Point-Process High-Resolution Representations of Heartbeat Dynamics for Multiscale Analysis: a CHF Survivor Prediction Study

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***Abstract*— Multiscale analysis of human heartbeat dynamics has been proved effective in characterizeing cardiovascular control physiology in health and disease. However, estimation of multiscale properties can be affected by the interpolation procedure used to preprocess the unevenly sampled R-R intervals derived from the ECG. To this extent, in this study we propose the estimation of wavelet coefficients and wavelet leaders on the output of inhomogeneous point process models of heartbeat dynamics. The RR interval series is modeled using probability density functions (pdfs) characterizing and predicting the time until the next heartbeat event occurs, as a linear function of the past history. Multiscale analysis is then applied to the pdfs' instantaneous first order moment. The proposed approach is tested on experimental data gathered from 57 congestive heart failure (CHF) patients by evaluating the recognition accuracy in predicting survivor and non-survivor patients, and by comparing performances from the informative point-process based interpolation and non-informative spline-based interpolation. Results demonstrate that multiscale analysis of point-process high-resolution representations achieves the highest prediction accuracy of 65.45%, proving our method as a promising tool to assess risk prediction in CHF patients.**

I. Introduction

The analysis of Human Heart Rate Variability (HRV) [1] has notably been used to discern healthy subjects from patients suffering from congestive heart failure (CHF) [2]. However, an important remaining challenge consists in improving the prediction of mortality risk for CHF patients, as well as risk stratification, to a level accurate enough to allow for application in clinical practice [2]–[5]. In particular, it has been accepted that linear features of heartbeat dynamics (often based on spectral analysis [1]) are not sufficient for CHF patients characterization, and need to be complemented by nonlinear features, ranging from Entropy rates to Non-Gaussian metrics (cf. [1], [6]–[13] and reference therein for reviews). In the last two decades, $1/f$ and fractal processes were used to model the temporal dynamics of HRV fluctuations [12]. More recently, multifractal [5], [11], or non Gaussian fat tail distribution models [14] have been involved in HRV descriptions. It was shown that the variations of scaling properties can be associated with pathologies and thus used as diagnostic tool [11], [15]. Furthermore, in CHF patients, departures from Gaussianity were used to evaluate increased mortality risk [2], and compared against fractal exponent [16]. Recently, a robust and efficient procedure relying on the use of multiscale representation and wavelet leaders, has been proposed to conduct multfractal analysis [17] and tested on HRV analysis [5], [18].

In this study, we evaluate the impact of point-process based interpolation strategies [8], [19] on wavelet leader based multiscale representations and we compare it against either a direct analysis of the raw data, or the use of a non informative standard spline-based interpolation. In fact, the R-R interval series extracted from the ECG are analyzed to characterize heart rate (HR) and heart rate variability (HRV). Whether raw data or interpolated and regularly re-sampled time series should be considered is a matter of debate. The former choice creates the difficulty of analyzing irregularly sampled data thus requiring to convert *number of beats* into *seconds* ; the latter choice raises the question of which interpolation should be envisaged and how much achieved results will depend on interpolation.

It has been demonstrated that, by means of a point process approach, it is possible to characterize the probabilistic generative mechanism of heartbeat events, even considering short recordings under nonstationary conditions. The RR interval series (RRi) is modeled using probability density functions (pdfs) characterizing and predicting the time until the next heartbeat event occurs. The unevenly spaced heartbeat intervals are then represented as observations of a state-space point process model defined at each moment in time, thus allowing to estimate instantaneous HR and HRV measures without using any interpolation method. We here illustrate these points on the study of a high quality database (described in Section II-C), comprised of 57 CHF patients, with the aim to accurately assess risk of posterior mortality. Results related to multiscale representations and (supervised) classification performance are presented and commented in Section III. Conclusions are drawn in Section IV, along with discussions and future endeavors.

