

Symbolic dynamic and frequency analysis in foetal monitoring

Maria Romano

DIETI, University of Naples, "Federico II", Naples, Italy

Interuniversity Centre of Bioengineering of the
Human Neuromusculoskeletal System

Giovanni D'Addio

S. Maugeri Foundation, Rehabilitation Institute of Telese,
Telese Terme, Italy

Fabrizio Clemente

IsIB-CNR, Monterotondo S., Roma, Italy

Alfonso Maria Ponsiglione, Gianni Improta,
Mario Cesarelli

DIETI, University of Naples, "Federico II", Naples, Italy

Interuniversity Centre of Bioengineering of the
Human Neuromusculoskeletal System

Abstract— Foetal heart rate variability is widely considered an important parameter to assess foetal reactivity and wellbeing. Traditional approaches to analyze foetal heart rate and its variability, such as Time and Frequency Domain Analyses, have shown some limitations, due to their inability to highlight nonlinear dynamics potentially relevant. Hence, in the last decades, nonlinear analysis methods have gained a growing interest and the integration of parameters derived from these techniques and traditional ones could be a way to improve the assessment of foetal development and/or distress. In this work, we proposed a comparison between new index obtained with a nonlinear analysis (Symbolic Dynamic Analysis) and more traditional parameters computed by the power spectral density of the foetal heart variability signals (Frequency Domain Analysis). A dataset of 579 cardiocographic signals from healthy foetuses, recorded from the 24th to the 42th gestation week, was examined using both above-mentioned methods. The obtained results demonstrate that Symbolic Dynamics, as much as Frequency Domain Analysis, could be a useful tool in foetal development assessing.

Keywords— *symbolic dynamics, frequency domain analysis, foetal heart rate variability, foetal development.*

I. INTRODUCTION

Cardiotocography (CTG) is the most widely used indirect diagnostic technique in clinical practice to monitor foetal health during pregnancy [1]. It can be used from the 24th week of gestation to delivery and consists in the simultaneous recording of foetal heart rate (FHR) and uterine contractions (UC) [2]. While the negative predictive value of CTG is very good, it is known that foetuses compromised not always manifest CTG changes [3]. In addition, since CTG interpretation is often carried out by a visual inspection, the efficiency of this method depends on the expertise and training of the observer, but obviously it lacks of objectivity and reproducibility. For this reason, many researchers have attempted to make it more reliable, introducing the computerized analysis [4]. In general, physicians mainly evaluate the following parameters: FHR mean value (related to week's gestation), FHR variability (FHRV), accelerations, decelerations, foetal movements and uterine contractions [2, 5]. Among these, FHRV is probably the most important feature of the FHR recording, due to its relationship with the

autonomic nervous system (ANS) and its development. Changes in FHRV are also correlated with foetal development. Nevertheless, even though foetal growth is correlated to the foetal well-being and ANS development, not many literature works inspect this issue. Besides, the great majority of these studies are old [6, 7] or use foetal magnetocardiography to record foetal heart activity [8, 9].

The FHRV, as the heart rate variability (HRV) of an adult subject, can be studied using two different approaches, historically known as linear and nonlinear analyses [10]. The linear analysis of FHRV (in time and frequency domain) provides significant noninvasive parameters to investigate the cardiac autonomic modulation; however, this methodology has shown some limitations in describing nonlinear structure of the sympatho-vagal interactions [11]. Therefore, methods developed from nonlinear systems theory have been applied, in recent years, to biological systems analysis and, in particular, to the study of HRV.

We focus the attention on the Symbolic Dynamic Analysis (SDA), a nonlinear technique which allows a simple description of a system's dynamics by means of a limited amount of symbols [12] and appropriate classification schemes. It already gets important results in adult subjects [13] and has been recently employed to quantify FHR regularity in the course of gestation [14]. Despite these facts, there are too few applications of SDA to FHRV analysis and it can't be yet considered a completely useful and reliable method.

Recently, SDA has been employed by the authors to study relationship between FHRV and neonatal wellbeing [15, 16]. Encouraged from the preliminary results, in this work we aimed to analyse FHRV from CTG recordings in healthy foetuses by means of SDA and correlate the results with more classical parameters computed with Frequency Domain Analysis (FDA).

Furthermore, we focused our attention on relationship between computed parameters and weeks of gestation, in order to investigate correlation with foetal development.

