Congr. Int. en Ing. Electrónica. Mem. ELECTRO, Vol. 41, pp. 148-153, Oct 2019, Chihuahua, Chih. México
http://electro.itchihuahua.edu.mx/memorias_electro/MemoriaElectro2019.zip
ISSN 1405-2172

DEVELOPMENT AND VALIDATION OF A COMPUTER PROGRAM AND GRAPHICAL USER INTERFACE FOR ASSESSMENT OF CARDIORESPIRATORY COUPLING

Figuerola Salvador[1], Quintanar Eduardo[2], Lerma Claudia[3]*
[1]Universidad La Salle Laguna, Canatlán 150, Parque Industrial Lagunero, Gómez Palacio, Durango.
[2] Universidad Autónoma Metropolitana, unidad Iztapalapa, Iztapalapa, Ciudad de México.
[3] Instituto Nacional de Cardiología Ignacio Chávez, Departamento de Instrumentación Electromecánica, Juan Badiano 1, Col. Sección 16. Tlalpan, Ciudad de México, 14080. Tel. +52 (55) 55732911 extensión 26202, Email: dr.claudialerma@gmail.com
*Author for correspondence

RESUMEN

La variabilidad de la frecuencia cardiaca (VFC) y la amplitud respiratoria (AR) son señales fisiológicas ampliamente utilizadas en la investigación científica. Para analizar estas señales existen programas comerciales que evalúan solamente la VFC, y para la AR los investigadores generan sus propios programas. El objetivo fue diseñar y desarrollar un programa de computadora para análisis del acoplamiento cardio-respiratorio, a través de la medición de la VFC y de la medición de la AR, la estimación de los espectros de potencia de cada una de las señales (VFC y AR) y su coherencia espectral. Se diseñó una interfaz que permite corregir automática y manualmente los errores de la detección de latidos (VFC) e inicio de la inspiración (AR) y calcular índices cuantitativos. El desempeño del programa se evaluó en datos de pacientes durante respiración espontánea y controlada. La interfaz permite estimar el acoplamiento cardio-respiratorio a usuarios no expertos.
Palabras clave: Procesamiento de señales, análisis espectral de potencia, desarrollo de programas de cómputo, movimientos ventilatorios, variabilidad de la frecuencia cardiaca.

ABSTRACT

Heart rate variability (HRV) and respiratory amplitude (RA) are two physiological signals widely used for scientific research. Analysis of these signals with commercial computer programs includes only HRV analysis and researchers develop their own programs for RA assessment. The aim was to design and develop a computer program for the analysis of cardiorespiratory coupling through the estimation of power spectrum of each signal (HRV and RA) as well as their spectral coherence. A graphical user interface was designed to allow automatic and manual correction of each beat (HRV) and inspiratory onset (RA), and to calculate standard quantitative indexes. Performance of this program was tested with data from patients during spontaneous and controlled breathing. The interface allows assessment of cardiorespiratory coupling to non-expert users.
Keywords: Signal processing, power spectral analysis, computer programs development, ventilator movements, heart rate variability

1. INTRODUCTION

Cardiovascular diseases are the main mortality cause worldwide [1], and there is great interest in methods for monitoring and diagnosis of cardiovascular health. The electrocardiogram (ECG) is an important physiological signal that allows identification of the occurrence of each heartbeat (usually in the R-wave) and the estimation of the time between consecutive heartbeats (RR interval). The beat-to-beat variations in the RR interval is known as heart rate variability (HRV) [2]. HRV analysis is used widely in scientific research [2]. HRV results from the modulation of the brain upon the heart's pacemaker, through the autonomic nervous system [2], but it has also influence of the quasi-periodic movements from respiration (breathing movements), a phenomenon known as respiratory sinus arrhythmia [3]. There are many methods for the analysis of HRV and the breathing movements amplitude, or respiratory amplitude (RA), including statistical and spectral methods [2, 3].

Some commercial systems created for clinical use include HRV analysis. However, most programs for HRV analysis created for research are custom-made. There are also some open-access programs for HRV analysis, including Physionet (https://www.physionet.org/physiotools/software-index.shtml), Kubios HRV (https://www.kubios.com/), ARTiiFact (http://www.artiifact.de/) and PhysioZoo (https://physiozoo.com/). The main limitation of these programs is that they only allow HRV analysis, or they include only simple estimations of the mean breathing frequency. The analysis of the respiratory signal and the cardiorespiratory interaction is usually performed with custom-made program developed by the researchers.