II. Materials and Methods

A. Point-Process Models of Heartbeat Dynamics

1) Model: Point-process interpolation is performed through a parametrized linear combination of the RR interval

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series. For $t \in (0, T]$, the observation interval, and $0 \leq u_1 < \cdots < u_k < u_{k+1} < \cdots < u_K \leq T$ the times of the events, we can define $N(t) = \max\{k : u_k \leq t\}$ as the sample path of the associated counting process. Its differential, $dN(t)$, denotes a continuous-time indicator function, where $dN(t) = 1$ when there is an event, or $dN(t) = 0$ otherwise. The left continuous sample path is defined as $\widetilde{N}(t) = N(t^-) = \lim_{\tau \to t^-} N(\tau) = \max\{k : u_k < t\}$. Although this framework can be applied to any phenomenon represented by unevenly observed events, we here define the point process model of the ventricular contraction events as the focus of our study. Therefore, given the R-wave events $\{u_j\}_{j=1}^{J}$ detected from the ECG, $\mathrm{RR}_j = u_j - u_{j-1} > 0$ denotes the j^{th} R–R interval. Assuming history dependence, the probability distribution of the waiting time $t - u_j$ until the next R-wave event follows an inverse Gaussian model [19]

$$f(t|\mathcal{H}_t, \xi(t)) = \left[\frac{\xi_0(t)}{2\pi(t-u_j)^3}\right]^{\frac{1}{2}} \times \exp\left\{-\frac{1}{2}\frac{\xi_0(t)[t-u_j-\mu(t,\mathcal{H}_t,\xi(t))]^2}{\mu(t,\mathcal{H}_t,\xi(t))^2(t-u_j)}\right\} \quad (1)$$

with $j = \widetilde{N}(t)$ the index of the previous R-wave event before time t.

In this study, we use the formulation where the instantaneous first-order moment statistic (mean) μ of the distribution is defined as

$$\mu_{\mathrm{RR}}(t, \mathcal{H}_t, \xi(t)) = \gamma_0 + \sum_{i=1}^{p} \gamma_1(i,t)\,\mathrm{RR}_{\widetilde{N}(t)-i} \quad (2)$$

with $\mathcal{H}_t = (u_j, \mathrm{RR}_j, \mathrm{RR}_{j-1}, ..., \mathrm{RR}_{j-p+1})$, $\xi(t) = [\xi_0(t), \gamma_0(t), \gamma_1(1,t), ..., \gamma_1(p,t)]$ the vector of the time-varying parameters, and $\xi_0(t) > 0$ the shape parameters of the inverse Gaussian distribution.

The use of an inverse Gaussian distribution $f(t|\mathcal{H}_t, \xi(t))$, characterized at each moment in time, is motivated both physiologically (the integrate-and-fire initiating the cardiac contraction [19]) and by goodness-of-fit comparisons [8]. In fact, if the rise of the membrane potential to a threshold initiating the cardiac contraction is modeled as a Gaussian random walk with drift, then the probability density of the times between threshold crossings (the R-R intervals) is indeed the inverse Gaussian distribution [19]. Since the IG distribution is characterized at each moment in time, it is possible to obtain an instantaneous estimate of $\mu_{\mathrm{e}}(t)$ at a very fine time scale (with an arbitrarily small bin size Δ), which requires no interpolation between the arrival times of two beats, therefore addressing the problem of dealing with unevenly sampled observations.

2) Parameter Estimation, Model Selection, Goodness-of-Fit: We effectively estimate the parameter vectors $\xi^a(t)$ using the Newton-Raphson procedure to compute the local maximum-likelihood estimate [8]. Because there is significant overlap between adjacent local likelihood intervals, we start the Newton-Raphson procedure at t with the previous local maximum-likelihood estimate at time $t - \Delta$. We determine the optimal order $\{p\}$ by the Akaike Information Criterion (AIC), and by prefitting the point process model goodness-of-fit to a subset of the data [19]. Model goodness-of-fit is based on the Kolmogorov-Smirnov (KS) test and associated KS statistics [8], [19]. The recursive, causal nature of the estimation allows to predict each new observation, given the previous history, independently at each iteration. The model and all its parameters are therefore also updated at each iteration, without priors. In other words, each test point RR_k is tested against one instance of a time-varying model trained with points $\{\mathrm{RR}_j\}$ with $j < k$. Autocorrelation plots are also considered to test the independence of the model-transformed intervals [19]. Once the order $\{p, q\}$ is determined, the initial model coefficients are estimated by the method of least squares [8].

