The CZF Method

Heart Rate Variability (HRV) refers to the variations in the heartbeat intervals or correspondingly in the instantaneous HR. It thus represents the variation over time of the period between consecutive heartbeats, and it represents a reliable expression of the many physiological factors of control that modulate the normal rhythm of the heart. It reflects the heart's ability to adapt itself to changing conditions by detecting and quickly responding to unpredictable stimuli.

R-R intervals provide a powerful mean of observing the interplay between the sympathetic and parasympathetic nervous systems. In studies of R-R intervals or HR we are mainly interested in autonomic neural regulation of the heart and the circulatory system. The balancing action of the sympathetic nervous system (SNS) and parasympathetic nervous system (PNS) branches of the ANS controls the HR. Increased SNS or diminished PNS activity results in cardio-acceleration and reduced variability. Conversely, a low SNS activity or a high PNS activity causes cardio-deceleration and more accentuated variability. Therefore, the degree of variability in the HR provides information about the functioning of the nervous control on the HR and the heart's ability to respond.

The R-R Methodology of Analysis

The analysis of R-R intervals has become a basic non-invasive tool for assessing the activities of the autonomic nervous system. As previously said, it covers mainly the need to evaluate overall cardiac health and the state of the autonomic nervous system (ANS) responsible for regulating cardiac activity. It is a useful signal for understanding the status of the ANS.

Let us consider the argument in more detail. The investigation of the cardiovascular system requires the measurement of the fluctuations in heart rate, in blood pressure and in the rate of respiration. Baroreflex mechanism plays an important role in time evolution of such system since sympathetic and parasympathetic nervous components act at this level in order to provide by competition to the increase and decrease of heart rate, respectively. Parasympathetic modulations result in an inhibitory activity in the sense that by their neural action they slow heart rate by decreasing SA node firing. Acceleratory sympathetic action, induced on the SA node, contributes instead, in a direct manner, to chronotropic cardiac activity. In detail, we must consider here the interaction of such two modulating components of the autonomic nervous system, and the manner in which they contribute to regulate cardiac activity. At the moment, the basic well known features are that the frequency of heart contractions, the speed of impulse conductivity on specific fibres and myocardium contractility increase the chronotropic, the dromotropic, and the inotropic functions of the heart in high correlation with heart enforcing sympathetic intensity. Of course, stimulation of parasympathetic heart innervation determines reduction of heart rate and myocardium contractility.

The studies started with Penaz et al. in 1968, Sayers et al. in 1973, and Akselrod et al. in 1981. Through the results of such studies it became clear at once that the regulative mechanism controlling the behaviors of heart rate, are reflected in some rhythmic oscillations on the beat-to beat set of data that in fact resulted to contain some well-defined rhythms. They were correlated to autonomic LF(low frequency band), and HF(high frequency band), activities, responding the

first mainly to sympathetic and the second to parasympathetic modulations., respectively. The VLF (very low frequency band) was connected to humoral regulation of the sinus pacemaker cell activity.

Starting with such studies, analysis was performed mainly in time and frequency domains. In frequency domain, spectral analysis of a beat-to-beat set of data (the currently known R–R time series) started to be performed, and still it is used, considering usually records of 260–300 consecutive heart beats, and giving HRV results using the fast Fourier transform (FFT). In principle, this technique is able to describe the R–R signal as a sum of several component oscillations at the fixed and equally spaced frequencies. FFT represents an indispensable method of analysis that is valid under extremely general conditions but at the same time it requires also the respect of some crucial restrictions, and in particular that the analyzed signal must be linear, it should be strictly periodic and stationary and all the input data should be sampled at equally spaced time intervals.

As previously outlined, R-R intervals express a net variability reflecting the condition that many physiological mechanisms of regulation and control modulate the rhythm of the heart. The structure generating the R-R signal is not only simply linear, but also involves nonlinear contributions. R-R is a non stationary signal, and just its variability contains important indicators of the functioning of the nervous control on the HR and the heart's ability to respond.

The CZF method has been introduced as a complementary technique of FFT just to account for such determinant factors of non linearity, of non stationarity, of instantaneous variability and complexity. The variability is the conceptual counterpart of such fundamental determinants in R-R dynamics.

