

# CMOS-Based Multifrequency Impedance Analyzer for Biomedical Applications

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**Abstract**—In this paper we present a monolithic microsystem, which can perform Bio-Impedance Analysis (BIA), and electro impedance tomography (EIT) measurements as well as record electrocardiogram (ECG) signals. In contrast to a full analog lock-in approach, a mixed analog/digital solution is adopted. The proposed solution has been designed, implemented and tested using a commercial 0.35- $\mu\text{m}$  CMOS technology. The tuning range of the signal generator and the detector is from 10kHz to 10MHz in 1kHz steps. The circuit ensures a CMRR of 81dB@10kHz, which increases to 84dB@10MHz. The measured equivalent input noise power spectral density is  $e_n=2.57\text{nV}/\sqrt{\text{Hz}}$  at 10kHz in the worst case, close to the 1/f corner frequency. It decreases until  $e_n=1.8\text{nV}/\sqrt{\text{Hz}}$  at 1MHz and  $e_n=1.9\text{nV}/\sqrt{\text{Hz}}$  at 10MHz. Measurements of a reference RC network performed with the proposed monolithic solution and compared with a Keysight E4980A Precision LCR Meter shows a maximal relative error of 0.8% over the whole operating frequency range.

**Index Terms**— Bioimpedance, Biomedical electronics, Biomedical monitoring, Biomedical telemetry, Demodulation, Digital modulation, Electrocardiography, Impedance measurement, System-on-chip

## I. INTRODUCTION

BIO-IMPEDANCE spectroscopy, BIA, and EIT techniques have been widely investigated for measuring many different human pathologies. The characteristic of being a noninvasive, low cost solution, makes the bio-impedance measurement technique an optimal candidate for IoT devices and portable systems (i.e. arm band, fitness tracker devices, smartphone, health monitor devices). Bio-impedance spectroscopy has been used to monitor the hydration level of subjects suffering from renal disease [1], to evaluate the status of human tissue [2], or to quantify the body composition [3]. Moreover, it has been reported that BIA has been successfully employed to measure breathing rate [4], glucose level [5], and pulse wave velocity [6]. In addition, by using the EIT approach, the measurement principle of bio-impedance spectroscopy has

been used to obtain time varying 2D images of the thorax for real-time lungs activities monitoring purposes [7].

Renal failure is the pathology where this organ loses its normal functional capacity. In advanced cases, when the renal function is severely impaired the dialysis therapy is the only available way to compensate for its malfunction. Dialysis therapies available today do not guarantee that at the end of a dialysis session the balancing of body fluid is adequately addressed. Recent findings have documented that fluid accumulation between dialysis sessions is a powerful predictor of death and cardiovascular complications [8]. Among all pathologies, hypervolemia is one of the most difficult to diagnose and one which may expose patients to an increased risk of death. Indeed, fluid accumulation will inevitably lead to hypertension. When the circulating volume is excessive, i.e. more than what the heart can effectively cope with, a congestive heart failure may arise. Hypervolemia usually manifests as pulmonary edema and peripheral edema.

With the BIA approach, the electrical impedance of the body is measured by injecting (through a couple of electrodes) a small alternating current into the body at controllable frequencies and by measuring the induced potential difference through others two electrodes [9]. Often the bioimpedance is measured in distributed manner over the body [10]. However the possibility to carry out a very precise and localized measurement allow to characterize the composition of the tissue. Applying the monitoring to the thorax region we have the possibility to learn in precise, accurate and not invasive way the amount water, which may accumulate in lungs, during the dialysis therapy. In the literature there are many studies that confirm the possibility to detect an edema state by measuring the thorax impedance. In particular, the study of Z.-Y Peng at al. [11] shows that changes of 2 - 6 $\Omega$  of transthoracic impedance in animals (dogs) can be directly correlated to the presence of a pulmonary edema. In the last few years, many BIA systems have been developed [12-14], but the resolution is

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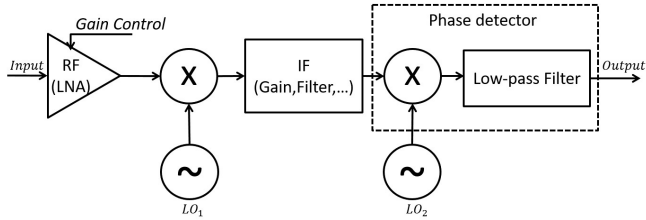


Fig. 1: General scheme of a heterodyne lock-in amplifier

often limited around  $1\Omega$  and the frequency response is not more than a few MHz. These current systems allow to make a qualitative assessment of the examined tissue, but they do not make it possible to obtain an image reconstruction of the liquid distribution in the lungs, which would allow to precisely identify the location of a possible edema.

On the other hand, Electrical Impedance Tomography (EIT) is a non-invasive, radiation-free technique of imaging, which can be used for the detection of pulmonary emboli, non-invasive monitoring of heart function and blood flow [15]. The principle of EIT is based on the back-image reconstruction of the voltage distribution obtained by stimulating a tissue with a current signal applied through electrodes distributed on the chest. A current application at the surface of a subject with homogenous bioelectric properties causes a reproducible distribution of potentials inside the subject. The regions in the chest with the same electrical potential, as a result of current application, are called isopotential lines. The distribution of isopotential lines contributes to a predictable voltage profile on the surface of the body. An increasing of impedance in a region results in a change in each of the voltage profiles which make up one frame. In the EIT case, image reconstruction requires voltage measurement with very high resolution of the order of nanovolts [16]. Thanks to the similarity between BIA and EIT measurements, it is possible to design and develop a system capable of providing both the characterization of impedances and the 2D image of a thorax's section. Moreover, it is also possible to monitor both ECG and respiration rate signals with the same system, which will allow having a complete monitoring of the patient's vital parameters during the dialysis therapy.

In this work, a monolithic mixed-signal (analog/digital) chip for a portable bio-impedance analyzer and EIT system is proposed. This device performs all of the tasks necessary to achieve bio-impedance/EIT measurements in the frequency range from 10kHz to 10MHz. Moreover, the proposed device allows measuring both bio-impedance and ECG signals. Furthermore, thanks to a programmable integrated routing network, which allows connecting in a flexible way the electrodes with the internal device building blocks, the same chip can be used to perform EIT.

The study and design of the proposed integrated system is the continuation of our previous work (see [1]) where we have developed a discrete device, which allowed us to study the correlation between the change in impedance and the hydration level. Based on [1] we have determined the levels of performance required to design the ASIC device in such a way

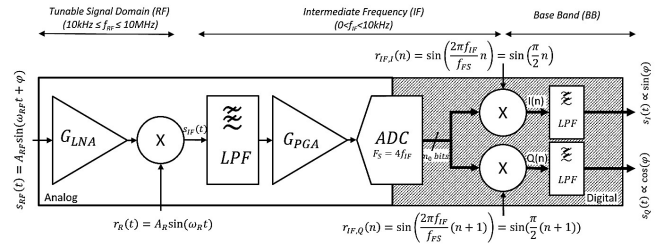


Fig. 2: Proposed improved heterodyne lock-in amplifier

to be able to cover all applications (BIA/EIT/ECG).

The paper is organized as follows: Section II describes the detection principle and the system architecture of the CMOS-Based Multifrequency Impedance Analyzer. Section III analyzes the key structures of the ASIC by providing more details on the working principle and by analyzing the ASIC from a theoretical point of view. Section III highlights the effectiveness of the proposed solution by means of computer simulation. Section V describes the circuit implementation. Section VI presents the measurements results and finally sections VII concludes the paper.

## II. DETECTION PRINCIPLE AND SYSTEM ARCHITECTURE

In literature over the years many solutions which incorporate a lock-in amplifier into an integrated circuit have been proposed. One of the most interesting approach was proposed by Davide Bianchi et al. [17]. A high performance lock-in amplifier capable of working up to 150MHz has been implemented in CMOS 0.35 $\mu$ m technology. However, the design was optimized for current mode measurement and the reference signal need to be provided by an external source. Another design able to perform high frequency impedance measurement was proposed by A.Manickam et al. [18], but also in this case only the lock-in core was integrated, and the input was optimized for current mode operation.

The solution proposed in this paper combines the lock-In approach with the dual step superheterodyne demodulation scheme. Furthermore, in alternative to the full analog approach a mixed analog/digital solution is adopted. The device is able to measure both currents used for stimulation and voltages available on the sensing electrodes. Impedance evaluation and signal processing, is carried out half on chip and half off chip, by means of a microcontroller.

