NONINVASIVE CARDIOVASCULAR SYSTEM IDENTIFICATION USING PULSE WAVE TRANSIT TIME

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Abstract: This work shows that it is possible to model the heart rate autonomic control from samples of ECG, PPG and respiratory flow waveform (RFW). Usually, such modelling is carried out with physiological signals that are more difficult to acquire during the clinical exams: ECG, arterial blood pressure and instantaneous lung volume. In this work, the ECG, PPG and RFW were recorded with a portable system from volunteers at two different postures: supine and standing. The ECG, PPG and RFW were processed off line in order to obtain the RR, the inverse of the pulse wave transit time (IPWTT) and the RFW series. These series were used as input for ARMA models and the obtained results were compared to the ones available in the literature. The qualitative and quantitative comparisons of the results reveal very similar performance.

1 INTRODUCTION

The power spectral density (PSD) analysis of the heart rate variability (HRV) is widely used for the non-invasive assessment of the autonomic nervous system (ANS). The higher frequency (HF) components of the HRV (0.15 to 0.4 Hz) are related to the breathing rate (Respiratory Sinus Arrhythmia - RSA) and mediated by the parasympathetic system (Pagani *et al.*, 1986; Berntson *et al.*, 1997). The lower frequency components (LF: 0.04 to 0.15 Hz) comprise the Mayer waves (around 0.1Hz) and contain oscillations due to the interactions between the heart rate (HR) and the blood pressure (BP). The LF power is affected by both sympathetic and parasympathetic systems. The LF/HF power ratio is often used as an index of the sympathovagal balance (Pagani *et al.*, 1986; Task Force, 1996).

Although the spectral analysis contributes to the understanding of the heart rate autonomic control, it characterizes the output and not the system itself. Modelling allows the system characterization, i.e., to obtain the transfer functions between each input and the output and their impulse responses (Xiao *et al.*, 2005).

The cardiovascular system neural control has been modelled by a multi-input/single-output (MISO) system, using as inputs, the arterial blood pressure (ABP) and the instantaneous lung volume (ILV) and, as output, the HRV (Perrott and Cohen, 1996). Systolic blood pressure (SBP) series obtained from the ABP waveform has also been used as input to discrete models instead of ABP samples (e.g., Baselli *et al.*, 1997).

The instantaneous ABP is registered by a catheter inserted into an artery or non-invasively, using commercial systems such as the Finapress (Ohmeda Inc). The ILV is usually measured using chest-abdomen inductance plethysmography.

Research on the cardiovascular models has provided useful data to characterize patients' clinical condition (Xiao *et al.*, 2005; Faes *et al.*, 2006). Nevertheless, the acquisition of the ILV and ABP as described above may hamper the broad use of models to obtain diagnosis indexes. The chest-abdomen inductance plethysmograph is cumbersome in procedures during which cardiac arrest may occur. The Finapress is not available in many clinical facilities and it is susceptible to movement artefacts. Besides, it is also difficult to synchronize

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signals acquired from different commercial systems since no information is usually provided on their processing (time delay).

As alternatives to the use of the SBP and ILV as model inputs, the pulse wave transit time (PWTT) and respiratory flow waveforms (RFW) are here investigated.

The PWTT, usually defined as the interval between the ECG R-wave and the base of the leading photoplethysmography (PPG) deflection within a same cardiac cycle (Figure 1), has been shown to be significantly correlated to the systolic blood pressure (SBP). The SBP is inversely proportional to the PWTT (Lass *et al.*, 2004; Teng and Zhang, 2006).

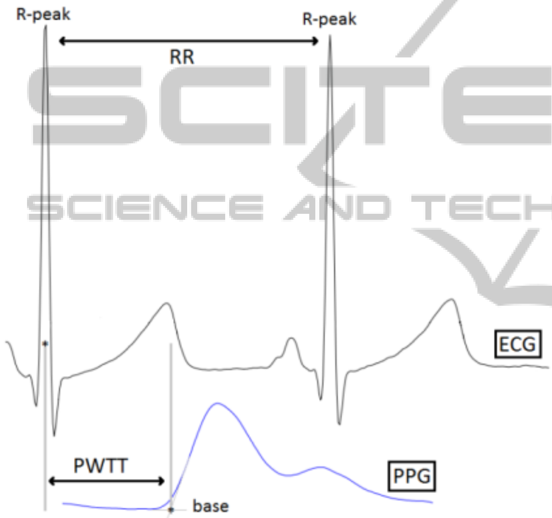

Figure 1: The PWTT is the interval between the ECG R-wave peak and the base of the leading edge of the PPG. The RR series is a measurements set of the time interval between consecutive ECG R-waves.

