# ESTIMATION OF BRS BY USING SIMULTANEOUS VARIABILITY OF RR-INTERVALS IN HEART AND SYSTOLIC BLOOD PRESSURE IN HUMANS

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**ABSTRACT**
We used a new method to estimate BaroReflex Sensitivity (BRS). The methodology, based on the CZF formulation, (see Conte et al 2009), enabled us to evaluate simultaneous variability of RR and SBP and to estimate the BRS. The method was applied to seven subjects (female and men with age ranging from 21 to 28 years old) and the results were compared with those that may be obtained by using the standard Fourier spectral analysis technique. The results also resulted in satisfactory agreement with previously obtained results by application of the same methodology.

**Keywords**: *Heart Rate Variability (HRV) analysis, new method for BRS calculation , autonomic disfunction, chaos and fractal analysis.*

## 1. On the Fundamental Role of Recurrences and Variability of Signals in Nature

According to Joseph Zbilut and Conte only few systems in Nature exhibit linearity. Natural systems, especially those who pertain to biological matter, and , in detail, to physiological, neuro-physiological and to psychological processes, possess a complexity that results in a great variedness and variability, linked to non linearity, to non stationarity, and to non predictability of their time dynamics. In time domain, traditional methods were used to describe the amplitude distribution of signals. Later, methodologies used spectral analysis. Unfortunately, they suffer of fundamental limits. They are applied assuming linearity and stationarity of signals that actually do not exist. The consequence is that such methods are unable to analyse in a proper way the important fluctuations that instead we may observe in signals , and particularly in signals of clinical electrophysiological interest.

Actually, fluctuations and apparent irregularities in the time dynamics behaviour constitute the essence of the inner structure of the signal that obviously is counterpart representative of the physiological and physio-pathological condition of the subject. The emerging indication is that we are very distant from traditionally accepted principles as it is the case of homeostatic equilibrium and of similar mechanisms of controls. The study of this very irregular behaviour has required and still continues to require the adoption of new principles supported from non linear methodologies, chaos and fractal analysis. Non linear science is becoming an emerging methodological and theoretical framework that makes up what is called the science of the complexity . Complexity does not represent a generic term having counterpart at epistemological and philosophical level, but a well established property of living matter that presently we are able to evaluate and estimate by direct indexes and parameters. An indication of such convincing new perspective results from existing chaotic and divergent behaviour in the physiology of the living beings

In detail, we may consider some accepted basic principles that may be reassumed as it follows:

1) Non linear systems under certain conditions may exhibit chaotic behaviour.
2) The behaviour of a chaotic system can change drastically in response to small changes in the system's initial conditions;
3) A chaotic system is often deterministic;
4) In chaotic systems the output system is no more proportionate to system input.

Chaos may be identified in systems also excluding the requirement of determinism. We term such behaviour non-deterministic chaos. This approach to chaos theory was initiated by Zak, Zbilut and Webber [Zak 1989,1992,1998; Zbilut et al. 1994, 1995, 1996, Zbilut et al. 2008] and recently authors have given several examples, theoretical and experimental verifications on this important chaotic behaviour [Conte et al. 2004, 2004, 2006].

## 2. Fractality and Non Linearity of Experimental Time Series

The so called CZF method was introduced rather recently [Conte et al. 2007, 2008, 2008, ] for analysis and quantification of sympathetic and vagal activity in variability of R–R time series in ECG signals.

CZF states for the surname (Conte, Zbilut, Federici) of the authors who introduced it. A software version of the method may be found by free download on the Nevrokard site http://www.nevrokard.eu/ ( a HRV) .

