

## Effect of Respiration in Heart Rate Variability (HRV) Analysis

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**Abstract – Beat-to-beat changes in cardiac signals or heart rate variability (HRV) is controlled by the two branches of Autonomic Nervous System (ANS) in a very complex manner. Although traditional HRV (tHRV) analysis has shown to provide information on cardiac ANS control, it often fails to isolate the effect of two branches in HRV signals. This problem becomes more obvious especially at low respiratory rates since parasympathetic activity shifts into lower frequencies and overlaps the frequency interval where sympathetic region is defined. To investigate the effect of respiration in HRV analysis we have analyzed the data of 17 healthy subjects while they were performing normal breathing (NB) and deep breathing (DB). Data were analyzed and compared using both tHRV analysis and enhanced HRV (eHRV) analysis where we used respiration to locate the frequency interval of parasympathetic activity in HRV signal. eHRV analysis provided proper isolation and more accurate detection of parasympathetic and sympathetic control of the heart.**

### I. INTRODUCTION

Most of the organs in human body including heart are controlled by Autonomic Nervous System (ANS). Beat to beat variations in heart rate (HR) is regulated by ANS activity. Therefore analyzing HR variability (HRV) data can provide a tool to understand the mechanisms of ANS. In recent years, interest has grown in the study of the changes in HR with the purpose of finding new parameters and new criteria for better diagnosis of diseases associated with abnormal ANS activity [1], [2]. The effects of drugs and of external stimuli can also be better understood with analysis of HRV. As shown by many studies, HRV signals contain well defined rhythms which include physiological information [3]-[6]. Rhythms in the low frequency (LF) range, between 0.04 to 0.15 Hz, are usually considered as markers of sympathetic modulation. The high frequency (HF) range, between 0.15 to 0.4 Hz, can contain the rhythms regulated by parasympathetic activity. Vagal activity is the major contributor to the HF component.

Although many researchers consider the LF area to involve sympathetic activity, some suggest that the LF area corresponds to both sympathetic and parasympathetic activity. On the other hand, an increase in normalized LF power is always observed as a result

of sympathetic activation. Therefore, an increase in LF power is accepted as a sign of sympathetic activation by most authors [7], [8]. Similarly there are questions if HF power of HRV signal is a true measurement of parasympathetic activity. Clearly there is a problem of isolating parasympathetic and sympathetic activity in traditional HRV analysis. Although there are predefined frequency intervals as described above, there are many situations where the measurement of sympathetic is not pure sympathetic or measurement of parasympathetic is a mixed measure. For example respiration has a significant effect on the HR oscillations and parasympathetic activity is very closely related to respiratory sinus rhythm. Recent studies have shown that respiratory peak can be used as a quantitative measure of vagal control [9],[10]. Alcalay et al. has shown that respiratory peak in HR spectrum decreased as the dose of atropine increased when administered to human volunteers. This type of behavior, a direct dose dependent change in vagal activity is a clear indication of the sensitivity of the respiratory peak as a tool for vagal control. Therefore if one uses traditional HRV (tHRV) analysis and ignores the effects of respiration in HRV spectra, problem of isolating two branches rises since respiration can entrain HR and Blood Pressure (BP) oscillations over a wide range of frequencies, from 0.01 to 0.5 Hz [11]. Slow respiration can cause a false-positive increase in LF power (an increase due to increased parasympathetic activity rather than sympathetic) in tHRV analysis. Related to the importance of respiration is the logical conclusion that once the actual breathing rate is known, detection of the HF power should be centered around the fundamental respiration frequency (FRF) and not a default fixed frequency which is the case with tHRV analysis [11]. Uijtdehaage et al also found that “the changes in cardiac activity resulting from changes in sympathetic control cannot be interpreted accurately unless concurrent vagal activity is taken into account as well.” Therefore, the respiratory peak can be used as a tool to estimate vagal activity, and isolate both branches of ANS (i.e., sympathetic and parasympathetic) [12]. Isolating both branches would eventually lead to more accurate evaluation of HRV and a better tool in diagnosing people with autonomic dysfunctions. There have been some studies analyzing the relationship between cardiovascular autonomic control and respiratory activity using time-domain analysis only [13].

