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Obstructive sleep apnea detection using spectrum and bispectrum analysis of single-lead ECG signal

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Abstract

A novel method for the automatic diagnosis of obstructive sleep apnea (OSA) from an electrocardiogram (ECG) is presented. This method aims to detect OSA utilizing exclusively ECG recordings during sleep and present a minute-by-minute signal processing technique. In the proposed algorithm, a wide range of features based on heart rate variability (HRV) and ECG-derived respiratory (EDR) signals are considered. The novelty of this study arises from employing bispectral analysis to the HRV and EDR signals in order to illustrate quadratic phase-coupling that can be observed among signal components with different frequencies. From this perspective, in the proposed algorithm, a new feature set based on a higher order spectrum of HRV and EDR signals is introduced and it is utilized to extract information regarding their non-linearity and nonGaussianity. This feature vector is then fed into the input of a least-square support vector machine classifier. To implement the proposed method, the apnea-ECG database, which contains 70 nocturnal ECG records gathered from volunteer men and women, is used in this work. Results obtained from cross-validating 35 data records show that the normal recordings could be separated from the apneic recordings with an accuracy of 95.57% and a sensitivity and specificity of 98.64% and 92.51%, respectively. In addition, 35 other records were used for a pure independent validation of the proposed method and the obtained accuracy, sensitivity and specificity was 94.12%, 93.46% and 94.79% respectively in OSA episode detection. The performance of our proposed technique is better than in other existing approaches. It can be used as a reliable tool for automatic OSA identification and as a result, it will improve medical services.

Keywords: bispectrum, ECG, EDR, HRV, obstructive sleep apnea, quadratic phase-coupling

1. Introduction

Obstructive sleep apnea (OSA) is a common disorder characterized by repetitive pharyngeal collapse during sleep, and it is receiving increased attention because of convincing data showing important neurocognitive and cardiovascular sequels (Malhotra and White 2002). It is known by the complete (apnea) or incomplete (hypopnea) cessation of breathing for more than 10 s, which causes oxygen saturation in the blood to decrease. Apnea and hypopnea occur as a result of a physical airway collapse during sleep. This happens as the upper airway dilating muscles, like all striated muscles, normally relax during sleep (Fauci *et al* 2008). Obesity is a strong causal factor for sleep-disordered breathing (SDB), and because of the ongoing obesity epidemic, estimates of sleep-disordered breathing prevalence have increased by up to 10% among 30–49 year old men, 17% among 50–70 year old men, 3% among 30–49 year old women, and 9% among 50–70 year old women (Peppard *et al* 2013). In OSA patients, dilating muscles were unable to overcome negative airway pressure during inspiration. It is possible that before the closure of the airway, patients start to snore which would lead to OSA. OSA terminates shortly after the patient wakes up. This disorder has several health consequences which would affect the patients' lifespan. OSA symptoms will manifest themselves as daytime drowsiness, impaired cognitive performance, depression, insomnia and hypertrophy. OSA leads to an augmentation in the mean 24 h blood pressure. Epidemiologic data in normal populations indicate that this increase in blood pressure would increase the risk of myocardial infarction by around 20% and stroke by about 40% (Fauci *et al* 2008). Continuous positive airway pressure (CPAP) is a device utilized for the treatment of this disorder. This device prevents obstruction through positive pressure (5–20 cm H₂O), reduces sleepiness and improves hypertension (Malhotra and White 2002). CPAP is a minimally invasive method and patients must consider choosing the one that suits them best.

Polysomnography (PSG), which must be performed in a sleep laboratory setting, is considered the reference standard for diagnosing OSA, but it is expensive and requires specialized resources (Qaseem *et al* 2014). Polysomnography measures or estimates the apnea–hypopnea index (AHI), which is a measure of the number of apnea or hypopnea events per hour during sleep. The AHI is used to diagnose and assess the severity of OSA. Polysomnography consists of continuous polygraphic recordings from surface leads for electroencephalography (EEG), electrooculography (EOG), electromyography (EMG), electrocardiography (ECG), and from non-invasive sensors for nasal airflow, oral airflow, tracheal sounds, thoracic and abdominal respiratory effort, and oxyhemoglobin levels.

However, polysomnography requires specialized facilities, is resource-intensive and expensive, and requires patients to spend the night under observation in a foreign environment (Qaseem *et al* 2014). In addition, as there is limited access to sleep clinics, most of the patients remain undiagnosed and untreated. Therefore, detection of OSA by means of a non-invasive tool with minimum interference in the patients' sleep would be valuable and it would lead to resolving these problems.

