Mixed-level simulation tool for design optimization of electrical impedance spectroscopy systems

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Abstract: The design of electrical impedance spectroscopy systems is driven by target applications. Moreover, system functions are inter-dependent. Thus, optimizing the design of each block without input from the others is impossible. Furthermore, simulating the whole system at transistor level is time consuming. This chapter presents a mixed-level simulation tool for the efficient development of bioimpedance spectroscopy measurement systems. We have developed *Verilog-AMS* models combined with transistor-level descriptions of several analog blocks. This allows us to run highly efficient system-level simulations for a whole circuit. We apply this tool to the design of an integrated circuit suitable for *in vivo* monitoring of bluefin tuna physiological parameters. In fact, the variation of biological processes offers significant insights into a host of key parameters such as growth, survival and reproduction. The obtained results show that the approach described in this chapter can reduce simulation time by 80 % while consistently reaching high simulation performances.

Keywords: bioimpedance spectroscopy, IC design, bluefin tuna, physiological parameter monitoring

1 Introduction

Electrical Impedance Spectroscopy (EIS) can be used to characterize matters governed by electrochemical processes. From material science to biosensing [1–3], the EIS range of applications is wide. In some of these applications, the system design is ruled by strong constraints. The simple choice between various potential system architectures is challenging. Moreover, system functions are inter-dependent. As a result, optimiz-

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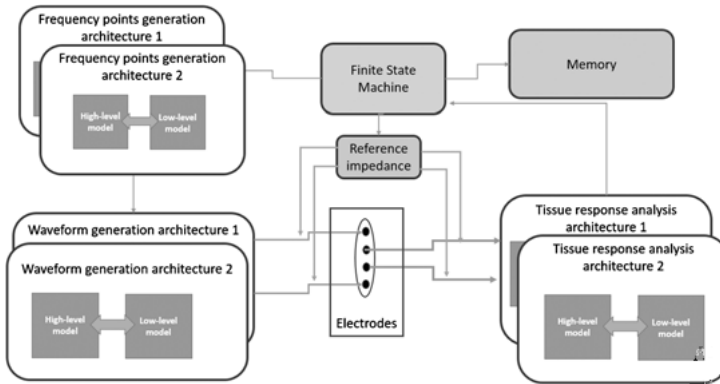**Sylvain Bonhommeau,** IFREMER, Rue Jean Bertho, 97822 Le Port, France

Fig. 1: The main blocks of the integrated circuit architecture.

ing the design of each block without input from the others is impossible. To address this issue, an efficient design strategy is needed.

The overall architecture consists of the main blocks presented in Fig. 1. The three principal system functions are the frequency components generation, the stimulation waveform construction and the system-under-test response analysis. The hardware implementation of each of these blocks differs depending on the application.

In general, three approaches are used for the design of integrated systems, i. e., the bottom-up, the top-down and the mixed-level approaches. The bottom-up approach consists in implementing each of the system blocks at transistor level, proceeding to the block verification, and then assembling all the blocks to build the system. This approach helps to achieve high performances at block level but without any system-level consideration. Thus, it is impossible to ensure optimal system-level performances. Moreover, a global simulation at transistor level is generally impractical because it is time consuming. Conversely, the top-down approach addresses architectural level first by describing each block by its functional model. This approach can optimize system-level specifications but without considering each block constraint. The high-level block requirements retrieved from the system-level simulation might be unsuitable at low level. The mixed-level approach combines high-level and low-level models for each block. The idea is to co-simulate some of the blocks at the transistor level with the others at high level. With this approach, we can address the inter-dependability of the system blocks to propose various optimized architectures, while customizing each block for better performances. Furthermore, by combining fast-simulated high-level models with accurate low-level models, we can drastically reduce the global simulation time. In this context, we develop a mixed-level simulation tool dedicated to help designers find the most suitable architecture for certain given system constraints.

