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Characterizing Nonlinear Heartbeat Dynamics within a Point Process Framework

Zhe Chen [Member, IEEE]
Neuroscience Statistics Research Laboratory, Harvard Medical School, Massachusetts General Hospital, Boston, MA 02114 USA, and also with the Department of Brain and Cognitive Sciences, Massachusetts Institute of Technology, Cambridge, MA 02139 USA (zhechen@neurostat.mit.edu)

Emery N. Brown [Fellow, IEEE]
Neuroscience Statistics Research Laboratory, Harvard Medical School, Massachusetts General Hospital, Boston, MA 02114 USA, and also with the Harvard-Massachusetts Institute of Technology (MIT) Division of Health Science and Technology, and the Department of Brain and Cognitive Sciences, MIT, Cambridge, MA 02139 USA (enb@neurostat.mit.edu)

Riccardo Barbieri [Senior Member, IEEE]
Neuroscience Statistics Research Laboratory, Harvard Medical School, Massachusetts General Hospital, Boston,MA02114 USA, and also with the Massachusetts Institute of Technology, Cambridge, MA 02139 USA (barbieri@neurostat.mit.edu)

Abstract

Human heartbeat intervals are known to have nonlinear and nonstationary dynamics. In this paper, we propose a model of R–R interval dynamics based on a nonlinear Volterra–Wiener expansion within a point process framework. Inclusion of second-order nonlinearities into the heartbeat model allows us to estimate instantaneous heart rate (HR) and heart rate variability (HRV) indexes, as well as the dynamic bispectrum characterizing higher order statistics of the nonstationary non-Gaussian time series. The proposed point process probability heartbeat interval model was tested with synthetic simulations and two experimental heartbeat interval datasets. Results show that our model is useful in characterizing and tracking the inherent nonlinearity of heartbeat dynamics. As a feature, the fine temporal resolution allows us to compute instantaneous nonlinearity indexes, thus sidestepping the uneven spacing problem. In comparison to other nonlinear modeling approaches, the point process probability model is useful in revealing nonlinear heartbeat dynamics at a fine timescale and with only short duration recordings.

Keywords

Adaptive filters; approximate entropy (ApEn); heart rate variability (HRV); nonlinearity test; point processes; scaling exponent; Volterra series expansion

Correspondence to: Zhe Chen.

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I. Introduction

The human heartbeat is regulated by the autonomic nervous system, and as a result, heart rate (HR) and heart rate variability (HRV) measurements extracted from the ECG are important quantitative markers of cardiovascular control [1]. A healthy heart is influenced by multiple neural and hormonal inputs that result in variations of the interbeat interval duration. Specifically, various nonlinear neural interactions and integrations occur at the neuron and receptor levels, and underlie the complex output of structures such as the sinoatrial (SA) node in response to changing levels of sympathetic and vagal activities [55]. The complex nature of heartbeat dynamics has been widely considered and discussed in cardiovascular literature. Although detailed physiology behind these complex dynamics has not been completely clarified, several nonlinearity measures of HRV have been pointed out as important quantifiers of complexity of cardiovascular control and have been proved to be of important prognostic value in aging and diseases [4], [25], [26],[46], [58], [60], [62].

Many physiological signals are known to be nonlinear and nonstationary. In biomedical engineering, various nonlinear indexes, such as the Lyapunov exponent, the fractal exponent, or the approximate entropy (ApEn), have been proposed to characterize the nonlinear behavior of the underlying physiological system (e.g., [2]). It has been suggested that such nonlinearity indexes might provide informative indicators for diagnosing cardiovascular or brain diseases. Notably, some difficulties have been often encountered when validating these indexes, such as the presence of noise or artifact, the limited size of data samples, or the low sampling rate of the observed signals. All these issues shall be kept in mind when new statistical indexes are estimated from real signals recorded from a nonlinear system.

In characterizing the nonlinear heartbeat dynamics, both linear and nonlinear system identification methods have been applied to R–R interval series [19], [20], [61]. Examples of higher order characterization for cardiovascular signals, include nonlinear autoregressive (AR) models, Volterra–Wiener series expansion, and Volterra–Laguerre models [2], [32], [33], [36]. Several authors have demonstrated the feasibility and validity of nonlinear AR models, suggesting that future HR dynamics studies should put greater emphasis on nonlinear analysis [19], [20], [31], [61]. However, none of these models have included nonlinear elements in a framework based on a precise statistical characterization of the heartbeat generation process, and all of mentioned studies used either beat series (tachograms) or discretionarily interpolated R–R time series instead of deriving model estimates. In this paper, we apply nonlinear modeling to heartbeat dynamics using a point process paradigm. The point process theory is a powerful statistical tool able to characterize the probabilistic generative mechanism of the heartbeat at each moment in time, thus allowing for estimation of instantaneous HR and HRV measures [7], [8]. Furthermore, inclusion of second-order nonlinear terms to the point process model offers an opportunity to monitor dynamic higher order spectra indexes [39], [40].