Among the biological signals, the ECG signal is the most widely used, and it contains useful information regarding cardiovascular activity and other adjacent systems. ECG is a time-varying semi-periodic signal representing the electric activity of different components of the heart during the cardiovascular cycle. Even though OSA does not take place in a cardiovascular system, it is possible to observe its effects on this system. Hence, one will be able to detect OSA effects in a cardiovascular system through ECG records. Over the last decade, several algorithms based on digital signal processing have been proposed for OSA screening using an ECG signal. Studies have shown that heart rate variability signals (HRV) and ECG-derived respiratory signals (EDR) contain useful information regarding OSA. De Chazal *et al* (2003) utilized HRV and EDR signals and derived 88 features both in time and frequency domains. Using these features, they trained linear discriminate (LD) and quadratic discriminate (QD) classifiers and achieved an accuracy of

90%. Hossen *et al* (2005) developed a subband decomposition soft-decision algorithm for HRV signals that accomplished an accuracy of 93% in discriminating normal and apnea episodes. Khandoker *et al* (2009) proposed an algorithm using wavelet decomposition of the ECG signal and a two-stage feed-forward neural network (NN) and reported an accuracy of 94.84% in the classification of OSA. Mendez *et al* (2009) proposed two other signals made out of EDR and HRV signals, which lacked any physiological meaning, and extracted features from these four signals. Moreover, they developed a time-varying autoregressive model for a beat-to-beat estimation of power spectrum density (PSD). They achieved an accuracy of 88% in the classification of OSA using a k-nearest neighbor (KNN) classifier. In another study, Mendez *et al* (2010) used an empirical mode decomposition of ECG signals for apnea detection and reported an accuracy of 85% for LD and QD classifiers. BSoul *et al* (2011) presented an application for Android operating systems based on a support vector machine (SVM) classifier which was able to detect OSA domestically. By using a wide range of features in time and frequency domains an SVM classifier was trained and it resulted in an accuracy of 89.88%. Gubbi *et al* (2012) also proposed a method using NN and separated hypopnea/apnea events from normal ones. In addition to that, using an extra stage, they detected central sleep apnea (CSA) episodes. Kesper *et al* (2012) focused on cyclic variations of HRV signals and EDR curves for the detection of OSAHS and reported an accuracy of 80.5% for independent classification. Lado *et al* (2011) analysed several databases for apnea detection and using the HRV signal evaluated the validity of both databases and algorithms. Nguyen *et al* (2014) used the nonlinear dynamics of HRV signals to detect OSA. The complexity of HRV is measured using recurrence quantification analysis (RQA). In order to achieve a more robust method they applied different fixed neighbor thresholdings for recurrence plot calculation. Using a soft decision fusion they were able to detect OSA events with an accuracy of 85.26%.

This study aims to develop an algorithm for OSA detection using novel features based on a spectrum and higher order spectrum (HOS) of HRV and EDR signals. HOS is the spectral representation of higher order statistics such as third order cumulants and beyond. The fact that it is possible to acquire information regarding non-stationary signals and their deviation from linearity and Gaussianity using HOS was the main motivation for this work. Previous applications of HOS on biological signals such as the mental task classification of EEG signals Zhou *et al* (2008), detection of epilepsy from EEG signals Chua *et al* (2011) and cardiac arrhythmia classification Khadra *et al* (2005) have been reported. In addition, Hadjileontiadis *et al* (2001) presented an algorithm for QRS detection during sleep using HOS. This method was used on data nocturnally recorded from patients with sleep apnea.

In this paper, by employing HOS and spectral analysis on HRV and EDR signals, several features have been extracted. The extracted features contain valuable information regarding OSA, which is used in the classification process. It is expected that by recovering the phase coupling (or lack of phase coupling) between different frequency bands of HRV and EDR signal, new information will be revealed that may be quantified and used in screening apnea episodes. Afterward, extracted features have been used to train a least-square support vector machine (LS-SVM). The SVM maps input feature space into a higher dimension and through solving an optimization problem, finds the optimal separating hyper-plane. The LS-SVM is a reformulated version of the conventional SVM that leads to solving a less complex linear optimization problem. According to the obtained results, it has been shown that the developed algorithm exhibits a high performance in discrimination between normal and apnea episodes and has potential for the initial assessment of patients with suspected OSA.