The aim of this work was to design and develop a computer program and graphical user interface for the analysis of cardiorespiratory coupling through the estimation of power spectrum of each signal (HRV and RA) as well as their spectral coherence. The signal

processing methods were selected based on previous research [4–7] and international recommendations [2, 3].

2. MATERIALS AND METHODS

2.1. Data and annotations

Data from healthy subjects and renal patients

Data from healthy volunteers and patients with end-stage renal disease (ESRD) were obtained (Table 1).

Table 1 Characteristics from participants. Data are shown as median (percentile 25 – percentile 75) or absolute value (percentage).

	Healthy (N = 12)	ESRD (N = 10)	p
Age (years)	41 (31 – 45)	31 (25 – 41)	0.314
Sex			0.206
Female	4 (33%)	6 (60%)	
Male	8 (67%)	4 (40%)	

Data from subjects were obtained with a device BioHarness 3.0 (Zephyr, TM) which records an ECG channel at 250 samples per second and a RA channel at 1 sample per second, both with an analog-to-digital converter resolution of 12 bits. The data was transferred to the computer by USB and data files were saved with CSV format.

From each participant, recordings were obtain with the following protocol: 10 minutes during resting (supine position) and spontaneous breathing, 10 minutes during active standing, 10 minutes in supine position (with 2 minutes of spontaneous breathing followed by 3 minutes with controlled periodic breathing at 0.1 Hz, then 3 minutes with controlled periodic breathing at 0.25 Hz, and 2 last minutes with spontaneous breathing). The app Breathe (developed for Android by Jatra, email apps@jatra.co.uk) was used as a visual guide to help the subjects to follow the controlled breathing pattern.

Each recording was processed with an algorithm to detect QRS complexes in the ECG (to identify each heartbeat) and an algorithm to identify the onset of each respiratory cycle in the RA signal. Detection of these events was supervised by and expert to obtain a set of fiducial points for each heartbeat and respiratory cycle, these supervised annotations were considered the gold standard to be compared with the automatic detection.

Simulated data

A set of synthetic ECG signals were generated with the function "ecgsyn" [8]. Each simulated ECG had 250 samples per second, a mean heart rate of 60 beats per minute and a total of 100 heartbeats. The function produced a vector with the occurrence time of each QRS, which was used as gold standard to compare the automatic QRS detection applied to the simulated ECG with additive noise. The additive noise included:

a) White noise, which was obtained with the function "rand" with amplitude values within the interval [a,-a].
b) A sinus function with frequency of 60 Hz and amplitude = 0.5*a.

The amplitude of this additive noise was incremented gradually during 100 iterations from an initial amplitude of noise = 0 until a final maximum amplitude of noise = 1.4 the root-mean-square value (RMS) of the simulated ECG, or RMS(ECG).

For each iteration, the relationship between the amplitude of the additive noise and the ECG was estimated as the RMS ratio = RMS(noise)/RMS(ECG).

2.2. ECG and AR signals processing

Peak detection algorithms

QRS complex identification in the ECG was performed with a second-derivative algorithm that was validated previously [4,7]. The ECG signal was rectified, and a threshold value was calculated to identify each QRS complex. Then, the time between each QRS complex was measured, to obtain the RR interval or HRV signal. After the automatic detection was performed, the user interface allows manual correction of the heartbeat detection. Additionally, the user has the option to apply a well-known adaptive filter to identify and correct automatically RR intervals from non-normal beats (i.e. arrhythmias or artifacts) [9].

In the RA signal a bandwidth FIR filter with cut-off frequencies between 0.1 and 0.35 Hz was applied before using MATLAB function "peaks" to identify the onset of each respiratory cycle (or inspiration, "I"). Then, the time between consecutive inspiration time was calculated to obtain the I-I intervals. The user interface allows manual correction of the "I" events detection.

Performance tests of peak detection

The performance of the automated detection in QRS complexes was tested on data from all participants (Table 1) by comparison of the supervised annotations (gold standard) versus the automated QRS detection.

