Hindawi
Computational and Mathematical Methods in Medicine
Volume 2018, Article ID 4860204, 8 pages
https://doi.org/10.1155/2018/4860204

*Research Article*

# Analysis of Exercise-Induced Periodic Breathing Using an Autoregressive Model and the Hilbert-Huang Transform

**Tieh-Cheng Fu,[1,2,3] Chaur-Chin Chen,[4] Ching-Mao Chang,[5,6] Hen-Hong Chang,[7,8] and Hsueh-Ting Chu[9,10]**

[1] *Department of Physical Medicine and Rehabilitation, Chang Gung Memorial Hospital, Keelung, Taiwan*
[2] *Heart Failure Center, Department of Internal Medicine, Chang Gung Memorial Hospital, Keelung, Taiwan*
[3] *College of Medicine, Chang Gung University, Tao-Yuan, Taiwan*
[4] *Department of Computer Science, National Tsing Hua University, Hsinchu, Taiwan*
[5] *Center for Traditional Medicine, Taipei Veterans General Hospital, Taipei, Taiwan*
[6] *Faculty of Medicine, National Yang-Ming University, Taipei, Taiwan*
[7] *School of Post-Baccalaureate Chinese Medicine, College of Chinese Medicine, Research Center for Chinese Medicine & Acupuncture, China Medical University, Taichung, Taiwan*
[8] *Department of Chinese Medicine, China Medical University Hospital, Taichung, Taiwan*
[9] *Department of Computer Science and Information Engineering, Asia University, Taichung, Taiwan*
[10] *Department of Department of Medical Research, China Medical University Hospital, China Medical University, Taichung, Taiwan*

Correspondence should be addressed to Ching-Mao Chang; magicbjp@gmail.com and Hsueh-Ting Chu; htchu.taiwan@gmail.com

Received 27 February 2018; Accepted 21 May 2018; Published 26 June 2018

Academic Editor: Dominique J. Monlezun



Evaluation of exercise-induced periodic breathing (PB) in cardiopulmonary exercise testing (CPET) is one of important diagnostic evidences to judge the prognosis of chronic heart failure cases. In this study, we propose a method for the quantitative analysis of measured ventilation signals from an exercise test. We used an autoregressive (AR) model to filter the breath-by-breath measurements of ventilation from exercise tests. Then, the signals before reaching the most ventilation were decomposed into intrinsic mode functions (IMF) by using the Hilbert-Huang transform (HHT). An IMF represents a simple oscillatory pattern which catches a part of original ventilation signal in different frequency band. For each component of IMF, we computed the number of peaks as the feature of its oscillatory pattern denoted by $\Delta_i$. In our experiment, 61 chronic heart failure patients with or without PB pattern were studied. The computed peaks of the third and fourth IMF components, $\Delta_3$ and $\Delta_4$, were statistically significant for the two groups (both *p values* $< 0.02$). In summary, our study shows a close link between the HHT analysis and level of intrinsic energy for pulmonary ventilation. The third and fourth IMF components are highly potential to indicate the prognosis of chronic heart failure.

## 1. Introduction

The rehabilitation of patients with chronic heart failure (CHF) is a slow process, and sometimes, good progress is difficult to obtain for some patients. Exercise-induced periodic breathing (EPB) was found to be an important evidence of poor prognosis [1–6]. Therefore, physiatrists commonly check exercise breathing patterns of patients with CHF by using cardiopulmonary exercise testing (CPET; Figure 1(a)) to guide the pharmacological and nonpharmacological treatments for these patients. CPET involves measurements of ventilation (VE) respiratory oxygen uptake ($VO_2$) and carbon dioxide production ($VCO_2$) during a symptom-limited exercise test [7]. On increasing the bicycle workload during a CPET test, the respiratory exchange rate and tidal volume increase simultaneously. For more respiratory exchanges, a periodic breathing (PB) pattern might occur in some patients with CHF. PB (Figure 1(d)), first described in the 1970s [8], is a phenomenon of abnormal hyperventilation that alternates apneas and hypopneas. In this study, we investigated the