This paper is organized as follows: in section 2 the database used in this study is introduced. The proposed algorithm is presented in section 3, which contains four subsections relating to the pre-processing of ECG signals and the extraction of HRV and EDR signals, spectral and bispectral feature extraction, a statistical significance test of extracted features, and classification using an

LS-SVM classifier. After the explanation of the proposed method, in section 4 we present the results of apnea detection. Section 5 provides the discussion and finally in section 6 the concluding remarks are presented.

2. Database

Throughout this paper, we adopt the apnea-ECG database developed by Moody *et al* (2001) and Penzel *et al* (2000). This database is publicly available on the PhysioNet website (Moody *et al* 2000). This database consists of 70 nocturnal ECG records of approximately 8 h in duration obtained from different patients. Each ECG signal was sampled with a sampling frequency of 100 Hz and 16-bit resolution, where each bit portrays 5 μ V. Records do not involve episodes of pure CSA and Cheyne–Stokes respiration and all of the apnea episodes are obstructive or mixed (containing both OSA and CSA). Besides this, for each 1 min segment of the record, there are annotations available that indicate the presence or absence of apnea during that minute. These annotations have been marked by a specialist using results obtained from volunteer patients' PSG records.

3. The proposed algorithm

In this study we present a novel algorithm using features based on the spectrum and HOS of HRV and EDR signals for the episode classification of OSA events. As can be seen in figure 1, the proposed algorithm is divided into three main stages: pre-processing, feature extraction, and classification. In the pre-processing stage, HRV and EDR signals are derived from nocturnal ECG records. Then, for feature extraction a set of novel features that have proper potential for discrimination between normal and apnea episodes have been proposed. Finally, in the last stage we employed a statistical classification method for episode status determination.

3.1. Pre-processing

Recent studies have shown that HRV and EDR signals contain beneficial information regarding this disorder. HRV is usually calculated from the elapsed time between two ventricular contractions which can be inspected from intervals between consecutive R peaks (Acharya *et al* 2004). In addition, during the respiration effort the filling and emptying of the lungs, chest movements and variations in the thorax impedance distribution result in a rotation of the electrical axis of the heart which affects beat morphology (Bailón *et al* 2006). These effects are observable from variations in the amplitudes of peaks in the ECG signal that make it possible to estimate the EDR signal.

In order to perfectly construct HRV and EDR signals from ECG records, the accurate detection of a QRS complex is required. Therefore, for QRS detection we have used an algorithm based on the wavelet decomposition of an ECG signal. Wavelet transformation analyses the signal at different frequency bands by decomposing the signal into an approximation signal and several detail signals. Using this method, we decomposed the ECG signal with a Daubechies6 (db6) wavelet by up to seven levels. Figure 2 illustrates a 1 min episode of the ECG signal with its related decomposition signals. It is worth mentioning that in wavelet

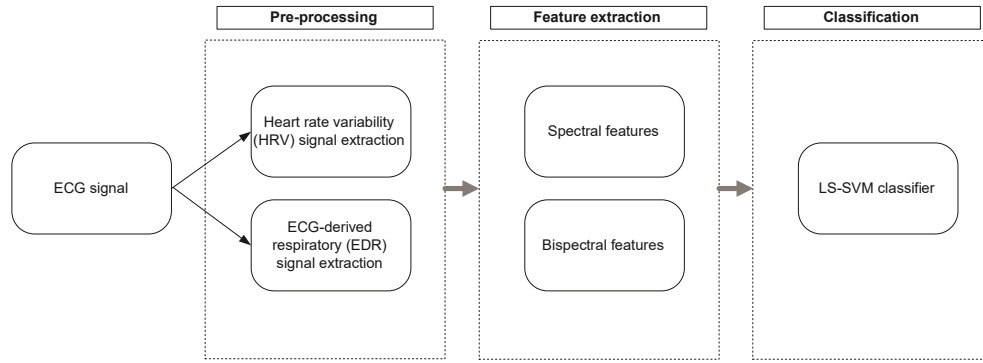


Figure 1. Schematic representation of the proposed method for OSA detection.

