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Application of dynamic point process models to cardiovascular control

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Abstract

The development of statistical models that accurately describe the stochastic structure of biological signals is a fast growing area in quantitative research. In developing a novel statistical paradigm based on Bayes' theorem applied to point processes, we are focusing our recent research on characterizing the physiological mechanisms involved in cardiovascular control. Results from a tilt table study point at our statistical framework as a valid model for the heart beat, as generated from complex mechanisms underlying cardiovascular control. The point process analysis provides new quantitative indices that could have important implications for research studies of cardiovascular and autonomic regulation and for monitoring of heart rate and heart rate variability measures in clinical settings.

Keywords: Heart rate variability; Point processes; Adaptive filters; State estimation

1. Introduction

Heart rate (HR) and heart rate variability (HRV) are important dynamic measures of the state of the cardiovascular system and the autonomic nervous system (Stauss, 2003; Task Force, 1996). Heart rate is traditionally estimated as the average of the reciprocal of the *R–R* intervals within a specified time window, or as the number of *R*-wave events (heart beats) per unit time on the electrocardiogram (ECG). The *R*-wave events mark the electrical impulses from the heart's conduction system that represent ventricular contractions. Hence, they are a sequence of discrete occurrences in continuous time, and as such, form a point process. Rather than modeling them to reflect the point process structure of the heart beats, most current methods either treat the heart beat *R–R* interval series as continuous-valued signals, or convert them into continuous-valued, evenly spaced measurements for analysis by interpolation of either the *R–R* intervals or their reciprocals. We have recently derived new definitions of HR and HRV based on an explicit point process Bayesian probability model for heart rate under the assumption that the stochastic properties of the *R–R* intervals are governed by an inverse Gaussian renewal model. We can estimate the time-varying inverse Gaussian parameters by either local maximum likelihood (Barbieri et al., 2005) or by adaptive point process estimation (Barbieri and Brown, 2006), and assess model goodness-of-fit by Kolmogorov–Smirnov (KS) tests based on the time-rescaling theorem. These models give a more physiologically sound representation of the stochastic structure in heart beat generation than those provided by current definitions and analysis methods. In particular, the adaptive filter algorithm can compute updates in an on-line fashion and at any desired temporal resolution, and it may be at the core of a new device to monitor heart beat dynamics in clinical settings such as the intensive care unit, the operating room and during labor and delivery (Fig. 1). We here show the application of our adaptive paradigm to data from 10 healthy subjects during postural changes.

2. Methods

In this section, we present the heart beat interval and the heart rate probability models, the heart beat interval model parameters, the point process adaptive filtering algorithm to derive instantaneous estimates of heart rate and heart rate variability, and the goodness-of-fit test to evaluate how well these estimates describe the stochastic structure of the *R*-wave events extracted from an ECG.

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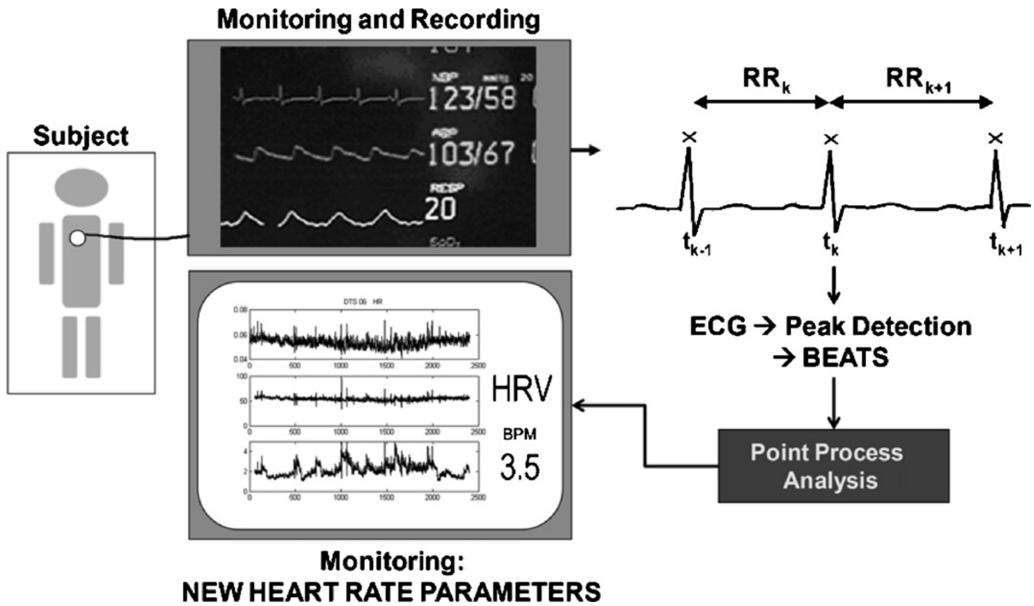

Fig. 1. From ECG non-invasive recordings, *R–R* interval peak can be detected, and the adaptive filter algorithm can compute instantaneous updates of heart rate and heart rate variability indices in an on-line fashion and at any desired temporal resolution. This framework poses the basis for a new device for monitoring of heart beat dynamics in clinical settings such as the intensive care unit, the operating room and during labor and delivery.