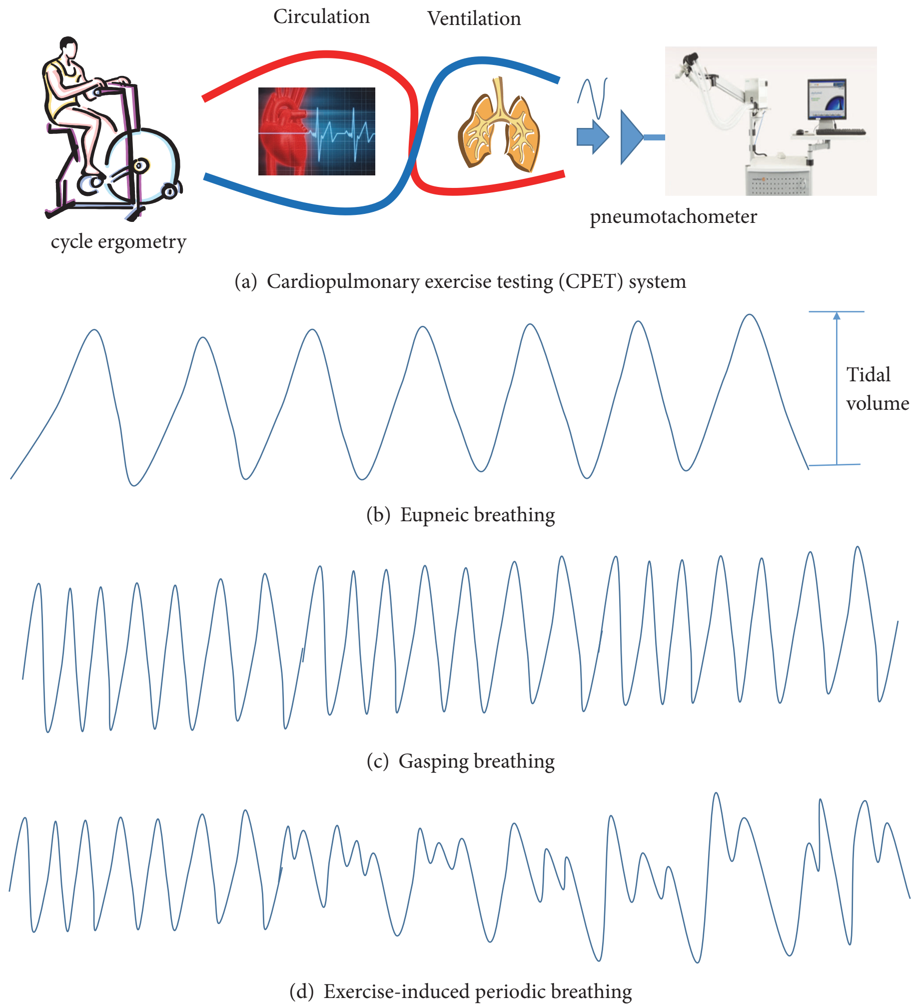


FIGURE 1: **A cardiopulmonary exercise testing (CPET) system and breathing patterns.** (a) A CPET machine is comprised of a cycle ergometer and pneumotachometer. During the test, the bicycle workload for the patient is increased until maximal exertion is reached. (b–d) Breathing patterns include eupneic, gasping, and periodic breathing (PB). Tidal volume is the volume of air exchange between inhalation and exhalation.

difference in ventilation signals between PB and non-PB patients [9].

From the analysis of cardiopulmonary exercise testing (CPET) measurements, two significant indicators have been studied in the literature, namely, peak $VO_2$ and $VE/VCO_2$ slope. Peak oxygen consumption (peak $VO_2$) was considered the gold standard assessment parameter of prognosis in CHF [10, 11]. Then, the ratio of ventilation-to-carbon dioxide production ($VE/VCO_2$ slope) was also studied later with the same importance as peak $VO_2$ [12, 13]. More recently, the quantification of PB patterns was investigated in both the spatial and frequency domains [3–5]. Here, we endeavored to link CPET measurements and the quantification of PB patterns by using the Hilbert-Huang transform (HHT) [14]. The Hilbert-Huang transform has been applied in many biomedical analyses [15], including blood pressure [16, 17], nasal flow [18], and electroencephalography [19, 20]. To apply the Hilbert-Huang transform on the analysis of ventilation measurements, we propose two important steps of preprocessing. In the first step, we examine the ventilation measurements from CPET tests. Some ventilation measurements are noisy and aberrant when the testing patient is gasping. The occurrence of such aberrant signals is caused by the limitation of a CPET system. The ventilation VE values are obtained from breath-by-breath calculation of gas exchange at the mouth. A nonrebreathing valve is connected to a mouthpiece to prevent mixing of inspired and expired air. Thus, one irregular gasping exhalation may be recorded as two or more breaths. As a result, we filter out those aberrant measurements.

Moreover, not all measurements from entire CPET tests were used in our analysis. To determine the meaningful difference in cardiopulmonary response between the PB and non-PB patients, we only selected the period before the patient's ventilation reached the maximal volume. The common respiratory rate for an adult at rest is 12–20 breaths per

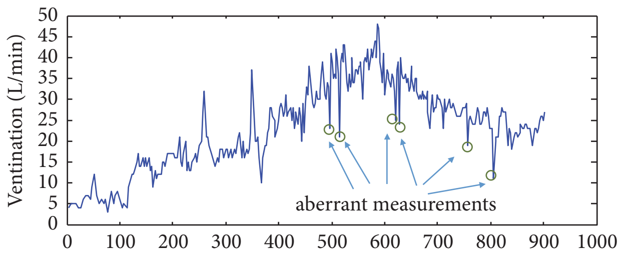


Figure 2: **Measured signals of exercise breath-by-breath ventilation.** Very low measurements usually occur when the patient is gasping. In this study, when the ventilation volume was high, these exceptional measurements were observed as noises.

minute, which will increase up to 30–50 breaths per minute during exercise testing. Thus, PB patterns are most likely to appear around the peak respiratory volume. Therefore, 200 ventilation measurements, that is, a period of 4–6 minutes before the peak volume, were used in the analysis.

