Trend and variability of the heart beat RR intervals during the exercise stress test

Camillo Cammarota and Mario Curione

Abstract—**The stress test is performed to evaluate the presence in the electrocardiogram of myocardial ischemia. The heart beat RR intervals extracted from the electrocardiogram recorded during this test show a non stationary profile consisting in a decreasing trend during the exercise phase, an increasing trend during the recovery and a global minimum (acme). In addition this time series exhibits a non constant variability. We decompose the series into a deterministic trend and a random fluctuation. The trend is obtained as an exponential fit of the data; the fluctuation is modeled as the evolution of a stochastic difference equation of Langevin type. Data analysis is performed on ambulatory recorded electrocardiograms of healthy subjects. In particular we show that the variance of the RR intervals is increasing with mean. This behavior, qualitatively similar to the one found in atrial fibrillation, is reproduced by our model.**

Index Terms—**exercise test, heartbeat, RR interval, time series**

I. Introduction

The exercise stress test is performed to evaluate the presence in the electrocardiogram (ECG) of myocardial ischemia. In multistage Bruce protocol [6] the patient on a bicycle ergometer is subjected at a workload linearly increasing in time (25 W every 2 minutes). The test is stopped when the heart rate reaches a maximum, usually 85% of the estimated top heart rate based on the patient's age. During the test 12-leads ECG is monitored.

Diagnosis of ischaemia is usually performed by visual inspection of the ECG signal. Recently our group has started an automated analysis of these ECG data in order to find clinical applications related to QRS area evaluation [4].

During the test the RR intervals, defined as the intervals between two consecutive R peaks, show a typical pattern. During the exercise (stress phase) the trend is decreasing, during the recovery the trend is increasing; these two phases are separated by a global minimum (acme) (fig. 1, first panel).

The variability of the RR intervals, known as Heart Rate Variability (HRV), is quantified by means of several indices both in time and in frequency domain, and it is used to extract informations on the control of autonomic system on heart rate [11]. The estimation of the HRV indices is usually performed on RR sequences recorded at rest, where the sequence can be supposed to be stationary. Evaluation of HRV during the exercise is difficult because the series is not stationary.

The heart rate during exercise was extensively investigated both in clinical studies and in signal analysis. A first approach focuses on the trend component of the RR data, considering mainly the heart rate recovery, defined as the maximum heart rate minus the heart rate at a specified time period during recovery (for instance 1 minute), measured in beats per minute. A heart rate recovery of less than 12 beats per minute in the first minute was found to be a predictor of overall mortality [3].

A second approach removes baseline trend induced by exercise in RR series using a suitable filtering and then evaluates HRV on the filtered sequence. Several indices estimated over intervals of two minutes were found to be predictors of cardiovascular mortality [5]. In this study it is recognized that the RR variability is related to the RR interval values.

In signal analysis time-frequency methods were applied to estimate how low frequency (LF) and high frequency (HF) spectral components vary in time. In application to real data low frequencies have been filtered out [8]. The above references show the usefulness of information contained both in the trend (heart rate recovery) and in residual after detrending (time and frequency domain indices).

In this report we analyze the RR series extracted during the routine ambulatory bicycle exercise test of normal subjects. We investigate the series using the decomposition of time series in two main components: deterministic trend and stochastic variability.

The first result confirms the observed dependence of the RR variability on the RR value, i.e. that the series is heteroschedastic. We try to quantify this dependence estimating the slope of the linear fit of standard deviation versus mean for blocks of adjacent beats. This was already observed in atrial fibrillation and was proposed to discriminate this pathology [12]. In that paper the coefficient of variation (defined as standard deviation over mean) was estimated. A linear dependence of standard deviation versus mean was also found in [1].

The evidence of heteroschedastic behavior in normal subjects during stress has stimulated the use of novel methods to investigate non stationary time series [2].

The second result concerns the trend: we propose a method for estimating the trend based on a simple mechanical model. The trend is defined by an exponential fit of the data series, separately in stress and recovery.

Finally we propose a dynamical model for the stochastic variability defined by a difference stochastic equation of Langevin type. These models have been recently used in the reconstruction of the RR series ([7], [9]). In our model we use a drift and a diffusion term that allow to reproduces some qualitative features of the data, in particular the heteroschedastic behavior.

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II. METHODS

The subjects of our analysis were selected from a group referred for symptoms and signs suggestive of myocardial ischemia to ECG Laboratory. They underwent to clinical examinations, exercise test, standard 12-leads ECG and scintigraphy. Multistage Bruce protocol diagnosis of inducible ischemia was used according to current guideline [6]. From the subjects who underwent the test, those of them who resulted healthy are the object of the present study; no other selection criteria has been adopted.