In this study, we performed HRV spectral analysis with and without using respiration signal and compared results. The FRF is obtained from the power spectrum of the respiration signal and used in separately computed HRV spectra to locate the HF area. The method which uses

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respiration information is called enhanced HRV (eHRV) analysis.

## II. METHOD

ECG and respiration signal of 17 normal subjects were collected while the subjects performed normal and deep breathing for approximately 1 minute each. During deep breathing, the patients were instructed to relax and breathe deeply at 6 breaths per minute. Data were analyzed and monitored in real time and stored in a computer. ECG signal was sampled at 250 Hz while respiration signal was sampled at 50 Hz. RR intervals were detected from the ECG, and ectopic beats were identified and excluded from calculations. RR time series were obtained as the time intervals between consecutive R peaks. They were later interpolated and evenly sampled at 4 Hz. Instantaneous heart rate (IHR) was obtained from RR time series by the mathematical relationship of  $60/(\text{RR-interval})$ . Then the mean value was subtracted from the signal and Time-Frequency analysis is performed.

Time-Frequency analysis method is based on continuous wavelet transforms (CWT) rather than FFT. For this type of signals, the CWT is better suited given its capability of adjusting to changes in signal characteristics. The FFT assumes that the signal is stationary in short segments and uses a fixed length window to do time varying analysis. Although the FFT provides good results for stationary signals, it does not completely reflect the time varying features of nonstationary signals. This is especially true for HRV signals where signal features, in response to the clinical exam, quickly change over time. Time and frequency resolution become an issue due to fixed length window used in the analysis. For longer windows, the time resolution gets better but the frequency resolution gets worse. For shorter windows, the frequency resolution improves but the time resolution gets worse. This is caused by the uncertainty principle where time and frequency resolution cannot be increased at the same time. The FFT forces a compromise or a trade off between time and frequency resolution. On the other hand if one can adjust the window size according to signal features, one can obtain better time-frequency resolution. This is exactly what wavelet analysis does. Window length in wavelet analysis is adjusted to the signal features and provides a better time frequency resolution. For slow changing signals it uses longer windows, for fast changing signals window length is shorter. CWT of a discrete time series  $x(n)$  is computed as the convolution of  $x(n)$  with a scaled and translated version of a basis function  $h(t)$  such that:

$$CWT(n, f) = \Delta t \kappa(s) \sum_{\mu} x(\mu) h^* \left( \frac{n - \mu}{s} \Delta t \right), \text{ for } s = f_0 / f \quad (1)$$

whereby:

$\Delta t$  is the sampling period;

$\kappa(s)$  is a normalizing parameter that depends on the scale factor 's';

\* represents complex conjugate;

$f_0$  is a constant reference.

Once the time-frequency analysis of the IHR is performed, sympathetic and parasympathetic measures are calculated using both tHRV and eHRV analysis. In tHRV analysis, standard LF, HF and LF/HF power parameters are estimated using previously determined fixed frequency ranges for these variables at each time. In literature, the frequency range between 0.04 Hz to 0.15 Hz is considered to be the Low Frequency (LF) range. The frequency range between 0.15 Hz to 0.4 Hz corresponds to HF range. LF and HF power are estimated as the area under spectrum of HR in above ranges. The LF/HF power is the mathematical ratio of LF power to HF power. Once all LF, HF and LF/HF values are estimated from time-frequency plot at each time, they are averaged to determine the values for the whole signal.