Eckberg (2003) suggests that the mechanical stretch of pulmonary and thoracic receptors has small contribution to the RSA, pointing out that the RSA is mainly generated by the central respiratory motoneurone activity. Therefore, the breathing rate obtained from the inspired and expired flow waveform (acquired by nasal thermometry) may convey information on the respiratory motoneurone discharges that affect the HRV.

This work investigates the feasibility of using the PWTT series and the RFW samples as inputs for the cardiovascular system neural control modelling. These signals can be acquired with a simple system, barely disturbing the usual clinical exams. Therefore, their use circumvents practical difficulties to obtain useful indexes from models in order to help assessing patients' health.

2 MATERIALS AND METHODS

This section describes the acquisition of the physiological signals from healthy volunteers and the methods used to model the HRV.

2.1 Subjects

Five volunteers (4 males; 1 female; age: 22-46 years; ASA1) took part of the study. The protocol (Project 529/10) was approved by the Research Ethics Committee of the Federal University of Santa Catarina (UFSC). These subjects were informed about the protocol and gave their written consent. The experiments were carried out at the Medical School Hospital of the UFSC.

2.2 Protocol

The experimental data were recorded from volunteers at two different postures: supine and standing. After changing the posture, five minutes were waited for hemodynamic stabilization before the data acquisition.

At each position, the subjects breathed according to two different patterns guided by a metronome.

The first pattern corresponds to a broadband respiratory signal (Poisson distribution) necessary as input to generate a reliable autonomic heart rate control model (Berger *et al*., 1989). This pattern consists of breathing cycles ranging from 1 to 15s (mean=5s) during 6 minutes.

The second pattern is paced breathing at the rate of 12 breaths/min. This pattern was recorded for each subject during 2 minutes.

2.3 Signal Acquisition and Discrete–time Signal Processing

A portable device developed in our laboratory was employed to acquire the required waveforms: RFW by nasal thermometry, EGC and PPG. The RFW, ECG and PPG were filtered by band-pass second order Butterworth filters to limit their bandwidths to 0-6Hz, 0.5-100Hz and 0.8-10Hz, respectively. The filtered waveforms were sampled at the rate of 1 kSPS and converted to 12-bit words. The sampled waveforms were transmitted via Bluetooth to a laptop computer where they were stored into separated files (16 bits Intel PCM format). More information on the developed system can be found elsewhere (Giassi Jr. *et al.*, 2011).

The sampled waveforms were processed off line in order to obtain the inputs series for the models.

The ECG, PPG and RFW were further filtered by digital FIR filters in order to attenuate interfering signals. The ECG, PPG and RFW bandwidths were limited to 0.5-40Hz, 0.26-15Hz and 0-0.75Hz, respectively.

The R-wave peaks of the ECG were detected using continuous wavelet transform (CWT) as proposed by Ghaffari *et al.* [9]. According to these authors, the algorithm achieved a sensitivity of 99.91% and a predictivity of 99.72% when applied to signals of the MIT/BIH database. The RR series is the measurements set of the time interval between consecutive R-waves of the ECG. As it corresponds to an irregularly sampled waveform, the RR series was linearly interpolated to achieve the sampling rate of 1.5 SPS. The HR consists of the inverse interpolated RR series.

The ECG and the PPG are used to obtain the PWTT series. The Figure 1 shows a PWTT measurement for a cardiac cycle. The PWTT is the time interval between the R-wave peak and the base point within the same cardiac cycle. Following Chiu *et al.* (1991), the base marker corresponds to the intersection of the tangent through the steepest part of the slope (determined by the maximum first derivative point) with its baseline. The PWTT series is the set of these consecutive measurements. The IPWTT series corresponds to 1/PWTT. The IPWTT series was also interpolated to achieve 1.5 SPS.

