33rd Annual International Conference of the IEEE EMBS
Boston, Massachusetts USA, August 30 - September 3, 2011

# Advances in Monitoring Cardiovascular Signals. Contribution of Nonlinear Signal Processing

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*Abstract*—**Monitoring procedures are the basis to evaluate the clinical state of patients and to assess changes in their status, thus providing necessary interventions in time. To obtain this important objective it is necessary to integrate technological development with systems performing biomedical knowledge extraction and classification. Methods extracting non linear characteristics from HRV signal are presented and discussed to stress that integrated and multiparametric signal processing approaches can contribute to new diagnostic and classification indices. Examples report heart rate variability analysis in long periods in patients with cardiovascular disease. Fetal ECG monitoring is another example. In this case, coupling nonlinear parameters and linear time and frequency techniques increases diagnostic power and reliability of the monitoring. The paper shows that integrated signal analysis is very helpful to describe pathophysiological mechanisms involved in the cardiovascular and neural system control. It is a reliable basis to set up knowledge-based monitoring systems.**

## I. Introduction

Monitoring biomedical signal is one of the primary tools for investigating disease state evolution. Measurement, quantification, evaluation and classification of biological signal properties, all contribute to global understanding of the biological system that act as input of the observed time course. The overall architecture of a monitoring system combines a technological support with signal analysis methods to extract useful parameters to classify and predict the patient status.

In order to reach this goal it is very important to identify processing methods enhancing pathophysiological signal properties thus linking parameters to a physiological meaning (and to physical quantities).

Traditional monitoring systems received a fundamental improvement by new technological devices allowing longer and deeper data collection as well as advanced clinical tools for data interpretation, visualization and storage. Signal processing analysis contributed to this development by providing new methods and algorithms tools for extracting reliable quantitative parameters.

Multiparametric analysis added clinical and diagnostic knowledge by measuring several physiological variables that are useful to fully understand and follow the development of disease states. Among analysis methods, advanced signal processing techniques both in time and in frequency domain played a key role for extracting information that either in cardiovascular and neural systems has been associated to pathophysiological events.

Most of these approaches were based on the simplified hypothesis of linearity even if it is now clearly established that biological systems are much more complex than they appear. The introduction of nonlinear signal processing methods provided new information about cardiovascular and neutral systems. Their description, based on nonlinear parameters estimating complex signal properties, completed and improved data description, providing new useful indices for monitoring purposes. Examples are described, related to heart rate variability analysis in long periods in patients with cardiovascular disease. Fetal ECG monitoring is another case in which coupling nonlinear parameters and linear time and frequency techniques increased diagnostic power and analysis and monitoring reliability.

## II. Signal Processing Approaches

The development of the nonlinear dynamical system analysis has led to the introduction of a large amount of signal analysis techniques aimed at the extraction of nonlinear parameters from experimental time series. The original goal was the evaluation of the characteristics generating the system. In many cases, however, the generation system is unknown and the output signal is the only information we can obtain about the system itself. This is the case of human life support systems among which the heart plays a dominant role.

The measurement of the electrical activity of the myocardial cells is the basic tool allowing the knowledge of the heart activity. The electrocardiographic signal (ECG) and more generally the cardiovascular monitoring are the main way to investigate heart function. Heart Rate Variability signal (HRV) measures spontaneous variability between successive beats. It has been shown that HRV signal changes can be related to the activity of several physiological control mechanisms of different nature. Their interaction produces changes in the beat rate assuring the system controlling heart beats reacts efficiently to different incoming stimuli.

Manuscript received 15th April , 2011.

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Frequency domain analysis of the HRV signal provides quantitative and noninvasive measures of the activity of the Autonomic Nervous System (ANS) [1]. This is obtained by a linear modeling approach that quantifies both the sympathetic and parasympathetic control activity and their balance through the measure of spectral low and high frequency components (LF and HF). Nevertheless, the analysis of HRV signal through classical linear methods, either in time or in frequency domain, provided the quantification of some important properties of the regulating action performed by the ANS in the short period [1] but confirmed that the information carried by this signal cannot be totally explained by a linear approach only [2]. Results on HRV signal analysis show that its dynamic behavior involves nonlinear components that contribute to the signal generation and control [2][3]. Signal structure appears erratic but it presents abrupt changes and patterns in which more regular behaviors appear. To investigate these properties of the physiological rhythms of the cardiac system and to assess nonlinear deterministic phenomena affecting HRV signal both in short and long temporal windows, nonlinear signal analysis is a fundamental tool [4].

