Point process time-frequency analysis of respiratory sinus arrhythmia under altered respiration dynamics

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Point Process Time-Frequency Analysis of Respiratory Sinus Arrhythmia under Altered Respiration Dynamics

Sandun Kodituwakku, Sara W Lazar, Premananda Indic, Emery N Brown (Fellow IEEE), and Riccardo Barbieri (Senior Member IEEE)

Abstract—Respiratory sinus arrhythmia (RSA) is largely mediated by the autonomic nervous system through its modulating influence on the heartbeat. We propose an algorithm for quantifying instantaneous RSA as applied to heart beat interval and respiratory recordings under dynamic respiration conditions. The blood volume pressure derived heart beat series (pulse intervals, PI) are modeled as an inverse gaussian point process, with the instantaneous mean PI modeled as a bivariate regression incorporating both past PI and respiration values observed at the beats. A point process maximum likelihood algorithm is used to estimate the model parameters, and instantaneous RSA is estimated by a frequency domain transfer function approach. The model is statistically validated using Kolmogorov-Smirnov (KS) goodness-of-fit analysis, as well as independence tests. The algorithm is applied to subjects engaged in meditative practice, with distinctive dynamics in the respiration patterns elicited as a result. Experimental results confirm the ability of the algorithm to track important changes in cardiorespiratory interactions elicited during meditation, otherwise not evidenced in control resting states.

I. INTRODUCTION

A large number of autonomic and hemodynamic parameters are influenced by respiratory activity. Among them, respiratory sinus arrhythmia (RSA) can be defined as the variations in the heart rate which occur simultaneously with the respiration cycle [1]. At typical resting respiratory frequencies, heart rate increases during inspiration, and decreases during expiration. RSA is usually considered as an indirect measure of vagal cardiac control, although at lower respiratory frequencies sympathetic cardiac control contributes to RSA as well [1]. A key problem in cardiorespiratory engineering is to efficiently and accurately quantify RSA under different physiological conditions, such as variations in respiration and changes in sympathetic-parasympathetic inputs. A solution to this issue could yield critical insights into the mechanisms involved in short-term cardiorespiratory coupling [1] [2].

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In previous work [3] [4], RSA was defined using simple time domain measures of beat interval series. Filtering and transfer function approaches were also used in quantifying RSA [5] [6], and a bivariate autoregressive model was further proposed to estimate the time-varying RSA gain [7] [8]. As most of these methods are not able to overcome stationarity issues and estimate fast changes in RSA at arbitrarily small time scales, a point process framework for heart beat dynamics [9] [10] has been proposed to assess RSA within an adaptive point process filtering algorithm [11].

In this paper, we use a novel local maximum likelihood method within a point process framework to allow for instantaneous estimation of RSA. Importantly, as measures based on the traditional subdivision in oscillatory frequency components might not be reliable in the presence of nonstationary respiratory patterns, we further propose a new method for dynamically selecting the RSA gain within the transfer function spectrum, based on a time-frequency characterization of the respiratory cycle and the time-varying coherence between respiration and heart beat series (pulse intervals, PI). Such combined method is capable of computing reliable, instantaneous estimates of RSA by accounting for rapid dynamic changes in both respiration patterns and autonomic inputs. The new algorithm is validated on simulated data, as well as applied to recordings from subjects practicing meditation.

II. METHODS

A. Point Process Model of Heart Beat Interval Dynamics

Integrate and fire models are regularly used to simulate heart beats, and such model postulates that the resulting times between two firing events (the PIs) have statistical properties of an inverse Gaussian process [9]. Additionally, autonomic inputs to the SA node are part of the cardiovascular control circuitry, thus the PI variations are dynamic or time-varying [9]. For this reason, we here model the pulse intervals as a history dependent, inverse gaussian point process model with time-varying model parameters. Assume in a given observation interval \( (0, T) \), K successive pulses are recorded: \( 0 < u_1 < u_2 < \ldots < u_K \leq T \). Given any pulse-timing \( u_k \), the waiting time until the next pulse-timing (ie. next PI), obeys a history dependent inverse gaussian probability density \( f(t) \) given by

\[
f(t|u_k) = \frac{\theta(t)}{2\pi(t-u_k)^3} \cdot \exp \left\{ -\frac{1}{2} \frac{\theta(t)(t-u_k - \mu_{PI}(t))^2}{\mu_{PI}(t)(t-u_k)} \right\},
\]

where \( t \) is any time satisfying \( t > u_k \), and \( \mu_{PI}(t) > 0 \) is the mean of the distribution, which is an estimation of the
instantaneous mean PI. \( \theta(t) > 0 \) is the shape parameter of the inverse gaussian distribution.