### A. The proposed hybrid heterodyne lock-in amplifier

The working principle of the lock-in amplifier relies on the orthogonality of sinusoidal functions. In particular, the locking amplifier takes advantage from the property of the multiplication of two sinusoids. Namely, when a sinusoidal function  $f_1(t)$  of frequency  $\omega_1$  is multiplied by another sinusoidal function  $f_2(t)$  at frequency  $\omega_2$ , different from  $\omega_1$ , and integrated over a time much longer than the period of the two functions, then the result converges to zero. Instead, when the two frequencies  $\omega_1$  and  $\omega_2$  are in phase, the average value is equal to half the product of the amplitudes.

Heterodyning is a technique used to generate a new frequency by combining or mixing two frequencies. In telecommunications this principle is widely used in the radio

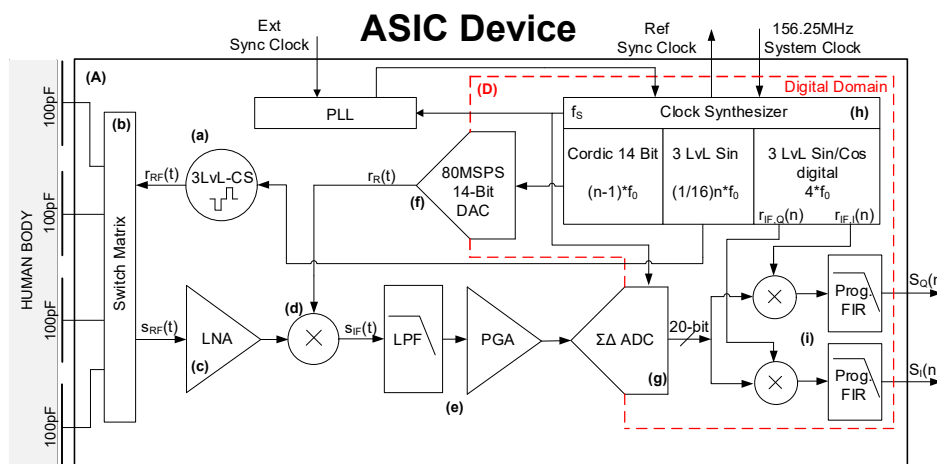


Fig. 3: System architecture [23]

receivers and transmitters.

The basic concept of the operation of the heterodyne structure can be described as follows (Fig. 1). The incoming signal, after being pre-amplified by a low noise amplifier in the radio frequency domain (RF), is mixed with a local oscillator (LO1) to produce sum and difference frequency components. The LO1 is selected to shift the RF signal to a fixed and known intermediate frequency (IF) ( $IF < RF$ ) where all the signal conditioning and processing can be carried out. By following this approach, it is therefore possible to optimize the signal processing at a fixed known frequency, without the need to retune the whole processing chain depending on the incoming signal.

In conventional approach [18], the full acquisition chain of a heterodyne lock-in amplifier is implemented in the analog domain (LNA, low-pass filter, and phase detector) and the output of the phase detector generates DC signals which correspond to the In-phase (I)/Quadrature (Q) components of the signal to be sensed. With the proposed solution (Fig. 2) the LNA amplified signal is first frequency-shifted to the intermediate frequency ( $f_{IF}$ ) domain, low-pass filtered (LPF) and then sampled by an analog-to-digital converter (ADC). At the end, the sampled signal is digitally demodulated and filtered to obtain the I/Q DC values. In this way, the phase detector is fully implemented in the digital domain. In general, when dealing with low noise and offsets, most of the analog circuits need to include chopping and active offset compensation techniques. On the other hand, by sampling the signal directly at intermediate frequency, these techniques turn out to be unnecessary. In fact, in the IF domain, the signal of interest is embedded in the AC component of the signal. This makes the detector immune to all DC signal components, which are added by the analog circuitry, or which were already present in the signal. Furthermore, by choosing the value of the intermediate frequency appropriately, it is possible to inherently limit the effects of noise (e.g. by placing  $f_{IF} >$  flicker noise corner frequency).

Digital demodulation normally requires complex digital circuits, which are capable of performing full precision multiplications. By choosing the sampling frequency equal to

four times the intermediate frequency, the digital demodulation can be achieved by means of simple digital circuits. Moreover, by implementing a fully programmable digital low pass filter after the digital demodulator, the bandwidth of the phase detector can be digitally tuned according to the type of measurements required. In addition, the proposed system turns out to be also optimal for sharing circuits blocks. In particular, thanks to the low sampling frequency, this solution allows the use of time-multiplexing resource sharing, implementing a double demodulator and a double digital low-pass filter, with a single digital structure. The first digital demodulator decodes the in-phase signal (I demodulator), and the second digital demodulator decodes the quadrature signal (Q demodulator). This approach always ensures absolute consistency between the I and Q samples, and thus guarantees the highest possible accuracy in the detection of magnitude and phase.

### B. System architecture

The system architecture is shown in Fig. 3. Compared to other solutions [18, 19], this new architecture combines the lock-in approach with the dual step super-heterodyne demodulation scheme. In contrast to the full analog approach, a mixed analog/digital solution is adopted. In particular, this solution performs a first frequency down-conversion in the analog domain (A) and shifts the I/Q demodulation in the digital domain (D). This has the big advantage of removing any sensible dual path from the analog domain (I and Q analog phase detectors) with important benefits in terms of circuit complexity, detector precision, and power consumption.

As shown in Fig. 3, the analog domain includes all the circuits required to generate the stimulation currents and to collect the induced voltage signals: (a) three level current source, (b) switch matrix, (c) low-noise amplifier, as well as the circuits necessary to perform the first step of the lock-in detection: (d) signal probing frequency (RF) to intermediate frequency (IF) demodulator mixer, (e) programmable gain amplifier and antialiasing filter, (f) digital to analog converter for generating a 86dB SNR sinusoidal demodulation signal, (LO) (g) sigma-delta modulator ADC. Fig. 3 also shows the digital domain blocks, including: (h) the synchronous signal generator, (i) the ADC decimator and the digital part of the lock-in detector, and

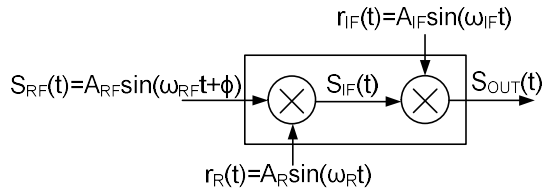


Fig. 4: Heterodyne demodulator

all control logic required to manage the chip and to communicate with an external microcontroller. Furthermore, the chip has a built-in PLL to provide the synchronization with other devices for a multichip operation (EIT operation mode).

### III. SYSTEM ANALYSIS

#### A. Heterodyning and intermediate frequency IF

In order to appreciate the effectiveness of the proposed approach we evaluate the signal transfer function of the ideal heterodyne modulator shown in Fig. 4 (for simplicity a single path is considered – the I phase detector), where  $\phi$  is the phase between the input signal (at  $\omega_{RF}$ ) and the two reference frequencies  $\omega_R$  and  $\omega_{IF}$ . By recalling the trigonometric product-to-sum identities and by noting that  $\omega_{RF} = \omega_R + \omega_{IF}$ , we can write the signal at the intermediate stage as:

$$S_{IF}(t) = \frac{A_{RF}A_R}{2} \left( \cos(\omega_{IF}t + \phi) - \cos((2\omega_R + \omega_{IF})t + \phi) \right) \quad (1)$$

from which it directly follows that:

$$S_{out}(t) = \frac{A_{RF}A_R A_{IF}}{4} \left( \sin(-\phi) + \sin(2\omega_{IF}t + \phi) - \sin(2(\omega_R + \omega_{IF})t + \phi) - \sin(-2\omega_R t - \phi) \right) \quad (2)$$

Eq. (1) shows that  $S_{out}(t)$  is the combination of "image" signals with frequencies higher than the intermediate frequency  $f_{IF}$ , and a DC component, which depends only on the phase  $\phi$  between the input signals. Furthermore from Eq. (1) it follows that if a DC signal  $k$  is superimposed to the incoming signal (i.e. an offset added by an input amplifier)

$$S_{RFdc}(t) = S_{RF}(t) + k \quad (3)$$

at the IF stage the DC signal will be moved at frequency  $f_R > f_{IF}$

$$S_{IFdc}(t) = S_{IF}(t) + k A_{IF} \sin(\omega_R t) \quad (4)$$

which allows removing the unwanted effects of any DC components by implementing a LPF in the IF domain, before performing the second demodulation step.

In the same way a DC component added in the IF domain will be translated at frequency  $f_{IF}$  at the output of the second modulator stage. Therefore, all DC signals added by the circuitry in the RF and IF domain will not affect the accuracy of the measurement.