In essence the method enables us to analyze the total variability, the VLF , the LF , and the HF contributions of a given tachogram of subjects in normal as well as pathological conditions.
Incidentally we remember that VLF states for Very Low Frequency and relates the FFT –frequency domain spectrum evidencing modulations on the heart rhythm arising possibly from thermoregulation as well as from hormonal contributions and also from the renin – angiotensin system. Of course this is the dominant interpretation at the present also if further studies are still required in order to establish with certainty the presence, the function and thus the meaning of such band. LF states for Low Frequency and relates modulation as due to sympathetic and possibly also to parasympathetic activity. Also this band is still affected from some residual indeterminacy in the interpretation since the dominant component in this band is usually attributed to the sympathetic activity.
The last band is the HF that states for High Frequency and relates vagal as well as respiration modulation .
The final interesting feature of the CZF method is that it enables estimation of the fractal dimension and in this manner the method covers a possible analysis disengaged from approximation and limits

## 3. Estimation of Baro Reflex Sensitivity (BRS) by the CZF Method.

It is well known that the baroreflex loop is an important cardiovascular control mechanism for short-term blood pressure (BP) regulation. Based on afferent information of arterial baroreceptors reacting on changes in BP, central cardiovascular control is exerted on different peripheral effector systems as in particular on heart rate, cardiac output, peripheral resistance in order to keep BP between narrow limits.
Baroreflex sensitivity (BRS) is a sensitive integrated measure of both sympathetic and parasympathetic autonomic regulation in which changes in heart rate due to variation in BP are reflected.
Different techniques, based usually on spectral analysis or on the so called sequence method, have been introduced to quantify baroreflex gain (Parlow et al. 1995). Traditionally, BRS is assessed pharmacologically, using the heart rate response to vasoactive drugs. Pharmacological and non-invasive
BRS measurements have been found to correlate significantly (Parlow et al. 1995, Watkins et al. 1996). The literature is boundless on this subject. However, no definitive agreement has been reached on which of the employed methods should be preferred (Lipman et al. 2003, Parati et al. 2004). On the other hand, BRS measurements represent an important prognostic tool to detect early subclinical autonomic dysfunction. In fact, reduced values of BRS may result largely from vagal withdrawal determining an high component of risk. Therefore it represents a valuable predictor of future cardiovascular morbidity and mortality in a variety of disease states that are associated with autonomic failure, (Gerritsen et al. 2001, La Rovere et al. 1998, Ditto 1990). An interesting connection has been shown between diminished BRS and psychopathology (Virtanen et al. 2003). The aim of the present paper is to evidence that the BRS may be estimated also by the CZF In detail we consider that this new BRS method introduced in literature in 2009 (**arXiv:0810.4090**) is essentially free from approximations.
Let us review the essence of the approach.
First we reconstruct variability by the variogram and its representation in frequency domain as previously explained in (Conte et al., 2009). One time we will use this method on *RR* time series and thus the same approach will be used for reconstructed *SBP* time series. In this condition, we will introduce two new BRS indexes of variability, $BRS_{LF}$ and $BRS_{HF}$ , respectively for the two bands (LF) and (HF) respectively , calculated in the following manner:

$$BRS_{LF} = \sqrt{\frac{TOTAL\quad VARIABILITY\quad CALCULATED\quad IN\quad THE\quad LF\quad BAND\quad FOR\quad R-R}{TOTAL\quad VARIABILTY\quad CALCULATED\quad IN\quad THE\quad LF\quad BAND\quad FOR\quad SBP}}$$

and

$$BRS_{HF} = \sqrt{\frac{TOTAL\quad VARIABILITY\quad CALCULATED\quad IN\quad THE\quad HF\quad BAND\quad FOR\quad R-R}{TOTAL\quad VARIABILTY\quad CALCULATED\quad IN\quad THE\quad HF\quad BAND\quad FOR\quad SBP}}$$

The results are obviously given in msec/mmHg
An accurate investigation requires to use variogram values calculated by using the mean blood pressure time series given by $\dfrac{SBP-DBP}{3}+DBP$ .
This last explanation completes the exposition of our method.

