Exploring the Short-Term Memory of Heart Rate Variability through Model-Free Information Measures

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Exploring the Short-Term Memory of Heart Rate Variability through Model-Free Information Measures

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Abstract—In this work, we perform a comparative analysis of discrete- and continuous-time estimators of information-theoretic measures quantifying the concept of memory utilization in short-term heart rate variability (HRV). Specifically, considering heartbeat intervals in discrete time we compute the measure of information storage (IS) and decompose it into immediate memory utilization (IMU) and longer memory utilization (MU) terms; considering the timings of heartbeats in continuous time we compute the measure of MU rate (MUR). All measures are computed through model-free approaches based on nearest neighbor entropy estimators applied to the HRV series of a group of 15 healthy subjects measured at rest and during postural stress. We find, moving from rest to stress, statistically significant increases of the IS and the IMU, as well as of the MUR. Our results suggest that both discrete-time and continuous-time approaches can detect the higher predictive capacity of HRV occurring with postural stress, and that such increased memory utilization is due to fast mechanisms likely related to sympathetic activation.

I. INTRODUCTION

Heart rate variability (HRV) series exhibit memory effects that determine to a different extent their predictability depending on cardiac autonomic regulation, cardiovascular mechanics, circadian rhythms and other physiological factors. Such memory effects are typically deployed over multiple different time scales: while long-range correlations are detected from HRV recordings lasting several hours [1], the so-called short-term HRV refers to memory effects spanning time scales in the order of a few minutes [2]. Short-term HRV is typically investigated using spectral analysis or, in the time domain, using linear parametric or nonlinear model-free measures of predictability [3]. The latter approach is often preferred because it allows to detect memory effects related to complex mechanisms of physiological regulation which may result in nonlinear correlations. The non-parametric analysis of HRV and other physiological time series is typically performed using information-theoretic measures such as the information storage (IS) [4], which allows to detect virtually any type of interaction and offers the flexibility to define measures able to capture specific aspects of the investigated dynamics. In this regard, information measures applied to physiological variability series have been used to infer the relevance of short-lag and longer memory effects respectively related to fast and slower physiological mechanisms, possibly associated to sympathetic and vagal short-term regulation [5].

The short-term memory of HRV is typically investigated using measures of information storage computed for discrete-time processes where the variable of interest is the interbeat interval [4]. However, continuous-time formulations have recently emerged to compute measures of coupling and causality which work for continuous processes where the variable of interest is an event (in the case of HRV, the heartbeat) [6]–[9]. In this context, in a recent preliminary work we have proposed an approach to quantify the rate of memory utilization in simulated heartbeat dynamics reproducing HRV [10]. The aim of the present study is to compare this continuous-time estimator of the predictive capacity of HRV with the model-free discrete-time estimator of the IS, also considering a decomposition of the latter into quantities measuring short-lag and longer memory effect. The work is focused on understanding the cardiovascular control mechanisms leading to HRV and on providing information about their latency in different physiological conditions (here, supine rest and postural stress).

II. INFORMATION-THEORETIC ASSESSMENT OF THE MEMORY OF HEART RATE VARIABILITY

In this work, we consider the cardiovascular system as a dynamical system whose activity is described by two types of random processes: a continuous-time point process \( R \) described by the times of occurrence of the heartbeats (times of each R peak in the electrocardiogram, ECG), and a discrete-time random process \( X \) described by the duration of the heartbeat intervals (heart periods). An exemplary realization of these processes is reported in Fig. 1a, showing the events \( t_i \) of the point process \( R \) and the observations \( x_i \) of the process \( X (i \in \mathbb{Z}, t_i \) is the time of the \( i \)th heartbeat and \( x_i = t_{i+1} - t_i \) is the duration of the \( i \)th heartbeat interval). In the following, we formulate measures of the predictive capacity of the observed dynamical system defined in discrete time for the process \( X \) (information storage [4] and its decomposition into short- and long-memory effects) and in continuous time for the process \( R \) (memory utilization rate [11]).

