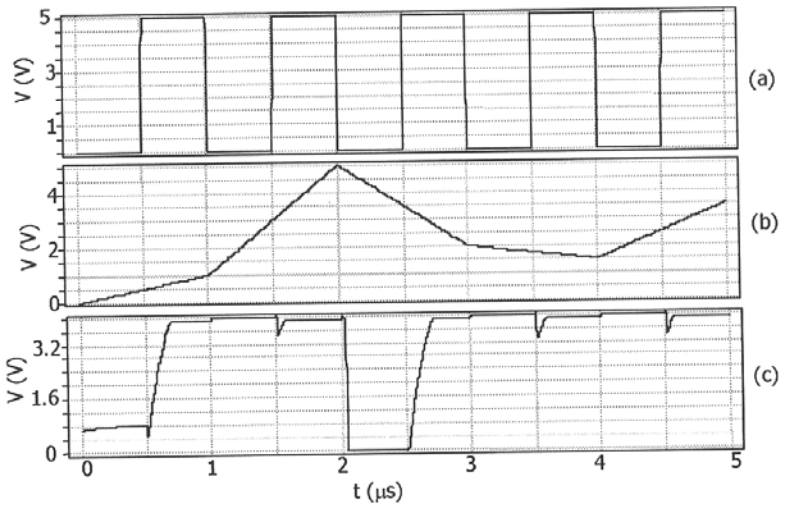

Figure 7: Waveforms of the comparator. (a) Clock. (b) Input voltage (randomly chosen). (c) Output voltage.

Figure 8 shows the schematic diagram of the one-bit digital to analog converter.

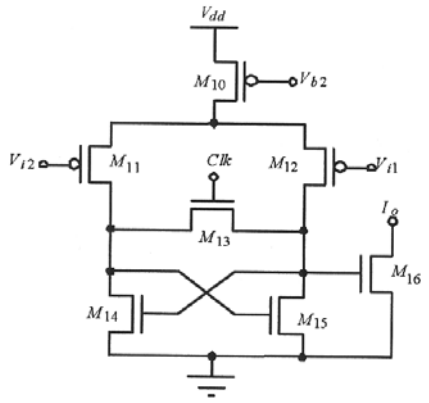

Figure 8: One-bit digital to analog converter.

The working principle of this circuit is identical to the one of the comparator. The signals that come from V_{o1} and V_{o2} of the comparator are connected to the inputs V_{i1} and V_{i2}. The transistor M_{16} works as a voltage to current converter, that is, it converts the digital output level into a current that will discharge the capacitor of the integrator, whenever it is necessary.

Figure 9 shows the whole circuit output as a function of the input current. The oversampling ratio is 64. It was used a digital filter with constant weights (simple average) and the Pearson coefficient of the curve is 0.996, which shows that the device has a good linearity. This result can even be improved by increasing the oversampling ratio and by using an optimum digital filter.

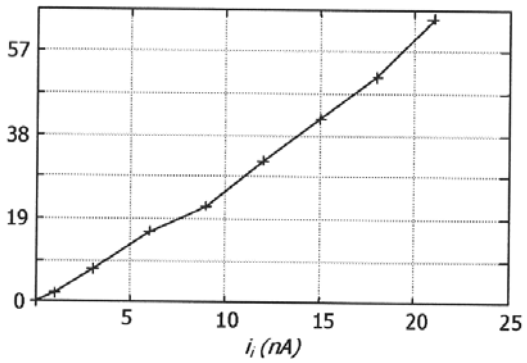

Figure 9: Analog to digital converter output values for input currents ranging from 0 to 21 *nA*. The oversampling ratio is 64.

FABRICATION

Figure 10 shows a picture of the complete device. It consists on two dies. The first one is the microfluidic die. It is composed by the three microfluidic cuvettes and was fabricated using SU-8 techniques. The second die, placed underneath, is the detection chip. It is composed by the three photodiodes of 200 μm × 200 μm and by the three sigma-delta converters, which were placed quite close to the photodiodes.

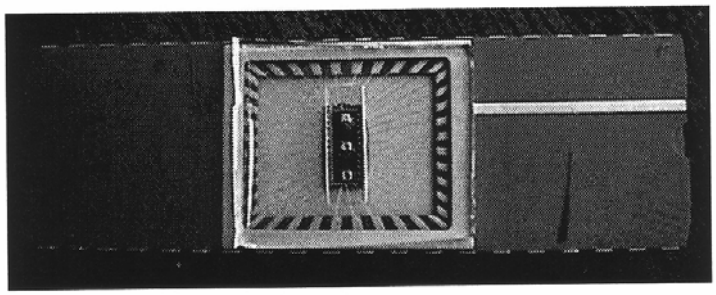

Figure 10: Picture of the complete device with the microfluidic cuvettes die on top of the CMOS detection die.

CONCLUSIONS

This article described a sigma-delta analog to digital converter, which was designed for use in lab-on-a-chip devices for application in the spectrophotometric analysis, by optical absorption, of biological fluids. For the biochemical substance analysis, the lab-on-a-chip operation requires the simultaneous measurement of the optical absorption of the fluid samples within the three fluid cuvettes. Therefore, it was designed a first order one-bit sigma-delta analog to digital converter for each optical channel (cuvette plus photodetector). The converter was designed with a small number of transistors, occupying a very small area in the device. The performance simulation of the device was shown very promising results, not only for this particular application, but for all applications where an array of photodetectors must be read. Meanwhile, the measurement and test setup are being developed to obtain the so desired experimental results of the device.

ACKNOWLEDGMENTS

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