2.1. Point Process Probability Model of Heart Beat Intervals

Each *R*-wave event is initiated by a coordinated depolarization of the heart's pacemaker cells that begins in the sino-atrial (SA) node and propagates throughout the cardiac muscle. Deterministic models of this integrate (rise of the transmembrane potential)-and-fire (depolarization) mechanism are used regularly to simulate heart beats or *R*-wave events (De Boer et al., 1985; Berger et al., 1986). An elementary, stochastic integrate-and-fire model is the Gaussian random walk model with drift, and the probability density of the first passage times for this random walk process, i.e., the times between threshold crossings (*R–R* intervals), is well-known to be the inverse Gaussian (Tuckwell, 1988; Chhikara and Folks, 1989). Therefore, we assume that given any *R*-wave event u_k, the waiting time until the next *R*-wave event, or equivalently, the length of the next *R–R* interval, obeys the following history-dependent inverse Gaussian (HDIG) probability density:

$$f(t|H_k,\theta)=\left[\frac{\theta_{p+1}}{2\pi(t-u_k)^3}\right]^{1/2}\exp\left\{-\frac{1}{2}\frac{\theta_{p+1}[t-u_k-\mu(H_k,\theta)]^2}{\mu(H_k,\theta)^2(t-u_k)}\right\}, \quad (1)$$

where $0<u_1<u_2<\cdots<u_k<\cdots<u_K\le T$ are the K successive *R*-wave event times from an ECG in an observation interval $(0, T]$, t is any time satisfying $t>u_k$, $H_k=\{u_k, w_k, w_{k-1}, \ldots, w_{k-p+1}\}$ is the history of the *R–R* intervals up to u_k, $w_k=u_k-u_{k-1}$ is the kth *R–R* interval, $\mu(H_k,\theta)=\theta_0+\sum_{j=1}^{p}\theta_j w_{k-j+1}>0$ is the mean, $\theta_{p+1}>0$ is the scale parameter, and $\theta=(\theta_0,\theta_1,\ldots,\theta_{p+1})$ is the vector of model parameters. The autoregression on the mean allows for consideration of the effect of the recent history of the sympathetic and parasympathetic inputs to the SA node.

The mean and standard deviation of the *R–R* probability model in (1) are respectively

$$\mu_{RR}=\mu(H_k,\theta), \quad (2)$$

$$\sigma_{RR}=[\mu(H_k,\theta)^3\theta_{p+1}^{-1}]^{1/2}. \quad (3)$$

Heart rate is often defined as the reciprocal of the *R–R* intervals, thus we define $r=c(t-u_k)^{-1}$ as the heart rate random variable and use the standard change-of-variables formula from elementary probability theory to derive the mean and standard deviation of the heart rate probability density defined as

$$\mu_{HR}=\mu^*(H_k,\theta)^{-1}+(\theta_{p+1}^*)^{-1}, \quad (4)$$

$$\sigma_{HR}=\left[\frac{2\mu^*(H_k,\theta)+\theta_{p+1}^*}{\mu^*(H_k,\theta)\theta_{p+1}^{*2}}\right]^{1/2}. \quad (5)$$

where $\mu^*(H_k,\theta)=c^{-1}\mu(H_k,\theta)$, $\theta_{p+1}^*=c^{-1}\theta_{p+1}$.

To track the non-stationary behavior in heart beat dynamics that occurs due to changes in state under both physiological and pathological conditions, we assume that the parameter θ is time-varying, and we model the time-varying behavior of θ using a state space model. To define the state model and the observation model, we choose J large, and divide $(0, T]$ into J intervals of equal width $\Delta=T/J$, so that there is at most one spike per interval. The adaptive parameter estimates will be updated at $j\Delta$ for $j=1,\ldots,J$.

From the heart beat probability model in (1) we define the associated conditional intensity function as

$$\lambda(j\Delta|H_j,\theta_{j\Delta})=\frac{f(j\Delta|H_j,\theta_{j\Delta})}{1-\int_{u_j}^{j\Delta}f(u|H_j,\theta_u)\,du}. \quad (6)$$

The conditional intensity function provides a canonical characterization of a point process that gives a history-dependent generalization of the rate function of a Poisson process (Brown et al., 2003).

Once the state model and the observation process model are defined (Barbieri and Brown, 2006), it follows from (Barbieri et al., 2004; Eden et al., 2004) that the point process adaptive filter algorithm for this system is

$$\text{One-step prediction}: \quad \theta_{j|j-1}=\theta_{j-1|j-1}, \quad (7)$$

$$\text{One-step prediction variance}: \quad W_{j|j-1}=W_{j-1|j-1}+W_\varepsilon, \quad (8)$$

$$\text{Posterior mode}: \quad \theta_{j|j}=\theta_{j|j-1}+W_{j|j-1}(\nabla\log\lambda_j)[n_j-\lambda_j\Delta], \quad (9)$$

$$\text{Posterior variance}: \quad W_{j|j}=[W_{j|j-1}^{-1}-(\nabla^2\log\lambda_j)[n_j-\lambda_j\Delta] - (\nabla\log\lambda_j)[\nabla\lambda_j\Delta]']^{-1}, \quad (10)$$

where $\lambda_j=\lambda(j\Delta|H_j,\theta_{j|j-1})$ and $\nabla(\nabla^2)$ denotes the first (second) derivative of the indicated function with respect to θ for $j=1,\ldots,J$. The notation $\theta_{j|k}$ defines the state at time $j\Delta$, given the observations from $(0, k\Delta]$.

Given $\theta_{j|j}$, the point process adaptive filter estimate of θ at time $j\Delta$, it follows from (2)–(5) that the instantaneous estimates of mean *R–R*, *R–R* interval