The paper is organized as follows. Section II presents some background on nonlinear system identification by Volterra–Wiener series expansion. Section III gives a brief exposition of probabilistic point process model theory for heartbeat intervals, derives the instantaneous HR and HRV indexes, and reviews the adaptive point process filtering algorithm as well as the goodness-of-fit tests. Section IV is devoted to the instantaneous higher order spectral analysis and derivation of the dynamic bispectrum estimate, as well as the nonlinearity test for R–R interval series. Section V describes the synthetic data generated to test the models, as well as two experimental heartbeat datasets. Section VI presents the experimental results on all datasets using the point process models, discussing model selection, nonlinearity assessment, performance comparison, and irregularity characterization. Finally, discussions and conclusion are given in Section VII.

II. Volterra Series for Nonlinear System Identification

The Volterra series expansion, based on the Volterra theorem, is a general method for nonlinear system modeling and identification [36]. In functional analysis, a Volterra series denotes a functional expansion of a dynamic, nonlinear, and time-invariant function. The Volterra series allows for representation of a wide range of nonlinear systems. Because of its generality, Volterra series expansion has been widely used in nonlinear modeling in engineering and physiology [2], [31], [36]. For instance, computational procedures based on a comparison of the prediction power of linear and nonlinear models of the Volterra–Wiener form have been applied to measure the complex dynamics of the heartbeats [6]. However, it shall be pointed out that all of these nonlinear models used only raw R–R intervals without modeling the point process nature of the heartbeats.

Consider a nonlinear single-input and single-output system $y = g(x)$. According to the Volterra series theory, the nonlinear system can be expanded by a (finite or infinite) set of kernel expansion terms

$$y(t) = k_0 + \sum_{m=0}^{M-1} k_1(m)\, x(t-m) + \sum_{m=0}^{M-1}\sum_{n=0}^{M-1} k_2(m,n)\, x(t-m)\, x(t-n) + \cdots \quad (1)$$

where M is the memory of the nonlinear system. Equation (1) only includes up to the second-order nonlinear term in the Volterra series expansion; however, inclusion of higher order terms is possible. The Volterra kernels $\{k_0,k_1,k_2,\ldots,\}$ describe the dynamics of the system, each of which is associated with Volterra coefficients at different kernel orders and different time lags. Estimation of the Volterra coefficients is generally performed by computing the coefficients of an orthogonalized series, and then recomputing the coefficients of the original Volterra series. A common method is based on the least squares optimization [36]. In this paper, we apply a point process adaptive filtering approach to recursively estimate the time-varying Volterra coefficients.

III. Heartbeat Interval Point Process Model

A random point process is a random element whose values are “point patterns” on a set, where a point pattern is specified as a locally finite counting measure [23]. Specifically in the time domain, a simple 1-D point process consists of series of binary (0 and 1) observations, where the variables 1 marks the occurrence times $t \in [0,\infty)$ of the random events. Mathematically, we let $N(t)$ define a continuous-time counting process, and let its differential $dN(t)$ denote a continuous-time indicator function, where $dN(t) = 1$, when there is an event (such as the ventricular contraction) or $dN(t) = 0$, otherwise. Point process theory has been widely used in modeling various types of random events (e.g., eruptions of earthquakes, queueing of customers, spiking of neurons, etc.) where the timing of the events are of central interest. Bearing a similar spirit, the point process theory has been used for modeling human heartbeats [7],[8],[16]. The point process framework primarily defines the probability of having a heartbeat event at each moment in time. A parametric formulation of the probability function allows for a systematic, parsimonious estimation of the parameter vector in a recursive way and at any desired time resolution. Instantaneous indexes can then be derived from the parameters in order to quantify important features as related to cardiovascular control dynamics.

A. Heartbeat Interval

Suppose we are given a set of R-wave events $\{u_j\}_{j=1}^{J}$ detected from the ECG, let $RR_j = u_j - u_{j-1} > 0$ denote the jth R-R interval, or equivalently, the waiting time until the next R-wave event. By treating the R-wave as discrete events, we may develop a point process probability model in the continuous time domain [7].

Assuming history dependence, the probability distribution of the waiting time $t-u_j$ until the next R-wave event follows an inverse Gaussian model:

$$p(t)=\left(\frac{\theta}{2\pi t^3}\right)^{\frac{1}{2}}\exp\left(-\frac{\theta\left[t-u_j-\mu_{\mathrm{RR}}(t)\right]^2}{2\left(t-u_j\right)\mu_{\mathrm{RR}}^2(t)}\right)\quad\left(t>u_j\right),$$