With the proposed hybrid approach, the second demodulator is implemented in the digital domain. Digital demodulation normally requires full precision multiplications. In general floating points units are implemented to minimize the effect of rounding and approximation. Instead, with the proposed

solution, we are able to perform the demodulation step in a simple way.

By sampling the IF signal at four times the IF frequency, it results that the demodulation has to be performed with a reference sine wave sampled at four times its fundamental frequency (sampling frequency  $f_S = 4f_{IF}$ )

$$(r_{IF}(n))_{@f_S} = \sin\left(\frac{2\pi f_{IF}}{f_S} n\right) = 0, 1, 0, -1, 0, \dots \quad (5)$$

By operating at four times the IF frequency, it means that the operation of demodulation is transformed into

$$s_{out}(t) = s_{IF}(t) \cdot r_{IF}(t) \quad (6)$$

$$(s_{out}(n))_{@f_S} = (s_{IF}(n))_{@f_S} \cdot (r_{IF}(n))_{@f_S} \quad (7)$$

$$(s_{out}(n))_{@f_S} = (s_{IF}(n))_{@f_S} \cdot \sin\left(\frac{2\pi f_{IF}}{f_S} n\right) \quad (8)$$

$$(s_{out}(n))_{@f_S} = (s_{IF}(n))_{@f_S} \cdot (n \& 0x01) \cdot (-1)^{(n \text{ shr } 1)} \quad (9)$$

where  $n$  is a positive integer number and **shr** is the logical shift right digital operation on integer numbers.

When implemented with digital circuits, the demodulator is obtained with a simple inversion of sign combined with some logic gates. This mathematical approach has the valuable property to implement an ideal demodulation without adding any inaccuracies due to the digital quantization and due to the digital multiplication. In other words, this means that the accuracy of this phase detector is only determined by the resolution of the AD converter.

#### B. Operating frequencies

An essential condition to ensure proper operation of the whole system is the absolute synchronization among all of the signals, as well as respecting the following relationships among the signals:

$$f_{RF} > f_R > f_{IF}, \quad f_{RF} = f_R + f_{IF} \quad (10)$$

$$r_R(t) = A_R \sin(2\pi f_R t) \quad (11)$$

$$r_{IF,I}(n) = \sin\left(\frac{2\pi f_{IF}}{f_S} n\right) = \sin\left(\frac{\pi}{2} n\right) \quad (12)$$

$$r_{IF,Q}(n) = \sin\left(\frac{2\pi f_{IF}}{f_S} (n + 1)\right) = \sin\left(\frac{\pi}{2} (n + 1)\right) \quad (13)$$

$$f_S = 4 \cdot f_{IF} \quad (14)$$

where  $f_{RF}$  is the frequency of the input signal  $s_{RF}$  resulting from the interaction of the current reference signal  $r_R(t)$  and the Device Under Test (DUT) attached to the terminals,  $f_R$  is the frequency of the reference signal  $r_R(t)$  for the analog demodulator (d),  $f_{IF}$  is the intermediate frequency,  $f_S$  is the base sampling rate of the ADC,  $r_{IF,I}(n)$  and  $r_{IF,Q}(n)$  are the reference signals of the digital modulators.

By considering the requirements of our application, the intermediate frequency  $f_{IF}$  has been placed at a higher value than the bandwidth of the incoming signal ( $f_{IF} > BW_{(s_{RF})} = 100\text{Hz}$ ). Moreover, the distance between the two spectral components  $f_{lo} = f_{RF} - f_R$  and  $f_{hi} = f_{RF} + f_R$  has been maximized to facilitate the design of the LPF ( $f_R$  as high as possible). In order to maximize the SNR the frequency  $f_{IF}$  has been selected higher than the flicker noise corner frequency of the PGA (1kHz) and set to  $f_{IF} = 1.192\text{kHz}$ .

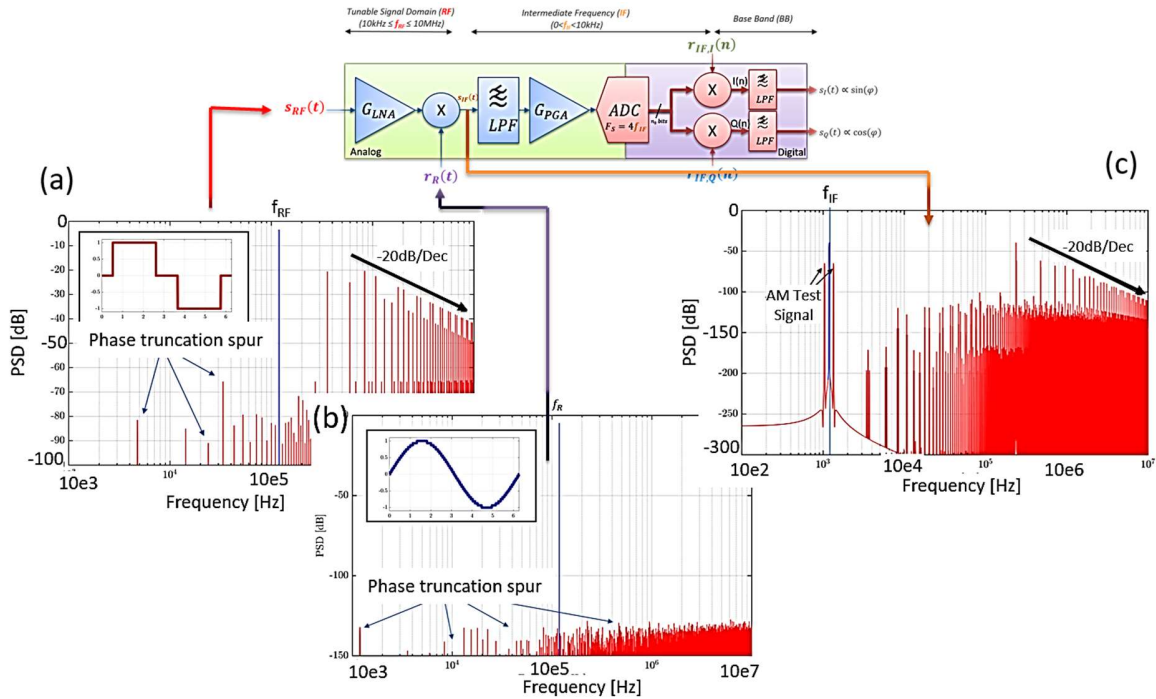


Fig. 5: PSD of the signals at different stages of the elaboration chain. (a) 3 level signal measured on the DUT, (b) PSD of the analog demodulator reference sinusoidal, (c) PSD of the demodulated signal

### C. Optimization of the excitation signal waveform

Ideally, both signals  $r_R(t)$  and  $r_{RF}(t)$  should be ideal sine waves, however, two high quality synchronous sine wave generators would increase the complexity of the system. As a more effective solution we chose to replace the ideal sine wave of the  $r_{RF}(t)$  signals with a sinusoid approximated by a three level signal  $s_{RF}(t)$ , (Fig. 5(a)) where  $\pm\sin(\beta)$  are the switching thresholds between 0, 1 and 0,-1.

The development of the Fourier series of the  $s_{RF}(t, \beta, \omega_0)$  function is:

$$s_{RF}(t) = \frac{1}{2}a_0 + \sum_{n=1}^{\infty}(a_n \cos(\omega_0 n t) + b_n \sin(\omega_0 n t)) \quad (15)$$

where  $a_n = 0$  since  $s_{RF}(t)$  is an odd function, and:

$$b_n = \frac{2\omega_0}{n\pi} (\cos(n\omega_0\beta) - \cos(n\pi - n\omega_0\beta)) \quad (16)$$

The optimal value of  $\beta$  can be identified as  $\beta = 1/(6f_s)$ , which gives  $b_2=b_3=0$ ,  $b_4=b_6=b_8=0$ ,  $b_9=\dots=0$  and  $b_5, b_7, b_{11}, b_{13} \neq 0$ , proving that the first visible harmonic is the fifth. This corresponds to a significant reduction in the number of harmonics present in  $r_{RF}(t)$ .

## IV. MODEL SIMULATION

In Fig.5(a) the Power Spectral Density (PSD) of  $s_{RF}(t)$  is depicted. On the plot the 20dB/dec roll off of the signal harmonics ( $f_n > f_{RF}$ ), which correlates to the  $1/n$  term of the Fourier Series of the 3-level sinusoid, is clearly visible. At the same time, the effect of the phase truncation in the phase accumulator shows up with spurs located at frequencies below  $f_{RF}$ . On the same plot, it is possible to note the positive effect produced by the use of a  $\beta$  value close to  $1/12$  times the signal

period. It is also possible to observe how the harmonics highlighted by the spectral analysis are in number and in amplitude lower than it would be with a classic square wave function.

