Feasibility of Ultra-short Term Complexity Analysis of Heart Rate Variability in Resting State and During Orthostatic Stress*

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Abstract— **In this work, we study ultra-short term (UST) complexity of Heart Rate Variability (HRV) and its agreement with analysis of standard short-term (ST) HRV recordings obtained at rest and during orthostatic stress. Conditional Entropy (CE) measures have been computed using both a linear Gaussian approximation and a more accurate model-free approach based on nearest neighbors. The agreement between UST and ST indices has been compared via statistical tests and correlation analysis, suggesting the feasibility of exploiting faster algorithms and shorter time series for detecting changes in cardiovascular control during various states.**

I. Introduction

Over the last decades an increasing interest has been devoted to understand the complex mechanism of the autonomic nervous system (ANS) regulation in different physiological and pathological conditions [1]. Since the cardiovascular system is strongly influenced by ANS, heart rate variability (HRV) is one of the most investigated time series for the characterization of heart rate control. Starting from the R-R intervals (RRI) time series extracted from electrocardiographic (ECG) signals, HRV analysis can be performed in time, frequency and also information-theoretic domain [1]. In particular, entropy-based measures such as Conditional Entropy (CE) can provide information about the neural autonomic regulation and specifically the degree of control system complexity. The analysis of 300 heartbeats time series (corresponding to about 5-minute recordings), usually referred to as short-term (ST) HRV, has been long considered a standard for assessing the cardiovascular dynamics and the autonomic regulation [1]. Recently, researchers have further explored whether and to what extent shorter time series, i.e. the so-called ultra-short term (UST) analysis, can be employed in place of ST for assessing cardiovascular dynamics, given the undoubted advantages in terms of real-time processing costs and storage [2].

In this work, we compute CE measures using two different estimators, i.e. a faster linear Gaussian approximation and the standard model-free approach, on UST time-series, compared to standard 300 beats recording, at rest and after eliciting orthostatic stress, to investigate their feasibility for assessing the complexity of cardiovascular dynamics during application of physiological stressor.

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II. Materials and Methods

A. Experimental protocol and time series extraction

The data analyzed in this work consisted of an historical dataset acquired on 61 healthy normotensive subjects (37 female; age: 17.5 ± 2.4 years) [3]. The measurement protocol included two phases: (i) a 15-minute long supine rest (R) during which the subjects were lying in the supine position on a motorized table; (ii) a 8-minute long head-up tilt phase (T) after tilting the table to 45 degrees to evoke postural stress. Starting from ECG signals acquired using a horizontal bipolar thoracic lead (CardioFax ECG-9620, NihonKohden, Japan, 1 kHz sampling rate), RRI time series were extracted as the temporal distance between the n-th and $(n+1)$-th QRS apexes. In order to ensure stationarity, the 300-beats long (ST) time series were obtained starting 8 min after the beginning of R and 3 min after the beginning of T phases, respectively. Further details on the ethical approval, data acquisition and preprocessing can be found in [3]. The shorter time series were then extracted repeatedly eliminating the last 30 points each time, thus obtaining UST segments ranging from N=270 down to N=120 heartbeats. Finally, all the time series were normalized to zero mean and unit variance before computing the complexity measures.

B. Complexity measures

For a stationary stochastic process $\boldsymbol{X}$, starting from the Shannon entropy theory it is possible to define CE as [4]:

$$CE(X) = H(X_n, \boldsymbol{X}_n^-) - H(\boldsymbol{X}_n^-) \quad (1)$$

where $H(\cdot)$ and $H(\cdot,\cdot)$ denote respectively entropy and joint entropy, whereas X_n and $\boldsymbol{X}_n^-$ are the random variables describing the current and the past states of the process $\boldsymbol{X}$, respectively. The CE reflects the amount of information available in the present sample which cannot be inferred from the past, measuring the average uncertainty about the present state of X when its past is known. In this study, the estimation of CE has been performed on RRI time series through two different estimation methods, i.e. a faster linear Gaussian approximation (herein referred as *lin*) and the standard more accurate, but also more time-consuming k-nearest neighbor (*knn*) technique. The linear parametric approach relies on the fact that many real data tend to a Gaussian distribution, while the *knn* method instead exploits the intuitive notion that the probability density of a point decreases as the distance from itself and its neighbors increases. We refer the reader to [5] for further information about the estimators employed for computing CE. In this work, an autoregressive model of order p=2 was employed in the *lin* approach, while k=10 neighbors and m=2 past components were used w.r.t. *knn* method.

C. Statistical analysis

The statistical significance of the results was assessed using the parametric Student's t-test, given the hypothesis of the CE distributions normality was verified through the Kolmogorov-Smirnov test. In detail, the t-test was used to compare T vs R CE distributions and, for a given phase, each UST (N<300) distribution to the reference ST (N=300 beats). For all the analyses, the significance threshold was set to $p<0.05$. The squared Pearson correlation coefficient r^2 was also computed as a measure of the agreement between each UST and the reference ST distribution. Finally, in order to assess the effect size between T and R distributions for a given N length, the Cohen's d measure was computed as the difference between the means of the distributions divided by the standard deviation.