B. Multiscale analysis

1) Hurst parameter and wavelets: Classical multiscale analysis is based on wavelet coefficients, which are obtained by comparing by inner product the data X to the collection $\{\psi_{j,k}(t) = 2^{-j}\psi(2^{-j}t - k)\}_{(j,k)\in\mathbb{N}^2}$ of dilated and translated templates of the so-called mother wavelet ψ: $d_X(j,k) = \langle \psi_{j,k} | X \rangle$. For detailed introductions to wavelet transforms, readers are referred to e.g., [20].

For *self-similar* processes, such as fractional Brownian motion, commonly used to model HRV (cf. e.g., [21], [22]), it can be shown that the so-called *structure functions*, consisting of sample moments of order $q > 0$, behave as power laws with respect to scales

$$S(q,j) = \sum_{k=1}^{n_j} |d_X(j,k)|^2 \simeq K_q 2^{jqH} \quad (3)$$

with n_j the number of $d_X(j,k)$ available at scale 2^j. The Hurst parameter H can (technically) be simply related to the repartition of energy along frequencies (hence to the Fourier spectrum or autocorrelation of X). It thus consists of a linear feature that can be efficiently estimated using wavelets [17], [18]. The function $S(q = 2, j)$ can also be deeply tied to Fourier spectrum [17], [18].

2) Multifractal models and wavelet leaders: In many applications and notably in HRV analysis, it was pointed out that self-similar models do not fully describe the scaling properties in data and that *multifractal* models could prove useful (cf. e.g., [11], [18]). Multifractality mostly implies that the linear behavior with respect to q of the scaling exponents qH in (5) must be replaced with a strictly concave function $\zeta(q)$. Parameter H alone thus no longer fully accounts for the scaling properties in data. It is now well-documented that the correct estimation of the scaling exponents $\zeta(q)$ for all values of q requires replacing wavelet coefficients with *wavelet leaders*, consisting of multiscale quantities that better capture the fluctuations of regularity in data by scanning all details finer than the chosen analysis scale [17].

The wavelet leaders are defined as local suprema of (fractionally integrated) wavelet coefficients, taken with a narrow temporal neighborhood and all finer scales

$$L_X^{(\gamma)}(j,k) := \sup_{\lambda' \subset 3\lambda_{j,k}} 2^{j'\gamma} |d_X(\lambda')|. \quad (4)$$

with $\lambda_{j,k} = [k2^j, (k+1)2^j)$ and $3\lambda_{j,k} = \bigcup_{m\{-1,0,1\}} \lambda_{j,k+m}$ [17]. The fractional integration parameter $\gamma \geq 0$ is chosen

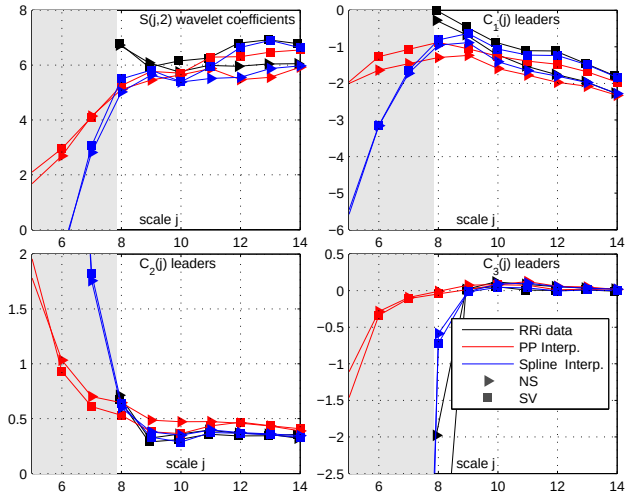

Fig. 1. Multiscale representations for the 3 different data modeling, for SV an NS subjects.

