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Frequency Modulation between Low- and High-Frequency Components of the Heart Rate Variability Spectrum May Indicate Sympathetic-Parasympathetic Nonlinear Interactions

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Abstract—**Interactions among physiological mechanisms are abundant in biomedical signals, and they may exist to maintain efficient homeostasis. For example, sympathetic and parasympathetic neural activities interact to either elevate or depress the heart rate, to maintain homeostasis. There has been considerable effort devoted to developing algorithms that can detect interactions between various physiological mechanisms. However, methods used to detect the presence of interactions between the sympathetic and parasympathetic nervous systems, to take one example, have had limited success. This may be because interactions in physiological systems are nonlinear and nonstationary. The goal of this work was to identify nonlinear interactions between the sympathetic and parasympathetic nervous systems in the form of frequency and amplitude modulations in human heart rate data. To this end, wavelet analysis was performed, followed by frequency analysis of the resultant wavelet decomposed signals in several frequency brackets we define as: very low frequency (f <0.04 Hz), low frequency (0.04-0.15 Hz) and high frequency (0.15-0.4 Hz). Our analysis suggests that the HF bracket is significantly modulated by the LF bracket in the heart rate data obtained in both supine and upright body positions. Furthermore, the strength of modulations is stronger in the upright than supine position, which is consistent with elevated sympathetic nervous activities in the upright position. However, there was no evidence of amplitude modulation among these frequencies.**

Keywords—**Frequency modulation, heart rate variability, nonlinear interaction, sympathetic, parasympathetic, nervous systems, wavelet, amplitude modulation.**

I. INTRODUCTION

Heart Rate Variability (HRV) is a marker of sympathetic and parasympathetic (vagal) influences on the modulation of heart rate [1]. It is through efficient interactions between the sympathetic and parasympathetic nervous activities that homeostasis of the cardiovascular system is properly maintained. Failure of the interactions may lead to sympathetic hyperactivity, promoting the occurrence of life-threatening ventricular tachyarrhythmias, whereas augmented vagal tone exerts a protective and antifibrillatory effect [2]. Experimental evidence suggests that myocardial ischemia, acute myocardial infarction, sudden cardiac death, and chronic heart failure all exhibit signs of autonomic function imbalance [3]. Consistent with autonomic imbalance, patients who have suffered a myocardial infarction (MI) have a marked decrease in HRV due to an increase in sympathetic and a decrease in vagal neural activities.

Spectral analysis of the R-R-intervals or heart rate has been widely used in HRV studies, and it has been shown reflect dynamics of the two nervous systems. Power spectra of human HRV can be divided into three main frequency zones: the PSD below 0.04 Hz is considered to be very low frequency (VLF), between 0.04 Hz and 0.15 Hz is the LF, and between 0.15 HZ and 0.4 HZ is the HF. The LF is found to be mediated by both the sympathetic and parasympathetic nervous influences and the HF is unequivocally believed to be dominated solely by the parasympathetic nervous system (including respiratory sinus arrhythmias) [2]. The VLF has been proven to be related to factors other than the ANS (e.g. temperature, hormones, regulation of vascular resistance etc.) [4]. The ratio of LF components to HF components of the PSD obtained from linear spectral analysis has been shown to be a useful marker of sympathetic-vagal balance in HRV in limited cases [2, 5], as stated earlier.

Interactions between the sympathetic and parasympathetic nervous activities can lead to variety of interesting nonlinear phenomena, such as entrainment or synchronization. In cases when synchronization does not occur, interactions between the two nervous systems may reveal itself in the form of either frequency or amplitude modulation in which one nervous system may be modulated by the presence of the other nervous system [6]. The interactions are believed to be nonlinear because physiological conditions would most likely involve ANS regulation based on dynamic and simultaneous activity of the sympathetic and vagal activities in response to physical environmental stressors [7]. These findings suggest that the autonomic imbalance seen in CHF and MI may result from abnormal interactions between the sympathetic and vagus nerves.

Methods used to detect the presence of interactions between the sympathetic and parasympathetic nervous systems, in particular, have had limited success. This may be because interactions in physiological systems are nonlinear and nonstationary [6, 8]. In addition, noise contamination compounds the complications of developing accurate nonlinear interaction detection algorithms. To this end, the goal of this study was to detect nonlinear interactions in the form of frequency and amplitude modulation bewteen the parasympathetic and the sympathetic nervous systems. Furthermore, possible frequency and amplitude modulations of the two nervous systems by the VLF component were also investigated.