II. METHODS

A. Data collection and CTG processing

CTG traces were recorded by healthy patients during the clinical practice, using commercially available cardiotocographs. Five hundred and seventy-nine antepartum recordings from the 24th to the 42th gestation week were considered for the study. The database was completed with other clinical information of patients and newborns. All patients gave their informed consent to participate in the research concerning foetal monitoring. CTG signals were processed by a software previously developed by the authors [17, 18] and recently updated in order to implement also the SDA.

B. Symbolic Dynamics Analysis

According to previous studies [15, 16, 17, 18], we applied SDA to the series of the differences between consecutive heart beat intervals (ΔRR). We calculated the interbeat intervals series (RR) using the known formula: $RR=60000/FHR$. From the RR time series, expressed in ms, we computed the ΔRR , to make the analysis independent of the mean heart rate. Then, an alphabet of five symbols was chosen to classify the full range of variability. In order to distinguish higher from moderate variations, the decision rule that associates each series sample with one alphabet symbol was the comparison between the sample value and two thresholds, named primary (PT) and secondary (ST) threshold [16]. The primary threshold (PT) was chosen to identify samples that are not due to the physiological variability of the cardiac rhythm but to the noise (mainly correlated to the resolution in FHR recording). ST was heuristically set to 3 ms, by considering the peak to peak amplitude of ΔRR series [20].

After the symbolization, a sliding window of length L was shifted along the codified series, with an overlap of L-1 points, transforming it in a sequence of patterns of L samples (called words). In this work, as in the previous one [16], the L value was chosen equal to 7 (considering a mean FHR of 140 bpm, this value corresponds to 3 s) in order to include in the word the burst peak of a sympathetic response. At this point, according to a method already introduced by the authors [15, 16, 20], the words were grouped in different word classes (WC) by the within-word symbol occurrence, using the criterion (called dominance criterion) described in Table 1. The criterion had the aim to highlight sympatho-vagal activations, considered associated to greater or less variability, and cases of absence of variability or random variations.

Finally, as carried out in a previous work of the authors [16], a new parameter, named Variability Index (V.I.), was estimated from the percentages of occurrence of the different WC (pH, pM, pO and pR), with the aim to put in evidence the amount of physiological variability of the signal at the expense of that null or random, at which we assign zero weight:

$$VI = \frac{p_H}{100} * 1 + \frac{p_M}{100} * 0.5 + \frac{p_O}{100} * 0 + \frac{p_R}{100} * 0 \quad (1)$$

TABLE I. "DOMINANCE CRITERION" TO GROUP THE CLASSES OF WORDS.

Description	Meaning	Code
At least 4 symbols "VP" or "VN"	high activation	H
At least 3 symbols "VP" and 1 symbol "P"		
At least 3 symbols "VN" and 1 symbol "N"		
At least 4 symbols "P" or "N"	moderate activation	M
At least 3 symbols "P" and 1 symbol "VP"		
At least 3 symbols "N" and 1 symbol "VN"		
At least 4 symbols "O"	absence of variability	O
All other cases	random	R

C. Frequency Domain Analysis

Because of the non-stationarity of the FHRV signal and according to the literature and methodologies previously used by the authors [21, 22, 23], the power spectral density (PSD) was estimated by means of the Short Time Fourier Transformation using a sliding Hamming window of 32 s [24]. Then, we computed the power in the main frequency bands of FHRV. Most of literature agrees that three bands can be detected in the FHR power spectrum, a very low frequency band (VLF), a low frequency band (LF) and a high frequency band (HF). However, despite to the spread use of FHRV spectral analysis, there is no agreement in definition of the frequencies bands. After a careful study of different literature works [25, 26, 27], the authors set the three bands of FHRV spectrum as follows: from 0 Hz up to 0.05 Hz (VLF); from 0.05 Hz up to 0.2 Hz (LF); from 0.2 Hz up to 1 Hz (HF).

As frequency parameters, we chose the power in low and high frequency bands (respectively named LF power and HF power), the total power (computed as the sum of LF and HF power) and the LF to HF power ratio, used as index of sympatho-vagal balance (SVB), a very important parameter which reflects the relations between vagal and sympathetic branches of the ANS.

D. Regression Analysis

Regression analyses were carried out for estimating the relationships among indexes extracted from SDA and FDA.

Then, after splitting data in 17 groups, according to gestational week, we computed mean and standard deviation of V.I. and LF power for each group and evaluated the respective regression curves.