Since the tool is intended to help design integrated circuit systems, the Cadence platform was chosen. We have developed a library of high-level and low-level mod-

els of the mainly used blocks for impedance spectroscopy from the literature [4–6]. For high-level models we use *Verilog-AMS*, which is a derivative of the *Verilog* hardware description language that enables designers to create analog and mixed-signal modules containing high-level behavioral descriptions of the system blocks. For the low-level model description, we use transistor-level models simulated by the *Cadence Virtuoso* suite.

We apply this tool to the design of an integrated circuit suitable for *in vivo* monitoring of bluefin tuna physiological parameters.

2 Bluefin tuna physiological parameter monitoring

Although marine ecosystem services are critical for human well-being, the necessary scientific information to conserve and manage them efficiently is currently lacking. A way to improve our understanding of marine species is to use implantable sensors for monitoring physiological parameters related to key biological processes such as feeding and spawning. Indeed, such processes offer significant insights into a host of key population parameters such as growth, survival and reproduction. For instance, a key physiological parameter is muscle fat content. The variation of this parameter in space and time is indeed related to the previously mentioned behaviors as fish feed to accumulate reserves, as the fat is used during reproduction.

2.1 System specifications related to the targeted application

The choice of the different elements constituting the architecture of the integrated circuit is related to the application. In our case, long monitoring periods in the wild are considered, typically 12 months. Therefore, the architecture should be characterized by low power consumption. As the device has to be implantable, solutions offering a low silicon surface area have to be preferred for the fish well-being.

Previous measurements conducted on bluefin tuna showed that the expected impedance values are of the order of $100\,\Omega$ at $50\,\mathrm{KHz}$ [7]. At higher frequencies, this value is expected to decrease. Using a handheld measurement device based on the AD5933 chip and a four-electrode configuration, bioimpedance spectroscopy ranging from $300\,\mathrm{Hz}$ to $100\,\mathrm{KHz}$ was performed on the bluefin tuna's back at the second dorsal fin level. The obtained results (Fig. 2) confirm the expected impedance range: from sub-Ohm levels at higher frequencies to hundreds of Ohms at lower frequencies.

The non-linear behavior of tissue could be linked to biological processes [8], thus allowing the collection of new data with substantial scientific potential. Therefore, the designed system must be able to measure non-linearity of the tissue.
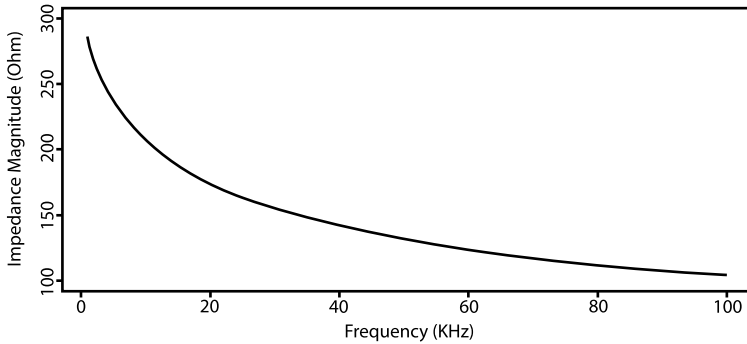
Fig. 2: Bluefin tuna impedance magnitude.

For a rigorous characterization of the biological tissue composition, the complex impedance needs to be analyzed over a large range of frequencies. Each type of tissue molecule has a different response to given frequencies. Three main frequency regions describing physiological processes have been identified [9]: the α dispersion (Hz–kHz), the β dispersion (kHz–MHz) and the γ dispersion (MHz–GHz). Since α and β dispersions are associated with the most relevant biological aspects [4] for our application and for integrated circuit (IC) design considerations, the exploration was limited to these two frequency regions: 500 Hz–10 MHz.

2.2 IC architecture definition

For the general principles of the measurement, current stimulation and voltage measurement were chosen, mainly for safety reasons since in that case the current passing through the biological tissue can be controlled. Also, a four-electrode configuration is used to get rid of the impedance at the interfaces.