Let us focus our attention on such concept. To be clear, let us repeat again that heart rate variability is an important variable whose quantitative measure evidences the basic features of cardiovascular regulation by the autonomic nervous system. Many recent studies have shown that non-linear phenomena are involved in the genesis of R-R interval dynamics because of the complex regulation mechanisms controlling it. Consequently linear statistical analysis in time and in frequency domain must be interplayed with non linear methods. The first consequence of acting non linear components is the Variability of the signal that is to say fluctuations of the heart beating in time. An appropriate method of analysis must aim to quantify such Variability. The CZF method accomplishes to such finality accounting for Variability that is due to all kind of modulating components that are involved in the R-R interval dynamics.

Let us help us with an example in order to illustrate better the appropriateness of the method. Linear or near-linear systems possess a regularity and simplicity that are readily recognizable by scientific investigation. Yet numerous other systems, and especially those pertaining to living beings, possess complexities that are at best nonlinear and often non-predictable. A common ground between living and nonliving systems resides in their shared property of recurrence. That is, within the dynamical signals expressed by living and non-living signals are stretches, short or long, of repeating patterns. As signals grow in complexity, however, recurrences become rarer. For so-called random systems such as it may be a radioactive decay, recurrences occur theoretically by chance alone. Variability represents the conceptual counterpart of recurrence.

Let us give an example on the manner in which variability may be estimated.
For simplicity, consider a series that, for brevity, is given only by six values of consecutive R–R time intervals. We call these data

$$R-R_1, R-R_2, R-R_3, R-R_4, R-R_5, R-R_6$$

The first time we select the time lag h = 1 and we will have

$$[(R-R_1)-(R-R_2)]^2+[(R-R_2)-(R-R_3)]^2+[(R-R_3)-(R-R_4)]^2+[(R-R_4)-(R-R_5)]^2+[(R-R_5)-(R-R_6)]^2 \quad \text{(A1)}$$

In this manner we have estimated the total variability of the considered R-R intervals in the time lag h=1. This is to say that for all the given R-R values we have estimated the total variability of

these values for the subsequent heart beats considered in their real sequence. Consider two subsequent values of R-R intervals, as example

$R-R_1$ *and* $R-R_2$ *or* $R-R_2$ *and* $R-R_3$ *or still* $R-R_3$ *and* $R-R_4$

(in general: R_i and R_{i+1}). For the physiological considerations that we have previously exposed, we obtain that in general $R-R_1, R-R_2, R-R_3, R-R_4, R-R_5, R-R_6$ are different values. The differences $(R_{i+1}-R_i)$ are revealing the fluctuations or the variations characterizing mainly the presence of instantaneous autonomic input modulations. By calculation of the (A.1) we obtain the total variability that is exhibited from our data along all the sequence that we have taken in consideration. In order to outline that we have calculated the Total Variability and only for subsequent heart beats, we will indicate such result by $V(1)$ where V states for the Total Variability that we have calculated and the lag (h=1) indicates instead that we have performed such calculation for subsequent heart beats.

Note some very important features of the method that we have taken in consideration:

a) $V(1)$ represents the Total Variability in correspondence of the time lag h=1. Instead of the Total Variability we could have calculated also properly its mean value as the CZF method really may do.

b) By calculation of $V(1)$ we estimate the total ***Instantaneous*** Variability of the R-R intervals that we have in consideration. Obviously, this is a parameter that is of great importance in the analysis of HRV.

c) The calculation of such total ***Instantaneous*** Variability relates the whole set of R-R interval data that we have under our consideration.

Now let us take a step on. This time we calculate the Total variability for the time lag h=2, that is to say taking differences (R_i - R_{i+1}). We have in this case to calculate the following expression

$$[(R-R_1)-(R-R_3)]^2+[(R-R_2)-(R-R_4)]^2+[(R-R_3)-(R-R_5)]^2+[(R-R_4)-(R-R_6)]^2$$

and in this manner we arrive to estimate the total *Instantaneous* Variability but this time not comparing variations for subsequent heart beats but shifted by one. Thus we estimate as autonomic input modulations induces variability in R-R intervals for heart beats shifted by one. This time we indicate such calculated values by $V(2)$ that is to say total *Instantaneous* Variability for shift equal to 2.

In the same manner we may calculate $V(3)$ that will represent the total *Instantaneous* Variability for a time lag h=3 that is a shift equal to 3.