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A. Discrete-time Formulation

The discrete-time process \( X \) is defined at each heartbeat time \( t_i \), and quantifies the duration \( x_i \) of the \( i^{th} \) R-R interval. The capability of this process to keep predictable information over time is quantified by the so-called information storage (IS), an information-theoretic quantity defined for a stationary process as \( S_X = I(X_i; X_{i-1}) \), where \( X_i \) is the random variable sampling the process at the current time \( t_i \), \( X_{i-1} = [X_{i-1}, X_{i-2}, \ldots] \) is the infinite-dimensional variable covering the past history of the process sampled at the times \( t_{i-1}, t_{i-2}, \ldots \), and \( I(\cdot; \cdot) \) denotes mutual information (MI).

The quantity \( S_X \) measures the amount of information about the present state of the process that can be explained by its own past states. As such, it reflects the predictability (regularity) of the process dynamics resulting from the presence of memory. Interestingly, the IS can be decomposed to evidence the separate contributions of “immediate” (one-lag) and longer-memory effects to the overall memory of the process \( X \), exploiting the chain rule for MI to get:

\[
S_X = I(X_i; X_{i-1}) + I(X_i; X_{i-1}|X_{i-1}) = I_X + M_X.
\]

(1)

In (1), the term \( I_X = I(X_i; X_{i-1}) \) quantifies the information shared by the current R-R interval \( X_i \) and the interval \( X_{i-1} \) immediately preceding it, while \( M_X = I(X_i; X_{i-1}|X_{i-1}) \) quantifies the information that the past intervals \( X_{i-2}, X_{i-3}, \ldots \) share with \( X_i \) but not with \( X_{i-1} \); these two measures are denoted as immediate memory utilization (IMU) and memory utilization (MU). These three measures can be expressed evidencing marginal and conditional probability distributions of the heartbeat intervals using the expectation operator \( \mathbb{E}[\cdot] \) as follows:

\[
S_X = \mathbb{E} \left[ \ln \frac{p(x_i|x_{i-1})}{p(x_i)} \right],
\]

(2)

\[
I_X = \mathbb{E} \left[ \ln \frac{p(x_i|x_{i-1})}{p(x_i)} \right],
\]

(3)

\[
M_X = \mathbb{E} \left[ \ln \frac{p(x_i|x_{i-1})}{p(x_i|x_{i-1})} \right].
\]

(4)

In sum, the decomposition (1) shows how the IS, quantified as the information carried by the present state of the observed system which is attributable to its past states, can be split into a contribution measuring the immediate usage of memory occurring within one single time step (i.e., the IMU) and a contribution measuring the usage of memory attributed to time lags longer than one (i.e., the MU).

B. Continuous-time Formulation

In this section, considering that event-based processes like the heartbeats are more naturally described by continuous-time point processes [9], [12], we describe the formalism introduced in recent theoretical works to compute measures of information dynamics in continuous time [11]. These works have highlighted the importance, when continuous-time information-theoretic measures are computed analyzing discrete-time processes in the limit \( \Delta t \to 0 \) (where \( \Delta t \) is the sampling time of the discrete-time process), of normalizing the measures by \( \Delta t \) so as to obtain rates quantified in [nats/sec], providing in this way their convergence. However, when the analysis aims at quantifying the predictive capacity of continuous-time processes, the same works have shown that a convergent rate of the IS does not exist; moreover, considering the decomposition (1) applied to information rates, the divergent properties of the IS rate are inherited solely by the MU rate term, while the so-called memory utilization rate rate (MUR) is convergent and quantifies the active memory usage of the process as it is understood in an intuitive manner [11].

