A Unified Point Process Framework for Assessing Heartbeat Dynamics and Cardiovascular Control

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***Abstract*— We present a unified probabilistic point process framework to estimate and monitor the instantaneous heartbeat dynamics as related to specific cardiovascular control mechanisms and hemodynamics. Assessment of the model's statistics is established through the Wiener-Volterra theory and a multivariate autoregressive (AR) structure. A variety of instantaneous cardiovascular metrics, such as heart rate (HR), heart rate variability (HRV), respiratory sinus arrhythmia (RSA), and baroreceptor-cardiac reflex (baroreflex), can be rigorously derived within a parametric framework and instantaneously updated with an adaptive algorithm. Nonlinearity metrics, as well as the bispectrum of heartbeat intervals, can also be derived. We have applied the proposed point process framework to a number of recordings under different experimental protocols. Results reveal interesting dynamic trends across different posture/pharmacological/age/ heart disease conditions, pointing at our mathematical approach as a promising monitoring tool for an accurate, noninvasive assessment of a large spectrum of cardiovascular diseases and disorders, including hypertension and congestive heart disease.**

I. Introduction

In recent years, advanced statistical models have been developed for evaluating the heartbeat dynamics [1-3]. Heartbeats, once detected from continuous electrocardiogram (ECG) signal, are treated as discrete events that can be modeled by a stochastic point process [2, 3]. Various probabilistic models (e.g., the inverse Gaussian, Gaussian, lognormal, or gamma distribution) can be used to model the heartbeat interval [4], whereas its mean is modulated by previous inter-beat intervals. In the meanwhile, nonlinearity of the heartbeat dynamics as well as the interactions between the heartbeat and other cardiovascular measures have always been the research interests. In light of the Wiener-Volterra theory, we present a unified point process framework to include the interactions between the heartbeat intervals and other cardiovascular measures such as respiration and arterial blood pressure, as well as assessing nonlinear heartbeat dynamics.

II. A Point Process Framework for Heartbeat Dynamics

A. Heartbeat Interval Point Process Model

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. By treating the R-waves as discrete events, and assuming history dependence, the waiting time $t-u_t$ until the next R-wave event can be modeled by an inverse Gaussian model [2, 3]:

$$p(t)=\left(\frac{\theta}{2\pi t^3}\right)\exp\left(-\frac{\theta(t-u_t-\mu_t)^2}{2\mu_t^2(t-u_t)}\right) \quad (1)$$

where u_t denotes the previous R-wave event occurred before time t, $\theta>0$ denotes the shape parameter, and $\mu(t)\equiv\mu_{\mathrm{RR}}(t)$ denotes the instantaneous R-R mean. In point process theory, the inter-event probability $p(t)$ is related to the *conditional intensity function* (CIF) $\lambda(t)$ by a one-to-one transformation: $\lambda(t)=\frac{p(t)}{1-\int_{u_t}^{t}p(\tau)d\tau}$. The estimated CIF can be used to evaluate the goodness-of-fit of the heartbeat point process model.

B. Instantaneous Indices of HR and HRV

Heart rate is defined as the reciprocal of the R-R intervals. For RR measured in seconds, the HR $r=c(t-u_t)^{-1}$ (where c=60 s/min) is a physiological measurement 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 $p(r)=\left|\frac{dt}{dr}\right|p(t)$, and the mean HR and the HRV can be derived [1, 2]:

$$\mu_{\mathrm{HR}}=a^{-1}+b^{-1},\quad \sigma_{\mathrm{HR}}=\left(\frac{2a+b}{ab^2}\right)^{1/2},$$

where $a=c^{-1}\mu_{\mathrm{RR}}$ and $b=c^{-1}\theta$.

III. Modeling of Instantaneous Heartbeat Interval

In general, let us consider a causal, continuous-time nonlinear mapping F between an output variable $y(t)$ and two zero-mean input variables $x(t)$ and $u(t)$. In light of the Wiener-Volterra theory, expanding the Volterra series of function F (up to the second order) with respect to $x(t)$ and $u(t)$ yields

$$\begin{aligned} y(t) &= F(x(t),u(t)) \\ &= \int_0^t a(\tau)x(t-\tau)d\tau+\int_0^t b(\tau)u(t-\tau)d\tau \\ &+ \int_0^t\int_0^t h_1(\tau_1,\tau_2)x(t-\tau_1)u(t-\tau_2)d\tau_1 d\tau_2 \\ &+ \int_0^t\int_0^t h_2(\tau_1,\tau_2)x(t-\tau_1)x(t-\tau_2)d\tau_1 d\tau_2 \\ &+ \int_0^t\int_0^t h_3(\tau_1,\tau_2)u(t-\tau_1)u(t-\tau_2)d\tau_1 d\tau_2 \end{aligned} \quad (2)$$