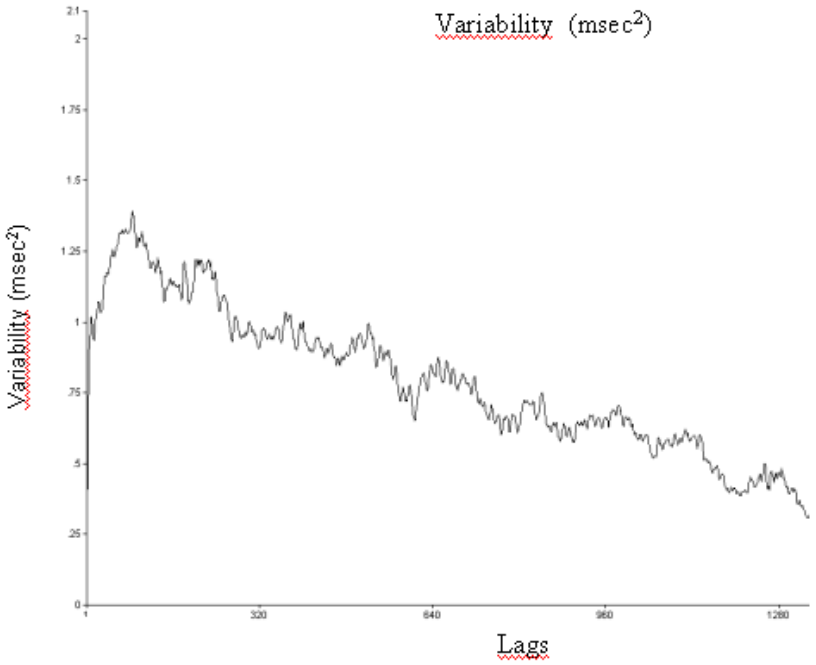
$$[(R-R_1)-(R-R_4)]^2+[(R-R_2)-(R-R_5)]^2+[(R-R_3)-(R-R_6)]^2$$

For $V(4)$ we have :

$$[(R-R_1)-(R-R_5)]^2+[(R-R_2)-(R-R_6)]^2.$$

Finally, we may now represent the results of our CZF analysis of variability by a graph. In abscissa the sign the values of the lags (h=1,2,3,….) and in ordinate the corresponding values of the total *Instantaneous* Variability, $V(1),V(2),V(3),....$ given in $m\sec^2$.

Let us consider as example a series of R-R intervals of $N=1300$ data points. Usually the CZF method computes h-lags=N-3. In this manner in abscissa we have values ranging from 1 to 1297, and in ordinate we have the Variability expressed in msec^2. Figure 1 illustrates the case:



We may now take a step on. We realize a conversion of the previously calculated Varibility data in the frequency domain obtaining this time in abscissa the values of the frequency in Hz ranging from zero to one and in ordinate the corresponding values of the Variability. At this point the analogies with the FFT are evident. In both cases, FFT and CZF method we have a spectral distribution in the frequency domain. In the case of the FFT we have the Power of the components expressed in $msec^2$ as well as in the case of the CZF method we have variability also expressed in $msec^2$.

In the case of the FFT we acknowledge three bands of interest that are the VLF, the LF, and the HF and in addition we calculate the PSD. In analogy, in the case of the CZF method we acknowledge the same three bands VLF,LF,HF and we calculate also the total spectral density of variability that we indicate also by the same PSD. In FFT we calculate the VLF(%),the LF(%), the HF(%) as well as the VLF, the LF, the HF values in normalized unities. Finally we calculate also some rations of interest as LF/HF or VLF/(LF+HF). All such values may be now calculated also in the case of the CZF method but accounting for the substantial conceptual differences that exist between the two methods. By FFT we evaluate the POWER of the modulating inputs in R-R intervals essentially in three bands of frequency, the VLF, the LF, and the HF. By the CZF method we evaluate the Variability in the same three bands of interest. Therefore we have introduced a very powerful instrument of analysis since by FFT we estimate the POWER of the modulating inputs, by the CZF method we estimate instead their instantaneous variability that is of great interest. In HRV analysis we need detailed information about the level of the tone and of the fluctuations that characterize the autonomic inputs in modulation of the R-R intervals. They determine the variability of the signal R-R. The CZF is devoted to analyse such basic features. In this manner we have two complementary instruments of analysis that both contribute to furnish a complete investigation on the dynamics of the considered R-R intervals under examination. Moreover, we are now in the condition to compare the Power of the input modulations with the Variability induced in the modulated R-R intervals. We may reach this objective by quantifying the ratios:

$$\frac{VLF_{PSD(FFT)}}{VLF_{CZF-method}};$$

$$\frac{LF_{PSD(FFT)}}{LF_{CZF-method}};$$

$$\frac{HF_{PSD(FFT)}}{HF_{CZF-method}};$$

obtaining in this manner a complete characterization of the dynamics that is under our analysis. More details on the CZF – method may be found by the following link:

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