Furthermore, in order to link V.I. and SVB, we divided CTG recordings in 16 groups according to their SVB values. In particular, we assembled every group selecting those signals whose SVB ranged from $x - 0.5$ up to $x + 0.5$, with x varying from 2 up to 17 and representing, in this way, the SVB mean of the group. Then, we calculated V.I. mean of each group and built the regression graph.

III. RESULTS

Scatter plots presented in the following figures (from 1 to 4) show relationships between V.I. and frequency parameters (power of both LF and HF bands, total power and SVB).

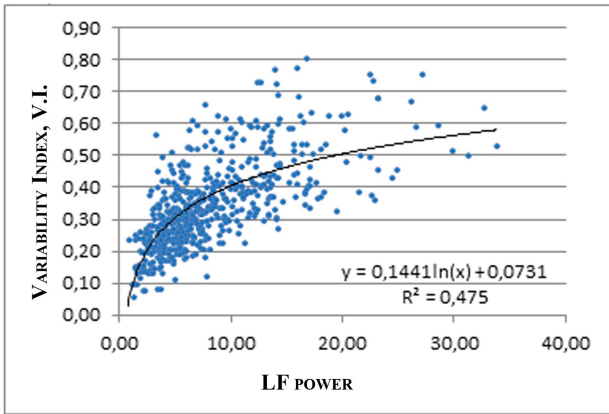


Fig. 1. Variability Index as a function of the power in low frequency band.

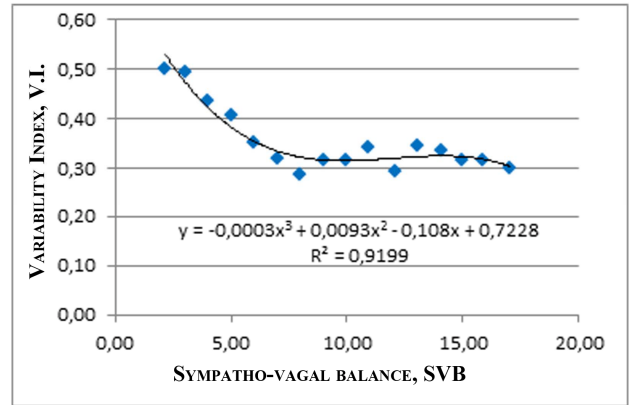


Fig. 4. Variability Index as a function of sympatho-vagal balance.

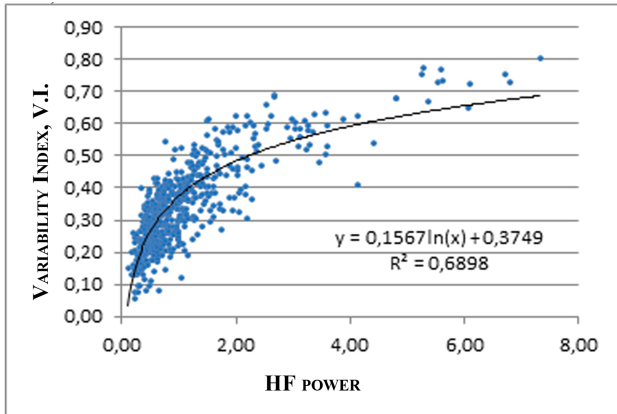


Fig. 2. Variability Index as a function of the power in high frequency band.

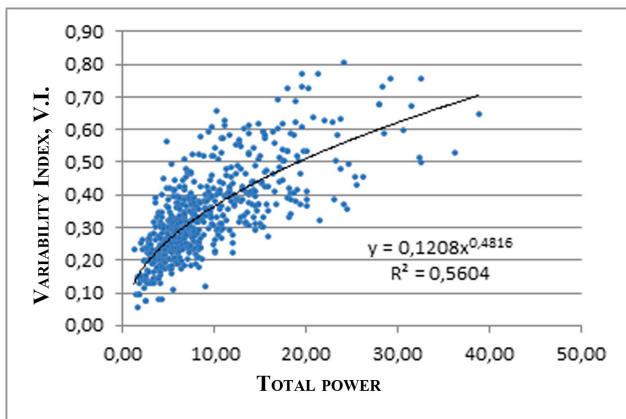


Fig. 3. Variability Index as a function of the signal total power.

TABLE II. MEAN AND STANDARD DEVIATION OF VARIABILITY INDEX AND LF POWER FOR DATA GROUPED ON THE BASIS OF GESTATIONAL WEEK. WEEKS 26 AND 27 ARE MISSING BECAUSE THERE ARE NO DATA AVAILABLE.