Importantly, when the analyzed continuous-time process reduces to a point process, the MUR measure can be formalized in a way that allows its practical computation [8], [9], [11]. In particular, following the formulations in [11], the MUR of the heartbeat point process \( R \) for which \( N \) heartbeats occur in a period \( T \), can be defined as

\[
\hat{M}_R = \lambda_R \mathbb{E}_{p_t} \left[ \ln \frac{\lambda_{R,t_i} R_t}{\lambda_{R,t_i} R_t} \right],
\]

(5)

where \( \lambda_{R,t} R_t \) and \( \lambda_{R,t_i} R_t \) are the instantaneous event-rates of \( R \) evaluated at the time of its \( i^{th} \) event \( t_i \) (i.e., the \( i^{th} \) heartbeat), conditioned respectively on its whole past history and on its previous event only, and \( \lambda_R = N/T \) is the average event-rate of \( R \) (i.e., the mean heart rate). The instantaneous event rate at the generic time \( u \) is defined as

\[
\lambda_{R,u} = \lim_{\Delta u \to 0} \frac{p_u(N_{R,u+\Delta u} - N_{R,u} = 1)}{\Delta u},
\]

(6)

where \( N_{R,u} \) is the number of events occurred up to time \( u \); \( p_u \) is a probability density evaluated in continuous time (i.e. at any time \( u \)), which differs from the probability \( p_t \) in (5) which is evaluated at the target events \( t_i \). Then, substituting (6) in (5), making a Bayes inversion and noting that \( \lim_{\Delta u \to 0} p_u(|N_{R,u+\Delta u} - N_{R,u} = 1) = p_t(\cdot) \), the MUR can be rewritten as [8]

\[
\hat{M}_R = \lambda_R \mathbb{E}_{p_t} \left[ \ln \left( \frac{p_t(R_{t_i}^1)}{p_t(R_{t_i}^1)}, \frac{p_u(R_{t_i}^1)}{p_t(R_{t_i}^1)} \right) \right],
\]

(7)

where \( R_{t_i}^1 \) and \( R_{t_i}^1 \) denote the short-term memory of the process and its whole past history.

C. Estimation Strategy

This section describes how the discrete-time IS, IMU and MU measures defined in (2-4) and the event-based MUR measure defined in (7) were computed in practice from a series of heartbeat events. For both discrete- and continuous-time measures, the estimation strategy is based first on building realizations of the short (one-lag) and long (>1 lag) past histories of the process by using time-delay embedding, and then computing the quantities in (2-4) and (7) via nearest neighbor estimator of the entropy measures [8], [13].
The quantities defined in discrete time (Fig. 1a) and referring to the time instant \( t_i \), a realization of the whole past history \( X_{t_i} \) needed to compute the IS is approximated by \( l = 3 \) intervals preceding the present moment \( t_i \); the history at the previous event \( t_{i-1} \) defines the present state (black arrows). The history at the previous event \( t_{i-1} \) is considered taking the intervals immediately preceding \( t_i \) (red arrows) or random event \( u_i \) (purple arrows); the history at the previous event \( t_{i-1} \) is approximated by \( x_{i-3}, x_{i-2}, x_{i-1} \), while longer-memory effects used to compute the MU are approximated by the vector of \( [x_{i-2}, x_{i-3}] \).

In the case of the continuous-time estimator (Fig. 1b), when histories are reconstructed for computing \( p_i \) (see Eq. 7), realizations of the whole history \( R_{t_i} \) are approximated using an embedding vector formed by the \( l \) inter-event intervals preceding the present moment \( t_i \) \((r_{t_i} \approx [x_{i-1}, x_{i-2}, x_{i-3}])\), of which \( r_{t_i}^1 = x_{i-1} \) represents the history at the previous event; when histories are reconstructed for computing \( p_u \), time points \( u_i \) are placed randomly along the time axis and the whole history \((r_{u_i} = [r_{u_i}^1, r_{u_i}^2])\) is approximated joining the history as the previous event \((r_{u_i}^1 = u_i - t_i)\) with the \( l - 1 \) inter-event intervals preceding \( t_i \) \((r_{t_i} \approx [x_{i-1}, x_{i-2}])\).

These history embeddings are then used to compute the entropies resulting from (2-4) and from (7) using the k-Nearest Neighbour (kNN) estimator. The estimator is implemented according to the strategies described in detail in Ref. [13] as regards the discrete-time estimator and in Refs. [8], [9] as regards the continuous-time estimator.