The performance of the automated detection in QRS complexes was also tested on the simulated data, by comparison of the QRS time produced by the ecgsyn function (gold standard) versus de automated QRS detection applied to each simulated ECG with additive noise.

The automated QRS detection was compared against the reference QRS annotations (or gold standard) to determine false positives (fp), false negatives (fn) and

true positives (tp). Then we calculated the following algorithm performance statistics [10]:

Sensitivity (Se) = tp/(tp+fn) (1)

Positive predictive value (PPV) = tp/(tp+fp) (2)

And the overall detection accuracy (ODA), defined as:

ODA = 2*(PPV*Se/(PPV+Se)) (3)

2.3 Heart rate variability (HRV) analysis

All the HRV indexes were calculated in accordance with the international recommendations [2].

The developed interface calculates the following time domain HRV indexes: mean value of all RR intervals (AvRR), standard deviation of the RR intervals (RRSD), root-mean-squared of the successive differences between RR intervals (RMSSD) and the percentage of successive RR intervals with difference greater than 20 ms (pNN20).

The time domain indexes obtained from the I-I intervals were: mean time between breathing cycles, or breath-to-breath intervals (AvBB), the standard deviation between breathing cycles (BBSD), and the root-mean-squared of the successive differences between breathing cycles (BMSSD).

The frequency domain analysis of both HRV and RA time series underwent the following steps: (a) elimination of linear trend, (b) re-sampling each time series at 5 samples per second, (c) application of a Hanning window, and (d) estimation of the power spectrum density with the Welch method.

From the estimated power spectrum density of HRV, the following spectral HRV indexes were obtained: the low frequency index (LF, from 0.04 to 0.15 Hz), high frequency index (HF, from 0.15 to 0.4 Hz), and LF/HF ratio. LF and HF were calculated in mean power units (ms^2) and normalized units (n.u.) [2].

To test the estimation of the HRV indices, the median value of all HRV indices were compared between the group of healthy subjects and the group of ESRD patients, using a Mann-Whitney U test. Also, the effect of a physiological stimulus (active standing) upon the spectral HRV indices was tested by comparing the median values of each spectral HRV index between supine position and active standing (within each group, Wilcoxon's rank test).

2.4 Spectral coherence analysis

The estimation of the spectral coherence was performed with the same steps described to estimate the power spectrum densities of HRV and AR (section 2.3).

The spectral coherence was obtained with the MATLAB function "mscoherence".

3 RESULTS AND DISCUSSION

3.1 Peaks detection

The performance of the QRS detection algorithm in ECG recordings from the participants of the study is shown in Table 2. The algorithm showed very good performance with more than 98% in the three performance statistics (Se, PPV and ODA).

Table 2 Performance of QRS detection algorithm in recordings from 12 healthy volunteers and 10 ESRD patients.

Group	Se	PPV	ODA
Healthy	98.6%	98.8%	98.7%
ERCT	98.8%	99.8%	99.3%

Performance of peak detection in the simulated ECG signals with additive noise are shown in Figure 1. A very good performance of the peak detection algorithm was shown with the three performance statistics above 90% for all tests with RMS ratio ≤ 0.8.

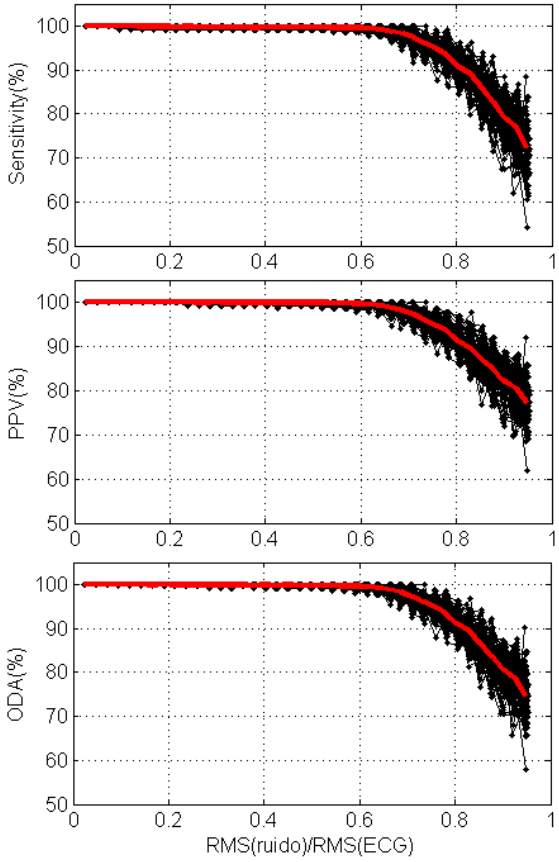

Figure 1 Performance of QRS detection algorithm in 100 tests with simulated ECG and additive noise. Black lines = individual tests, red line = mean from all tests.