In Fig.5(b) the PSD of the sinusoid generated by DDS is shown. The PSD is characterized by a strong signal centered at  $(n-1)f_{IF}$ . The quantization noise and the phase noise introduced by the phase accumulator are well below -86.6 dB.

In Fig.5(c) we can observe the folding effect of the demodulator on the  $s_{RF}(t)$ .

Fig.6(a) is the PSD of the 1-bit digital data stream of the sigma-delta modulator. Here the spurs caused by harmonics in the signal  $s_{IF}(t)$  are easily recognizable and are concentrated in the noise shaping region of the modulator, and thus have no impact on the overall system performance (spurs in the noise shaping region will be suppressed together with noise in the digital decimation stage (Fig. 6(b)).

The last PSD depicted in Fig. 7(a), highlights the frequency translation made by the digital I demodulator. Please note that the PSD of the signal at the output of the demodulator is not degraded but only mirrored around the Nyquist frequency. Low frequency noise is shifted to high frequency. With regards to the signal components at high frequencies, these are eliminated by the digital low pass filters (LP) located after the digital mixer, which makes the contribution of out of band signals negligible on the overall system accuracy.

## V. CIRCUIT IMPLEMENTATION

### A. Switch Matrix

The switch matrix (SM) is an analog structure located between the chip PIN and the front-end circuits.

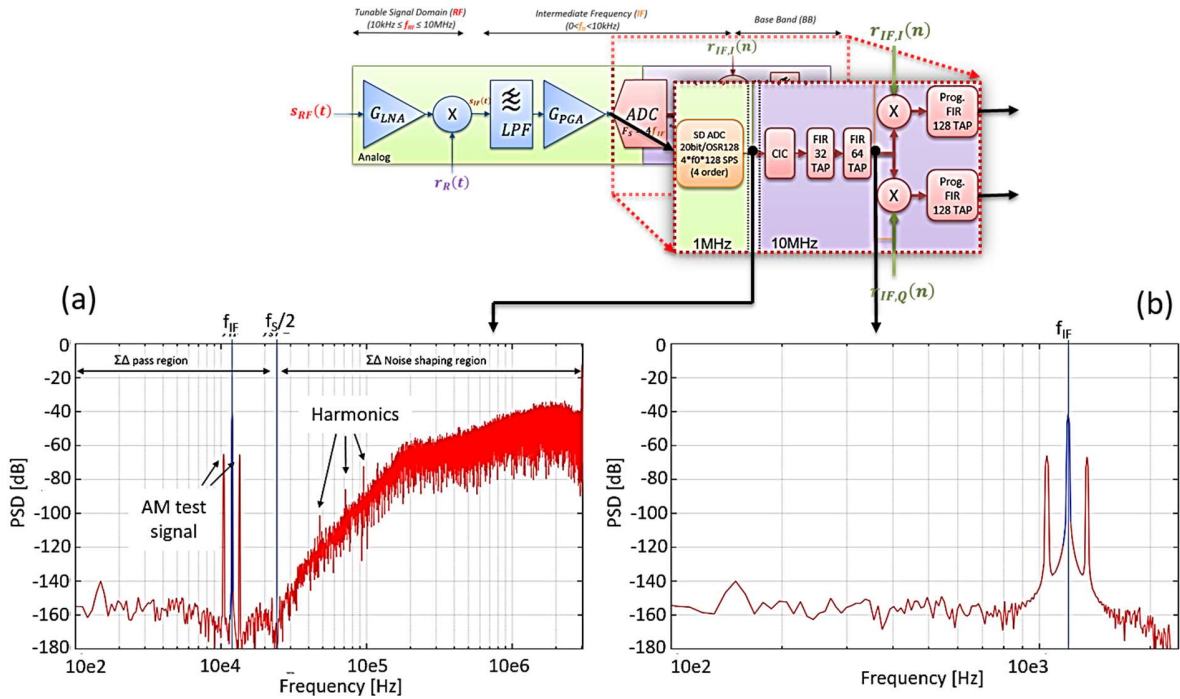


Fig. 6: ADC sampled signal (a) PSD of the 1-bit sigma delta modulator output, (b) PSD of the decimated and filtered digital signal at 4F<sub>0</sub> sampling rate

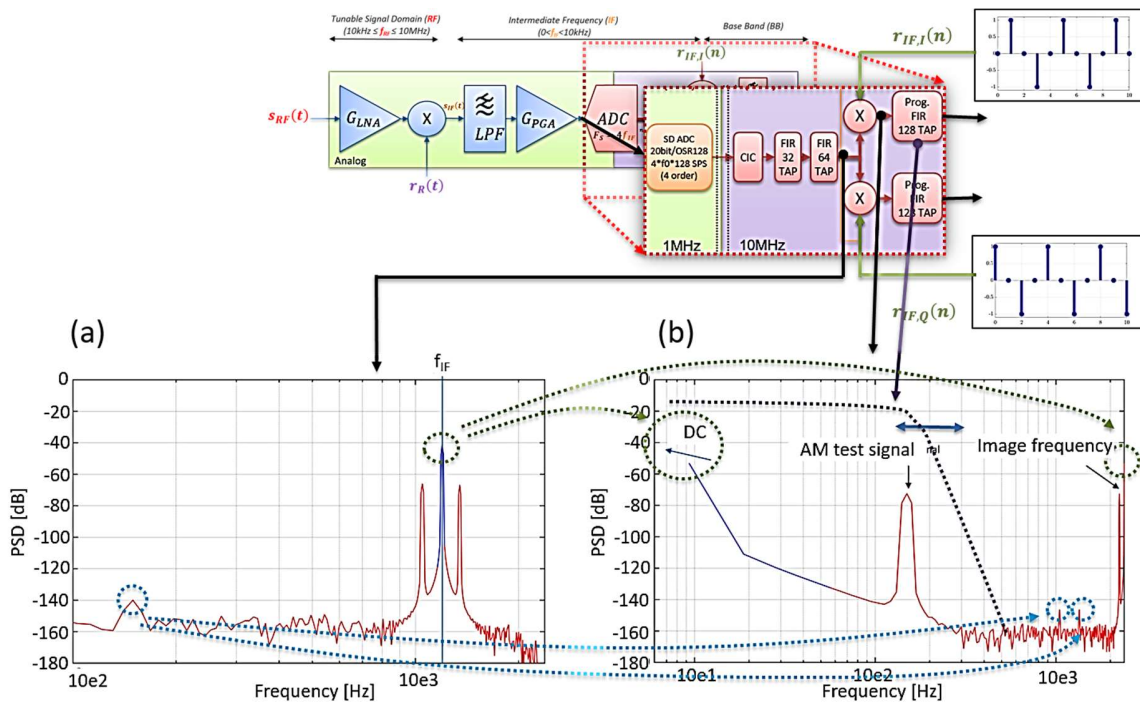


Fig. 7: Digital phase detector (a) PSD of the decimated and filtered digital signal (b) PSD of the digital demodulated signal

It allows to dynamically map the externally connected elements to the internal circuitry (current source and LNA). In particular, in order to perform correct measurements, the stimulation and the readout terminals are constantly exchanged. Furthermore, the SM is of fundamental importance for performing the auto calibration procedure of the entire measurement chain. The SM allows to connect eight possible

input terminals (IO) with four function lines.

The configurability of the structure is guaranteed for each function line independently by a 4-bit binary code.

### B. Low noise amplifier

Fig. 8 shows the main structure of the LNA consisting of a folded-cascode topology with two diode-connected transistors

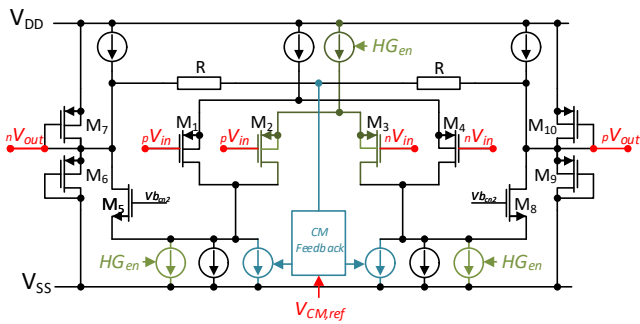


Fig. 8: Schematic of the LNA [23]

and a linearization resistor acting as a load. The differential input pair acts as a voltage controlled current source. It is implemented with P-MOS transistors (M1, M2, M3, and M4), in order to control the body voltage and to reduce both the body effect and the flicker noise contribution. The choice of a P-MOS transistor as active load is an important point for the design of an amplifier where the dependence of the gain on technology parameter changes has to be minimized. Another peculiarity of the circuit is the pair of low transconductance diode-connected transistors used as active loads (M6-M7 and M9-M10). Thanks to this configuration, the linearity of the amplifier is increased by reducing the dependence of the LNA gain on the input differential voltage. N-MOS transistors M5 and M8 allow folding the current from the input pair to the output node, thus reducing the voltage swing caused by the input signal and stabilizing the operating point of the output load.