In our experimental setting the standard 12 leads ECG was performed using PC-ECG 1200 (Norav Medical Ltd.) which provides in output digital signal with resolution of 2.441 microV and 500 Hz sampling frequency. The analysis of raw data, R peak detection, and subsequent computations were performed using a software written in R [10]

III. THE LOCAL MEAN AND VARIANCE

We model the observed RR time series $x_1, ..., x_n$ as the realization of a sequence of random variables (r.v.) $X_1, ..., X_n$, with joint continuous distribution P. Hence X_t denotes the RR interval at the t-th beat. A sequence of r.v. is called stationary if the probability distribution of any collection extracted from it is invariant under time shift. In particular if μ_t and σ_t denote mean and standard deviation of X_t, in a stationary case these functions are constant with respect to time. In RR series during stress both the mean and the variance are time dependent. Hence it is natural to ask if there is a relationship between mean and variance. At first glance from the plots of the RR series m_t and σ_t appear to be positively dependent. In other words when the RR interval takes its minimum (acme) the variance takes its minimum, and when the RR interval is maximum the variance is large (fig. 1 first panel). In order to estimate both the mean and the variance, we divide the time series into a set B of blocks made of $D = 40$ successive beats and compute the mean m_b and the standard deviation σ_b for each block $b \in B$. Since the trend introduces a bias in the estimation of the variance, we perform a linear detrending in each block. The standard deviation is then computed on the residuals after detrending. The plot of residuals is shown in fig. 1 (second panel). The pairs m_b and σ_b are plotted and the slope of the linear fit of σ_b versus m_b is computed. A typical plot is in fig. 1 (third panel). The use of different values for the block size D do not substantially alter the plot. We have selected in our database 11 cases of normal subjects in which the linear dependence appears to be more evident and statistically significant. The mean of slopes over these cases is 0.043 with a standard deviation of 0.017. The value 0.043 in normal subjects is much smaller than the one 0.24 found in atrial fibrillation [12].

IV. TIME SERIES DECOMPOSITION

The RR series shows a global minimum called 'acme' whose value is denoted m. We define as 'stress phase' the sequence of beats before the acme and as 'recovery phase' the ones after the acme. The duration of the stress phase is t_1 beats; the global duration is t_2 beats; typical values are $t_1 = 1500, t_2 = 2500$. We introduce a simple mechanical model to describe the time evolution of the RR interval in the two phases. The stress phase is characterized by an external action due to the increasing workload that causes an increasing of the heart rate. In both phases there is a so called 'equilibrium' M, corresponding to the mean value of the RR intervals immediately before and after the test. Of course $M > m$; typical values are $M = 800$ msec, $m = 400$ msec (see fig.1, first panel). The equilibrium values may be slightly different: for instance in the case of fig. 1 the equilibrium value at the beginning is larger than the one at end of the recovery. We denote them as M_1 and M_2.

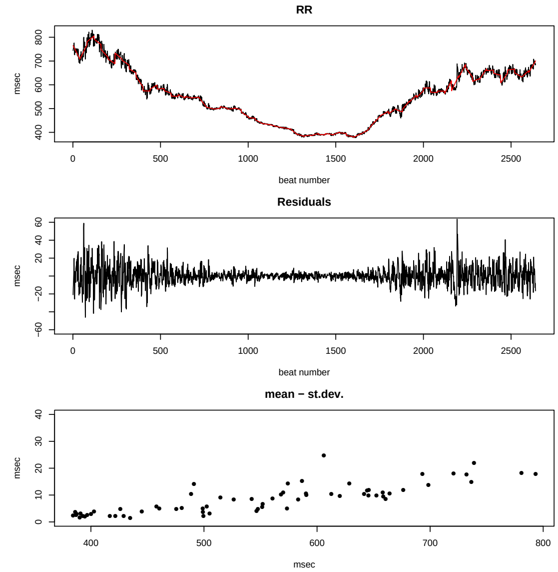

Fig. 1. First panel: Sequence of RR intervals (in msec) of the exercise test of a normal subject versus the beat number. Second panel: the residuals after detrending. Third panel: the standard deviation of residuals versus mean for blocks of 40 beats.