In eHRV analysis, time-frequency representation of the respiratory signal is estimated using the same method as for the HR signal, and the highest peak is identified at each time. Before the time-frequency analysis, the respiratory signal is high pass filtered to remove very low frequencies. The frequency corresponding to highest peak in time-frequency plot at each time is called as the Fundamental Respiratory Frequency (FRF). This frequency allowed us to locate the HF area in IHR time-frequency representation. HF area is chosen to be proportional with the FRF. It was chosen as from  $\text{FRF} \cdot 0.65$  to  $\text{FRF} \cdot 1.35$ . This interval was found to be optimal for locating parasympathetic region concentrated around respiration frequency. Furthermore since wavelet spectrum is taller and narrower in low frequencies and shorter and wider in high frequencies, parasympathetic area is not selected to be fixed width frequency interval. The interval is chosen to be proportional with FRF to provide accurate parasympathetic measure. For higher values of FRF, parasympathetic interval will be wider and for low FRF values it will be narrower. LF area is chosen to be from 0.04 Hz to 0.1 Hz but for very low FRF values below this range was adjusted to isolate LF and HF components. The LF area is chosen so that the effect of respiration can be isolated in low frequencies. Since the respiration may easily entrain frequencies 0.1 to 0.15, LF area excluded those frequencies. We will denote the LF area with LFa, HF area with RFa ('R' for respiration) and LF/HF with LFa/RFa respectively to prevent confusion with variables LF, HF, LF/HF estimated using tHRV analysis. LF, HF, LF/HF are also compared with LFa, RFa and LFa/RFa using a non-parametric Wilcoxon Matched Pair test.

## III. RESULTS

We have compared the LFa with LF, RFa with HF and LFa/RFa with LF/HF at normal breathing and deep breathing exercises. Fig. 1 (a) shows a representative example of IHR signal of a subject during normal breathing. Fig. 1 (b) displays the normal breathing signal. Time-frequency representation of IHR and respiration during normal breathing is provided on Fig. 1 (c) and (d) respectively. Fig. 1 (e) is the spectrum of the respiration

signal obtained from time-frequency plot at time n. FRF is found to be 0.26 Hz as indicated in the figure. Fig. 1 (f) shows the spectrum of IHR at time n. RFa and LFa are indicated in Fig. 1 (f) and they are close to HF and LF areas as it can be seen from the figure. For normal breathing rate, tHRV and eHRV analysis produced close results although eHRV was more specific to indicate the low and high frequency regions. On the other hand when respiration slows down, difference between tHRV and eHRV analysis becomes very obvious. Fig. 2 (a) indicates the IHR signal when the subject is performing deep breathing. Fig. 2 (b) displays the deep breathing signal. Time frequency plots of the IHR and deep breathing signal are provided in Fig. 2 (c) and (d) respectively. Fig. 2 (e) and (f) are the spectrum of the respiration and IHR signals that are obtained from time-frequency plot of respiration and IHR at time n respectively. Due to deep breathing, FRF is 0.085 Hz and RFa shifts into lower frequencies as indicated in Fig. 2 (f). This is an expected result since parasympathetic activity is mediated by respiration and respiration rate is low. On the other hand in tHRV analysis, HF power would be located in the interval 0.15-0.4 Hz where there is almost no power (Fig. 2 (f)).

Results from all 17 subjects are displayed in Table 1. Although mean values of LF, HF, LF/HF and LFa, RFa, LFa/RFa were close to each other at normal breathing, small differences were significant for LF power and the ratio. On the other hand, mean values of LF, HF, LF/HF and LFa, RFa, LFa/RFa were very different at deep breathing and the differences were significant for all values. As it is seen from Table 1 that eHRV provided more accurate numbers especially when the respiration is low. An expected increase in HF power (Parasympathetic measurement) when breathing rate is low is only indicated by eHRV analysis. On the other hand a high LF power in tHRV when the breathing is low indicates increase in sympathetic activity to deep breathing which is not expected.