Week	# CTG recordings	Variability Index	LF power
		Mean ± Std	Mean ± Std
24	1	0.08	2.09
25	2	0.13 ± 0.08	4.37 ± 3.04
28	2	0.19 ± 0.08	5.28 ± 3.55
29	3	0.24 ± 0.06	6.67 ± 1.36
30	4	0.26 ± 0.12	7.17 ± 2.19
31	8	0.27 ± 0.15	6.98 ± 3.59
32	9	0.24 ± 0.08	5.00 ± 2.02
33	22	0.31 ± 0.14	7.76 ± 4.39
34	38	0.33 ± 0.63	7.70 ± 4.43
35	47	0.38 ± 0.16	8.49 ± 4.64
36	54	0.38 ± 0.15	9.29 ± 5.09
37	93	0.36 ± 0.14	8.84 ± 5.95
38	109	0.36 ± 0.13	8.73 ± 6.03
39	100	0.34 ± 0.12	7.54 ± 5.23
40	48	0.33 ± 0.13	6.51 ± 4.14
41	33	0.37 ± 0.11	8.90 ± 6.95
42	6	0.33 ± 0.06	10.09 ± 5.20

Fig. 5 and 6 illustrate regression graphs relating mean values of V.I. and LF power to gestational week (mean and standard deviation are summarized in Table 2).

On every scatter diagram we displayed the trend line equation and the coefficient of determination (R^2).

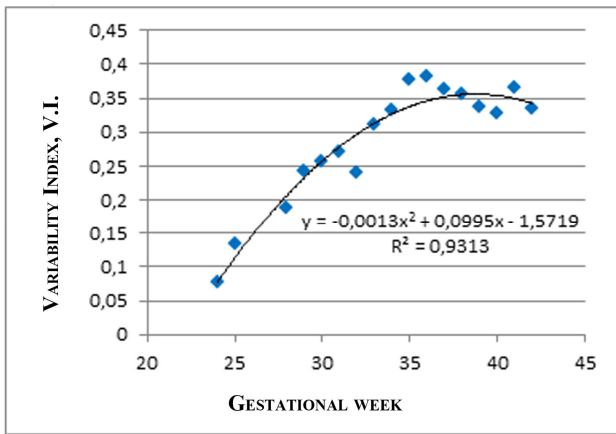


Fig. 5. Variability Index as a function of gestational week.

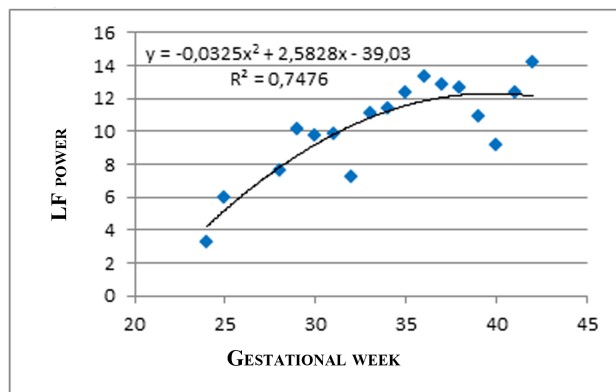


Fig. 6. Power in low frequency band as a function of gestational week.

IV. CONCLUSION

The paper describes an analysis of FHRV in computerised CTG monitoring by means of SDA and FDA. In particular, we propose a comparison between these two different methods to check advantages and disadvantages that both techniques could provide in foetal development assessment.

Regression analyses allowed us to evaluate the reliability of a novel index (V.I.) compared with traditional frequency parameters (LF and HF power and SVB). Curves in Fig. 1-3 show that the SDA index (V.I.) increases in correspondence of higher values of the power parameters. V.I. may then be considered also as an indicator of signal power. However, the correlation between V.I. and frequency parameters is stronger for HF power. A rough explanation of this result can be that, the computation of the ΔRR series corresponds to perform a high-pass filtering of the signal and, hence, an underestimation of the low frequencies.

We can further observe that, as shown in Fig. 4, a more complex polynomial curve is required to describe the relation between V.I. and SVB but to explain this result, it is necessary a more detailed study.

Particularly interesting are results shown in figures 5 and 6. Both curves have trend comparable with literature result [7], for the analysed weeks gestation, but with higher R^2 values.