In order to introduce an extra degree of freedom in controlling the linearity of the circuit, a resistor has been connected between the output nodes. A current controlled feedback loop has been added in order to control the output common mode voltage by directly adjusting the current in the input branch. In order to cover the 140dB of input dynamic range, the circuit has been made programmable (using the High Gain signal  $H_{Gen}$ ) to reduce the gain from 40 dB to 28dB when the input signal exceeds 10mV. The input branches are, therefore, split in two parts: transistors M2 and M3 are activated in high-gain mode, while in low-gain mode M2 and M3 are deactivated, reducing the gain and increasing the noise contribution, which however allows keeping unchanged the dynamic performance, thus increasing the voltage input range up to 80mV. The circuit ensures a CMRR of 81dB at 10kHz, which increases to 84dB at 10MHz.

### C. Mixer

The analog mixer stage (Fig. 9) has been implemented through a current steering Gilbert cell. The circuit is responsible for mixing both the LNA output signal and the signal  $V_{sen}$  from the 3-level current source (3L $\nu$ L-CS). The choice of integrating a "double" mixer into a single structure is dictated by the need to avoid degradation of the LNA performance by placing a multiplexer in front of the mixing stage. The two signals LNA $\nu$ -n and  $V_{sen}\nu$ -n are directly connected to the RF input transistors and the multiplexing function is realized through the selector inSel. The output current signal from the 14-bit-DAC is directly mirrored on the mixer through programmable current mirrors

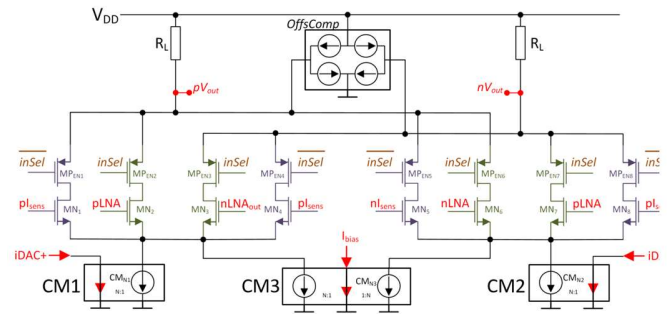


Fig. 9: Schematic of the mixer [23]

(CM1 and CM2), which allow setting the gain value. At the same time, to ensure proper operation of the structure, the bias current is adjusted (via CM3), ensuring a constant operating point. Furthermore, a programmable current source has been implemented as offset compensator (Offs Comp). This structure is directly connected to the two mixer outputs ( $V_{outp}$  and  $V_{outn}$ ) to adjust the output common-mode level and to compensate for any offset arising from mismatches within the mixer structure.

### D. PGA

The PGA and low-pass filter (LPF) blocks are realized with a chain of 3 stages. Two stages are optimized to generate an overall gain of 80dB (40dB + 40dB), while the third stage is optimized to realize the low-pass filter with cutoff frequency  $f_{3dB}$  at 5.9kHz. Both the amplification stages and the filtering circuit are implemented with fully differential multiple feedback topology (MFB). The use of a MFB structure in each stage, although not essential, has the advantage of improving the circuit performance in terms of anti-aliasing filtering.

After the last stage gain stage, a differential unity gain buffer has been inserted. This buffer is required to drive the high input capacitive load of the  $\Sigma\Delta$ -Modulator.

Given the large gain of the PGA, a programmable offset compensation circuit was introduced before the last amplification stage. This circuit is capable of compensating in a static manner (digitally programmable via a digital control word) a possible DC offset, which could be present at the input of the last PGA gain stage. It should be noted that a possible DC component (offset) in the signal may represent a problem in terms of PGA saturation, but does not constitute a theoretical limitation to the accuracy of the measurement, which can be still carried out. Indeed, an offset in the  $s_{IF}(t)$  signal would correspond to a signal at  $f_{IF}$  in demodulated digital signal. This unwanted signal is removed by the digital filters with no effect on the digital demodulated DC value.

### E. 20-bit sigma-delta ADC

The ADC is a 4th-order single-bit, single-loop, switched-capacitor  $\Sigma\Delta$ -Modulator, with a topology incorporating both feedback and feedforward paths. To improve the stability and to ensure a flat-band around  $f_{IF}$  the transmission zeroes have been placed at DC,  $f_0=1.19kHz$  and  $2\cdot f_0=2.38kHz$ . This is achieved by connecting the outputs of the first integrator and the output of second integrator to the input of the fourth

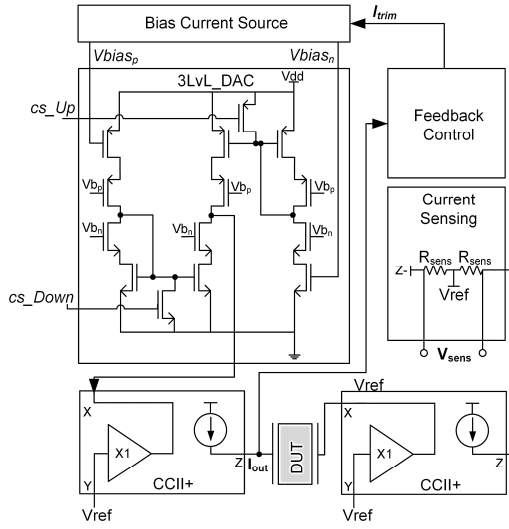


Fig. 10: Three-level current source

integrator through feed-forward paths. The feed-forward factors are both equal to  $1/4$ . The local feedback around the first two and last two integrators form two local resonators, which allows placing a couple of complex zeroes at the desired frequency.

To ensure that the ADC noise is dominated only by the quantization noise, the integrating and sampling capacitor of the first integrator stage has been sized to  $C1=240\text{pF}$  and  $C2=120\text{pF}$ ; while the capacitors of the following integrators were kept small (few tens of picofarads), because their noise contribution is negligible on the total noise contribution. Indeed, only the noise contribution of the first integrator appears unaffected at the output of the modulator (the input noise undergoes the same transfer function as the input signal), while the noise due to other sources inside the feedback loop undergoes to the noise shaping transfer function, which makes the noise requirements for the second, third and fourth integrator less stringent than that of the first integrator.

The oversampling factor is 128, which sets the sampling frequency at  $f_{s,ADC}=512 \cdot f_{IF}=610\text{kHz}$  and allows achieving the measured resolution of 96.8dB.

#### F. 14-bit 80MS/s DAC

The DAC, which is used to synthesize the LO signal, is a current steering DAC implemented by subdividing the bit coding in two structures: part of the bits is coded in the thermometric mode (the 12 most significant bits) and part in binary mode (the 2 least significant bits). Furthermore, in order to maintain a compact structure, the thermometric decoding section has been further divided in two sub-group of 6-bit (MSB and ISB) with the segmentation technique.

Linearity degradation has been reduced by means of a scrambler system, consisting of a butterfly randomizer which has been placed in front of the current sources. According to the analysis reported in [20] the randomization of elements transforms the mismatch error that produces tones in the output spectrum into a pseudo-noise, which improves the SFDR of the DAC.

All current sources are the parallel implementation of a single

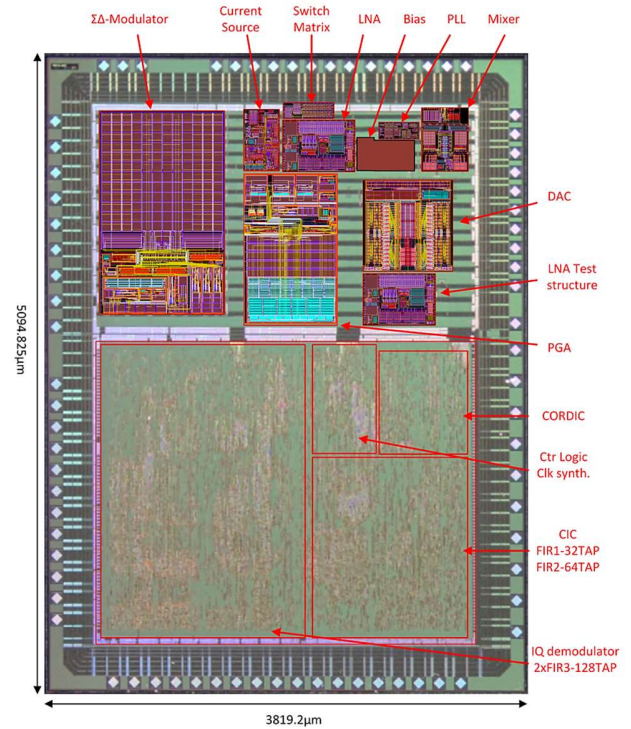


Fig. 11: Micrograph of the implemented ASIC [23]

current mirror cell composed by two cascoded P-MOS transistors, which allows increasing the output impedance. P-MOS transistors in the current cells allow achieving better shielding from substrate noise than N-MOS devices, thanks to their better isolation from the substrate. Furthermore, in order to reduce the charge-injection caused by the clock feed through, the P-MOS switches are followed by dummy switches with the scope of injecting an equal and opposite amount of charge into the channel.