## 2. Materials and Methods

*2.1. Breath-by-Breath Ventilation Signals for 61 Patients with Chronic Heart Failure.* Exercise ventilation signals were recorded from CHF patients who received rehabilitation at the Chang Gung Memorial Hospital-Keelung Branch in Taiwan. All the subjects were studied in accordance with a protocol previously approved by the local ethics committee and registered at the ClinicalTrials.gov website with ID No. NCT01053091. The respiratory signals were acquired using a pneumotachometer connected to a mask and analyzed using the machine MasterScreen CPX Metabolic Cart. In common cases, the signals, including $VO_2$ and $VCO_2$, are output per 30 seconds, although they are measured breath by breath. More information about the collected CPET data can be found in Fu et al. (2017). For this study, we output the original breath-by-breath signals of ventilation instead. The total measurement period was 10–15 minutes. We obtained 61 deidentified ventilation samples marked as PB (n = 20) or non-PB (n = 41) by physiatrists.

*2.2. Filtering of Ventilation by an Autoregressive Model.* Many observations of biosignal series exhibit serial autocorrelation and can be modelled with autoregressive (AR) models. Garde *et al.* showed that ventilation signals can also be fitted by AR models [18]. They used the coefficients of AR models to characterize the respiratory pattern of PB or non-PB patients. However, the average ventilation measurements per minute were adapted in their study. In our study, we analyzed breath-by-breath signals and applied the AR model method to fit the curve of exercise ventilation as shown in Figure 2.

The AR models predict $y_t$ as a function of past observations, $y_{t-1}, y_{t-2}, \ldots, y_{t-p}$. The form of the AR model is

$$\overline{y_t} = c + \phi_1 y_{t-1} + \cdots + \phi_p y_{t-p}, \tag{1}$$

where $p$ is the degree of the AR model and denoted by AR($p$) and $\overline{y_t}$ is the predicted term.

For the analysis of PB or non-PB exercise ventilation, 200 serial measurements before the largest ventilation volume were chosen, and an AR(6) model is applied to the series. By using the equation to fit the exercise ventilations, we filtered out the observed measurement of ventilation $y_t$ if $y_t < 0.8\overline{y_t}$. This filtered series of ventilation signals is called "the most exhausted exercise ventilations (MEE-Ve)" in this paper.

*2.3. Decomposition of the Chosen Ventilation Signals by the Hilbert-Huang Transform.* The Hilbert-Huang transform (HHT) is a signal decomposition method developed by Norden E. Huang in the 1990s [14]. By using this processing method, biosignals are decomposed into a set of IMFs by an empirical mode decomposition (EMD) process. The instantaneous frequencies and amplitudes of all IMFs can be used to identify embedded signal structures.

The HHT representation of series *X(t)* is

$$X(t) = \Re \sum_{j=1}^{n} a_j(t)\, e^{i\theta_j(t)} = \Re \sum_{j=1}^{n} \left[ C_j(t) + iY_j(t) \right], \tag{2}$$

where $C_j(t)$ and $Y_j(t)$ are, respectively, the $j$-th IMF component of $X(t)$.

To obtain IMFs, EMD [14], which is an iterative process that output a set of signal components called IMFs, is performed. Figure 3 shows an example of decomposed IMFs for a series of MEE-Ve. The original signals are decomposed into the components $\mathrm{IMF}_1$, $\mathrm{IMF}_2$, ..., $\mathrm{IMF}_5$. Different IMF components may imply particular factors. We calculated the peaks of the oscillations in each IMF with MATLAB's "mspeaks" function [21]. The estimated peaks of the IMF components of $\mathrm{IMF}_i$ are denoted as $\Delta_i$ to compare the PB and non-PB samples.

*2.4. Statistical Analyses.* Student's t-tests were used to identify statistically significant differences between two groups of features of PB and non-PB samples.

## 3. Results

*3.1. The Computation of IMFs of Most Exhausted Exercise Ventilations (MEE-Ve) for PB and Non-PB Patients.* The measurements of ventilation (VE) obtained from cardiopulmonary exercise testing (CPET) were analyzed using the proposed method. The programs were written in MATLAB. We analyzed the extracted exercise ventilations in this section by using HHT for 20 patients with or without PB as judged by physiatrists. The empirical mode decomposition (EMD) process is applied to the VE data and several IMFs are extracted. Figure 3 depicts the HHT decomposition result for IMF1-IMF5. In addition, we show the corresponding instantaneous frequency of the decomposed $\mathrm{IMF}_1$-$\mathrm{IMF}_4$ in Figure 4. All figures of HHT decomposition results for the 61 patients are available at our Github repository (https://github.com/htchu/EpbAnalysis).