Moreover, multiparametric signal processing showed that the integration of different parameters can provide a more robust descriptive support. We will show several examples in physiological and pathological conditions where a nonlinear dynamic model can explain the regulating mechanisms of the cardiovascular system. In the same time parameters obtained from the analysis can lead to a classification of different pathological states.

## III. Methods

The evaluation of the HRV signal characteristics by a nonlinear approach, considers a set of methods investigating both geometric and dynamic aspects. Differently to what happens when we have a well known deterministic system, we can only study experimental time series. Nevertheless important indications can be extracted from the parameters estimating nonlinear characteristics and their statistical use is of great importance, improving diagnostic performances and helping clinical knowledge in different cardiovascular pathologies [3][4].

*Self-Similarity indexes: H and α slope.*

A time series can show fractal characteristics in their patterns, as well as in the temporal scales. Time series, under different degrees of magnification of time step, can show patterns with self-similar characteristics. Other techniques exist, aimed at quantifying the degree of self-affinity in a time series by providing the estimation of the scaling exponent $H$[0,1], which can be computed directly on the RR series [5]. Among them, *Detrended Fluctuation Analysis (DFA*) demonstrated its usefulness in characterizing biological time series. Hurst exponent, $H$ estimates the level of self-similarity providing information on the recurrence rate of similar patterns in time, at different scales [6].

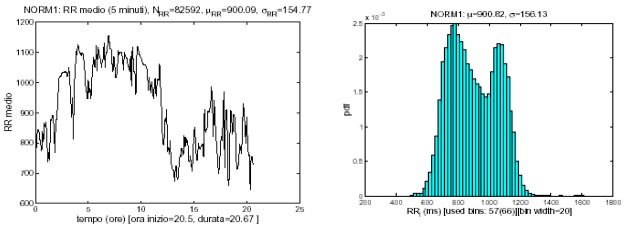


Fig.1. 24 h RR signal for a normal subject. Left panel: HRV time series as a function of beat number; Right: RR histogram

Hurst exponent, $H$ characterizes the level of self-similarity providing information on the recurrence rate of similar patterns in time, at different scales [6].

Several methods are available to estimate the H parameter: one is based on the periodogram. where α is the spectrum slope. $\alpha$ slope is usually computed by regressing power values in the frequency range (0.02-0.04] Hz in log-log scale. It was found that $\alpha \approx 1$ identified the HRV of normal subjects

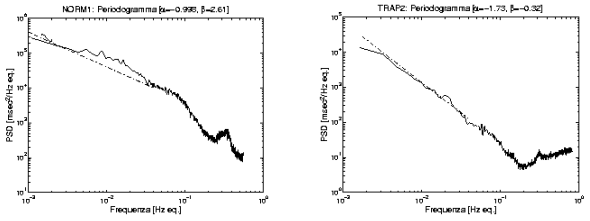


Fig.2. 1/$f$ Power-Law Spectrum. Periodogram calculated from 24 h RR signal in a normal (Left) and a transplanted (Right) subjects. $\alpha$ slope value is higher in disease state where the heart control systems are compromised

We adopted it for fetal HRV analysis as it does not require an a priori knowledge of the properties of the series. Moreover it can be used also in case of nonstationary time series, such in our case [6].

*DFA* is a fractal-related method estimating the scaling exponent (the slope of the power spectrum) [4] [7]. *DFA* provides a couple of scaling exponents $\alpha_S$ (Short-term fractal exponent, computed on short scales) and $\alpha_L$ (Long-term fractal exponent related to scaling on longer scales). Regularity properties can be estimated by Entropy indexes: *Approximate, Sample and MultiScale Entropy.*

*ApEn* quantifies regularity and complexity of a time series even if short (>100 values) or noisy. *ApEn* depends on the length $m$ of compared runs and on the percentage $r$ of the signal std, which fixes a filtering level. In practice, we evaluate within a tolerance $r$ the regularity, or frequency, of patterns similar to a given pattern of window length $m$. Statistical validity of *ApEn (m, r, N*) requires $m$=1, 2, $r$: 0.1 - 0.25 std of the input data [8]. Other methods estimate entropy-like indexes in time series. Among them, *Multiscale Entropy (MSE)* has been largely employed in biomedical signal analysis as it allows measuring signal properties at different time scales (Figure 4). The original *MSE* method [9] is based on a new entropy measure, *Sample Entropy (SampEn),* whose statistic depends on parameters $r$ (filtering level) and $m$ (detail level at which the signal is analyzed)

[10]. *SampEn* estimates entropy in single series. *MSE* measurements are plotted as a function of the scale factor $\tau_{sf}$. *MSE* and *ApEn* were estimated in the same time series by the same parameter set as in the *SampEn*. A subset of 5000 point was selected from corrected sequences. Parameters for the computation of *ApEn* and *SampEn* were: $m$=1 $r$=0.1, $m$=2 $r$=0.15 and 0.2. Scale factors ranged from 1 to 15.