II. MATERIALS AND METHODS

A. Detection of Frequency Modulation by Wavelet Transform

Wavelet transform was used on the heart rate data to separate the low and high frequency oscillatory components. Wavelet transform, specifically, was used because of its intrinsic properties of high frequency resolution in the low frequencies and high time resolution in the high frequencies. These properties are especially advantageous for extracting frequency oscillations in both low and high frequency ranges. The wavelet transform of a signal $x(t)$ is obtained as follows [4]:

$$T_x(f,t) = \sqrt{f}\int_{-\infty}^{\infty} x(u)\cdot\psi\cdot f\cdot(u-t)du$$

where ψ is a "mother" function, $T_x(f,t)$ are the wavelet coefficients, and f is frequency. The Morlet wavelet function is often selected to analyze rhythmic components. A simplified expression of the Morlet function is:

$$\psi(\tau) = \pi^{1/4}\exp(j2\pi f_0\tau)\exp\left[-\frac{\tau}{2}\right]$$

The time-frequency representation of the energy density of $x(t)$ can be obtained from the wavelet coefficient:

$$T_x(f,t) : E_x(f,t) = C\cdot f\cdot\left|T_x(f,t)\right|^2$$

where C is a constant determined by the wavelet mother function. $E_x(f,t)$, known as the "scalogram", is essentially a time averaged power spectrum. The scalogram, $E_x(f,t_i)$, is comprised of a frequency vector, $V_{t_i}(f)$, for every time point t_i. After a scalogram is generated, the local maxima of the $V_{t_i}(f)$ (representing instantaneous frequencies) are detected for every time point within the desired frequency bands (e.g., low and high frequency bands associated with heart rate spectra). Likewise, instantaneous amplitudes of the low and high frequency bands associated with the heart rate spectra can also be extracted.

To determine modulation characteristics of the high and low frequency oscillations, both extracted instantaneous amplitudes and frequencies are then subjected to the Fourier transform. This last step provides information about all modes involved in the modulation process. All the scalograms in this study were calculated with wavelet window length set to 4.

B. Validation with Simulation Example

In order to test the validity of this approach to determining the presence of frequency modulation, we consider a time series with three frequency components: very low frequency (VLF, below 0.04 Hz, center frequency $f_o = 0.02Hz$), low frequency (LF, 0.04-0.15 Hz, center frequency $f_1 = 0.08Hz$) and high frequency (HF, 0.2-0.4 Hz, center frequency $f_2 = 0.3Hz$). In this example, the LF is designed to be modulated by the VLF frequencies and the HF is modulated by both the LF and VLF frequencies.

C. Heart Rate Data Collection

Heart rate data from 7 healthy people (20-40 years old) were obtained with an instruction to breathe at a fixed frequency of 0.2 Hz (we used 0.2 Hz because it is close to the spontaneous respiration frequency of the subjects we studied), aided by a computer-generated sound. Twelve minutes of ECG data were collected for both supine and upright postures. Subsequently, the data sets between R-R markers were converted into 4 Hz instantaneous heart rate signals by interpolation. Each HR data set contained 2400 data points, which is equivalent to a 10 minute recording of HR (transition data between posture change was excluded).

III. RESULTS

1. Simulation Example: Detection of Frequency Modulation by Wavelet Transform

Fig. 1a shows the time tracing of the simulated frequency modulated signal as described in section B of Material and Methods. Fig. 1b shows the corresponding scalogram of the signal shown in Fig. 1a, which exhibits VLF activity near 0.02 Hz, LF activity at ~0.08 Hz and HF activity at ~0.3 Hz. From Fig. 1b, the highest frequency for each time point within each respective LF and HF band is extracted, and the resultant maximum frequency oscillations within the LF and HF bands are provided in Fig. 1c. Clearly, there are time-invariant oscillations in these plots. To determine the frequencies associated with these oscillations, power spectral densities (PSD) are calculated, and their results are provided in Fig. 1d for the HF and Fig. 1e for the LF bands. Fig. 1d (obtained from high frequency oscillations in Fig. 1c shows two distinct frequency bands centered at 0.02 Hz and 0.08 Hz. On the other hand, Fig. 1e shows a single distinct frequency centered at 0.02 Hz. Therefore, these results suggest that the HF is modulated by both the VLF (0.02 Hz) and LF (0.08 Hz) frequencies, while the LF is modulated by only the VLF (0.02 Hz). These results are the expected outcome since the data were generated to produce modulation of the LF by the VLF frequencies, and HF modulation by both the LF and VLF frequencies.