Heart rate is often defined as the reciprocal of PIs [12]. For PIs measured in seconds, \( r = c/(t - u_k) \), where \( c = 60 \text{s/min} \), gives the estimation of heart rate in beats per minute (bpm). By using a standard change of variables formula [13], mean and standard deviation of the heart rate probability density are given by [9]

\[
\mu_{HR}(t) = c \left( \frac{1}{\mu_{PI}(t)} + \frac{1}{\theta(t)} \right),
\]

\[
\sigma_{HR}(t) = c \left[ \frac{2\mu_{PI}(t) + \theta(t)}{\mu_{PI}(t)\theta^2(t)} \right]^{\frac{1}{2}},
\]

and they respectively define the instantaneous estimates of heart rate and heart rate variability.

**B. Bivariate Model for RSA analysis**

The influence of past autonomic inputs and respiration activity on the PIs are incorporated into the model by defining a bivariate regression on the mean of the point process probability density(1),

\[
\mu_{PI}(t) = a_0(t) + \sum_{k=1}^{p} a_k(t) P_{I_{t-k}} + \sum_{k=1}^{q} b_k(t) R_{P_{I_{t-k}}}. \tag{4}
\]

Note that the respiration signal (RP) is sampled at the pulse timings, so that both respiration and PIs are synchronized.

RSA can then be defined as the transfer function from RP to PI,

\[
H_{12}(\omega, t) = \frac{\sum_{k=1}^{q} b_k(t) z^{-k} |_{z=\omega^{2\pi f_s}}}{1 - \sum_{k=1}^{p} a_k(t) z^{-k} |_{z=\omega^{2\pi f_s}}}. \tag{5}
\]

We propose two methods of estimating the RSA gain from the above transfer function. First, the time-varying respiration spectrum \( P_{RP}(\omega, t) \) is used to estimate the frequency \( \omega_{RP}(t) \) where maximum respiration power is concentrated at each time instance, i.e.,

\[
\max_{\omega} [P_{RP}(\omega, t)] = P_{RP}(\omega_{RP}, t). \tag{6}
\]

Then, RSA gain can be estimated by evaluating (5) at \( \omega_{RP} \),

\[
RSA^A_{gain}(t) = [H_{12}(\omega_{RP}, t)]. \tag{7}
\]

Second, we evaluate the RSA gain at the frequency where maximum interaction between PIs and respiration occur. In this regards, we use the time-varying autoregressive coherence spectrum \( Coh(\omega, t) \) [5] to estimate the frequency \( \omega_{coh}(t) \) where coherence is maximum, i.e.,

\[
\max_{\omega} [Coh(\omega, t)] = Coh(\omega_{coh}, t), \tag{8}
\]

and the RSA gain is evaluated at \( \omega_{coh} \),

\[
RSA^B_{gain}(t) = [H_{12}(\omega_{coh}, t)]. \tag{9}
\]

**C. Local Maximum Likelihood Estimation**

A local maximum likelihood method [14] was used to estimate the unknown time-varying parameter set \( \xi = \{ \{a_k\}_{k=0}^{p}, \{b_k\}_{k=1}^{q}, \theta \} \). In estimating \( \xi \) at time \( t \), we take a local likelihood interval \( (t-l, t] \), where \( l \) is the length of the local likelihood observation interval. Within \( (t-l, t] \), we may observe \( n \) pulses, \( t-l < u_1 < u_2 < \ldots < u_n \leq t \). Then, we consider the local joint probability density of \( u_{t-l:t} = \{u_1, \ldots, u_n\} \). Log likelihood of joint probability density is given by