We use the classical method of time series decomposition in trend and fluctuation. In order to estimate the trend we first introduce a function $\alpha(t)$, where t is a real number in the interval $[0, t_2]$, which is solution of a differential equation. We use that both the phases are characterized by a restoring term that drives the system towards the equilibrium M. For sake of simplicity we assume that this term is linear: $-a(\alpha - M)$, where a is a positive constant. In addition the stress phase is characterized by a constant negative contribution $-b$ that reflects the workload. We assume $\alpha(t)$ to be solution of the two following ordinary differential equations in different time intervals

$$\begin{array}{l} \alpha_1' = -a_1(\alpha_1 - M_1) - b \\ \alpha_1(0) = M_1; \quad t \in [0, t_1] \end{array} \tag{1}$$

$$\begin{array}{l} \alpha_2' = -a_2(\alpha_2 - M_2) \\ \alpha_2(0) = m; \quad t \in [t_1, t_2] \end{array} \tag{2}$$

These equations have exponential solutions:

$$\alpha(t) = \begin{cases} M_1 - \frac{b}{a_1}(1 - e^{-a_1 t}) & t \in [0, t_1] \\ M_2 + (m - M_2)e^{-a_2(t-t_1)} & t \in [t_1, t_2] \end{cases} \tag{3}$$

Hence the trend of our series can be defined as the discretization of $\alpha(t)$, denoted α_t.

The fluctuation is now defined according to the following equation in both phases:

$$\Delta X_t = -k(X_t - \alpha_t) + (\alpha_t - m)\epsilon_t; \quad t \in [1, t_2] \qquad (4)$$

We assume that the initial value is $X_1 = M_1$ and ϵ_t is a stationary sequence with zero mean and variance σ_ϵ^2. For the proposes of the present study we shall assume that the ϵ_t are independent and identically distributed (i.i.d.) normal variables.

The eq.(4) is a finite difference stochastic equation of Langevin type. The investigation of its theoretical properties is outside the scope of the present report. We recall that the simple equation $\Delta X_t = \epsilon_t, \quad X_0 = 0$ has as solution a random walk, that is non stationary; in particular if ϵ_t is normal, the sequence X_t is a sequence of normals with mean zero and variance $\sigma_\epsilon^2 t$. The term $-k(X_t - \alpha_t)$ drives the random walk towards the deterministic trend α_t. The coefficient $\alpha_t - m$ of the diffusion term produces the dependence of standard deviation versus mean. The use of this type of equation in the analysis of RR series is not new ([7], [9]), but the presence of an explicit trend was not considered before.

V. Estimation of the parameters and data analysis

The parameters m, M_1, M_2, t_1, t_2 are estimated just by observation of the time series. In particular M_1, M_2 are estimated by the mean of say 20 values at both the extremes. In order to estimate t_1 the RR series is smoothed so that there is only one time in which the series takes its minimum. The values are reported in the Table I. The parameters a_1, a_2, b are not observable directly and have to be estimated from the model. From the solutions (3) a rough estimate of the parameters a_1, a_2, b can be obtained. These values are used as starting ones in a non linear least squares estimation of the same parameters from the data series. The values obtained are reported in Table II. The exponential fitting obtained is satisfactory in all cases; a typical case is in fig. 2.

The estimation of the parameters in the second member of eq. (4) is outside the scope of the present communication. We limit ourselves to verify that for suitable values of the parameters the model qualitatively reproduces the data series and the plot of standard deviation versus mean reproduces the observed one.

In fig. 3 an example of a simulated series is shown in the second panel. The parameters of the trend are in the 3th row of the two tables. The parameters of the model in eq.(4) are $k = 0.1, \sigma_\epsilon = 0.06$. The third panel shows the relationship between mean and standard deviation.

VI. Conclusion

The plot of standard deviation versus mean has revealed that in normal subjects there is a positive correlation between the two variables, of the same type that was found in atrial fibrillation [12], but much smaller. In order to better understand the dynamics we have performed a decomposition of the RR series in trend and random fluctuation. We have simulated the series using a small number of parameters, if compared to the complexity of this type of data. We have used 8 parameters: each of the two exponential fits requires 3 parameters and the stochastic evolution requires 2 parameters. We are able to reproduce both some qualitative features of the data and the observed dependence mean - standard deviation.