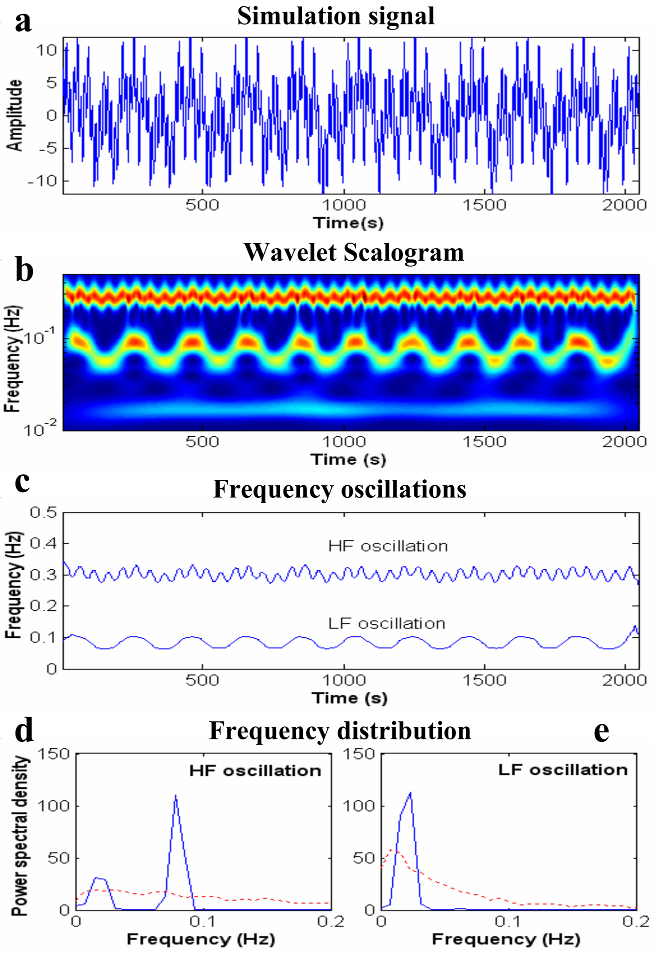

Fig. 1 a: simulated time series with FM; b: wavelet scalogram; c: maximum frequency oscillations extracted from the HF and LF bands of the scalogram in b; d-e: power spectral densities of the HF and LF oscillations in c (solid lines), respectively. Dotted lines in d-e represent the statistical threshold lines.

To quantitatively determine if the spectral power of the frequency oscillations shown in Figs. 1d-e are statistically significant, 20 independent realizations of Gaussian white noise (GWN) time series of the same data length as the simulation example data were generated. Each of these 20 realizations of GWN time series were subjected to the identical data processing described earlier as the simulation example data. The mean plus two standard deviations of the 20 realizations of PSD was used as the statistical threshold. Any spectral power above this statistical threshold indicates 95% probability that the frequency or amplitude modulation does exist and did not occur by some random occurrence. Note that both the HF and LF oscillation data obtained (see Fig. 1c) for GWN and the simulated example were all normalized to a unit variance prior to computation of PSD. This procedure allows a comparable comparison between the data of interest and the statistical threshold data obtained via noise sources. Superimposed on Fig. 1d-e are dotted lines to represent the statistical threshold. The fact that these statistical lines are below the spectral peaks associated with the simulation example data suggests a high probability of the validity of the frequency modulation of the VLF and LF on HF as well as VLF on LF.

2. *Detection of Frequency Modulation in Heart Rate*

We analyzed heart rate data from 7 subjects in both supine and upright positions with subjects instructed to breath at 0.2 Hz (12 breaths/min). Heart rate time series data were subjected to the identical data processing steps as detailed in the simulation example described above. Fig. 2a shows a representative heart rate from both postures, and the corresponding power spectra are shown in Fig. 2b. The frequencies with maximum magnitude were extracted at each time point in the HF (centered at 0.2 Hz) and LF (centered at 0.08-0.012 Hz) bands and their results are shown in Figs. 2c-d for both postures. The PSD of the HF and LF oscillations for both postures are shown in Figs. 2e-g for the supine and Figs. 2f-h for the upright posture. Both postures show significant FM of the HF by the frequencies in the LF range (spectra of HF frequency oscillations surpass threshold lines in LF band). However, no significant FM was found in the LF oscillations by VLF (spectra of LF frequency oscillations are lower than the threshold lines in VLF band) for any of the 7 subjects. The presence of FM of the HF by the LF in this subject is especially prevalent for the upright posture.