*3.2. Numbers of Peaks as the Features of IMFs.* We used MATLAB's "mspeaks" function to perform the peak fitting of IMFs and the source ventilations. Figure 5 illustrates

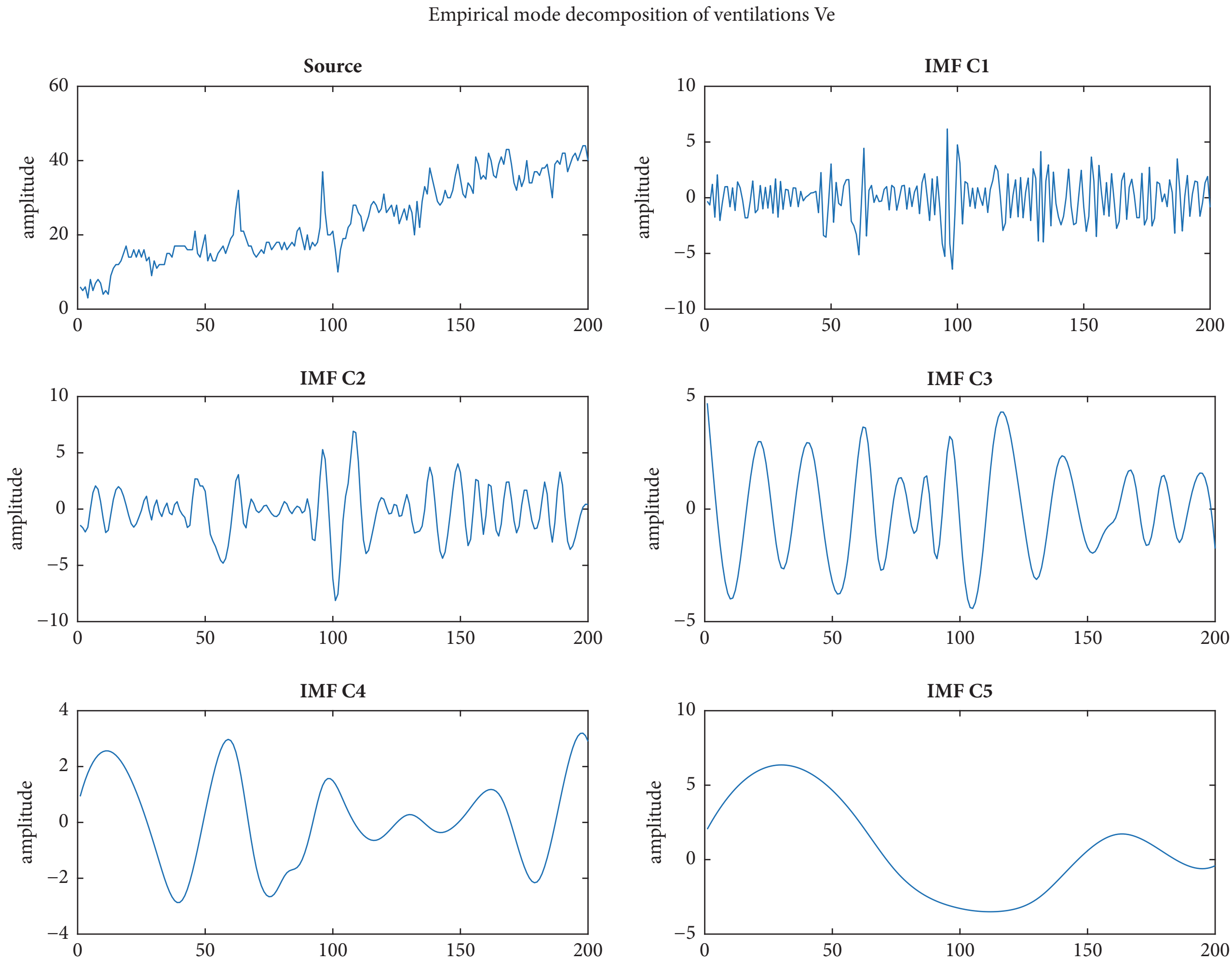


Figure 3: **An example of empirical mode decomposition of most exhausted exercise ventilations (MEE-Ve).** The MEE-Ve signals are $k$ ventilations before the peak volume. The number $k$ is 200 in this paper. The illustration is from the analysis of the patient ID: pb0001 which was judged as a periodic breathing (PB) case. All results of the EMD analysis for the PB or non-PB cases can be found at the Github repository (https://github.com/htchu/EpbAnalysis).

the computed locations of peaks for the same experimental data in Figure 3. Obviously, the peak fittings for the source ventilations and the first IMF (Figures 5(a) and 5(b)) are not as good as the peak fittings for the other IMFs (Figures 5(c)–5(f)). Table 1 lists the numbers of computed peaks of $IMF_1$-$IMF_5$ for first 20 patients (10 PBs and 10 non-PBs). Supplemental Table 1 provides all of the computed peaks for the entire test dataset.