\[
\log f(u_{t-l:t}) = \sum_{j=2}^{n} w(t - u_j) \log f(u_j - u_{j-1})
\]

\[+ w(t - u_j) \log \int_{t-u_j}^{\infty} f(v)dv, \tag{10}\]

where \( w(t - u_j) = \alpha^{t-u_n}, 0 < \alpha < 1 \), is a weighting function for the local likelihood estimation [14]. The weighting time constant \( \alpha \) governs the degree of influence of a previous event observation \( u_j \) on the local likelihood at time \( t \). Second term of (10) represents the likelihood of partially observed interval since the last observed pulse \( u_n \) (right censoring). To maximize the local log likelihood in (10) we use a Newton-Raphson method, and obtain the local maximum likelihood estimate of \( \xi \). Of note, the time increment \( \Delta \) for computing the next \( \xi \) from \( t \) to \( t + \Delta \) can be chosen as arbitrarily small, thus yielding instantaneous estimates of heart rate and heart rate variability.

Goodness-of-fit of the proposed model was evaluated using a Kolmogorov-Smirnov (KS) test based on the time-rescaling theorem [15]. The test uses the conditional intensity function \( \lambda(t) = f(t)/[1 - \int_{0}^{t} f(v)dv] \) to transform pulse events into independent observations on the interval \([0, 1]\), and the KS plot allows to test the agreement of the transformed observations and the ideal uniform probability density. The transformed quantiles’ autocorrelation function is further computed to check independence of the transformed intervals.

**III. RESULTS**

**A. Experimental Protocol**

Meditation essentially consists of subjects focusing on their breath and passively ignoring everyday thoughts. For this reason, mastering meditation techniques has been often mischaracterized as “simply resting”. To such extent, the present experiment considers two groups of subjects, one group consists of experienced meditators, whereas the other group consists of subjects with no meditation experience. The experiment starts with 6 minutes of control period, followed by 1 minute of fixation, then 24 minutes of meditation, followed by 1 minute of fixation, and finally 6 minutes with the subject silently counting random numbers [16]. The control subjects are asked to simply rest during the “meditation” period. During the experiment, blood volume pressure (BVP) signal, and a belt signal proportional to lung volume changes were recorded at 1 kHz. BVP was used to identify the PIs, and the belt signal was sampled at these pulse timings to obtain the respiration values at the beats.

**B. PI and HRV Estimation**

First, optimal values for regression orders of the bivariate model \( p \) and \( q \), maximum-likelihood interval \( l \), and weighting time constant \( \alpha \) were obtained by minimizing the Akaike Information Criterion for maximum likelihood estimation, as well as the KS distance on the KS plot. This empirical optimization yields to \( p = 4 \), \( q = 6 \), \( l = 90s \), and \( \alpha = 0.98 \).
The KS plot and autocorrelation function for this final model are shown in Figure 1 for a representative subject.

Then, the proposed maximum likelihood point process model was applied to both meditating and control subjects with model parameters as described above. The resulting instantaneous mean PI estimate $\mu_{PI}(t)$ (4), and HRV index $\sigma^2_{HR}(t)$ (3) for two representative subjects are shown in Figures 2 and 3. In particular, sudden variations can be observed in the original PI series of the experienced meditator (Fig. 2). These distinctive contractions are not classifiable as ectopic beats, but could be attributed to fast tachycardic and/or bradycardic events, possibly due to sharp shifts in the sympatho-vagal balance. Sharp increases in the HRV index are consequently observed at corresponding timings. Of note, similar transients were less frequent in the control subject (Fig. 3).

Average statistics for 6 subjects from each group were performed for mean PI, HRV, and the LF/HF index [12]. Results show no significant changes in all parameters in the control group, whereas a general increase in HRV was observed in the meditating group. Importantly, we observed that the respiratory cycle often tends to slow down during both meditation practice and relaxation, and some of the respiratory variability may fall well within the low frequency (LF) band of the standard HRV frequency band division [12]. As a consequence, the RSA-elicited PI variability would mirror the respiratory spectral distribution, with vagal modulated cardiac dynamics distributed between both LF and HF bands, thus potentially biasing the LF/HF index.