III. Results

Fig. 1 panels (a.1) and (b.1) show the distributions of CE values across 61 subjects in R and T computed through *lin* and *knn* estimator, respectively. For both estimators and for all the N lengths, CE values are significantly lower during orthostatic stress if compared to rest, with a high effect size (i.e., d>0.8) as well (panels a.2 and b.2). When comparing UST distributions with the ST reference, *knn* estimator led to significantly higher values of CE for all the N lengths (panel b.1), while the linear one reported this result only during T for lower N values (150 and 120 beats). Finally, the squared Pearson correlation coefficient r^2 decreases with N for both estimators, remaining higher than 0.81 (panels a.3 and b.3).

IV. Discussion and Conclusion

Our results prove the feasibility of employing CE measures computed through *lin* and *knn* estimators to detect changes from rest to tilt phases, also when using shorter time series. Physiologically, the decrease in complexity shown during T is due to the activation of the sympathetic system and the withdrawal of the parasympathetic one and is in agreement with previous short-term HRV studies [6]. We complement such findings demonstrating that alterations in dynamics complexity are also detectable analysing shorter time series, down to 120 heartbeats. The agreement with the reference ST time series decreases with the length N, in accordance to previous studies demonstrating that the reliability of UST analysis in assessing physiological changes may be lower when reducing sample length [2], [7]. In agreement with Castaldo *et al.* [2] setting a threshold of the correlation coefficient (r=0.9) to assess the agreement of the results obtained between UST and standard ST analysis, herein we set r^2=0.81, and all the obtained results are above this threshold. Besides, the significant increase in the complexity revealed by *lin* estimator (Fig.1 panel a.1) at decreasing N length (N >= 150 beats) if compared to N=300 beats (even if only during T) evidences that nonlinear mechanisms dominant in the cardiovascular dynamics (reported e.g. in [6]) may be lost when analyzing shorter time series [2]. This is confirmed analyzing the results obtained through *knn* analyses (panel b.1), demonstrating significant variations already at N=270 beats.

Overall, the obtained results suggest that ultra-short term time series are still feasible to assess the degree of control system complexity, and that the linear estimator could be the most appropriate choice given its computational and timing advantages with respect to the nonlinear one [5]. Future studies should foresee the computation of further information domain indices to have a better insight in employing UST analysis for cardiovascular dynamics assessment.

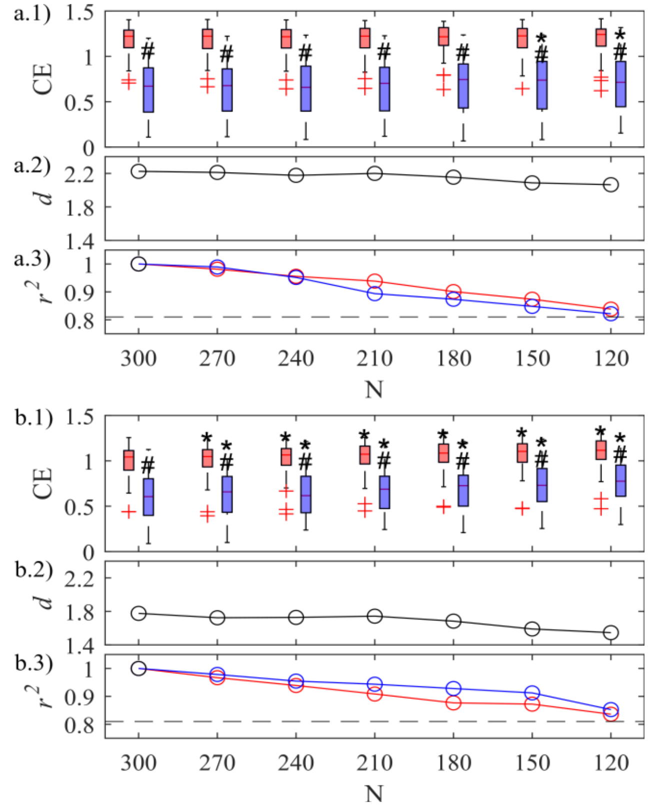

Fig. 1. Results of complexity analysis for different time series length N using both *lin* (a. subplots) and *knn* (b. subplots) estimators during R (red) and T (blue) conditions. (.1) subplots: boxplot distribution of CE values; statistical test results: #, $p<0.05$ paired Student t-test between conditions (T vs R); *, $p<0.05$ paired Student t-test between each UST (N<300 beats) and ST (N=300 beats) distributions; (.2) subplots: Cohen's d computed between T and R distributions for each N. (.3) subplots: squared Pearson correlation coefficients computed between a given UST distribution and the reference ST. Dotted line: threshold r^2=0.81.

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