The output current of the DAC is collected by a diode connected transistor, which acts as load (and is part of the current mirrors, which mirrors the DAC current into the mixer).

In order to allow changing the mixer gain, the DAC current has been made configurable through a 4-bit programmable resistor. The LSB can vary between  $5.6\text{nA}$  and  $103\text{nA}$  for a total current consumption between  $115\mu\text{A}$  and  $2.1\text{mA}$ .

#### G. Three level current source and current sensing

The 3-level current source (3LvL-CS) (Fig. 10) is the circuit responsible for the generation of the current required to stimulate the tissue (DUT). According to typical BIA and EIT specifications, the 3LvL-CS needs to be capable of generating a sine wave, approximated by a 3-levels signal, from DC up to a frequency of 10MHz.

The 3LvL-CS is composed by: a bias current source responsible for generating a symmetrical stimulus current on the DUT that is driven by the 3-level DAC through a CCII+ buffer; a second CCII+ buffer which act as current collector or virtual ground; a current sensing circuit for measuring the current through the DUT and finally a current control feedback circuit, which ensures the symmetry of the currents throughout the cycle of the signal.



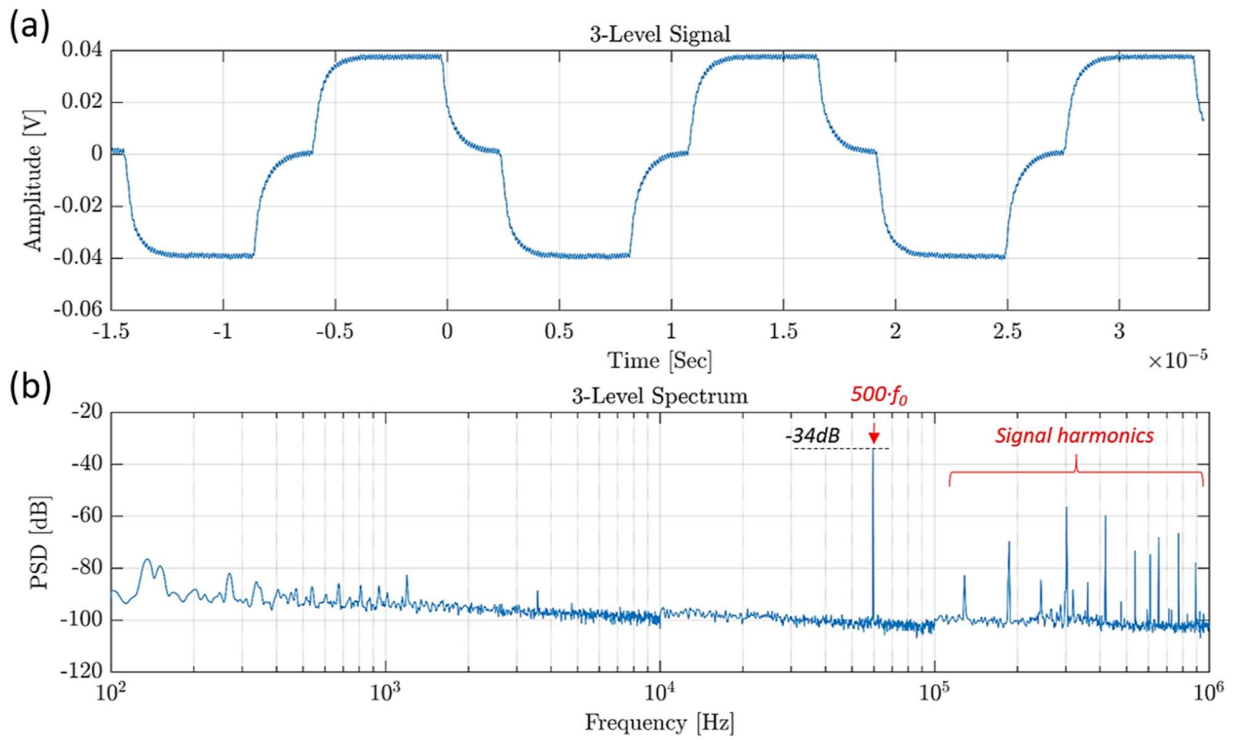


Fig. 12: LNA output (a) Time domain (b) Signal PSD

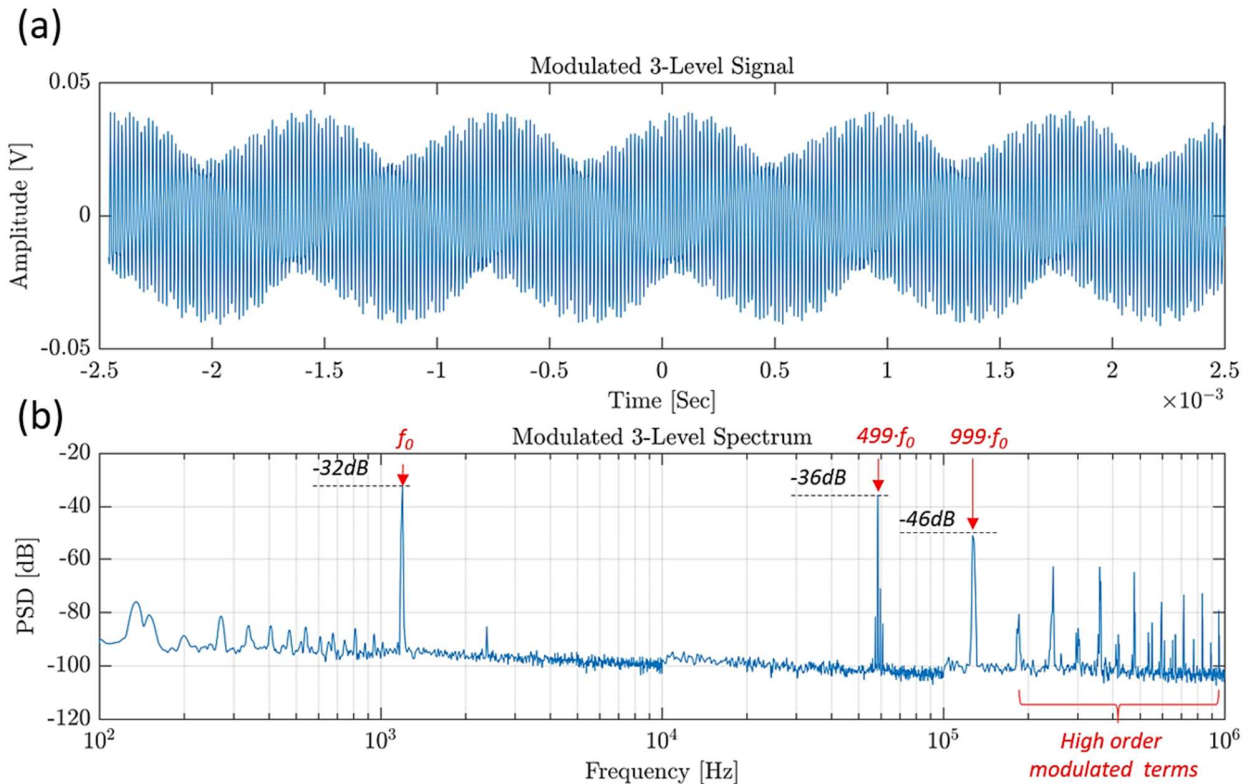


Fig. 13: Mixer Output for a  $499f_0$ Hz demodulator reference signal (a) Time domain (b) Signal PSD

The current amplitude is programmable through the 4-bit register between two ranges: from  $1\mu A$  to  $15\mu A$  for the low current mode, and from  $10\mu A$  to  $150\mu A$  for the high current

mode. The clock generator controls the timing of the 3LVL-CS through the cs-Up, cs-Down and cs-Reset signals. The cs-Up and cs-Down phases controls the  $I_{out}$  polarity alternatively

