# Multifrequency simultaneous bioimpedance measurements using multitone burst signals for dynamic tissue characterization.

# **B.Sanchez and R.Bragos**

Center for Research in Biomedical Eng. (CREB), Dept. of Electronic Eng., UPC, Barcelona, Spain

E-mail: bsanchez@eel.upc.edu

Abstract. In this paper we present the keypoints to perform multifrequency simultaneous bioimpedance measurements using multitone signals. Concerning the frequency distribution, tones are spread over 1kHz to 1MHz range using a custom frequency distribution which we called Bilateral Quasi Logarithmic (BQL). BQL concentrates a higher number of tones around the impedance relaxation and contains a frequency plan algorithm. It minimizes the intermodulation effects due to non-linearities behaviours of the DUT and electrodes by slightly shifting the original tones in order to guarantee a guard bandwith. Regarding the multitone phase distribution, a Genetic Algorithm (GA) has been developed to minimize multitone Crest Factor (CF). This allow us to maximize the resultant Signal to Noise Ratio (SNR) of the acquisition system. This paper also presents the relation between parameters such as sampling frequency and ADC bits with the SNR and the effect in the overall amplitude and phase error when using multitone signals as excitation waveforms. Finally, we present characterization results from a measurement system based on a modular PXI architecture.

#### 1. Introduction

Multitone signals are useful for fast impedance spectroscopy characterization of biological systems whose electrical properties change along within time. Using this technique, is possible to obtain the impedance spectrum free of the errors induced by asynchronous undersampling of the mechanical modulation of the biological system under test. Essentially, a multitone is composed by the sum of M tones, each one with its own amplitude and phase (eq.1).

$$x[n] = \sum_{m=0}^{M-1} a_m \cos\left(2\pi \frac{f_m}{f_s} n + \varphi_m\right), \quad n = 0, ..., N-1$$
 (1)

# 1.1. Measures of Signal Quality: Crest Factor

When comparing signals it is necessary to have a quality measure in the form of a performance index. A classical index is the Crest Factor (CF), which gives an idea of signal's compactness but there are other options like *Performance Index for Perturbation Signals* (PIPS) [1] or *Time Factor* (TF) [2]. Thus, CF of a function x(t) is defined as the ratio of its peak value (also known

as Chebyshev norm) and its Root Mean Square value (RMS) [3] is given by:

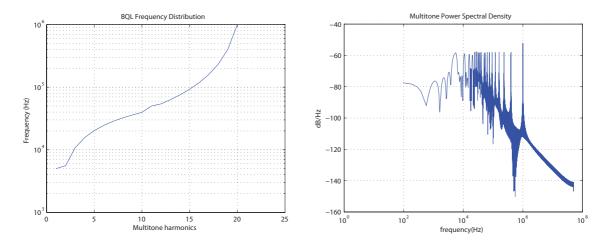
$$CF(x) = \frac{l_{\infty}(x)}{l_{2}(x)} = \frac{\max_{n \in [0, N-1]} |x[n]|}{\sqrt{\frac{1}{N} \sum_{n=0}^{N-1} |x[n]|}}$$
(2)

The classical ways to minimize CF use heuristic approaches [4], [5]. Other approaches consisted on analytical methods. They use different iterative methods [6], [7] or employ natural selection and evolutionary-inspired operators like Genetic Algorithms (GA) [8], [9].

## 1.2. Frequency distribution

Typically, multitone frequencies are either distributed logarithmically or equally spaced [10]. However, both have important disadvantages when measuring impedance. In one hand, equidistant frequency distribution needs a high number of tones to cover a wide frequency range ands avoid losing spectral resolution. Moreover, intermodulation products will appear at the same measurement frequencies if the global system presents non-linearities, provoking errors in the amplitude and phase determination. In the case of logarithmic distribution there is a big number of tones at low and high frequencies content where the relaxation do not include much information.