### III. Application to Heart Rate Variability

#### A. Experimental Protocol and Data Analysis

The proposed methods were applied to investigate memory utilization in time series of heart rate variability measured from healthy subjects during a protocol of postural stress [14]. Specifically, fifteen young healthy subjects (25 ± 3 yrs) were considered for the analysis and were monitored recording the ECG (lead II, sampling frequency of 1 kHz) for 15 minutes in the resting supine position, and for 15 minutes in the 60° upright position reached passively after tilting the motorized bed table. The data analyzed consisted of sequences containing the timings of the consecutive R peaks in the ECG (event series of the R times). For each subject, the series were cleaned up from artifacts and windowed to \( N = 300 \) events in each of the two experimental conditions (REST and TILT). The estimation approaches described in Sect. II were implemented to compute the IS and decompose it into the IMU and MU components in discrete time, and to compute the MUR in continuous time. Computations were carried out using \( k = 15 \) neighbors to estimate entropies via the kNN method, and varying the embedding length in the range \( l = 2, 3, 4 \).

The method of surrogate data was used to assess the statistical significance of each estimated measure, in order to establish the presence of non-negligible memory effects [3], and to compensate the bias of the MUR estimate via the approach proposed in [9]. Specifically, for each original heartbeat series, 100 sequences of surrogate event series were obtained by randomly shuffling the inter-event intervals, and then the considered measure was deemed as statistically significant if its value obtained on the original series exceeded the 95\textsuperscript{th} percentile of its distribution evaluated on the surrogate series. The statistical significance of the differences in the median value of each measure evaluated in the REST and TILT conditions was assessed by means of the non-parametric Wilcoxon signed-rank test for paired values, assuming a 5\% significance level.

#### B. Results and Discussion

Fig. 2 reports the distributions across subjects of the measures quantifying the predictive capacity of heart rate variability in the two analyzed experimental conditions. When the process is analyzed in discrete time considering heartbeat intervals, we see that the IS is statistically significant in all subjects and increases significantly moving from rest to tilt (Fig. 2a). This result confirms previous findings in the literature and is in agreement with the presence of regular oscillations in the heart period time series and with the increase of the regularity of these oscillations related to the sympathetic activation induced by postural stress [3], [9], [14]. The decomposition of the IS defined in (1) reveals that the IMU term behaves like the IS, being significant in all subjects and increasing with tilt (Fig. 2b), while the MU term displays an opposite behavior, being smaller and showing a tendency to decrease with tilt (statistically significant for \( l = 2 \), Fig. 2c). These results suggest that immediate memory effects prevail in
the storage of information within heart rate variability, while longer effects (interval > 1) are often negligible and further dampened during the orthostatic stress. The importance of fast memory effects and their prevalence during tilt compared to rest was shown also regarding cardiovascular interactions in a previous work computing lag-specific transfer entropy [5].

The continuous-time analysis shows that the rate of memory utilization computed for the sequences of heartbeat times behaves similarly to the overall and immediate predictive capacity of the process computed for the series of heartbeat intervals. Indeed, the MUR measure shows a statistically significant increase while moving from the supine to the upright position (Fig. 2d), similarly to what observed for the discrete-time measures of IS and IMU (Fig. 2a,b). These findings provide an empirical confirmation of the fact that the MUR measure is able to capture fast memory effects, where a "fast" effect is here intended at a discrete-time resolution—considering the interval preceding the current one.

IV. CONCLUSIONS

This study performed a comparative analysis between information-theoretic approaches for quantifying the concept of memory utilization in short-term HRV: the standard discrete-time interval-based method, and a novel continuous-time event-based method. Our results indicate that the two approaches can detect equally well the increased predictive capacity of HRV occurring with postural stress, and that the event-based measure correlates with the interval-based measure of fast memory effects.

Future studies should better explore the link between discrete- and continuous-time approaches for the analysis of short-range correlations in HRV, particularly regarding the assessment of time-lagged interactions which can be associated to the latency of the physiological mechanisms evoked by different patho-physiological conditions.

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