*3.3. Statistical Significance Test of IMFs.* The statistical significance test derived by Wu and Huang [22] is illustrated in Figure 6. The five extracted IMFs are shown along with the 95% and 99% confidence limits. All IMFs are above the 99-percentile confidence limit except for the IMF5. Therefore, only the IMF5 is not statistically significant from noise [22].

*3.4. More Peaks of $IMF_3$ and $IMF_4$ for Better Prognosis of Chronic Heart Failure Cases.* Student's t-tests were used to identify statistically significant differences between the two groups (PB and non-PB patients). Table 2 lists the $p$ values for the comparison between the two group for the computed peaks of IMFs. The $p$ values for first two IMFs are greater than 0.1 such that the peak computations are not statistically significant for $IMF_1$ and $IMF_2$. By contrast, the $p$ values for $IMF_3$ and $IMF_4$ are less than 0.02 such that the peak computations are statistically significant for $IMF_3$ and $IMF_4$.

## 4. Discussion and Conclusion

This paper conducted a new analysis on exercise ventilation signals to predict the prognosis of CHF patients. We defined MEE-Ve as a breath-by-breath ventilation measurement filtered using an AR model. We ran our correlation analysis through IMFs, extracted from the EMD process, and found that PB patterns were highly correlated to $IMF_3$ and $IMF_3$. To clarify the correlation, we introduced peak computation of

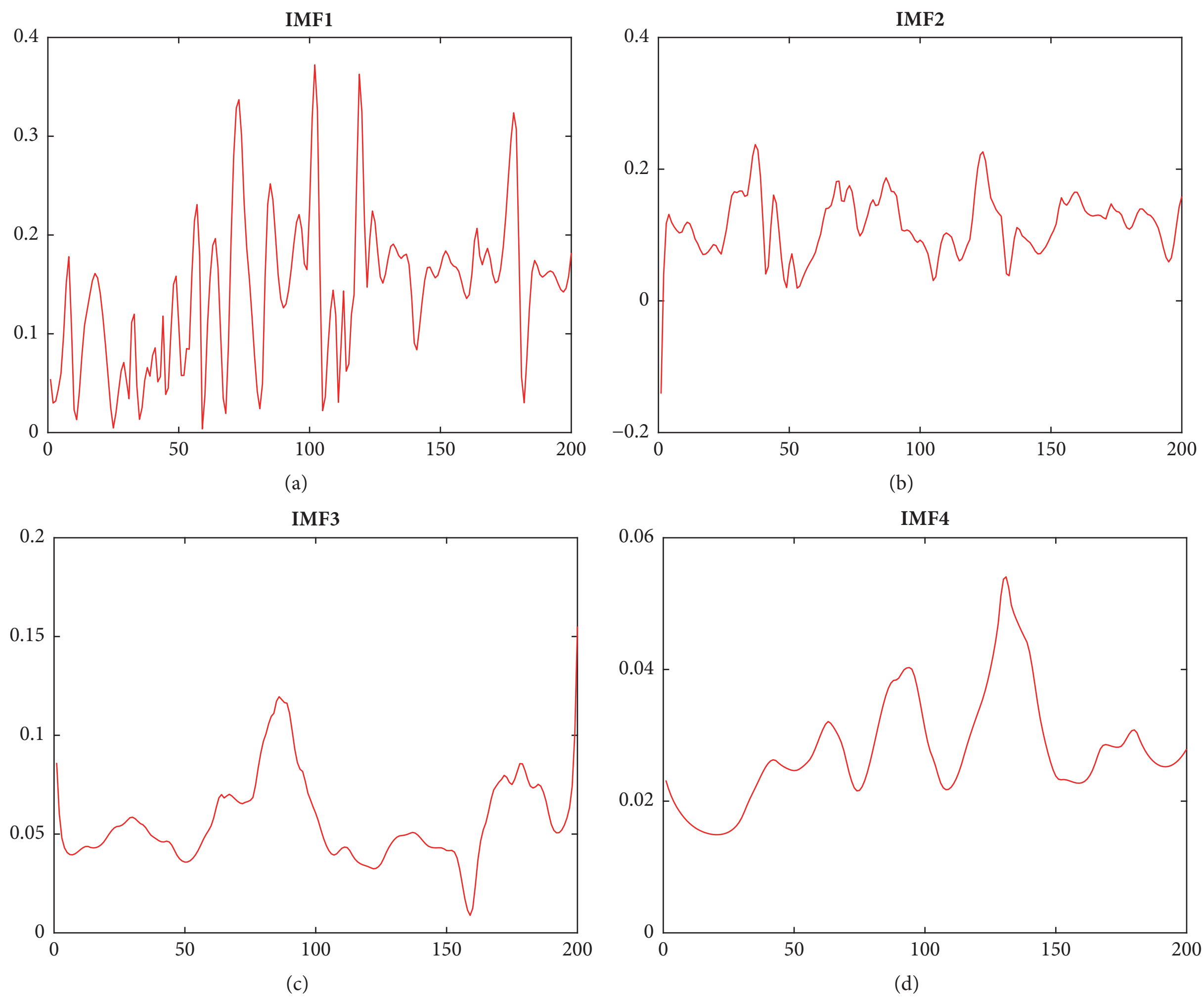


FIGURE 4: The corresponding instantaneous frequency of the decomposed $IMF_1$-$IMF_4$ (Figure 3).