3.2 HRV indexes estimation

Compared with the healthy subjects, ESRD patients during supine position had shorter AvRR (i.e. faster heart rate), lower short-term variability (smaller RMSSD and pNN20), larger LF and LF/HF and smaller HF.

Table 3 HRV indexes. Data is shown as median (percentile 25 – percentile 75).

	Healthy (N = 12)	ESRD (N = 10)	p
Supine position			
AvRR (s)	0.9 (0.8 – 1.0)	0.7 (0.6 – 0.9)	0.02
RRSD (ms)	107 (92 – 143)	109 (61 – 119)	0.49
RMSSD(ms)	61 (48 – 76)	15 (10 – 22)	<0.01
pNN20 (%)	53 (46 – 61)	13 (5 – 25)	<0.01
LF (n.u.)	44 (32 – 61)	68 (38 – 80)	0.05
HF (n.u.)	56 (41 – 68)	35 (20 – 62)	0.05
LF/HF	0.8 (0.5 – 1.5)	1.9 (0.6 – 4.0)	0.04
Active standing			
LF (n.u.)	82 (71 – 87) *	77 (54 – 83)	0.23
HF (n.u.)	20 (14 – 29) *	25 (20 – 47)	0.09
LF/HF	4.3 (2.5 – 6.3) *	3.2 (1.1 – 4.1)	0.09

* $p < 0.01$ compared to supine position

These differences are consistent with larger sympathetic nervous system predominance in the ESRD patients compared to healthy controls [6].

In response to active standing, the healthy groups had increased LF and LF/HF. This indicate an increment of the sympathetic nervous system activity (LF) and decrement of the parasympathetic nervous system activity (HF) with predominant sympathetic activity (higher LF/HF) in response to active standing [6].

3.3 Spectral coherence analysis

Results of the spectral coherence analysis between HRV and RA of 12 healthy volunteers during spontaneous respiration showed a highly disperse coherence in all frequencies (Figure 2, upper panel). In contrast, during controlled breathing at 0.1 Hz (middle panel) and 0.25 Hz (lower panel), coherence was very high with low dispersion in their respective breathing frequencies. This shows an expected increase in cardiorespiratory interaction induced by controlled breathing [11].