TABLE 1

Comparison of mean and standard deviation of low and high frequency power of HRV data estimated from tHRV and eHRV analysis over 17 patients

	tHRV		eHRV		p
NB	LF	4.46±3.18	LFa	2.66±1.85	.0003*
	HF	3.08±2.03	RFa	2.72±1.81	.0059
	LF/HF	1.58±0.71	LFa/RFa	1.12±0.55	.0004*
DB	LF	50.66±33.59	LFa	2.07±2.32	.0003*
	HF	6.94±6.12	RFa	46.11±30.15	.0003*
	LF/HF	9.22±3.64	LFa/RFa	0.11±0.26	.0003*

#### IV. CONCLUSION

It is clear that HRV spectral analysis with and without using respiration provides different results. The differences become more obvious when respiration rate is low. Although differences were more obvious in low breathing rates, using eHRV in general would provide more accurate results due to accurate localization of parasympathetic activity in HRV signal. Accurately locating parasympathetic would lead to isolation of sympathetic and parasympathetic activity which

has been the problem with tHRV analysis. Furthermore many standard ANS tests include deep breathing test which is to stimulate parasympathetic branch of the ANS. Therefore for accurate assessment of the ANS activity one must include the effect of respiration in HRV analysis. As an expected result of DB testing, parasympathetic activity should increase. This kind of a change is only observed when respiratory peak is used in HRV analysis to locate the high frequency area (RFa) then estimating the power. On the other hand, using a fixed frequency range provided a decrease in HF power and increase in LF power at DB which can be misleading. As a result, employing respiratory signal in HRV analysis provides more accurate isolation of sympathetic and parasympathetic activity which provides a better diagnostic tool in assessing human ANS.

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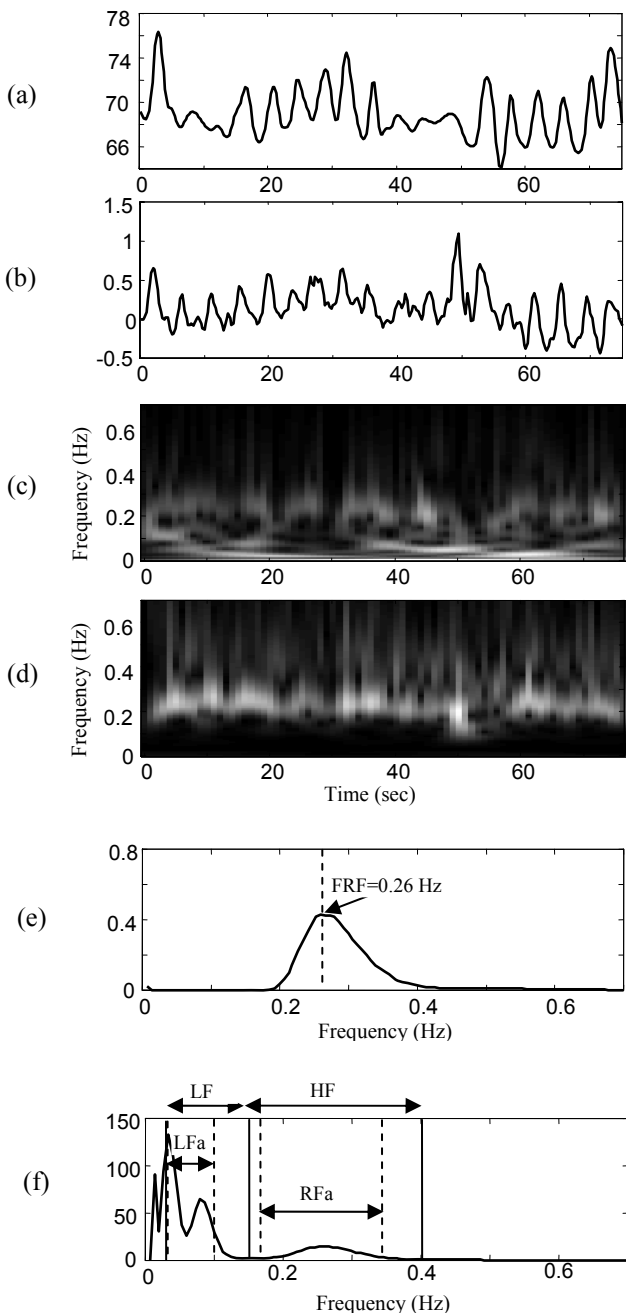