One of the main issues is how to arrange multitone frequencies to minimize intormodulation products effects. One option is generate each tone as a result of a fundamental frequency multiplied by a sequence values. This solution is based on special sets of multipliers in order to accomplish as many as possible disjunct distortion signal frequencies and to test signal frequencies is presented in [11]. In our case, BQL algorithm algorithm combines exponential and logarithmic functions to concentrate more frequency components close to the relaxation slope band. Moreover, it spreads the remaining tones at low and high frequencies (fig.1) [9] and also redistributes original tones taking into account where the intermodulation frequencies would appear.



**Figure 1.** Example of BQL fundamental harmonics to characterize impedance relaxation around 50kHz.

## 2. Precision of Transfer Function Measurement using Multitone Signals

In single frequency impedance measurements is well known the relationship between the SNR with parameters such as ADC bits or sampling frequency. In the case of multitone measurements

there are more hidden parameters that have to be taken into account. In fact, the SNR of an ideal b-bit AD converter measured over the Nyquist bandwidth  $(DC - F_s/2)$  when using a multitone input signal as excitation is decreased due to the Crest Factor and the number of tones M according to eq.3:

$$SNR_{multitone} = 6.02b + 1.76 - 20log_{10} \left(\frac{CF}{\sqrt{2}}\right) - 10log_{10} \left(M\right) \quad [dB]$$
 (3)

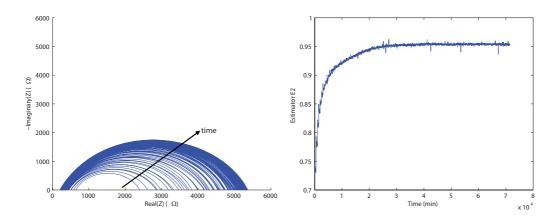
Finally, has been shown in [12] the relationship between SNR when using multitone and the magnitude and phase measurement accuracy:

$$\epsilon_l = 20log_{10} \left( 1 + 10^{\frac{-SNR_{multitone}}{20}} \right) [dB] \qquad \epsilon_{\theta} = \frac{180}{\pi} 10^{\frac{-SNR_{multitone}}{20}} [\circ]$$
 (4)

where  $\epsilon_l$  and  $\epsilon_{\theta}$  are magnitude and phase accuracy. Eq.4 allows to find the minimum system that satisfies quality measurement requirements in terms of SNR or accuracy using multitone signals only with the a priori information of Crest Factor, number of bits and number of tones.

#### 3. System characterization

The measurement system has been build around a PXI architecture from National Instruments. The system includes an embedded controller PXIe-8130, 2 channel digitizer card PXIe-5122 (100Ms/s, 64MB/channel, 14bits) and an arbitrary waveform card PXI-5422 (200Ms/s, 32MB, 16 bits). The system has been characterized measuring resistors and RC networks with a custom 4-wire wideband front-end. The set up has been carried out performing 100 measurements (2ms burst length) of a set of resistors (1% tolerance). Multitone signal was designed with 21 tones spread from 5kHz to 1.313MHz, 1mA of amplitude current and crest factor 2.7. Theoretical SNR obtained with this system parameters is 67.2dB which corresponds to a measurement error of 0.0038dB and 0.023° in magnitude and phase respectively. Magnitude and phase accuracy has been validated with the standard desviation obtained from the measurements. Also a preliminary dynamic scenario have been characterized based on yeast cell suspension settlement (fig.2) over interdigitated 4-electrode located at the bottom of a small bioreactor [13]. Multitone parameters used were the same as described before. System performed 100 measurements (10ms) every 5 minutes up to 12 hours, with a a total amount of 14400 measurements.



**Figure 2.** Time evolution of Cole-Cole arcs and cell growth estimator's described in [14].

At this moment, our work is focused on characterizing human stem cells for tissue engineered applications. The goal is to characterize stem cells differentiation into cardyomiogenic cells when applying electrical and mechanical stimuli in regenerative medicine.