The *Lempel Ziv Complexity (LZC)* is a method to assess algorithmic complexity [8]. *LZC* measure is associated to the number of distinct signal sub strings and to their recurrence rate; namely it reflects the gradual increase of new patterns along the given sequence.

The measure of complexity introduced by Lempel and Ziv assess the so-called algorithmic complexity, defined according to Information Theory as the minimum quantity of information which is needed to define a binary string. In case of random strings, algorithmic complexity is the length of the string itself. In fact any compression effort produces an information loss. *LZC* quantifies the rate of new patterns arising with the signal evolution. In order to estimate the *LZC* for the FHR time series, we need to code signals into symbolic sequences.

## IV. HRV Monitoring in Cardiovascular Disease

Estimation of $\alpha$ spectrum slope was made in 24 hours RR series (100000 beats) belonging to normal, hypertensive heart failure and transplanted patients (N=10 in each group). $\alpha$ significantly separates different groups. $\alpha$ value is near 1 for Normal subjects and it increases as the disease states become more critical. Moreover, subjects at risk of sudden cardiac death exhibit higher $\alpha$ values even inside pathological groups allowing their early classification [10] [4]. Holter 24 ECG monitoring equipments took advantage from these results introducing the new indices in their parameter classification systems.

Figure 3 shows results of DFA in HRV series of Heart failure patients. Both the slope in short S, (4,000 beats) and in long period L, (10,000 beats) significantly separate Normal vs. Heart failure. HRV of Normals show random walk in S period, 1/f noise in long period ($\alpha_{S,N}>\alpha_{S,HF}$ $p<0,01$) as HF patients exhibit 1/f noise both in short and in long period. HRV series of Normals were more correlated than HF patients in L period and less correlated in S period ($\alpha_{L,N}<\alpha_{L,HF}$ $p<0,01$)

## V. Fetal ECG and HRV Monitoring

Monitoring of fetal conditions during pregnancy is a challenging point for people working in the obstetric field.

The first goal is to assure that fetus is and remains in a wellbeing state as the pregnancy develops.

Till now, standard monitoring approaches use Doppler ultrasound measurements to detect Fetal Heart frequency. In the same time, the monitoring system records uterine contractions. The first goal is to assure that fetus is and remains in a wellbeing state as the pregnancy develops.

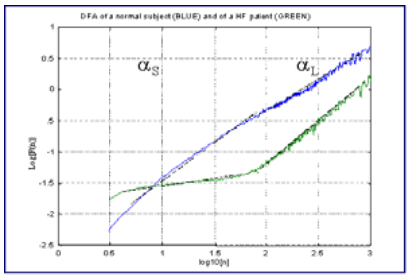


Fig. 3. DFA of a normal (blue) and Heart failure subject( green). The short (S, 4000 RR values ) and long term (L, 10000 RR) slope are shown.

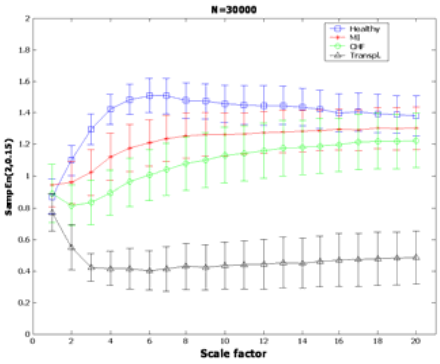


Fig.4. MSE results in Normal, Hypertensive, CHF and Transplanted subjects. RR length is 30,000 points. Similar results were obtained for 60,000 and 80,000 points.

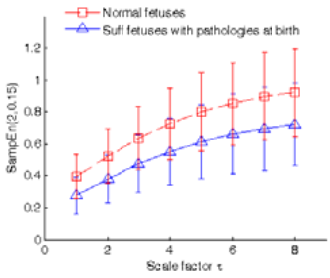


Fig. 5. Results of *MSE* computed by *SampEn* in Normal and recognized as Suffering fetuses. Differences are noticed in population that will show pathological conditions with disease at delivery.