to ensure minimal regularity (cf. [17] and references therein for theoretical developments and details on multifractal analysis). It has also been shown [17] that multifractal properties are well assessed when using multiscale representation based on the log-leaders $\ln L^{(\gamma)}(j,\cdot)$

$$C_p^{(\gamma)}(j) \equiv \mathrm{Cum}_p \ln L^{(\gamma)}(j) \simeq c_p^0 + c_p \ln 2^j \qquad (5)$$

with coefficients c_p related to $\zeta(q)$ (and the multifractal spectrum [17]) via the polynomial expansion $\zeta(q) \equiv \sum_{p\geq 1} c_p q^p/p!$. Thus, the leading coefficient c_1 is closely related to H, and $C_1^{(\gamma)}(j)$ to $S(2,j)$. $C_1^{(\gamma)}(j)$ hence constitutes a vector of linear features, associated to the autocorrelation of X [17], [18], while $C_2^{(\gamma)}(j)$ and $C_3^{(\gamma)}(j)$ (the variance and skewness of $\ln L^{(\gamma)}(j)$, respectively) probe information beyond correlation and are thus non linear features.

C. Experimental Data

Recordings from a cohort of 57 patients suffering from Congestive Heart Failure (CHF) were made available by the Nagoya Hospital or Fujita Health University Hospital, Japan. Of these patients, 30 died within 33 ± 17 months (range, 1-59 months) after Hospital discharge, whereas 27 survived for a longer time. The former group is referred to as non-survivors (NS) and the latter as survivors (SV). Further clinical details can be found in [2]. For each patient, R peak arrival times were carefully extracted from 24-hour Holter ECG recordings. Missing data and outliers stemming from atrial or ventricular premature complexes were handled by preprocessing automated tools. Subjects with sustained tachyarrhythmias were excluded from the study.

III. Results

A. Analysis setting

From the R peak arrival time lists $\{t_n, n = 1,\ldots,N\}$, three different time series are constructed and studied using the multiscale representations described in Section II-B: i) The raw data $X_n \equiv t_n - t_{n-1}$, referred to as the RRi time series ; ii) X is interpolated using the informative Point Process based interpolation (described in Section II-A), referred to as the PP Interp. time series ; iii) X is interpolated using a standard non informative Spline-based interpolation, referred to as the Spline Interp. time series. The 24h-long data are analyzed in one block. Analysis is conducted using Daubechies2 wavelets. Inspection of the database lead to choose $\gamma = 1$ in what follows. Note that for large subclass of multifractal processes one can show that $C_1(j) \equiv C_1^{(\gamma)}(j) - \gamma \ln 2^j$ for $p \geq 2$ does not depend on γ. This is assumed to hold for the data analyzed here.

B. Scaling properties

The wavelet coefficient based $\log_2 S(2,j)$ and wavelet leader based $C_1(j), C_2(j), C_3(j)$ representations are computed for data obtained from two different interpolations, as well as directly from raw RRi data. For interpolated time series, scale 2^j can be associated to $2^j T_S$ms. Raw RRi data consist of the list of RR interarrival times and scale 2^j can qualitatively be related to $2^j \overline{R}$ ms, where $\overline{R}$ denotes the sample mean estimate of the mean of the RR interarrival times for each subject. This permits to compare multiscale representations obtained from each methods, as functions of equivalent scales, for NS and SV subjects. Fig. 1 clearly show that the multiscale representations $\log_2 S(2,j)$ and $C_1(j), C_2(j), C_3(j)$ for the three time series are quasi-identical at large j, hence validating that interpolation strategies do not impact the coarsest time scales (above $j \geq 11$, i.e., above $\simeq$ 10s). Obviously, fine scales (below $j \leq 7$, i.e., below $\simeq$ 0.6s) do not exist for the raw RRi data, whereas fine scales are available for the PP Interp. and Spline Interp. time series. Their being different is a direct signature of the nature of the interpolation procedures more than of the content of the data. Intermediate time scales ($8 \leq j \leq 10$, i.e., from 1s to 5s) are the scale of interest, where the interplay between the content of the data and the interpolation procedures occurs. RRi data at scales $j = 8$ and 9 show clear departures from the scaling behavior observed at coarser scales. The non informative Spline Interp. time series suffer from the same drawback. On the contrary, the informative PP Interp. time series shows scales $j = 8$ and 9 in agreement and continuation of the scaling behavior seen at coarser scales. This clearly illustrates that point-process modeling of heartbeat dynamics allows to extend the possibility of extracting relevant information, already existing in data at coarse scales, also at finer scales.