Fig. 1. (a) IHR signal during NB (b) NB waveform (c) Time-Frequency representation of IHR signal during NB (d) Time-Frequency representation of NB (e) A slice of Time-Frequency representation of NB at time  $n$  (f) A slice of Time-Frequency representation of IHR at time  $n$ . While the eHRV provides better separation of sympathetic and parasympathetic modulation (RFa and LFa regions), eHRV and tHRV produce similar regions.

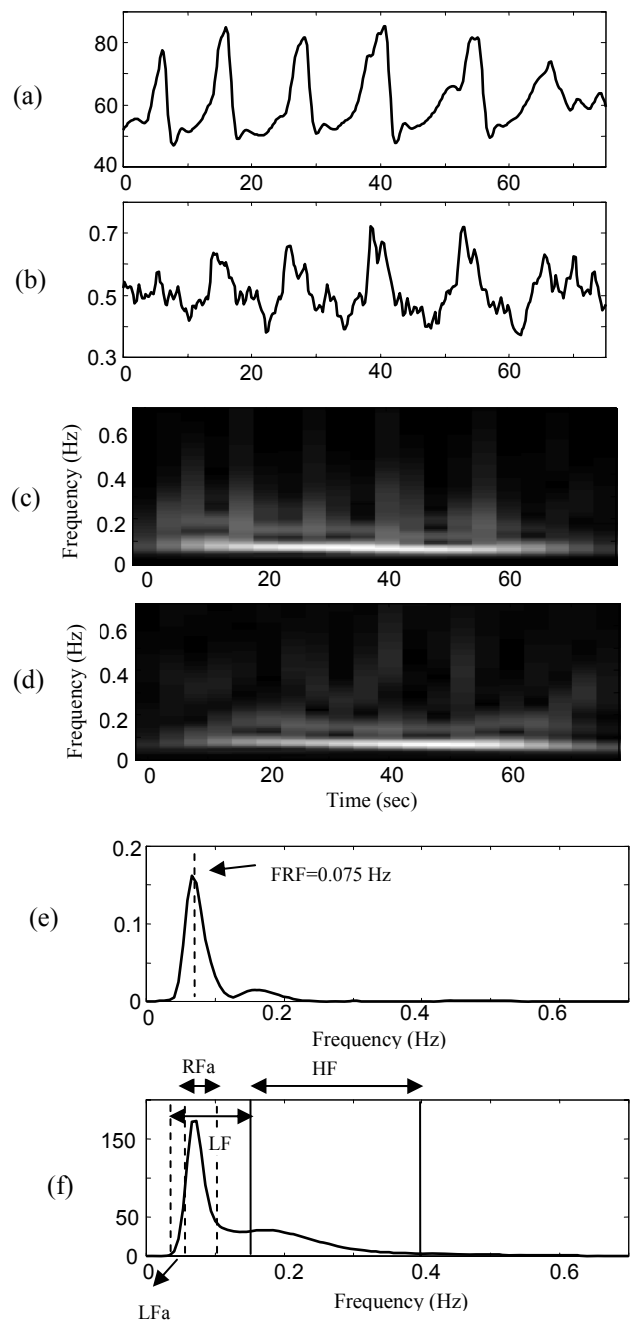


Fig. 2. (a) IHR signal during DB (b) DB waveform (c) Time-Frequency representation of IHR signal during DB (d) Time-Frequency representation of DB (e) A slice of Time-Frequency representation of DB at time  $n$  (f) A slice of Time-Frequency representation of IHR at time  $n$ . Isolation of high and low frequency power (RFa and LFa regions) is very clear. Region corresponding to parasympathetic modulation (RFa) is missed in tHRV analysis. tHRV indicates the HF area as a measure of parasympathetic.