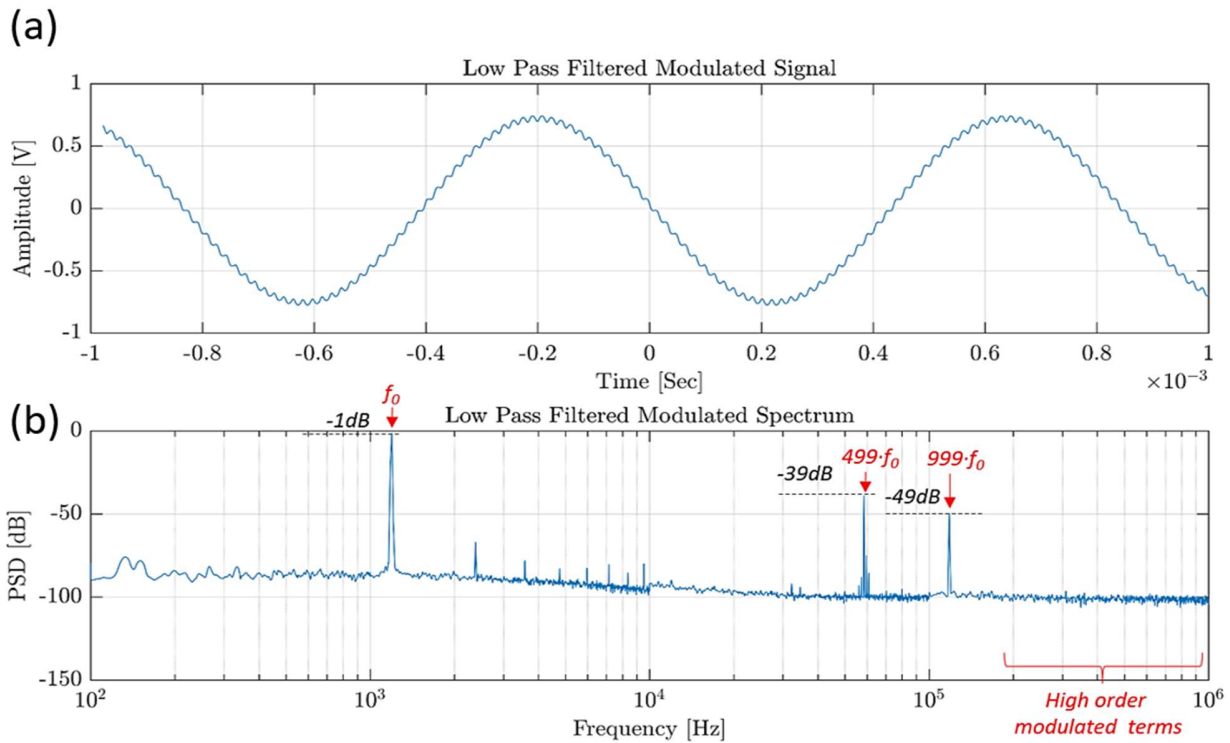


Fig. 14: PGA output (a) Time domain (b) PSD

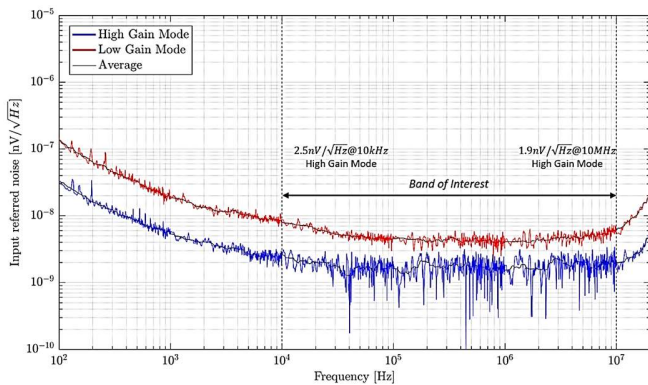


Fig. 15: LNA measured input referred noise

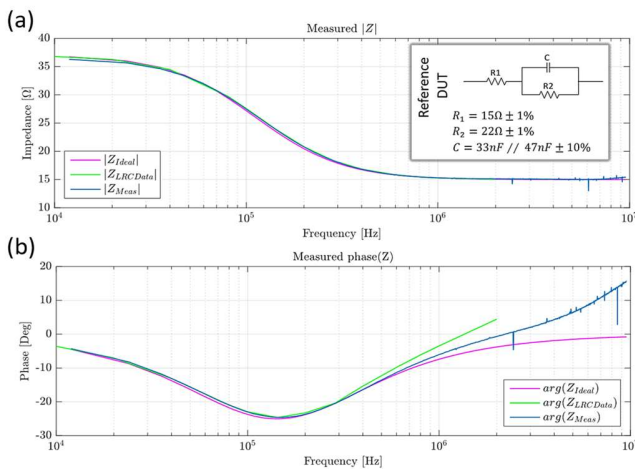


Fig. 16: ASIC, LRC Meter electrical impedance measurement performance comparison (a) amplitude (b) phase [23]

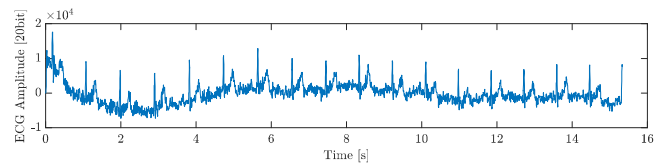


Fig. 17: ECG measurements [23]

enabling the P and N current mirrors.

Current mirrors are controlled by shorting the reference current to ground (or to  $V_{dd}$ ). This approach in controlling the reference current has the advantage of minimizing (or even eliminating) any overshoot in the transients.

To ensure an optimal and constant operating point for the current mirrors of the 3LvL-DAC, and, at the same time, to optimally isolate the current sources from the DUT, a current-conveyor (CCII+) structure has been implemented. The CCII+ behaves as a voltage follower between the Y terminal (current mirror output node) and the X terminal (voltage reference), and as a current follower between the X terminal and the Z terminal.

The current sense circuit has been implemented by means of a CCII+. The symmetry of the currents flowing into the DUT is ensured by the feedback control circuit, which, at the end of each cycle (0,+1,0,-1), ensures that the voltage measured at the 3LvL-DAC output node is equal to the reference voltage  $V_{ref}$ . In case of unbalancing between the currents, the feedback circuit generates a  $I_{trim}$  current compensating the unbalancing on the bias current source.

## VI. EXPERIMENTAL RESULTS

Fig. 11 shows a micrograph of the implemented ASIC. All circuit blocks have been fully experimentally characterized in

terms of both functionality and performance.

Fig. 12 shows the graph of the LNA differential output signal (a) and its spectrum (b). In the upper image (a), the 3-levels ( $f_{RF}=500f_0$ ) signal generated by the CS is plotted. The slow level transitions are the consequence of the limited signal bandwidth available on test PIN. PIN which, due to the parasitic capacitances and ESD protection resistances, form a low pass filter with a cutoff frequency of approximately 1MHz. In the frequency spectrum the fundamental frequency and its harmonics are easily distinguishable.

Fig. 13 shows the signal measured after the analog demodulation stage, and before the PGA amplification stage. For this measurement the DAC has been configured with a frequency of  $f_R=499f_0$ . The spectral component (b) which can be identified at  $499f_0$  is the result of the product between the DC component found on the LNA signal and the DAC demodulation signal. At higher frequencies, some harmonics of the signal are visible. In particular, it has to be noted that, after the demodulation process, the harmonics around the signal at  $f_0$  are minimal.

Fig. 14 refers to the signal measured after the PGA (PGA set at the nominal gain of 32dB). In this plot the effect of the anti-aliasing filter can be appreciated, which has greatly reduced the amplitude of the signal components located beyond the Nyquist frequency of the  $\Sigma\Delta$ -Modulator.

Fig. 15 shows the LNA measured equivalent input noise power spectral density, which is  $en=2.57nV/\sqrt{Hz}$  at 10kHz in the worst case, close to the flicker noise corner frequency. It decreases to  $en=1.8nV/\sqrt{Hz}$  at 1MHz and  $en=1.9nV/\sqrt{Hz}$  at 10MHz.

In a first system validation experiment, the device has been employed to measure a reference RC network and the results have been compared with values obtained with a Keysight E4980A Precision LCR Meter (Fig. 16). The upper plot shows both the measured impedance and the expected value. The lower plot shows the corresponding phase behavior. The measured relative error between the ASIC and the LCR meter is lower than 0.8%. Measurements have been performed by stimulating the reference RC network with an excitation current of  $25\mu A$  and by setting the phase detector bandwidth to 100Hz, which gives an effective impedance resolution of  $1m\Omega$  (note that with an excitation current of  $150\mu A$ , it should be possible to reach the theoretical limit of  $0.17m\Omega$ ).