where u_j denotes the previous R-wave event occurred before time t, $\mu_{\mathrm{RR}}(t)$ represents the first-moment statistic (mean) of the distribution, and $\theta > 0$ denotes the shape parameter of the inverse Gaussian distribution, whose role is to model the tail shape of the distribution (when $\theta \to \infty$, the inverse Gaussian distribution becomes more like a Gaussian distribution). As $p(t)$ indicates the probability of having a beat at time t given that a previous beat has occurred at u_j and $\mu_{\mathrm{RR}}(t)$ can be interpreted as signifying the most probable moment when the next beat could occur. By definition, $p(t)$ is characterized at each moment in time, at the beat as well as in-between beats. We can also estimate the second-moment statistic (variance) of the inverse Gaussian distribution as $\sigma_{\mathrm{RR}}^2(t)=\mu_{\mathrm{RR}}^3(t)/\theta$. The use of an inverse Gaussian distribution to characterize the R–R intervals' occurrences is motivated by the fact that 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 [7]. In [16], we have compared heartbeat interval fitting point process models using different probability distributions, and found that the inverse Gaussian model achieved the overall best fitting results. The parameter $\mu_{\mathrm{RR}}(t)$ denotes the instantaneous R–R mean that can be modeled as a generic function of the past (finite) R–R values $\mu_{\mathrm{RR}}(t)=g(RR_{t-1},RR_{t-2},\ldots,RR_{t-h})$, where RR_{t-j} denotes the previous j^{th} R–R interval occurred prior to the present time t. In our previous work [8], [14], [16], the history dependence is defined by expressing the instantaneous mean $\mu_{\mathrm{RR}}(t)$ as a linear combination of present and past R–R intervals (in terms of an AR model), i.e., function g is linear. Here, we propose to include the nonlinear terms of past R–R intervals by defining the instantaneous RR mean as follows:

$$\mu_{\mathrm{RR}}(t)=a_0(t)+\sum_{i=1}^{p}a_i(t)RR_{t-i}+\sum_{k=1}^{q}\sum_{l=1}^{q}b_{kl}(t)(RR_{t-k}-<RR>_t)(RR_{t-l}-<RR>_t) \tag{2}$$

where $<RR>_t=1/h\sum_{k=1}^{h}RR_{t-k}$. Here the coefficients $a_0(t)$,$\{a_i(t)\}$, and $\{b_{kl}(t)\}$ correspond to the time-varying zero-, first-, and second-order Volterra kernel coefficients. The zero order coefficient a_0 accounts for the nonzero mean of the R–R series. Equation (2) can be interpreted as a discrete Volterra–Wiener series with degree of nonlinearity $d = 2$ and memory $h = \max\{p, q\}$ [6]. As $\mu_{\mathrm{RR}}(t)$ is defined in a continuous time fashion, we can obtain an *instantaneous* R–R mean estimate at a very fine timescale (with an arbitrarily small bin size Δ), which requires no interpolation between the arrival times of two beats. Given the proposed parametric model, the nonlinear indexes of the HR and HRV will be defined as a time-varying function of the parameters $\xi(t)=[a_0(t),a_1(t),\ldots,a_p(t),b_{11}(t),\ldots,b_{qq}(t),\theta(t)]$.

B. Instantaneous Indices of HR and HRV

HR is defined as the reciprocal of the R–R interval. For t measured in seconds, a new variable $r=c(t-u_j)^{-1}$ (where c = 60 s/min) can be defined in beats per minute (bpm). By the *change-of-variables* formula, the HR probability $p(r)=p(c(t-u_t)^{-1})$ is given by

$$p(r)=\left|\frac{dt}{dr}\right|p(t), \tag{3}$$

and the mean and the standard deviation of HR r can be derived [7], [8], as given by μ_{HR} and standard deviation σ_{HR}, respectively

$$\mu_{HR}=\tilde{\mu}^{-1}+\tilde{\theta}^{-1} \tag{4}$$

$$\sigma_{HR}=\sqrt{\left(2\tilde{\mu}+\tilde{\theta}\right)/\tilde{\mu}\tilde{\theta}^{2}} \tag{5}$$

where $\tilde{\mu}=c^{-1}\mu_{RR}$ and $\tilde{\theta}=c^{-1}\theta$.

It is known from point process theory [7], [8], [13] that the *conditional intensity function* (CIF) $\lambda(t)$ is related to the interevent probability $p(t)$ with a one-to-one relationship

$$\lambda(t)=\frac{p(t)}{1-\int_{u_t}^{t}p(\tau)\,d\tau}. \tag{6}$$

The estimated CIF can be used to evaluate the goodness-of-fit of the proposed probability model for the heartbeat interval point process probability model. The quantity $\lambda(t)\Delta$ yields approximately the probability of observing a beat during the $[t,t+\Delta)$ interval in the sense that [23]

$$\lambda(t)=\lim_{\Delta\to 0}\frac{\Pr\{N(t+\Delta)-N(t)=1|H_t\}}{\Delta}$$

where H_t denotes all of available history information (subject to causality) up to time t.

C. Adaptive Point Process Filtering

In order to track the unknown parameters of vector ξ in a nonstationary environment, we can recursively estimate them via adaptive point process filtering [8]. Upon time discretization, we have the following equation updates at discrete-time index k:

$$\xi_{k|k-1}=\xi_{k-1|k-1} \tag{7}$$

$$P_{k|k-1}=P_{k-1|k-1}+W \tag{8}$$

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