C. SV versus NS classification

Exploring the extent to which the proposed multiscale representations permit to discern SV from NS subjects, we focus of the intermediate scales $8 \leq j \leq 10$ where interpolation procedures yields different behavior.

The obtained feature set is taken as an input of the Leave-One-Out (LOO) procedure for a Support Vector Machine (SVM)-based pattern recognition [23] (nu-SVM with $\mathrm{nu} = 0.5$ and radial basis kernel function). A class label, among SV or NS, given by clinical assessment, was associated to each point in the feature space, which, for each fixed scale j independently, takes as input the 4-dimensional feature vector $\log_2 S(2,j), C_1(j), C_2(j), C_3(j)$. In order to compare the proposed methodology with other standard approaches, we evaluated the LOO-SVM performance in predicting SV vs.

NS patients using the 4-dimensional feature vector estimated on RRi data, PP Interp. and Spline Interp.

Classification performance (measured in terms of accuracies, i.e., $\%$ of overall — True Negative and True Positive — total correct classification) are reported in Table I. Considering the SV vs. NS classes, accuracy of 50% is the change.

TABLE I
CLASSIFICATION ACCURACY IN %

scale (j)	PP Interp.	RRi data	Spline Interp.
5	41.82	0	20.00
6	49.09	0	7.27
7	52.73	0	3.64
8	**65.45**	21.82	30.91
9	63.64	10.91	30.91
10	54.55	50.91	45.45

Table I shows that accuracies at fine scales are small and irrelevant, which is consistent with the fact that fine scales do not contain information related to actual data. It also shows that performances at coarse scales are equivalent for all 3 time series (PP Interp., RRi data, and Spline Interp.) and barely beyond 50%. Finally and interestingly, Table I show that the maximum discrepancies between all 3 time series occur around scales $j = 8$, 9 and 10, and that, at these scales the point-process derived time series achieves the best accuracies (up to 65.45%).

IV. CONCLUSION AND DISCUSSION

This study aimed at testing a novel approach of multiscale analysis on high-resolution time series derived by point-process models of heartbeat dynamics on 57 long-term ECG recordings gathered from patients with CHF. To this extent, three multiscale representations are considered and compared: the $\log_2 S(2,j)$ and $C_1(j), C_2(j), C_3(j)$ is estimated from (a) the raw data (RRi time series), (b) RR interval series interpolated using a standard non informative spline-based interpolation, and (c) RR interval series interpolated using the informative point-process based interpolation. All representations are used to predict the mortality of CHF patients through a simple SVM classifier.

Results demonstrate that the analysis using the point-process derived time series achieves the best prediction accuracy, with a maximum of 65.45% for scale 8. This result is in agreement with our previous studies [8], [19] demonstrating that the use of an inverse Gaussian distribution, characterized at each moment in time, inherits both physiological (the integrate-and-fire initiating the cardiac contraction [19]) and methodological information. The parameter $\mu_{\mathrm{RR}}(t, \mathcal{H}_t, \xi(t))$ denotes the instantaneous R-R mean that can be modeled as a generic function of the past (finite) R–R values. Indeed, this is something unique of the point-process approach. This study poses a solid basis for devising a tool capable of performing accurate assessments of CHF morbidity and mortality, which still remain unacceptably high despite effective ongoing drug therapies. Future endeavors will focus on the study of a comprehensive set of features gathered from multiscale analyses, as well as investigating the multiscale and multifractal properties of instantaneous parasympathetic activity assessed by point-process estimates of HF power.

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