$IMF_3$ and $IMF_4$ ($\Delta_3$, $\Delta_4$) as the feature of ventilation signals from cardiopulmonary exercise testing (CPET).

However, the effectiveness of the proposed method needs more clinical examinations in the future. Meanwhile, the range selection of exercise ventilations is another issue for more studies. We plan to examine this method with more cardiopulmonary tests.

## Data Availability

The MATLAB programs and EPB data of this work are available at https://github.com/htchu/EpbAnalysis/.

## Disclosure

A preliminary study of the article had been presented in the conference ICS2014 (http://ics2014.thu.edu.tw/).

## Conflicts of Interest

The authors declare no conflicts of interest.

## Authors' Contributions

Tieh-Cheng Fu and Hsueh-Ting Chu coordinated the project and prepared the test dataset. The programs were written by Chaur-Chin Chen and Hsueh-Ting Chu. Hsueh-Ting Chu, Chaur-Chin Chen, Tieh-Cheng Fu, Hen-Hong Chang, and Ching-Mao Chang discussed the project and jointly wrote the manuscript. Ching-Mao Chang and Tieh-Cheng Fu interpreted the analysis results.

## Acknowledgments

This work is supported by the Ministry of Science and Technology, Taiwan, under Grant no. 102-2628-B-182A-001-MY3, and Chang Gung Medical Research Program (CMRPG2A0162 and CMRPG2C0402).

## Supplementary Materials

Supplemental Table 1: computed peaks for the decomposed intrinsic mode functions (IMFs) from exercise ventilation