Fig. 17 shows an example of ECG measurement, which has been carried out by setting  $r_R(t)=1$ ,  $r_{F,Q}(t)=1$  and by using two measuring electrodes connected to the arms of a volunteer and one reference electrode connected to ground.

## VII. CONCLUSIONS

We designed, implemented, and measured a new monolithic microsystem capable of (a) performing bio-impedance analysis, (b) record signals which can be used for electro impedance tomography, and (c) capture ECG traces. The device has been implemented in a commercial  $0.35\mu m$  CMOS technology. Table 1 summarizes the measured performance of the proposed ASIC and compares it with the most relevant integrated circuits

Specifications	H. Ko, et al. Ref [21]	S. Rodriguez, et al. Ref[22]	AD5933 Network Analyzer	This work
Measurements	BIA	BIA	Impedance	BIA, EIT, ECG
Impedance Range	0 $\Omega$ ... 800 $\Omega$	50 $\Omega$ ... 2k $\Omega$	1k $\Omega$ ... 10M $\Omega$	1 $\Omega$ ... 1k $\Omega$
Impedance Resolution	8.6 m $\Omega$	1 $\Omega$	244m $\Omega$	1 m $\Omega$
Voltage Resolution	N.A.	N.A.	N.A.	2.5 nV/ $\sqrt{Hz}$
Frequency Range	250Hz...1.24MHz	2kHz...2MHz	1Hz...100kHz	10kHz ... 10MHz
Frequency Bandwidth	0.5Hz...100Hz	50Hz	500Hz	100 Hz (digitally configurable)
Relative error	0.26%	1%	0.5%	0.8%
Power Consumption	52 $\mu W$	298 $\mu W$	125mW	100 mW
Power Supply	1.2V	1.8V	5.0V	3.3V
Silicon Area	13.8 mm <sup>2</sup>	1.44 mm <sup>2</sup>	N.A.	19.38 mm <sup>2</sup>
Technology	0.13 $\mu m$ CMOS	150 nm CMOS	N.A.	0.35 $\mu m$ CMOS
ADC	12 Bits	Off-Chip	12 Bits	20 Bits
Signal Generation	Off-Chip	Off-Chip	On-Chip	On-Chip
I/Q calculation (DSP)	Off-Chip	Off-Chip	On-Chip	On-Chip

Table 1: Comparison table [23]

for impedance measurements [21, 22, 23], demonstrating that no other monolithic solution in literature allows performing BIA, EIT and ECG measurements by using the same circuit.

## REFERENCES

- [1] D. Allegri, D. Vaca, D. Ferreira, M. Rogantini and D. Barretino, "Real-time monitoring of the hydration level by multi-frequency bioimpedance spectroscopy," 2017 IEEE International Instrumentation and Measurement Technology Conference (I2MTC), Turin, 2017, pp. 1-6.
- [2] S. Kun, B. Ristic, R. A. Peura and R. M. Dunn, "Algorithm for tissue ischemia estimation based on electrical impedance spectroscopy," in IEEE Transactions on Biomedical Engineering, vol. 50, no. 12, pp. 1352-1359, Dec. 2003.
- [3] J. R. Matthie, "Bioimpedance measurements of human body composition: critical analysis and outlook," Expert Review of Medical Devices, vol. 5, pp. 239-261, Mar. 2008.
- [4] M. C. Mlyńczak, W. Niewiadomski, M. Żyliński and G. P. Cybulski, "Ambulatory impedance pneumography device for quantitative monitoring of volumetric parameters in respiratory and cardiac applications," Computing in Cardiology 2014, Cambridge, MA, 2014, pp. 965-968.
- [5] C. E. F. Amaral and B. Wolf, "Effects of glucose in blood and skin impedance spectroscopy," AFRICON 2007, Windhoek, 2007, pp. 1-7.
- [6] M. C. Cho, J. Y. Kim and S. Cho, "A bio-impedance measurement system for portable monitoring of heart rate and pulse wave velocity using small body area," 2009 IEEE International Symposium on Circuits and Systems, Taipei, 2009, pp. 3106-3109.
- [7] S. Hong, J. Lee and H. J. Yoo, "Wearable lung-health monitoring system with electrical impedance tomography," 2015 37th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC), Milan, 2015, pp. 1707-1710.
- [8] K. Kalantar-Zadeh, D. L. Regidor, C. P. Kovesdy, D. Van Wyck, S. Bunnapradist, T. B. Horwich, and G. C. Fonarow, "Fluid retention is associated with cardiovascular mortality in patients undergoing long-term hemodialysis," Circulation, vol. 119, no. 5, pp. 671-679, 2009.
- [9] J. G. Webster, Medical Instrumentation: Application and Design, 4th ed. Hoboken, NJ: Wiley, 2009
- [10] M. Birkemose *et al.*, "Electrode placement in bioimpedance spectroscopy," 2013 35th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC), Osaka, 2013, pp. 3028-3031.
- [11] Z.-Y. Peng, L. a. H. Critchley, and B. S. P. Fok, "An investigation to show the effect of lung fluid on impedance cardiac output in the anaesthetized dog," British Journal of Anaesthesia, vol. 95, no. 4, pp. 458-464, 2005.
- [12] S. Rodriguez, S. Ollmar, M. Waqar and A. Rusu, "A Batteryless Sensor ASIC for Implantable Bio-Impedance Applications," in IEEE Transactions on Biomedical Circuits and Systems, vol. 10, no. 3, pp. 533-544, June 2016.
- [13] P. Kassanos, H. M. D. Ip and G. Z. Yang, "A tetrapolar bio-impedance sensing system for gastrointestinal tract monitoring," 2015 IEEE 12th International Conference on Wearable and Implantable Body Sensor Networks (BSN), Cambridge, MA, 2015, pp. 1-6.
- [14] J. Xu, P. Harpe, J. Pettine, C. Van Hoof and R. F. Yazicioglu, "A low power configurable bio-impedance spectroscopy (BIS) ASIC with

simultaneous ECG and respiration recording functionality," *European Solid-State Circuits Conference (ESSCIRC), ESSCIRC 2015 - 41st*, Graz, 2015, pp. 396-399.

- [15] T. Kriz and Z. Roubal, "Practical application of electrical impedance tomography and electrical resistive tomography," *2016 Progress in Electromagnetic Research Symposium (PIERS)*, Shanghai, China, 2016, pp. 1499-1503.
- [16] Y. Wu, P. Langlois, R. Bayford and A. Demosthenous, "Design of a CMOS active electrode IC for wearable electrical impedance tomography systems," *2016 IEEE International Symposium on Circuits and Systems (ISCAS)*, Montreal, QC, 2016, pp. 846-849.
- [17] D. Bianchi, et al., "CMOS impedance analyzer for nanosamples investigation operating up to 150MHz with sub-aF resolution", *IEEE J. Solid-State Circ.*, vol. 49, no. 12, pp. 2748-2757, 2014.
- [18] A. Manickam, A. Chevalier, M. McDermott, A. D. Ellington, and A. Hassibi, "A CMOS electrochemical impedance spectroscopy biosensor array for label-free biomolecular detection," in *2010 IEEE International Solid-State Circuits Conference - (ISSCC)*, 2010, pp. 130-131.
- [19] A. Rottigni, M. Carminati, G. Ferrari and M. Sampietro, "Handheld bio-impedance measurement system based on an instrument-on-chip," *2011 7th Conference on Ph.D. Research in Microelectronics and Electronics*, Trento, 2011, pp. 49-52.
- [20] Franco Maloberti, "Data Converters", Springer (US), 2007.
- [21] H. Ko, et al., "Ultralow-Power Bioimpedance IC with Intermediate Frequency Shifting Chopper", *IEEE Trans. Circuits Syst. II, Exp. Briefs*, vol. 63, no. 3, pp. 259-263, 2016.
- [22] S. Rodriguez, et al., "A Batteryless Sensor ASIC for Implantable Bio-Impedance Applications," *IEEE Trans. Biomed. Circuits Syst.*, vol. 10, no. 3, pp. 533-544, 2016.
- [23] D. Allegri, A. Donida, P. Malcovati and D. Barrettino, "CMOS-Based Multifrequency Impedance Analyzer for Biomedical Applications," *2018 IEEE International Symposium on Circuits and Systems (ISCAS)*, Florence, Italy, 2018, pp. 1-5.

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