Till now, standard monitoring approaches use Doppler ultrasound measurements to detect Fetal Heart frequency. In the same time, the monitoring system records uterine contractions. Fetal HR signal is usually analyzed by detecting morphological signal characteristics whose clinical relevance is judged by eye inspection. Thus, automatic computerized estimation of variability time domain parameters represented an improvement. Computation of short term (STV) and long term (LTV) variability provided quantitative data supporting diagnostic process. Nevertheless results remained poor in predicting fetal morbidity as the adopted approaches do not consider parameters that can enhance the activity of physiological control mechanisms.

This is the reason why we tried to integrate the traditional morphological approach with frequency domain analysis and with physiologically related non-linear analysis [11].

As a matter of fact the HR signal is much more complex than it can be judged by traditional approaches, even in the fetal life. Our experience over more than 2000 selected cases shows that using advanced signal processing techniques can

provide better classification results of the fetal states. Through this analysis, fetuses whose condition appears at risk can be evidenced in order to receive special attention. Figure 5 shows complexity index values that allow different classification of fetal stress states.

Thus a multiparametric set of diagnostic parameters is an improvement toward the classification of fetal pathologies and the related risk [11]. A parameter set including Frequency domain parameters from autoregressive power spectrum estimation (LF, MF, HF power and LF/(MF+HF)); Time domain parameters (FHR std, Delta FHR, Short term variability (STV), Long term irregularity (LTI), Interval Index (II)); and Regularity and Complexity parameters (ApEn, MSE, DFA, LZC), all were applied to analyze FHR.

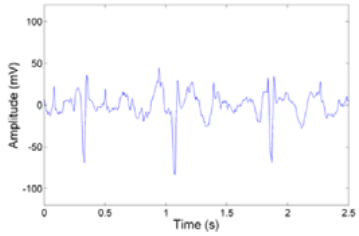


Fig.6. Abdominal ECG recording by a wearable system prototype showing Maternal and Fetal ECG peaks. An elastic belt includes textile electrodes that record 8 abdominal ECG traces. The objective is the home monitoring of the fetal wellbeing conditions during the last 2 months of pregnancy.

By this approach we performed classification of fetal states as well as we obtained diagnostic indications about intrauterine growth retardation (IUGR) and fetal distress [12][13].

*Fetal ECG from abdominal recordings*

Fetal monitoring could be also performed by measuring Fetal ECG through electrodes that are posed over the maternal abdomen after the 26$^{th}$ week of pregnancy [14]. In this way one can have a direct measure of the FECG. Unfortunately, the recording of FECG is very difficult both for the low SNR, due to noise superimposed and Maternal ECG interference and for the position of the fetus which almost continuously changes his/her position inside the uterus. The recording can be made only at the hospital and requires the presence of expert personnel. Even in that case, measurement of FECG remains a difficult operation,
Nevertheless, the direct FECG could provide information on the beat structure (long QT, T Wave morphology and slope which are related to heart diseases and to hypoxic fetal states. A possible solution can be provided from new textile biosensors. A new monitoring system has been designed that uses wearable textile technologies to measure FECG. A first example of the signal obtained by a wearable elastic belt sensorized with 8 ECG electrodes equipped with a simple acquisition system is illustrated in figure 6. The objective is to build up a system that woman can use at home sending data to the hospital for evaluation [14].

## IV. Discussion

Monitoring biological signals requires using and integrating different analysis methods to correctly classify signal behaviors. Examples were shown, confirming that not only time domain analysis should be employed. Frequency domain and nonlinear indices enrich the signal description providing new indicators for diagnostic and classification purposes. The importance of integration among advanced signal processing approaches, working at different time scales and in frequency domain was confirmed. The multiparametric approach provides an improvement in statistical analysis of biological signals. Examples we reported showed that monitoring systems can be improved by adding diagnostic and classification power through novel signal processing techniques. Some problems remain which are related to the quality of recordings and to the intrinsic complexity which characterizes pathologies thus complicating their prediction and control. Moreover we also need to develop personalized monitoring systems allowing almost continuous non invasive evaluation of the subject state. Knowledge based systems contribute to the patient care improvement. New technologies based on textile and/or wearable sensors can help personalization of the monitoring sessions maintaining high level performances in data analysis. The wearable monitoring system we are building up has been designed to allow a reliable and continuing assessment of fetal states at home leading to a significant improvement in the quality of fetal wellbeing assessment.

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