To generate the α and β dispersions we use a phase-locked loop as a frequency multiplier. The low-frequency signal coming from a crystal oscillator is multiplied to get the higher frequency. On the negative feedback path, successive divisions are then performed to get the frequency points.

To analyze non-linearity of the tissue, sine waves have been chosen for the stimulus. In order to measure harmonics of the system (tissue), the generated sine wave should have the lowest total harmonic distortion THD possible, so that harmonic intermodulation does not affect the measured result. To cancel harmonics of the sine wave, scaled and delayed versions of the signal at the output of the frequency sweep generation block are added (Fig. 3). The scale coefficients and the phase shifts are computed so that the constructed signal matches the expression of a pure sine wave.

The result is then fed to a voltage-controlled current source (VCCS) that generates the stimulation current. The VCCS is designed in such a way to have high stability current in the targeted frequency range. Synchronous detection has been chosen as the
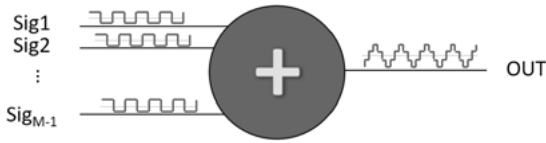
Fig. 3: Sine wave generation technique.

response analysis technique for its simplicity and its ability to single out the wanted frequency response even for the smallest AC signals obscured with noise. Since the frequency components of interest are translated into the baseband by the synchronous detection, the constraints on the analog-to-digital converter (ADC) are then relieved, and simple low-rate ADCs could be used to feed the memory with bit words representing the real and the imaginary parts of the impedance. A finite-state machine is used to control the different signals of the architecture, ensuring the sequentiality of the frequency sweep. Since the bluefin tuna is expected to migrate in several regions, the environmental parameters of the measurement (temperature, pressure, etc.) may vary drastically. A reference impedance is added to the overall architecture (Fig. 4) to compensate for the system drifts.
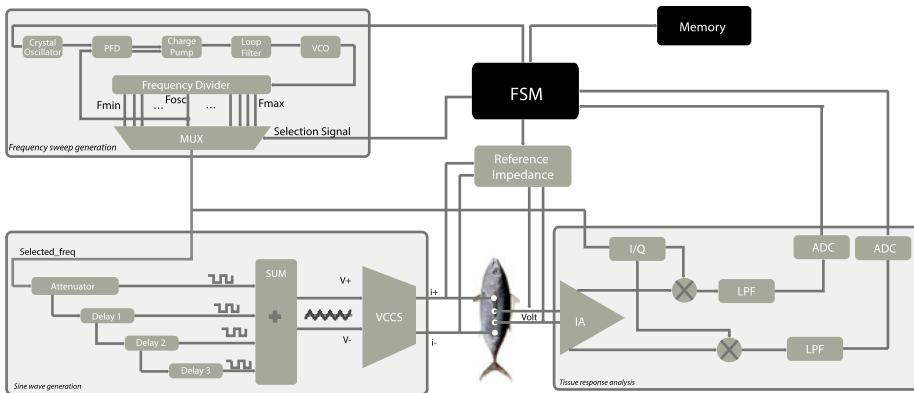

Fig. 4: The system-on-chip architecture.

2.3 Mixed-level simulation of the architecture

The VCCS is a critical component in bioimpedance spectroscopy architectures. It should deliver a high-accuracy current to the tissue under test over the frequency range of use. Unfortunately, at higher frequencies, the stray capacitance shunts the output impedance of the current driver, which causes its performance to decrease. To illustrate the mixed-level simulation approach on the proposed architecture, we chose to implement the VCCS at the transistor level to target its performances and the other blocks at high level using Verilog-AMS.