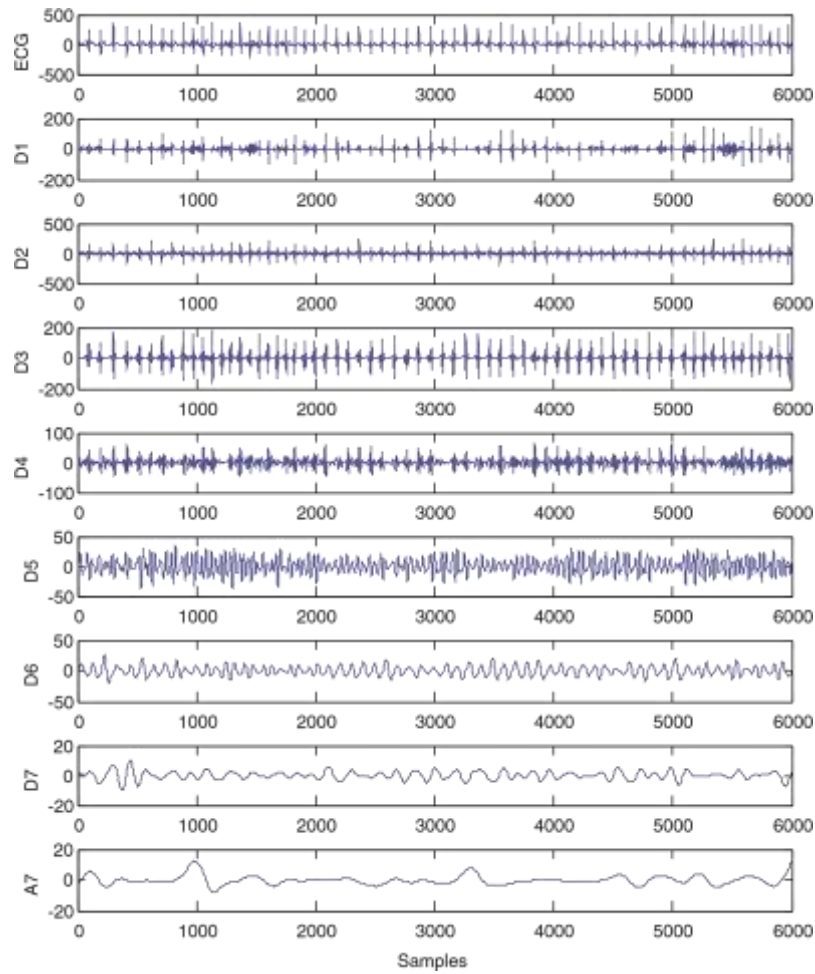


Figure 2. A one-minute ECG episode with its details and approximation signals decomposed using a Daubechies wavelet.

decomposition, after passing the signal through a low-pass filter, half of the samples can be eliminated according to Nyquist's rule, since the signal now has a highest frequency of half the frequency of the signal prior to filtering (Polikar 1996). However, in figure 2, up-sampled detail signals are illustrated so that the time resolution would be the same as the main ECG signal. Since

the second detail signal (D2) contains most of the QRS complex energy (Yildiz *et al* 2011), it is used for the estimation of the QRS complex. To determine the accurate time of QRS occurrence, the following procedure is applied. First, the absolute value of the second detail signal (D2) is calculated. Then, a hard threshold equal to 200% of the root mean square of the absolute value of D2 is applied to remove irrelevant noisy samples. After that, the maximum value for this signal is calculated within a 200 ms window. This approach results in an approximate calculation of QRS complex occurrence. Once the approximate QRS complex occurrence time is determined, the original ECG signal is scanned in a 70 ms window around the estimated time of the QRS complex which would result in the exact time of R peak. Due to the presence of spurious or missed QRS in the detection algorithm, obtained results were evaluated once more. For this purpose, the RR interval series was calculated from differences in consecutive R peaks. If the calculated RR interval is more than 180% of the mean RR interval value, there seems to be a missed QRS. In addition, if it is less than 60% of the mean RR interval value, there is an extra QRS detected and it is omitted. In addition to QRS detection, the ECG signal is detrended through the exclusion of approximation signals from the main signal.

Since premature ventricular contractions (PVCs) are known to have a serious impact on the results of RR interval analysis, we have edited the RR interval signal to handle the PVC beats. To this end, we have used the method recommended by Kamath and Fallen (1995) in which RR interval segments with a duration of less than 75% of the duration of the previous normal beat have been regarded as PVC beats and they have been eliminated from the RR interval signal. Accuracy of the R peak detection algorithm is evaluated with the help of a specialist. The accuracy for R peak detection was more than 94%. The small error in R peak detection was observed in the highly noisy episodes. In figure 3, the results of R peak detection using this method are illustrated for five different episodes.

After the exact extraction of R peaks, it is possible to construct HRV and EDR signals. An HRV signal is extracted from the difference between two consecutive R peak times. In addition, for the extraction of the EDR signal the summation of amplitudes in an R peak centered window of 100 ms (50 ms prior to R peak and 50 ms after that) is calculated.