The capability of this model to reproduce finer features of the data should be investigated. In heart rate variability studies a lot of indices both from linear and non linear modeling are used in time domain and in frequency domain. Most of them are defined only if the series is stationary. Thus they can not be applied to these RR data series. The proposed model suggests which are the components responsible for non stationary behavior. With reference to equation (4) they are the restoring term $-k(X_t - \alpha_t)$ and the coefficient of the diffusion $(\alpha_t - m)$; some other information should be contained in the

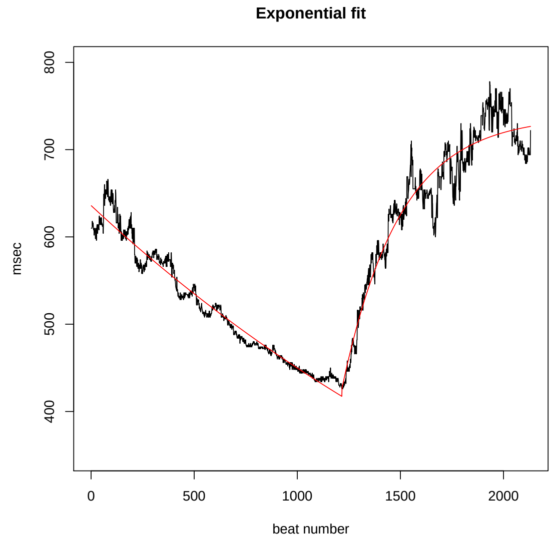

Fig. 2. The RR series and the exponential fit both for the stress and for the recovery phases.

TABLE I
Parameters of the RR series: from the left: duration in beats of the stress phase, total duration of the test, minimum RR in msec, maximum in stress, maximum in recovery.

t1	t2	m	M1	M2
1218	2373	377	665	701
2021	3223	331	534	593
1601	2662	383	749	679
2094	3217	342	571	597
2098	2883	369	814	642
1303	2213	418	855	762
1225	2459	389	634	544
1147	2062	395	678	723
1219	2131	421	610	696
2030	3097	365	492	594
986	1764	411	624	583

TABLE II
ESTIMATED PARAMETERS OF THE EXPONENTIAL MODEL: RESTORING COEFFICIENT OF THE TRESS, RESTORING IN RECOVERY, DRIFT.

a1	a2	b
0.0004	0.0040	0.357
0.0008	0.0021	0.236
0.0010	0.0022	0.529
0.0002	0.0018	0.175
0.0007	0.0004	0.433
0.0005	0.0030	0.433
0.0004	0.0044	0.253
0.0003	0.0062	0.324
0.0007	0.0036	0.269
0.0002	0.0037	0.159
0.0005	0.0004	0.334

random sequence ϵ_t. This sequence could be estimated from the data, after estimation of the parameter k, using the equation (4):

$$(\Delta X_t + k(X_t - \alpha_t))/(\alpha_t - m) = \epsilon_t \quad (5)$$

The sequence ϵ_t should be close to stationary so that a residual information could be extracted using standard methods.

There are several other possible improvements concerning the estimation of the parameters of the dynamical model. The values of M_1 and M_2 are in many cases different; this can be caused by the fact that the recovery phase is shorter than the stress. Also the parameters a_1 and a_2 are different. They reflect the strength of the restoring towards equilibrium which in turn is regulated by the neuroautonomic control. It is an interesting problem to test if these differences are significant. Another problem concerns the form of the diffusion term $(\alpha_t - m)\epsilon_t$. This simple form assumes that the variance reduces to zero at the acme, i.e. if $\alpha_t = m$. One can introduce another parameter to have a non zero variance. A reliable estimation of the variance close to the acme requires a higher resolution of the RR intervals and could be achieved using an ECG signal of higher sampling frequency. Other forms can be considered for the diffusion and in particular to assume that the variance increases non linearly in the difference $(\alpha_t - m)$.

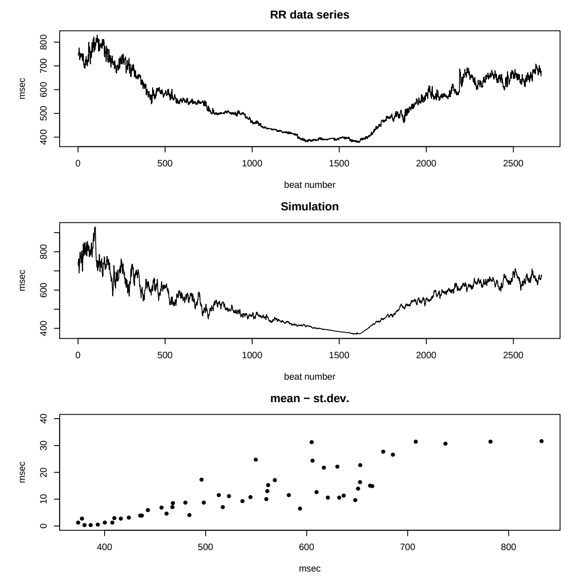

Fig. 3. First panel: data series of RR intervals; second panel: series obtained after simulation of the model with trend parameters estimated from the above; third panel: plot of standard deviation versus mean of the simulated series

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