2.3.1 Voltage controlled current source design

The current driver is implemented using a symmetrical operational transconductance amplifier (OTA) (Fig. 5). It is composed of a differential pair (M1, M2) driving two loads (M3, M4) connected as diodes, three current mirrors (M3–M5, M4–M6, M7–M8) and a current source M9 [10]. The first stage (M10, M11, M12, M13) is designed to bias the OTA with a current I_b.
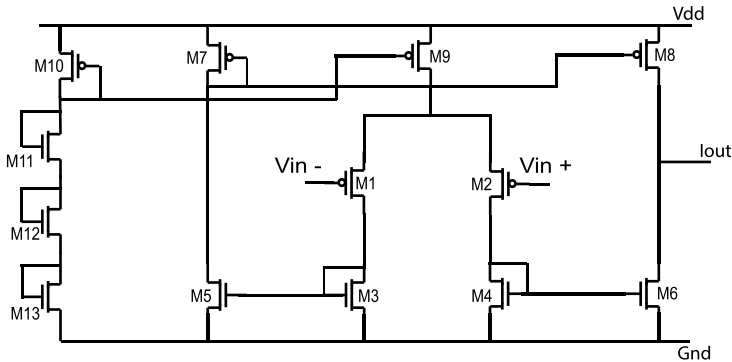

Fig. 5: The current driver architecture.

The OTA is designed with a 180-nm CMOS process, for a bias current I_b of 50 µA, a dynamic input range of ±0.3 V (Fig. 6) around a common mode voltage of 0.6 V, a transconductance of 200 µS and a bandwidth of 10 MHz.
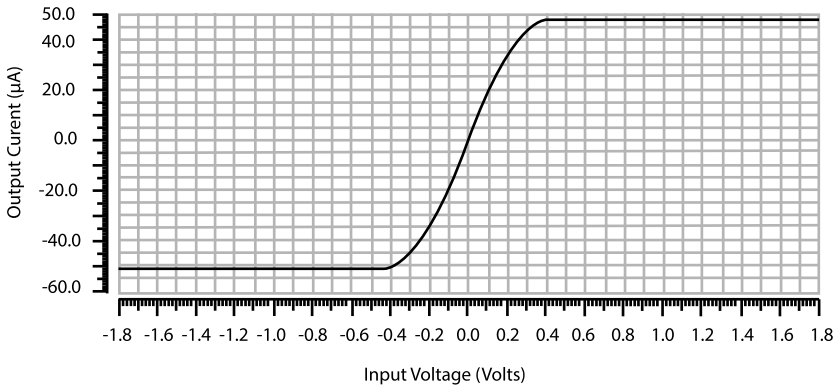

Fig. 6: The OTA differential DC input–output transfer curve.