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where $F(\bullet)$: $\Re^2 \rightarrow \Re$, and $a(\bullet)$, $b(\bullet)$, $h_1(\bullet,\bullet)$, $h_2(\bullet,\bullet)$, and $h_3(\bullet,\bullet)$ are Volterra kernels with appropriate orders. In our case, $y(t)$ is replaced by $\mu_{\mathrm{RR}}(t)$, $x(t)$ by previous R-R intervals, $u(t)$ by either blood pressure or respiration as covariate, and the continuous-time integral will be approximated by a finite and discrete approximation.

1) Case 1: Dropping of all second-order terms in (2), we obtain a bivariate discrete-time linear system [4, 6, 8]:

$$\mu_t = a_0(t) + \sum_{i=1}^{p} a_i(t) RR_{t-i} + \sum_{j=1}^{q} b_i(t) u_{t-j} \tag{3}$$

2) Case 2: Dropping of the last two quadratic terms in (2), we obtain a discrete-time bilinear system [7]:

$$\begin{aligned}\mu_t = a_0(t) &+ \sum_{i=1}^{p} a_i(t) RR_{t-i} + \sum_{j=1}^{q} b_i(t) u_{t-j} \\ &+ \sum_{i=1}^{r}\sum_{j=1}^{r} h_{ij}(t)(RR_{t-i} - \langle RR \rangle) u_{t-j}\end{aligned} \tag{4}$$

3) Case 3: Dropping of the terms that involve the covariate measure $u(t)$ in (2), it follows that [5]:

$$\begin{aligned}\mu_t &= a_0(t) + \sum_{i=1}^{p} a_i(t) RR_{t-i} \\ &+ \sum_{i=1}^{r}\sum_{j=1}^{r} h_{ij}(t)(RR_{t-i} - \langle RR \rangle)(RR_{t-j} - \langle RR \rangle)\end{aligned} \tag{5}$$

Therefore, by taking different terms from the Wiener-Volterra series expansion, we may derive and study the interactions between the random variables of interest.

IV. Assessment of Cardiovascular Functions and Instantaneous Spectral Analysis

From (3), depending on specific covariate measurement $u(t)$, we can evaluate the transfer function and frequency response of the $u \rightarrow RR$ feedback loop as follows:

$$H_{12}(f) = \frac{\left.\sum_{j=1}^{q} b_j(k) z^{-j}\right|_{z=e^{j2\pi f_2}}}{\left.1 - \sum_{i=1}^{p} a_i(k) z^{-i}\right|_{z=e^{j2\pi f_1}}} \tag{6}$$

where f_1 and f_2 denote the sample rate for the RR and covariate measurements, respectively. For instance, if $u(t)$ is a respiration measure, we can compute the RSA from (6) [4, 8]; if $u(t)$ is a blood pressure measure, then the baroreflex gain can be evaluated [6, 7]. Of note, when blood pressure is considered, the interaction is modelled by a bivariate closed-loop AR structure to acknowledge the observed cardiovascular physiology [1].

In light of (3)-(5), we can also perform various types of parametric spectral analysis, which may include the autospectrum and bispectrum of the instantaneous R-R interval, as well as the coherence and cross-bispectrum between the R-R and the covariate measures [4-8]. Therefore, our probabilistic model offers a convenient framework to assess heartbeat dynamics and cardiovascular control in both time and frequency domains.

We can update the model parameters in an online fashion using an adaptive point process filter [3]. By virtue of online estimation, we can compute various instantaneous indices regarding the heartbeat dynamics and the cardiovascular control in a nonstationary environment. Finally, model goodness-of-fit of can be evaluated with a *Kolmogorov-Smirnov* (KS) test based on the so-called *time-rescaling theorem* [2, 3].

V. Summary of Results and Conclusion

Results on application of our model framework include instantaneous assessment of sympatho-vagal balance and RSA during autonomic blockade, of nonlinear dynamics in cardiac heart failure subjects, and of instantaneous baroreflex gain in healthy subjects during a tilt procedure and under progressive stages of anesthesia [4-8]. All instantaneous indices are estimated to accommodate the nonstationary nature of the experimental recordings. Overall, our observations have confirmed established findings regarding the most important physiological and pathological mechanisms involved in cardiovascular control, and they also reveal interesting dynamic trends across different conditions.

In summary, a unified point process framework is proposed which enables us to simultaneously assess the linear and nonlinear indices of HRV, together with important cardiovascular functions of interest, under a wide range of experimental protocols.

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