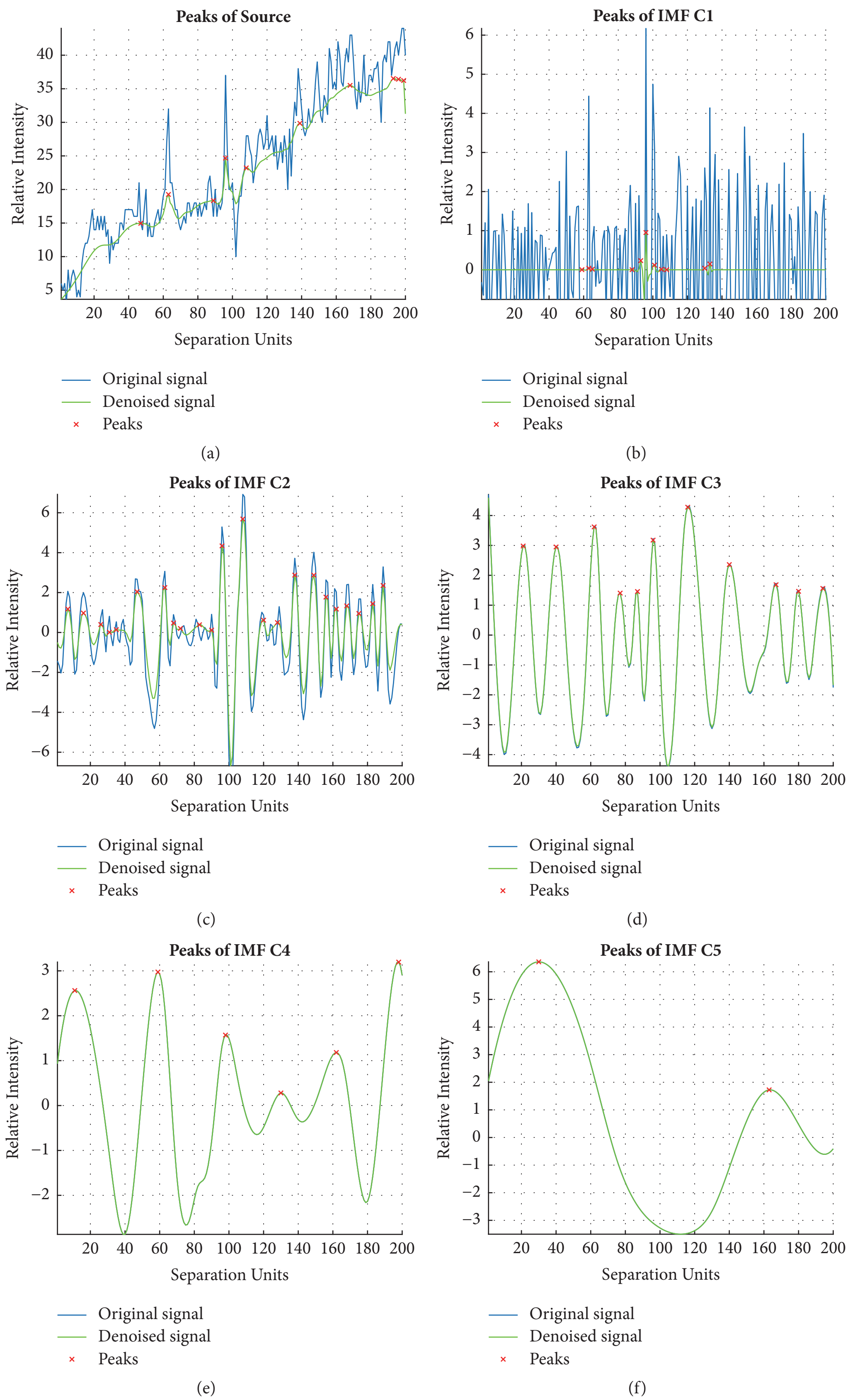


Figure 5: Peak Computations of IMFs (Figure 3).

Table 1: Computed peaks $\Delta_i$ of IMFs by mspeaks.

| PB or non-PB Patient | $\Delta_1$ | $\Delta_2$ | $\Delta_3$ | $\Delta_4$ | $\Delta_5$ |
|---|---|---|---|---|---|
| PB-1 | 11 | 23 | 11 | 6 | 2 |
| PB-2 | 2 | 28 | 17 | 7 | 3 |
| PB-3 | 11 | 29 | 13 | 5 | 2 |
| PB-4 | 9 | 30 | 13 | 7 | 3 |
| PB-5 | 14 | 27 | 14 | 4 | 2 |
| PB-6 | 8 | 25 | 13 | 5 | 2 |
| PB-7 | 0 | 28 | 14 | 6 | 3 |
| PB-8 | 21 | 25 | 16 | 8 | 3 |
| PB-9 | 0 | 30 | 15 | 7 | 3 |
| PB-10 | 3 | 23 | 9 | 5 | 2 |
| nPB-1 | 7 | 26 | 16 | 6 | 3 |
| nPB-2 | 7 | 29 | 15 | 8 | 2 |
| nPB-3 | 8 | 28 | 16 | 9 | 4 |
| nPB-4 | 2 | 24 | 14 | 7 | 3 |
| nPB-5 | 4 | 28 | 17 | 10 | 5 |
| nPB-6 | 0 | 30 | 17 | 7 | 5 |
| nPB-7 | 15 | 26 | 15 | 6 | 2 |
| nPB-8 | 8 | 27 | 15 | 7 | 3 |
| nPB-9 | 9 | 26 | 16 | 8 | 4 |
| nPB-10 | 2 | 31 | 17 | 8 | 3 |

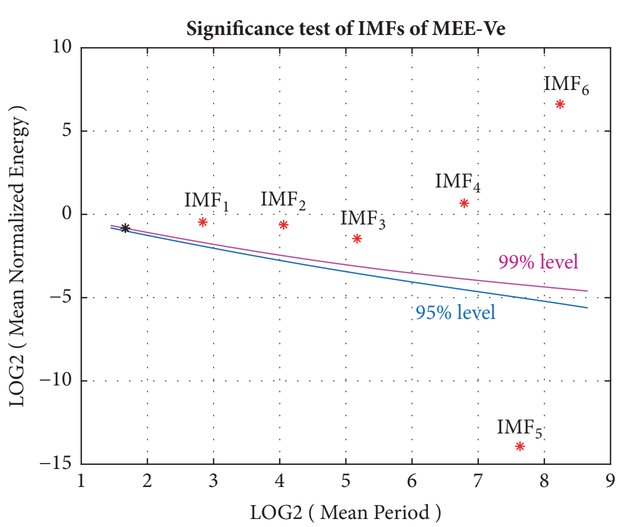


Figure 6: Statistical significance test for the decomposed IMFs. The $IMF_5$ is below the 95% confidence limit and is therefore considered statistically insignificant.

Table 2: P values of Student's t-test for IMFs.

| IMF component | Δ1 | Δ2 | Δ3 | Δ4 |
|---|---|---|---|---|
| *P value* | 0.6330 | 0.1103 | 0.016 | 0.017 |

signals of 61 chronic heart failure patients. *(Supplementary Materials)*

## References

[1] P. Agostoni, U. Corrà, and M. Emdin, "Periodic breathing during incremental exercise," *Annals of the American Thoracic Society*, vol. 14, pp. S116–S122, 2017.

[2] B. P. Dhakal, R. M. Murphy, and G. D. Lewis, "Exercise Oscillatory Ventilation in Heart Failure," *Trends in Cardiovascular Medicine*, vol. 22, no. 7, pp. 185–191, 2012.

[3] J. J. Leite, A. J. Mansur, H. F. G. De Freitas et al., "Periodic breathing during incremental exercise predicts mortality in patients with chronic heart failure evaluated for cardiac transplantation," *Journal of the American College of Cardiology*, vol. 41, no. 12, pp. 2175–2181, 2003.