## 4. Methods

Seven healthy subjects (4 women, 3 men) (age included between 21 and 28 years old) underwent continuous non-invasive blood pressure (BP) recording using a Finapres 2300 device together with an ECG recording using a BioPac system. Subjects were recorded 10-12 min in standing position.
Data were provided as BP and ECG signals sampled at 250 Hz with a 16-bit resolution. Systolic BP (SBP) values were obtained by software for peak maximum identification, and R-R values were obtained by software for time intervals identification in ECG. Pieces of 400 points were selected for analysis of variability. Lags in the variogram calculation were considered from 1 to 397.

## 5. Estimation of BRS and Results

The BRS estimates included the procedure exposed in the previous section, obtained by the CZF method. To this method we added also the investigation performed by the traditional spectral analysis previously discussed in the framework of the standard methods used currently to calculate BR*S.*
The results appear to be in satisfactory agreement with the previous results that were obtained in **arXiv:0810.4090** and are reported in Table 1
By inspection of Table 1 , we deduce that while Fourier method gives rather fluctuating values , the CZF method instead furnishes more coherent and uniform values.
In addition , in Figures 1, 2, 3, 4 we report the results of a brief statistical analysis based on correlation estimation. It is seen that the correlation between $BRS_{LF}$ and $BRS_{HF}$ in the CZF method results very high , the correlation between $BRS_{LF}$ and $BRS_{HF}$ using the Fourier Spectral Method results modest, in addition it does not result correlation between $BRS_{LF}$ of CZF vs $BRS_{LF}$ Fourier Spectral Method and between $BRS_{HF}$ of CZF Method vs $BRS_{HF}$ Fourier Spectral Method. This result gives further support to the thesis that calculation of BRS by using CZF method is very promising and able to take in consideration linear as well as non linear components.

**Table 1: Estimation of BaroReflex Sensitivity (BRS) by different methods (unities: msec/mmHg)**

| Subject | CZF Method | | Fourier Spectral Method | |
|---|---|---|---|---|
| | $BRS_{LF}$ | $BRS_{HF}$ | $BRS_{LF}$ | $BRS_{HF}$ |
| M. A. | 4.72 | 3.78 | 8.74 | 4.74 |
| R. C. | 7.14 | 6.96 | 6.12 | 6.01 |
| P. C. | 6.78 | 5.16 | 8.36 | 8.54 |
| D. V. | 4.15 | 4.43 | 5.37 | 4.28 |
| C. B. | 8.25 | 7.84 | 10.13 | 18.55 |
| B. V. | 5.95 | 5.23 | 14.03 | 20.94 |
| B. M. | 6.88 | 7.27 | 8.31 | 11.17 |