The achieved output impedance of the current driver is 270 kΩ at frequencies below 5 MHz; it drops to 259 kΩ at 10 MHz (Fig. 7). The output impedance value could be increased by cascoding the output stage, for example, at the price of decreasing the output swing of the current driver. Although these values of output impedance are
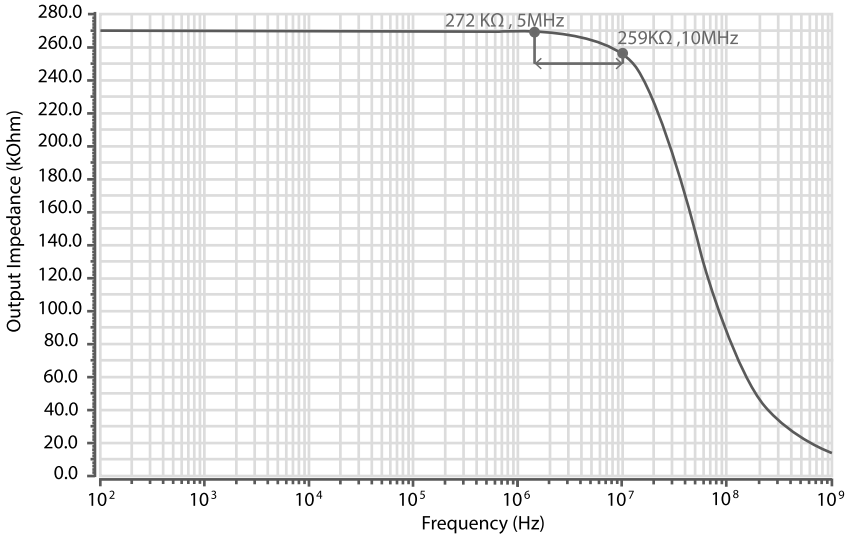
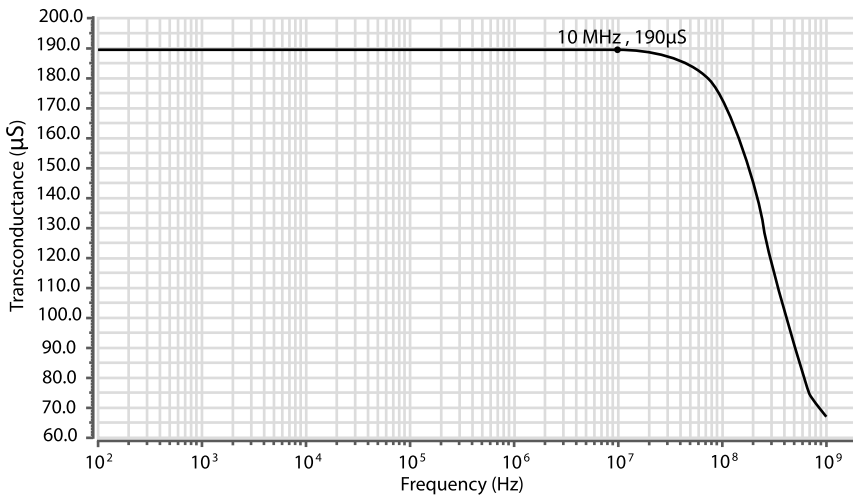**Fig. 7:** The current driver output impedance vs frequency, with a load of 1 kΩ/3 pF.

Fig. 8: The current driver transconductance vs frequency, with a load of 1 kΩ/3 pF.

not high, they are suitable for our application since the expected impedance of the bluefin tuna does not exceed 100 Ohms (Fig. 2). The achieved transconductance value is 190 µS and remains stable over the desired bandwidth (Fig. 8).

Monte Carlo simulation was performed on the transconductance of the OTA for 1000 runs with both process and mismatch; the results are shown in Fig. 9. The transconductance has a mean value of 190.64 µS and a standard deviation of 3.68 µS. The value of the standard deviation could be decreased by increasing the dimensions
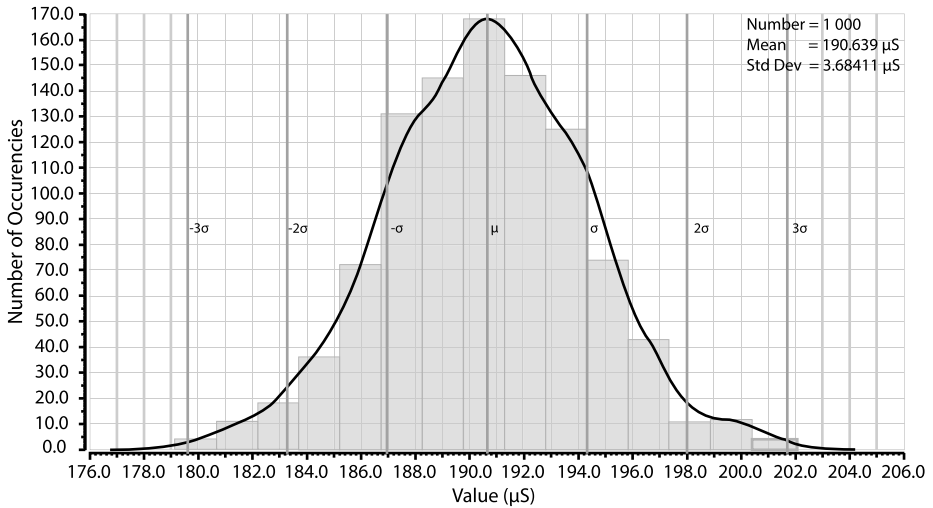
Fig. 9: Monte Carlo simulation of the transconductance of the current source.

of the current mirrors of the output stage, at the price of decreasing the bandwidth due to larger parasitic capacitances. Since 97 % of the runs are within 3.8 % of the deviation from the mean value, the design is considered as robust under process variation and device mismatch, and the transistor dimensions are kept unchanged.