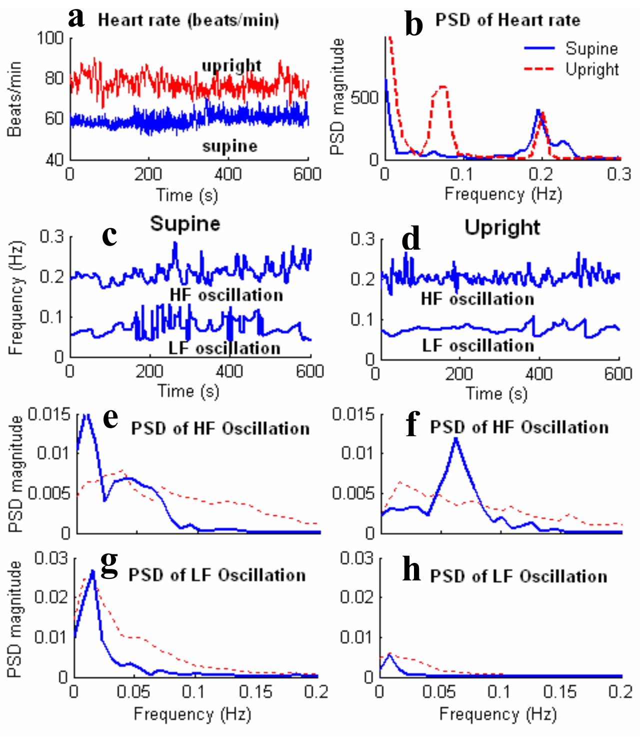

Fig. 2 a: representative instantaneous heart rate signals for supine and upright postures; b: PSD of heart ratet; c-d: HF and LF oscillations ectracted for supine and upright postures; e-h: PSD of HF and LF oscillations in c and d.

The averaged PSD of heart rate as well as HF oscillations from 7 subjects are shown in figure 3. Elevated LF and depressed HF power is seen with upright posture when compared to the supine position (Fig. 3a). The presence of the FM of the HF by the LF is consistently significant for both postures (Figs. 3b-3c). Further more, a considerably stronger FM in the upright is observed than supine position, as shown in Fig. 3d.

While not shown, we did not find consistent evidence of amplitude modulations among the VLF, LF and HF bands.

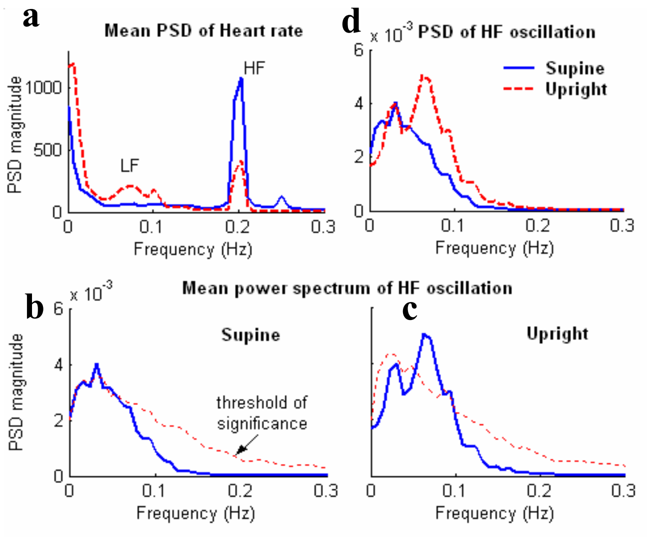

Fig. 3 a: mean PSD of heart rate for both postures; b-c: mean PSD of the FM (solid lines) and the statistical threshold (dotted lines) in the HF band for both postures; d: compare PSD magnitude of the FM strength between supine and upright posture.

IV. CONCLUSION AND DISCUSSION

A recent work by Sosnovtseva et al., using a double-wavelet approach, has found both frequency and amplitude modulation in renal autoregulation [6]. Similar to their work, we have employed a wavelet analysis followed by the stationary power spectrum, and found evidence of the frequency modulation (FM) of the HF by the LF bands. The presence of FM is an indication of a particular form of nonlinear interaction between the LF and HF bands. Physically, it may represent nonlinear interactions between the sympathetic and parasympathetic nervous systems. In this study, the strength of FM between the LF and HF bands was found to be stronger in upright than supine posture, which further supports our conjecture that this FM phenomenon in HR is induced by autonomic nervous interactions. As the sympathetic nervous activities increase, its modulating effect on the parasympathetic nervous system gets stronger.

Surprisingly, we did not find consistent amplitude modulation between LF and HF of the heart rate spectra. This is might be due to the sensitivity of HF amplitude to the depth of respiration and noises.

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