**Fig. 1: Correlation estimation between $BRS_{LF}$ vs $BRS_{HF}$ CZF Method**

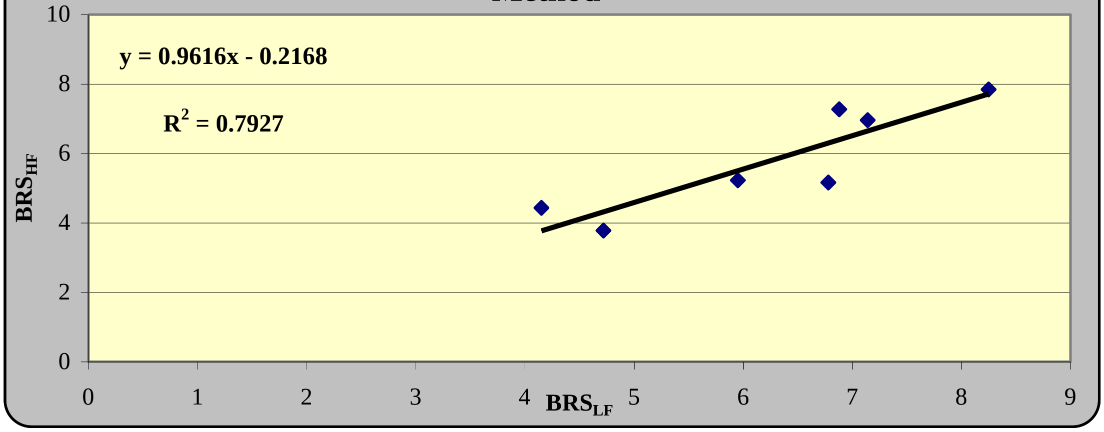


**Fig. 2: Correlation estimation between $BRS_{LF}$ vs $BRS_{HF}$ Fourier Spectral Method**

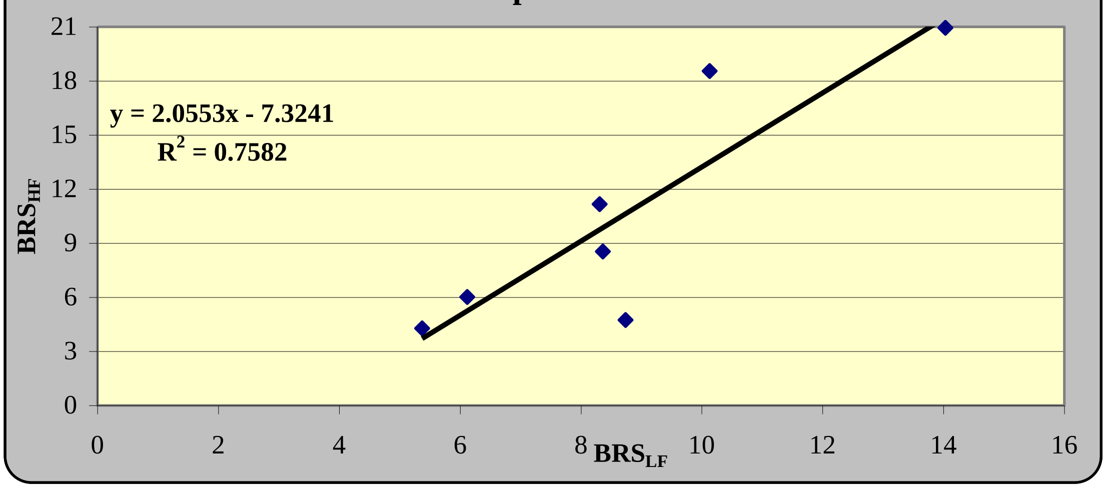

**Fig. 3: Correlation estimation between $BRS_{LF}$ CZF Method vs $BRS_{LF}$ Fourier Spectral Method**

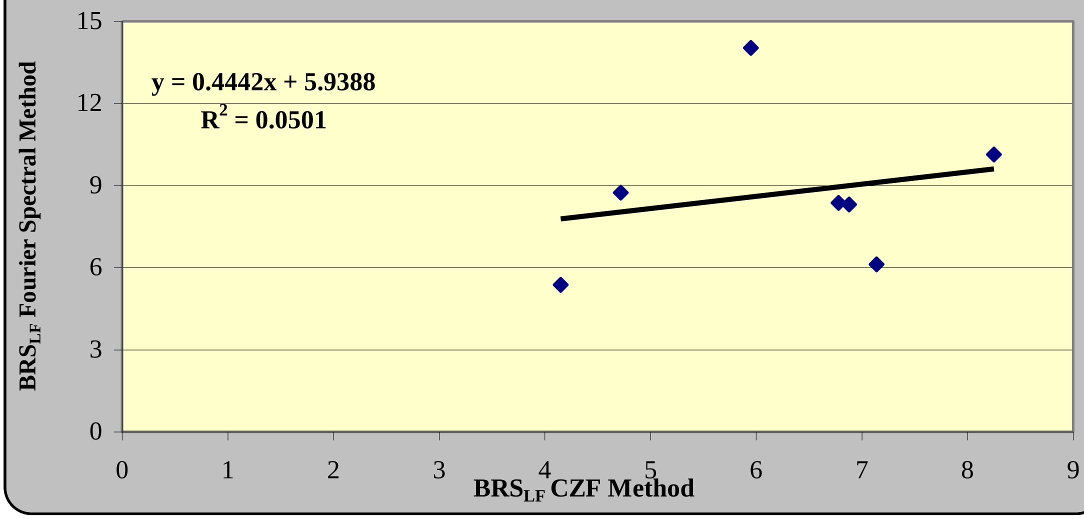


**Fig. 4: Correlation estimation between $BRS_{HF}$ CZF Method vs $BRS_{HF}$ Fourier Spectral Method**

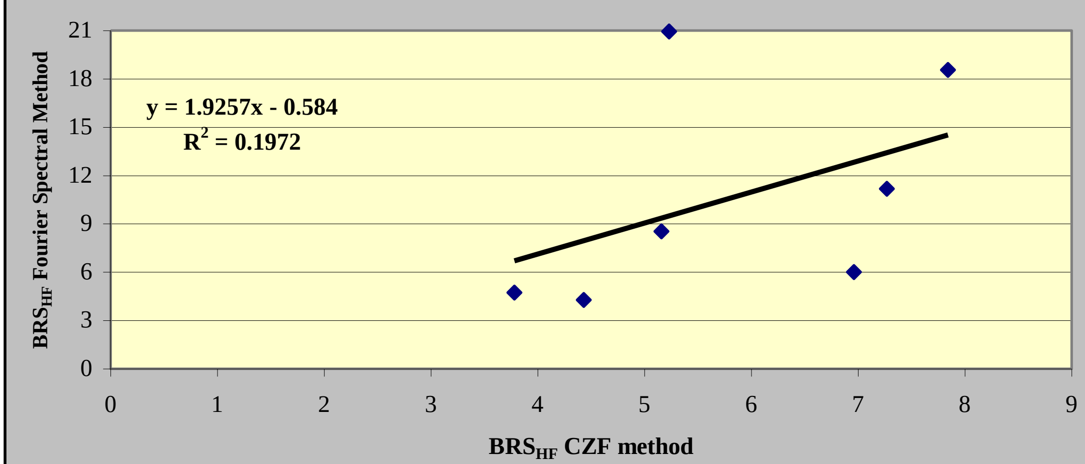



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**Table 1: Estimation of BaroReflex Sensitivity (BRS) by different methods (unities: msec/mmHg)**

| Subject | CZF Method | | Fourier Spectral Method | | Lomb-Scargle | |
|---|---|---|---|---|---|---|
| | $BRS_{LF}$ | $BRS_{HF}$ | $BRS_{LF}$ | $BRS_{HF}$ | $BRS_{LF}$ | $BRS_{HF}$ |