The RFW was decimated to 1.5 SPS in order to have all the input signals sampled at the same rate. The use of this sampling rate allows the comparison of the obtained impulse responses to those of Perrott and Cohen (1996).

The smoothness priors approach (Tarvainen *et al.*, 2001) was used to detrend the HR, IPWTT and RFW. For that, the lambda value used was 50 that makes the detrending to correspond to a high-pass filter with a cut-off frequency of 0.0375 Hz.

The HR, RFW and the IPWTT series were then normalized by their respective standard deviation.

2.4 The Model

Closed-loop systems have been proposed to model the cardiovascular system neural control to take into account the SBP and heart rate (HR) interactions (Appel *et al.*, 1989). Nevertheless, Takalo *et al.* (2004) showed that the transfer functions obtained from the open-loop model proposed by Perrott and Cohen (1996) were not significantly different from those obtained by the closed-loop model. In order to assess the adequacy of the IPWTT and RFW as model inputs, this work employs the open-loop model.

Briefly, the open-loop model is described by the Eq. 1 where the usual ILV and SBP inputs are replaced by RFW and IPWTT, respectively.

$$\begin{aligned} HR[n] &= -\sum_{i=1}^{N} a[i] HR[n-i] \; + \\ &+ \sum_{j=m}^{M} b[j]\, RFW[n-j] \; + \\ &+ \sum_{k=q}^{Q} c[k]\, IPWTT[n-k] \; + \; e[n] \end{aligned} \tag{1}$$

where **n**, **i**, **j** and **k** are discrete time indexes; a[i] are the autoregressive (AR) coefficients; b[j] and c[k] are the moving average (MA) coefficients and e[n] is the estimation error of the model. **N**, **M** and **Q** define the order of the model. **m** and **q** stand for delays between each input and the output.

Due to the non-causal coupling between the breathing and the HR (RFW→HR) (Mullen *et al.*, 1997), **m** was made equal to -4.

The interactions of the SPB and HR are mediated by their autonomic coupling (IPWTT→HR) and also, by the mechanical effects of the HR on the SBP (HR→IPWTT). To disentangle that, it is necessary to impose causality (Mullen *et al.*, 1997) that is achieved by making **q** equal to 1.

The coefficients estimates are calculated using the least square method. The multivariate model order was determined by means of the autoregressive moving average (ARMA) parameter reduction method: APR (Perrot and Cohen, 1996).

Applying the Z transform to the Eq. 1, the transfer functions between each input and the output are given by:

$$H_{HR,RFW}(z) = \frac{B(z)}{A(z)} = \frac{\sum_{j=m}^{M} b(j)\, z^{-j}}{1 + \sum_{i=1}^{N} a(i) z^{-i}} \tag{2}$$

$$H_{HR,IPWTT}(z) = \frac{C(z)}{A(z)} = \frac{\sum_{k=q}^{Q} c(k)\, z^{-k}}{1 + \sum_{i=1}^{N} a(i) z^{-i}} \tag{3}$$

From these equations, each impulse response (RFW→HR and IPWTT→HR) can be obtained by applying the inverse Z transform for RFW(z)=1 and IPWTT(z)=1.

2.5 Statistical Analysis

The Student's t-test was used to compare the power of the LF and HF bands between the PSD curves obtained from the measured ($LF_{measured}$ and $HF_{measured}$) HR and from the modelled (LF_{model} and HF_{model}) HR. This was repeated for the different postures and breathing patterns. A p-value below

0.05 was chosen as threshold for statistical significance.

3 RESULTS

From the data recorded during the broadband respiratory protocol, the ARMA model order and its coefficients were estimated for each volunteer.

With the estimated ARMA model parameters of each subject, HR output series were generated from the IPWTT and RFW series obtained for irregular (broadband) and paced breathing patterns at the supine and standing postures.

Figures 2 and 3 show the typical impulse responses (RFW→HR and IPWTT→HR, respectively) obtained from the ARMA model for a subject at supine posture breathing according to the broadband pattern.