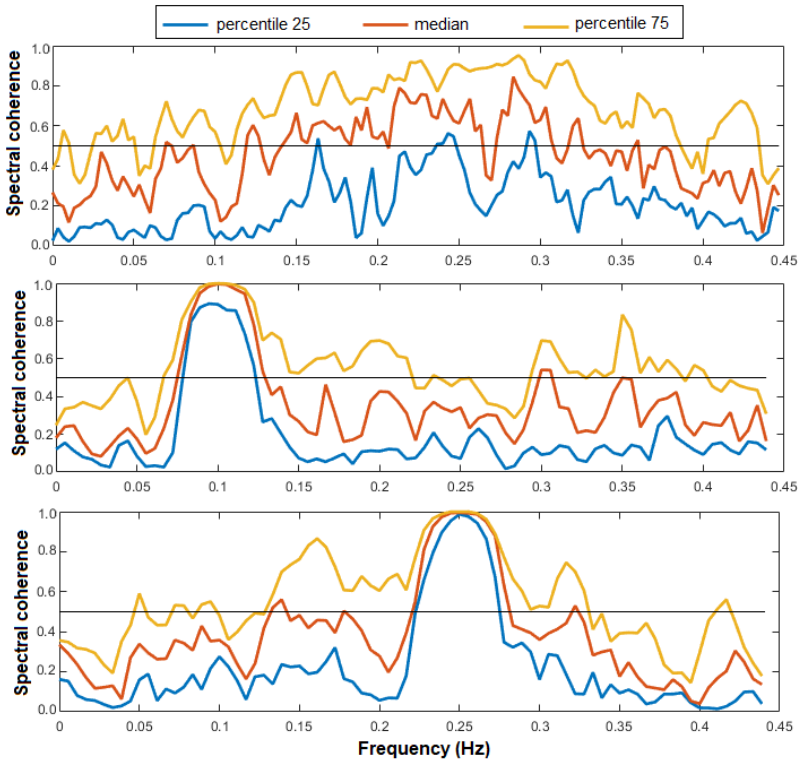

Figure 2 Results of the spectral coherence analysis between HRV and AR in 12 healthy subjects during spontaneous breathing (upper panel), controlled breathing at 0.1 Hz (middle panel) and controlled breathing at 0.25 Hz (lower panel). All recordings were obtained during supine position.

3.4 Graphical user interface

Figure 3 shows the screen presentation of the graphical user interface. The control bars are located at the left side and include options to load ECG and RA files, to apply the peak detector algorithms, to apply the adaptive filter for automatic identification and substitution of non-normal heartbeats in HRV ("Extrasystoles filter"), and the options to select a window size for spectral analysis.

The interface shows plots of the following signals as a function of time: ECG, RR interval (HRV), RA signal, I-I interval (BB interval) and RA at each I peak (Max RA). The bottom plots correspond to the power spectrum density of the RR intervals and the AR signal (bottom left) and the corresponding spectral coherence (bottom right).

In the example of Figure 3, the green shadows indicate a segment of HRV and AR time series which include a part with periodic breathing at 0.1 Hz followed by periodic breathing at 0.25 Hz. The power spectral densities and spectral coherence spectrum show correct identification of the harmonic components in both frequencies.

The graphical user interface includes the option "File" in the menu bar which allows the user to save the processed data (including HRV and I-I time series) in files with CSV format.

4 CONCLUSIONS

The developed computer program allows the analysis of cardiorespiratory coupling through the assessment of spectral coherence between HRV and RA.

The program includes a reliable automatic algorithm for peaks detection to obtain HRV and I-I time series, which can be retrieved from CSV files for further use with other methods.

The graphical user interface includes useful options such as interactive manual correction of the identified peaks, which allows the study of respiratory coupling to non-expert users.

5 ACKNOWLEDGMENTS

The authors thank Hortensia González, Juan Carlos Echeverría, Héctor Pérez Grovas and Raúl Martínez for their helpful suggestions. We also thank Marco García and Moisés Hernández their support with data gathering. S. Figuerola was supported with a scholarship from the Academia Mexicana de Ciencias. This work was partially supported by the Universidad Nacional Autónoma de México (the Autonomous National University of Mexico) [grant number PAPIIT-RN2163188].