This coefficient computed for SDA index (V.I.) is far higher than FDA parameters' one (LF power).

In summary, the results obtained, also considered together with the previous [15, 16], indicate that SDA, as much as FDA, could be a helpful tool in foetal monitoring. Moreover, indexes derived from SDA resulted more reliable than frequency parameters in assessing foetal development during the course of pregnancy.

Before the conclusion, it is worth to mention that we chose SDA for its ease of use, for immediate interpretation that one can do and for the successes already achieved in the adult subjects; however, other methodologies can be employed in HRV processing [28, 29].

For further studies, we would involve also not healthy foetuses and modify SDA methodology, for example by applying it directly to the FHRV signal.

ACKNOWLEDGMENT

This study was partially supported by QUAM project – funded by Italian Ministry of Economic Development - and by DRIVE IN2 project - funded by the Italian National Program Piano Operativo Nazionale Ricerca e Competitività 2007/13.

The authors thank Dr. Mario Russo of the Gesan S.r.l. for the support provided to the study.

REFERENCES

- [1] H.P. Van Gejin, "Developments in CTG analysis", *Baillieres Clin. Obstet. Gynaecol.*, vol. 10, 1996, pp. 185–207.
- [2] M. Romano, P. Bifulco, M. Cesarelli, M. Sansone and M. Bracale, "Fetal heart rate power spectrum response to uterine contraction", *Medical & Biological Engineering & Computing*, 2006, vol. 44, Issue 3, pp. 188-201.
- [3] Royal College of Obstetricians and Gynaecologists (RCOG), *The use of electronic fetal monitoring, The use and interpretation of cardiotocography in intrapartum fetal surveillance*. Royal College of Obstet. and Gynaecol, 2001, Evidence-based Clinical Guideline Number 8.
- [4] M. Cesarelli, M. Romano and P. Bifulco, "Comparison of short term variability indexes in cardiotocographic foetal monitoring", *Computers in Biology and Medicine*, 2009, vol. 39, Issue 2, pp. 106-118.
- [5] M. Cesarelli, M. Romano, G. D'Addio, M. Ruffo, P. Bifulco, G. Pasquariello, et al., "Floatingline estimation in FHR signal analysis", 5th European IFMBE Conference, 14-18 September 2011, Budapest, Hungary, IFMBE Proceedings 37, pp. 179–182.
- [6] Y. Kimura, K. Okamura, A. Yajima, "Spectral analysis of beat-to-beat intervals of the fetal heart obtained by Doppler ultrasound", *Gynecologic and Obstetric Investigation*, 1996, vol. 41, pp. 5-9.
- [7] T. Ohta, K. Okamura, Y. Kimura, T. Suzuki, T. Watanabe et al., "Alteration in the low-frequency domain in power spectral analysis of fetal heart beat fluctuations", *Fetal Diagnosis and Therapy* 1999, vol. 14, pp. 92-97.
- [8] R.T. Wakai, "Assessment of fetal neurodevelopment via fetal magnetocardiography", *Experimental Neurology*, vol. 190, 2004, pp.65-71.
- [9] N. S. Padhye, A. Brazdeikis and M. T. Verklan, "Monitoring fetal development with magnetocardiography", *Proceedings of the 26th Annual International Conference of the IEEE EMBS*, San Francisco, CA, USA, September 2004.
- [10] Task Force of the European Society of Cardiology and The North American Society of Pacing and Electrophysiology, *Heart Rate Variability – Standards of measurement, physiological interpretation, and clinical use*, *European Heart Journal*, 1996, vol. 17, pp. 354-381.
- [11] A. Voss, S. Schulz, R. Schroeder, M. Baumert and P. Caminal, "Methods derived from nonlinear dynamics for analysing heart rate variability", *Phil. Trans. R. Soc. A*, 2009, vol. 367, pp. 277-296.