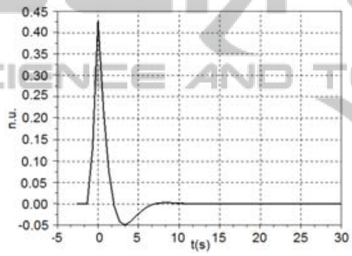

Figure 2: Typical RFW→HR impulse response of the ARMA model obtained from a subject at supine position, breathing according to the broadband pattern.

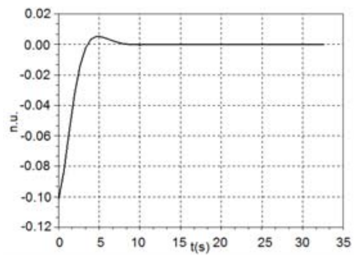

Figure 3: Typical IPWTT→HR impulse response of the ARMA model obtained from a subject at supine position, breathing according to the broadband pattern.

The fitness of the models could be verified by observing their responses to the RFW and IPWTT series that were acquired from the same subjects during the paced breathing. As illustrated by the Figure 4, the models outputs were able to follow up the measured HR, showing their suitability.

In order to compare the model output (HR_{model}) to the measured HR ($HR_{measured}$) in the frequency domain, each of these two series were segmented in three non-overlapping 40s segments and Hamming window was applied to all them. For each series, the DFT of the three segments were averaged. Next, the PSD curves of the $HR_{measured}$ and HR_{model} obtained from all five subjects were averaged. Figures 5 and 6 show the averaged PSD curves obtained from the subjects at supine and standing postures, respectively, breathing at irregular pace. These averaged PSD curves were also obtained for the subjects breathing at 12 breaths/min during supine (Figures 7) and standing (Figures 8) positions.

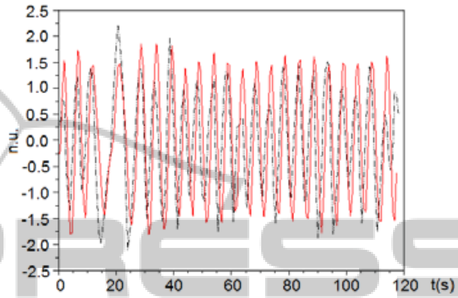

Figure 4: Typical result of HR series generated by the model (continuous red line) that follows up the HR (dashed black line) measured from a subject at supine posture breathing at 12 breaths/min.

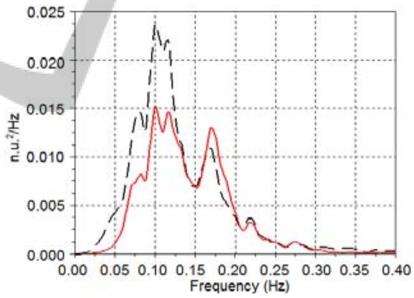

Figure 5: Averaged PSD of the $HR_{measured}$ (dashed black line) and the HR_{model} (continuous red line) for all subjects at supine posture, breathing at irregular pace.

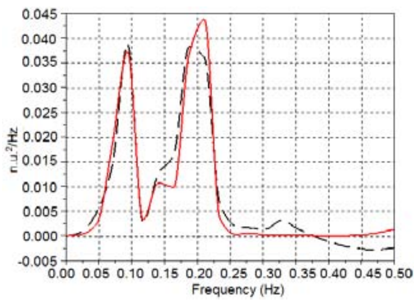

Figure 6: Averaged PSD of the $HR_{measured}$ (dashed black line) and the HR_{model} (continuous red line) for all subjects at standing posture, breathing at irregular pace.

Measurements of LF and HF power were carried out in normalized units (Task Force, 1996).

Table 1 contains the HR power values within the LF and HF bands that were obtained from the averaged PSD curves of all subjects breathing at irregular breathing pattern in the different postures. Table 2 shows the same for the subjects breathing at 12 breaths/min.

The Student's t-test does not show significant differences between $LF_{measured}$ and LF_{model} and neither between $HF_{measured}$ and HF_{model} for the two different postures and for the two different breathing patterns.