#### 4. Conclusions

One of the multitone signal strengths is that it is very rapid for those systems that have a short settling time and are not plagued by significant noise. In addition, SNR can be increased by aplying more energy in the desired spectral components in applications where the total amount of energy applied is not restricted. In applications where the energy is limited, a single multitone shot characterization obtains greater SNR than using Pseudo-Random Binary Sequences (PRBS). This is due the fact that the energy is focused on the measurement frequencies and it is not spread in the whole frequency band. One of the weaknesses of multitone signals is the crest factor. However, it is possible to minimize the impact of the crest factor over the measurement quality using common algorithms proposed in the literature.

### Acknowledgments

This work has been suported by grant from Spanish Ministry MICINN SAF2008-05144-C02-02.

#### 5. References

- [1] K. R. Godfrey, H. A. Barker, A. J. Tucker 1999 Comparison of perturbation signals for linear system identification in the frequency domain vol. 146 (IEEE Proc.-Control Theory Appl.) pp. 535–548.
- [2] J. Schouckens, P. Guillaume, R.Pintelon 1991 Design of multisine excitations vol. 40 (International Conference on Control) pp. 638–643.
- [3] P. Guillaume, J. Schoukens, R.Pintelon and I. Kollar 1991 Crest-factor minimization using nonlinear Chebyshev approximation methods vol. 40 (IEEE Transactions on Instruments and Measurement) pp. 982–989.
- [4] E. Beller and D. J. Newman 1965 An 11 Extremal Problem for Polynomials vol. 16 no. 3 (Proceedings of the American Mathematical Society) pp. 1287–1290.
- [5] M. Schroeder 1970 Synthesis of low-peak-factor signals and binary sequences with low autocorrelation vol. 16 no. 1 (IEEE Transactions of Information Theory) pp. 85–89.
- [6] A. Van den Bos 1987 A new method for synthesis of low-peak-factor signals vol. 35 no.1 (IEEE Transactionss on Acoustics, Speech and Signal Processing) pp. 120–122.
- [7] E. Van der Ouderaa, J. Schoukens and J. Renneboog 1988 Peak factor minimization using a time-frequency domain swapping algorithm vol. 37 no.1 (IEEE Transactions on Instruments and Measurement) pp. 145–147.
- [8] A. Horner and J. Beauchamp 1996 A genetic algorithm-based method for synthesis of low peak amplitude signals vol. 99 (Journal of the Acoustical Society of America) pp. 433–443.
- [9] B. Sanchez and R. Bragos Fast Electrical Impedance Spectroscopy for Moving Tissue Characterization Using Bilateral QuasiLogarithmic Multisine Bursts Signals vol. 22 no. 9 (4th European Conference of the International Federation for Medical and Biological Engineering) pp. 1084–1087.
- [10] A. Romsauerova, A. McEwan and D.S. Holder 2006 Identification of a suitable current waveform for acute stroke imaging vol.27 (Physiol. Meas.) pp. 211–219
- [11] C. Evans and D. Rees 2000 Nonlinear distortions and multisine signals. I. Measuring the. best linear approximation vol. 49 no.3 (IEEE Transactions on Instrumentation and Measurement) pp. 602–609
- [12] H. Kitayoshi, S. Sumida, K. Shirakawa and S. Takeshita 1985 DSP synthesized signal source for analog testing stimulus and new test method vol. 49 no.3 (IEEE Transactions on Instrumentation and Measurement) pp. 602–609.
- [13] R. Bragos, E. Sarro, A. Fontova, A. Soley, J. Cairo, A. Bayes-Genis, and J. Rosell 2006 Four versus twoelectrode measurement strategies for cell growing and differentiation monitoring using electrical impedance spectroscopy (Proc. 28th Annual International Conference of the IEEE Engineering in Medicine and Biology Society EMBS) pp. 2106-2109.
- [14] R. Bragos, X. Gamez, J. Cair, P. Riu, F. Godia 1999 Biomass monitoring using impedance spectroscopy vol.873 (Annals of the NewYork Academy of Sciences), pp 299–305.