C. Instantaneous RSA Estimation

Instantaneous time-frequency RSA estimates are computed using the bivariate AR point process and transfer function methods described in Section II-B. The algorithms were first tested with artificial series simulating both sudden and gradual shifts in RSA gain, as well as shifts in the main frequency where the two series are coupled. Results (not shown) demonstrate that the proposed algorithm is very robust and stable even under sudden changes in the foremost oscillatory (respiratory) frequency, while still being capable of accurately estimating sudden and gradual changes in the RSA gain.

As applied to the considered experimental data, the first important finding was that both $RSA^a_{gain}(t)$ and $RSA^b_{gain}(t)$ gave very similar estimates in all subjects considered. This finding was somehow expected, as PIs are often highly correlated with respiration activity at the main respiratory frequency, and indicates both $RSA^a_{gain}(t)$ and $RSA^b_{gain}(t)$ as reliable estimates of instantaneous RSA. Results are shown for one experienced meditator in Figure 4, and for a control subject in Figure 5. For both subjects we generally observed a high coherence (> 0.8), with only one evident exception in the experienced meditator where coherence drops below 0.8 at the timings corresponding to some of the fast transients in the heart beat dynamics mentioned before. Here, the significant increase in RSA gain during meditation is clearly noticeable, whereas in the control example RSA gain seems to fluctuate around baseline levels along the entire experiment\textsuperscript{1}.

Average RSA statistics for 6 subjects from each group are shown in Table 1. Results point at a major increase (58\%) in RSA during meditation, with high statistical significance ($p = 0.031$) compared to the baseline epoch. On the other hand, the control group does not show any significant change in RSA during relaxation ($p > 0.2$). During the silent random number generation phase, RSA values are statistically comparable to baseline levels for both groups.

Differently from the LF/HF assessment, our proposed method is robust to variations in respiration patterns as we

\textsuperscript{1}Note that for a fair comparison across subjects, the RSA gain (9) was normalized by the standard deviation of the corresponding respiration signal.

\begin{table}[h]
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\hline
 & Meditation & Control \\
\hline
Baseline & 0.029 & 0.028 \\
Practice & 0.035 ($+58\%$, $p = 0.031$) & 0.026 ($-7\%$, $p > 0.2$) \\
Numbers & 0.024 ($-10\%$, $p > 0.2$) & 0.024 ($-14\%$, $p > 0.2$) \\
\hline
\end{tabular}
\caption{Average RSA gain of 6 subjects each in the meditation and control groups. The percentage change, and Wilcoxon signed rank test results compared to the baseline epoch are also reported.}
\end{table}
relies on the respiratory spectral power distribution and the dynamic coherence between respiration and PIs, without any artificial subdivision in frequency bands. As a further proof that RSA gains are not considerably biased by possible shifts in respiration frequency, we have computed similar indices at a fixed frequency, where coherence is the highest on average along each experiment, and verified that average statistics using these quantities confirm the presented results.

In summary, while traditional HRV indices confirm previous findings pointing at an autonomic assessment not necessarily reflective of quiescent cardiac dynamics [17], and possibly biased by altered breathing patterns [18], our statistical RSA appraisal substantiates previous reports of a marked increase of RSA during meditation [19].

IV. CONCLUSIONS

We have proposed a maximum likelihood point process model for instantaneous RSA estimation combined with a time-frequency RSA evaluation based on respiration spectrum and coherence. Our novel framework allows for robust tracking of RSA changes at any time resolution, as well as overcoming potential problems associated with traditional subdivision in standard frequency bands in the presence of distinctive respiratory dynamics. The new algorithm was applied to subjects either practicing meditation, or just asked to relax under equal conditions. Results show a significant increase in RSA under meditation practice which is not evident in the control group, encouraging further investigation into the effects of meditation techniques on cardiovascular control and into the potential benefits of meditation on cardiovascular health. Overall, the dynamic statistical measures computed from our point process framework provide the basis for potential real-time indicators for ambulatory monitoring and instantaneous assessment of autonomic control in clinical practice.

REFERENCES