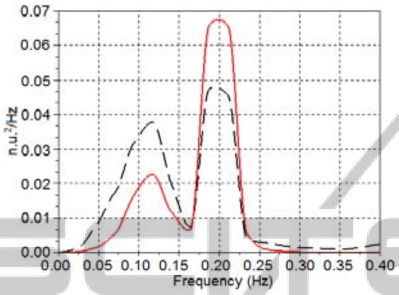

Figure 7: Averaged PSD of the $HR_{measured}$ (dashed black line) and HR_{model} (continuous red line) for all subjects at supine posture, breathing at 12 breaths/min.

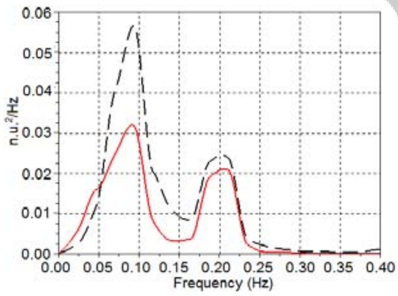

Figure 8: Averaged PSD of the $HR_{measured}$ (dashed black line) and the HR_{model} (continuous red line) for all subjects at standing posture, breathing at 12 breaths/min.

4 DISCUSSION

According to Payne *et al.* (2006), the variable cardiac pre-ejection period constrains the use of the IPWTT as a reliable estimate of the SBP; however, these authors point out that it may be useful for assessing the SBP variability.

When compared to non-invasive SBP measurements carried out with an arterial tonometer, the IPWTT has lower cost and does not offer risk of interrupting the perfusion due to the application of excessive pressure to the finger-cuff (Teng and Zhang, 2006).

Using the IPWTT and RFW as inputs, the model parameters were generated for each volunteer from data recorded when they were breathing according to an irregular pattern (Berger *et al*, 1989). The APR method was used to define the model orders (Perrott and Cohen, 1996).

Table 1: LF and HF powers (nu) measured from the averaged PSD curves for subjects breathing at irregular pace (Mean±SD).

	$LF_{measured}$	$HF_{measured}$	LF_{model}	HF_{model}
Supine	70.42 ±10.36	29.58 ±10.36	58.74 ±11.60	41.25 ±11.60
Standing	84.71 ±6.02	15.29 ±6.02	73,24 ±10.74	26.76 ±10.74

Table 2: LF and HF powers (nu) measured from the averaged PSD curves for subjects breathing at 12 breaths/min (Mean±SD).

	$LF_{measured}$	$HF_{measured}$	LF_{model}	HF_{model}
Supine	46.8 ±27.14	53.82 ±27.14	27.59 ±22.35	72.41 ±22.35
Standing	66.46 ±11.52	33.54 ±11.52	60.00 ±24.70	40.04 ±24.70

As can be seen in Figure 4, the generated models were able to follow the measured HR when the subjects were breathing at a constant rate.

It is possible to note in the Figures 2 and 3 that the model impulse responses are, respectively, very similar to the ILV→HR and SBP→HR impulse responses obtained, for instance, by Perrott and Cohen (1996) and by Chen and Mukkamala (2008).

The averaged PSD obtained for the $HR_{measured}$ and HR_{model} from the different volunteers breathing at irregular pace (Figures 5 and 6) and at 12 breaths/min (Figures 7 and 8) presented similar trends.

The statistics results do not point significant differences between the LF powers and HF powers calculated for the $HR_{measured}$ and HR_{model}.

5 CONCLUSIONS

This work investigated the use of the IPWTT and RFW as inputs to generate ARMA models of the heart rate autonomic control.

The assessment of the presented results allows us to conclude that the generated models are able to follow up the HR of subjects not submitted to nervous blockade.

It is much safer and easier to get these two series to model the autonomic control during routine clinical exams as alternatives to ILV and SPB. Therefore, they can be recorded from a larger number of patients under different clinical conditions, speeding up the investigation of parameters obtained from the models that may be useful to assist diagnosis.

Additional experiments using the RFW and IPWTT series as inputs are going to be carried out under sympathetic, vagal and double blockade to evaluate the model output generated in these scenarios. Furthermore, the effect of the IPWTT on the causal analysis as proposed by Faes *et al.* (2006) will be also investigated.

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