- [12] A. Porta, G. D'Addio, G. Pinna, R. Maestri, T. Gneccchi Ruscone et al., "Symbolic analysis of 24h Holter heart period variability series: comparison between normal and heart failure patients", *Comp Cardiology*, 2005, vol. 32, pp. 575-578.
- [13] A. Voss, J. Kurths, H.J. Kleiner, A. Witt, N. Wessel et al., "The application of methods non-linear dynamics for the improved and predictive recognition of patients threatened by sudden cardiac death", *Cardiovascular Research*, 1996, vol. 31, pp. 419-433.
- [14] P. Van Leeuwen, D. Cysarz, S. Lange, D. Geue and D. Grönemeyer, "Quantification of fetal heart rate regularity using symbolic dynamics", *Chaos*, 2007, vol. 17 (015119).
- [15] M. Cesarelli, M. Romano, P. Bifulco, G. Improta and G. D'Addio, "Prognostic Decision Support using Symbolic Dynamics in CTG Monitoring", *Data and Knowledge for Medical Decision Support*, B. Blobel et al. (Eds.) IOS Press, 2013.
- [16] M. Cesarelli, M. Romano, P. Bifulco, G. Faiella, G. Improta et al., "Symbolic Dynamics in Cardiotocographic monitoring", *The 4th IEEE International Conference on E-Health and Bioengineering - EHB 2013*, Grigore T. Popa University of Medicine and Pharmacy, Iași, Romania, November 21-23, 2013.
- [17] M. Cesarelli, M. Romano, P. Bifulco, F. Fedele and M. Bracale, "An algorithm for the recovery of fetal heart rate series from CTG data", *Computers in Biology and Medicine*, vol. 37, Issue 5, pp. 663-669, 2007.
- [18] G. Improta, M. Romano, F. Amato, M. Sansone and M. Cesarelli, "Development of a software for automatic analysis of CTG recordings", *GNB2012*, June 26th-29th 2012, Rome, Italy.
- [19] S. Guzzetti, E. Borroni, P.E. Garbelli, E. Ceriani, P. Della Bella et al., "Symbolic Dynamics of Heart Rate Variability. A Probe to Investigate Cardiac Autonomic Modulation", *Circulation* July 26, 2005.
- [20] M. Cesarelli, M. Romano, P. Bifulco, G. Improta and G. D'Addio, "An Application of Symbolic Dynamics for FHRV assessment", *Stud Health Technol Inform.*, 2012, vol. 180, pp. 123-127.
- [21] M. Cesarelli, M. Romano, M. Ruffo, P. Bifulco and G. Pasquariello, "Foetal heart rate variability frequency characteristics with respect to uterine contractions", *Journal of Biomedical Science and Engineering*, 2010, vol. 3, pp. 1014-1021.
- [22] M. Romano, M. Bracale, M. Cesarelli, M. Campanile, P. Bifulco et al., "Antepartum cardiotocography: a study of fetal reactivity in frequency domain", *Comput Biol Med J*, 2006.
- [23] J. Karin, M. Hirsch, C. Sagiv and S. Akesselrod, "Fetal autonomic nervous system activity monitoring by spectral analysis of heart rate variations", *IEEE Comput. Cardiol.*, 1992, pp. 479-482.
- [24] M. Romano, M. Cesarelli, P. Bifulco, M. Ruffo, A. Fratini, G. Pasquariello, "Time-frequency analysis of CTG signals", *Current Develop. in Theory and Applications of Wavelets*, 2009, vol.3, Issue 2, pp. 169-192.
- [25] L. W. Oppenheimer, R.M. Lewinsky, "Power spectral analysis of fetal heart rate", *Baillieres Clin Obstet Gynaecol.*, 1994 Sep, vol. 8, Issue 3, pp. 643-661.
- [26] S. Cerutti, S. Civardi, A. Bianchi, M.G. Signorini, E. Ferrazzi, G. Pardi, "Spectral analysis of antepartum heart rate variability", *Clin. Phys. Meas.*, 1989, 10 (suppl. B), pp. 27-31.
- [27] L.J. Groome, D.M. Mooney, L.S. Bentz, K.P. Singh, "Spectral analysis of heart rate variability during quiet sleep in normal human fetuses between 36 and 40 weeks of gestation", *Early Human Development*, 1994, vol. 38, pp. 1-10.
- [28] D. Labate, F. La Foresta, G. Occhiuto, F.C. Morabito, A. Lay-Ekuakille, P. Vergallo, "Empirical Mode Decomposition vs. Wavelet Decomposition for the extraction of respiratory signal from single-channel ECG: a comparison", *IEEE Sensors Journal*, 2013, vol.13, n.7, pp. 2666-2674.
- [29] M. Cesarelli, P. Bifulco, M. Bracale, "Evaluating time-varying heart-rate variability power spectral density: a multiple weighted-least-square identification process for recognizing changes in ICU patient status", *IEEE Engineering in Medicine and Biology*, 1997, vol. 16, n.6, pp.76-79