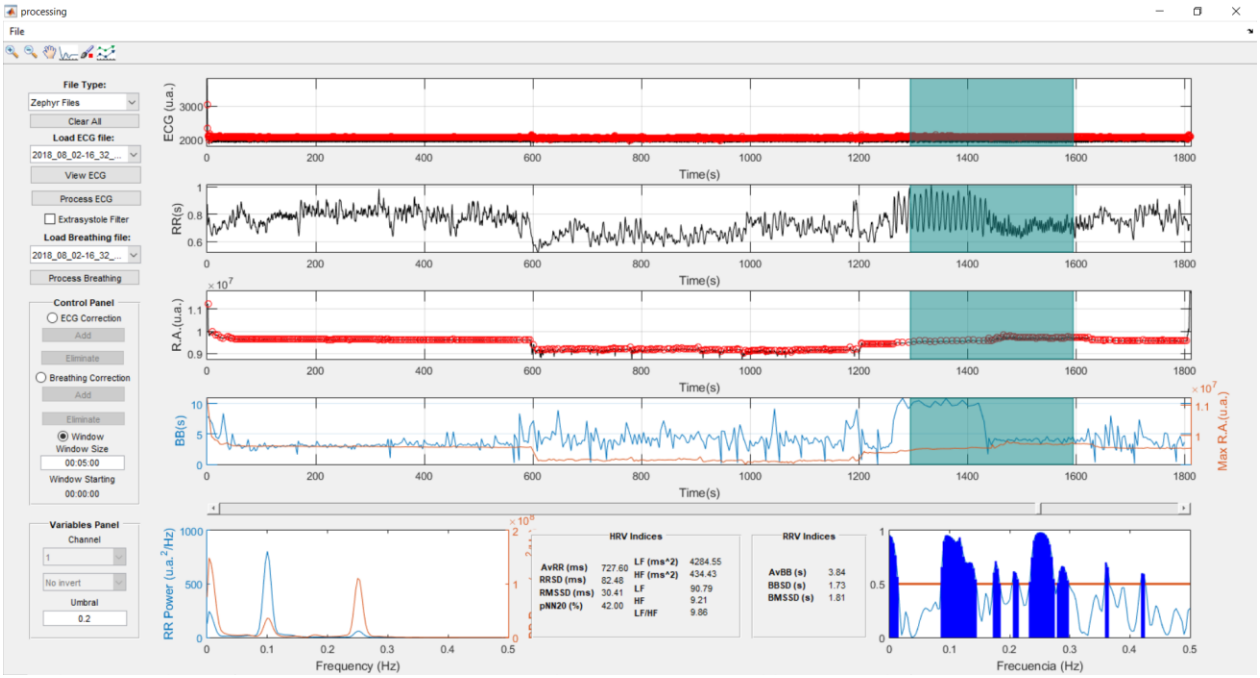

Figure 3 Example of the graphical user interface. The shadow indicates the window selected for the spectral analysis and spectral coherence, which includes a part with periodic breathing at 0.1 Hz followed by a part of periodic breathing at 0.25 Hz.

6 REFERENCES

[1] G.A. Roth, C. Johnson, A. Abajobir, et al, "Global, regional and national burden of cardiovascular diseases for 10 causes", J. Am. Coll. Cardiol. vol. 70, no. 1, 2017, pp 1-25.

[2] Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. "Heart rate variability. Standards of measurement, physiological interpretation, and clinical use", Eur. Heart J. vol. 17, no. 3, 1996, pp. 354-381.

[3] A.J. Garcia, J.E. Koschnitzky, T. Dashevskiy, J.M. Ramirez, "Cardiorespiratory coupling in health and disease", Auton. Neurosci. vol. 175, no. 1-2, 2013, pp. 26-37.

[4] C. Lerma, O. Infante, M.V. José, "Sistema de captura y análisis de la variabilidad del pulso arterial y la frecuencia cardiaca", ELECTRO, vol. 24, 2002, pp. 74-77.

[5] C. Lerma, E.I. De la Rosa-Vega, "Modelo matemático del control cardiovascular barorreflejo para evaluar el efecto de los movimientos de la respiración sobre la frecuencia cardiaca", ELECTRO, vol. 36, 2014, pp. 149-155.

[6] C. Lerma, H. González, H. Pérez-Grovas, M.V. José, O. Infante, "Preserved autonomic heart rate modulation in chronic renal failure patients in response to hemodialysis and orthostatism", Clin. Exp. Nephrol, vol. 19, no. 2, 2015, pp. 309-318.

[7] O. Infante, F. Valenzuela, S. Polo. "Algorithm that uses the second derivative to identify the QRS complex in real time", Rev. Mex. Ing. Biomed, vol, 13, 1992, pp. 23–32.

[8] P.E. McSharry, G.D. Clifford, L. Tarassenko, L.A. Smith, "A dynamical model for generating synthetic electrocardiogram signals", IEEE Trans. Biomed. Eng. vol. 50, no. 3, March 2003, pp. 289-294.

[9] N. Wessel, A. Voss, H. Malberg, C. Ziehmann, H.U. Voss, A. Schirdewan A, et al. "Nonlinear analysis of complex phenomena in cardiological data", Herzschr Elektrophys, vol. 11, 2000, pp. 159-173.

[10] J.A. Behar, A.A. Rosenberg, I. Weiser-Bitoun, "PhysioZoo: A novel open access platform for heart rate variability analysis of mammalian electrocardiographic data", Frontiers Physiol, vol. 9, no. 1390, 2018, pp. 1-14.

[11] G. Baselli, S. Cerutti, S. Civardi, D. Liberati, F. Lombardi, A. Malliani, M. Pagani, "Spectral and cross-spectral analysis of heart rate and arterial blood pressure variability signals", Comput. Biomed. Res, vol. 19, no. 6, 1986, pp. 520-534.