[4] T. P. Olson and B. D. Johnson, "Quantifying oscillatory ventilation during exercise in patients with heart failure," *Respiratory Physiology & Neurobiology*, vol. 190, no. 1, pp. 25–32, 2014.

[5] J. P. Ribeiro, "Periodic breathing in heart failure: Bridging the gap between the sleep laboratory and the exercise laboratory," *Circulation*, vol. 113, no. 1, pp. 9-10, 2006.

[6] G. Tumminello, M. Guazzi, P. Lancellotti, and L. A. Piérard, "Exercise ventilation inefficiency in heart failure: Pathophysiological and clinical significance," *European Heart Journal*, vol. 28, no. 6, pp. 673–678, 2007.

[7] K. Albouaini, M. Egred, A. Alahmar, and D. J. Wright, "Cardiopulmonary exercise testing and its application," *Postgraduate Medical Journal*, vol. 83, no. 985, pp. 675–682, 2007.

[8] G. Preiss, S. Iscoe, and C. Polosa, "Analysis of a periodic breathing pattern associated with Mayer waves," *American Journal of Physiology-Endocrinology and Metabolism*, vol. 228, no. 3, pp. 768–774, 1975.

[9] T. Fu, W. Lin, J. Wang et al., "Detection of exercise periodic breathing using thermal flowmeter in patients with heart failure," *Medical & Biological Engineering & Computing*, vol. 55, no. 8, pp. 1189–1198, 2017.

[10] G. A. MacGowan and S. Murali, "Ventilatory and heart rate responses to exercise: better predictors of heart failure mortality than peak exercise oxygen consumption.," *Circulation*, vol. 102, no. 24, p. E182, 2000.

[11] M. Robbins, G. Francis, F. J. Pashkow et al., "Ventilatory and heart rate responses to exercise better predictors of heart failure mortality than peak oxygen consumption," *Circulation*, vol. 100, no. 24, pp. 2411–2417, 1999.

[12] R. Arena, J. Myers, S. S. Aslam, E. B. Varughese, and M. A. Peberdy, "Peak VO2 and VE/VCO2 slope in patients with heart failure: A prognostic comparison," *American Heart Journal*, vol. 147, no. 2, pp. 354–360, 2004.

[13] F. M. Sarullo, G. Fazio, I. Brusca et al., "Cardiopulmonary exercise testing in patients with chronic heart failure: Prognostic comparison from peak vo2 and ve/vco2 slope," *The Open Cardiovascular Medicine Journal* , vol. 4, pp. 127–134, 2010.

[14] N. E. Huang, Z. Shen, S. R. Long et al., "The empirical mode decomposition and the Hilbert spectrum for nonlinear and non-stationary time series analysis," *Proceedings A*, vol. 454, no. 1971, pp. 903–995, 1998.

[15] C.-F. Lin and J.-D. Zhu, "Hilbert-Huang transformation-based time-frequency analysis methods in biomedical signal applications," *Proceedings of the Institution of Mechanical Engineers, Part H: Journal of Engineering in Medicine*, vol. 226, no. 3, pp. 208–216, 2012.

[16] C.-C. Chang, T.-C. Hsiao, and H.-Y. Hsu, "Frequency range extension of spectral analysis of pulse rate variability based on Hilbert-Huang transform," *Medical & Biological Engineering & Computing*, vol. 52, no. 4, pp. 343–351, 2014.

[17] Q. Zhang, Y. Shi, D. Teng et al., "Pulse transit time-based blood pressure estimation using hilbert-huang transform," in *Proceedings of the 2009 Annual International Conference of the IEEE Engineering in Medicine and Biology Society*, pp. 1785–1788, Minneapolis, MN, September 2009.

[18] C. Lin, M. Lo, and C. Guilleminault, "Exploring the Abnormal Modulation of the Autonomic Systems during Nasal Flow Limitation in Upper Airway Resistance Syndrome by Hilbert–Huang Transform," *Frontiers in Medicine*, vol. 4, 2017.

[19] M. Han and M. Wang, "Multichannel EEG feature extraction based on Hilbert-Huang transform and extreme learning machine," vol. 2013, pp. 5406–5409, 2013.

[20] R. Kumar, R. Ramaswamy, and B. Nath Mallick, "Local Properties of Vigilance States: EMD Analysis of EEG Signals during Sleep-Waking States of Freely Moving Rats," *PLoS ONE*, vol. 8, no. 10, Article ID e78174, 2013.

[21] J. S. Morris, K. R. Coombes, J. Koomen, K. A. Baggerly, and R. Kobayashi, "Feature extraction and quantification for mass spectrometry in biomedical applications using the mean spectrum," *Bioinformatics*, vol. 21, no. 9, pp. 1764–1775, 2005.

[22] Z. H. Wu and N. E. Huang, "A study of the characteristics of white noise using the empirical mode decomposition method," *Proceedings of the Royal Society A Mathematical, Physical and Engineering Sciences*, vol. 460, no. 2046, pp. 1597–1611, 2004.