| AM-A-1 | 7.414 | 7.264 | 6.445 | 6.327 | 6.327 | 6.347 |
| CR-A-1 | 4.523 | 3.632 | 10.475 | 4.147 | 10.834 | 4.266 |
| DPC-A-1 | 7.012 | 5.367 | 8.636 | 8.896 | 8.848 | 9.425 |
| IC-A-1 | 24.877 | 24.340 | 28.175 | 34.804 | 28.399 | 34.250 |
| RR-A-1 | 24.661 | 27.874 | 28.169 | 31.060 | 28.385 | 30.253 |
| SC-A-1 | 14.284 | 12.301 | 14.190 | 17.042 | 14.637 | 18.285 |
| VD-A-1 | 3.758 | 4.233 | 5.737 | 4.497 | 5.758 | 4.529 |
| AM-B-1 | 9.433 | 9.125 | 8.190 | 18.054 | 8.114 | 18.177 |
| CR-B-1 | 8.885 | 8.247 | 10.935 | 21.551 | 11.637 | 21.601 |
| DPC-B-1 | 5.456 | 4.831 | 15.003 | 21.934 | 9.392 | 9.321 |
| IC-B-1 | 21.959 | 22.082 | 18.778 | 31.635 | 19.388 | 32.240 |
| RR-B-1 | 26.350 | 20.140 | 33.454 | 36.362 | 33.822 | 36.537 |
| SC-B-1 | 10.389 | 6.351 | 11.791 | 22.349 | 11.617 | 23.009 |
| VD-B- 1 | 6.688 | 7.097 | 8.016 | 10.967 | 8.117 | 11.068 |