2.3.2 Simulation performances

To illustrate the efficiency of the mixed-level approach, two transient simulations of the overall architecture described below were launched. The first simulation contained the current source designed at the transistor level and the other blocks at high level. The second simulation contained all the blocks of the architecture at high level; a realistic Verilog-AMS model of the current source was used.

The Verilog-AMS model takes into account the values of the transconductance and the output resistance extracted from the simulation results presented in the previous part. The model could also be used to evaluate at high level the impact of process variation and device mismatch by using the results of the Monte Carlo simulation. In fact, the impedance error introduced by process and mismatch variation is ±1.9 % within one standard deviation from the mean value.

Simulations were performed on a machine with 25 cores (2 GHz) and 263 Gb of memory. The entire high-level simulation with the Verilog-AMS model of the current source took 15 minutes. On the other hand, the simulation with the current source at transistor level and the other blocks at high level took 75 minutes. The obtained results show that the mixed-level approach described in this chapter can reduce the simulation time by 80 % while consistently reaching high performances for each block.

3 Conclusion

This chapter presents a mixed-level simulation tool to support the design of bio-impedance spectroscopy ICs. The mixed-level simulation addresses the inter-depend-ability of the different blocks of the architecture, while enabling the designers to test different architecture solutions. Furthermore, the tool permits to go further in the design customization, allowing designers to enhance system performances with the significant advantage of having reduced simulation times. Moreover, this approach could also be useful to estimate the influence of process variation and device mis-match on the overall architecture. The influence of the measurement environment could also be estimated. In fact, Verilog-AMS blocks modeling sources of inaccuracies (such as the effect of the temperature and flicker noise) could simply be added to the model, permitting the evaluation of the impact and if needed refining the architecture for robustness.

Bibliography

[1] P. Aberg, N. Ingrid, J. Hansson, P. Geladi, U. Holmgren, and S. Ollmar, "Skin cancer identification using multifrequency electrical impedance", IEEE Transactions on Bio-Medical Engineering, 2004.
[2] T. Dai and A. Adler, "In vivo blood characterization from bioimpedance spectroscopy of blood pooling", IEEE Transactions on Instrumentation and Measurement, 2009.
[3] S. Grimnes and O. G. Martinsen, "Bioimpedance and Bioelectricity Basics".
[4] H. M. Dastjerdi, R. Soltanzadeh, and H. Rabbani, "Designing and implementing bioimpedance spectroscopy device by measuring impedance in a mouse tissue", Journal of Medical Signals and Sensors, 2013.
[5] Y. Long, B. Joonsung, L. Seulki, and Y. Hoi-Jun, "A 3.9 mW 25-electrode reconfigured sensor for wearable cardiac monitoring system", IEEE Journal of Solid-State Circuits, 2011.
[6] S. Rodriguez, S. Ollmar, M. Waqar, and A. Rusu, "A batteryless sensor ASIC for implantable bio-impedance applications", IEEE Transactions on Biomedical Circuits and Systems, 2016.
[7] J. Willis and A. J. Hobday, "Application of bioelectrical impedance analysis as a method for estimating composition and metabolic condition of southern bluefin tuna (Thunnus maccoyii) during conventional tagging", 2008.
[8] T. Yamamoto and Y. Yamamoto, "Non-linear electrical properties of skin in the low frequency range, Medical and Biological Engineering and Computing", 1981.
[9] H. P. Schwan, "Electrical properties of tissue and cell suspensions".
[10] M. C. Sansen, "Analog Design Essentials", The Springer International Series in Engineering and Computer Science, 2016.