3.2. Feature extraction

In order to specify the status of ECG segments using pattern recognition approaches, the extraction of several quantitative features is required. In this study, we considered a set of spectral-based as well as bispectral-based features for both HRV and EDR signals. As the acceptable performance of a classifier depends primarily on the successful selection of proper features, we attempted to extract features that represent maximal separation between two classes.

3.2.1. Spectral analysis. Many biomedical systems exhibit innate rhythms and periodicity that is more readily expressed and appreciated in terms of frequency than time units (Rangayyan 2001). The power spectral density (PSD) of a signal shows the strength of energy variations as a function of frequency. In other words, it illustrates how much power is contained in each of the frequency spectrums of the signal. Prior usage of spectral information of HRV signals for OSA detection has been reported (de Chazal *et al* 2003, Hossen *et al* 2005, Khandoker

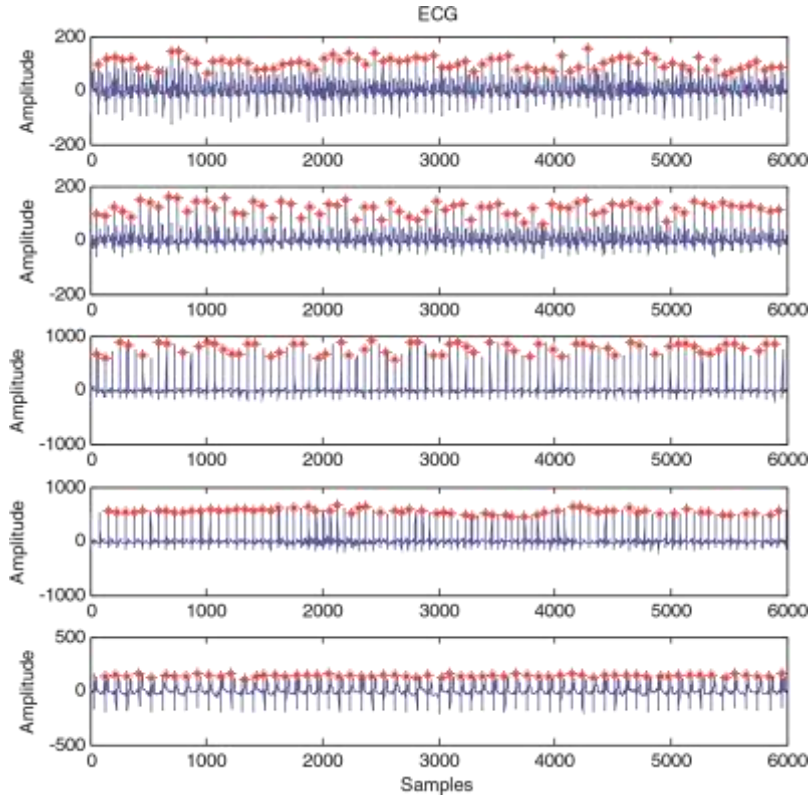


Figure 3. The result of R peak detection using the proposed method for five different ECG episodes.

et al 2009, Mendez *et al 2009*). In addition, previous studies have demonstrated that the spectral pattern of an HRV signal consists of three main frequency bands: a very low frequency band (VLF) from 0–0.04 Hz, a low frequency band (LF) from 0.04–0.15 Hz and a high frequency band (HF) from 0.15–0.4 Hz (Acharya *et al 2006*). It has been proven that the LF component is related to the sympathetic activation and power of the HF component which provides a quantitative index of the influence of respiration on the ECG signal and may be connected to vagal activity (Bailón *et al 2006*). As a result, extracting this information from an HRV signal could be helpful for OSA detection and the improvement of the algorithm performance. In order to calculate the power of an HRV signal in different frequency bands, we used the method proposed in (Ebrahimi *et al 2012*). In this method, using wavelet decomposition of HRV signals, these frequency bands have been extracted. To do so, the HRV signal is decomposed up to five levels using Daubechies4 discrete wavelet transform. Using these detail and approximation signals, the frequency components of an HRV signal are calculated as follows:

1. The VLF band could be estimated using the approximation coefficient.
2. The LF band could be estimated using the fifth detail signal (d_5).
3. The HF band could be estimated using the first four detail signals (d_1, d_2, d_3, d_4).

It should be noted that in the wavelet decomposition method, the choice of which bands to allocate to VLF, LF and HF depends on the original sampling rate of the signal and the

Normal

Apnea

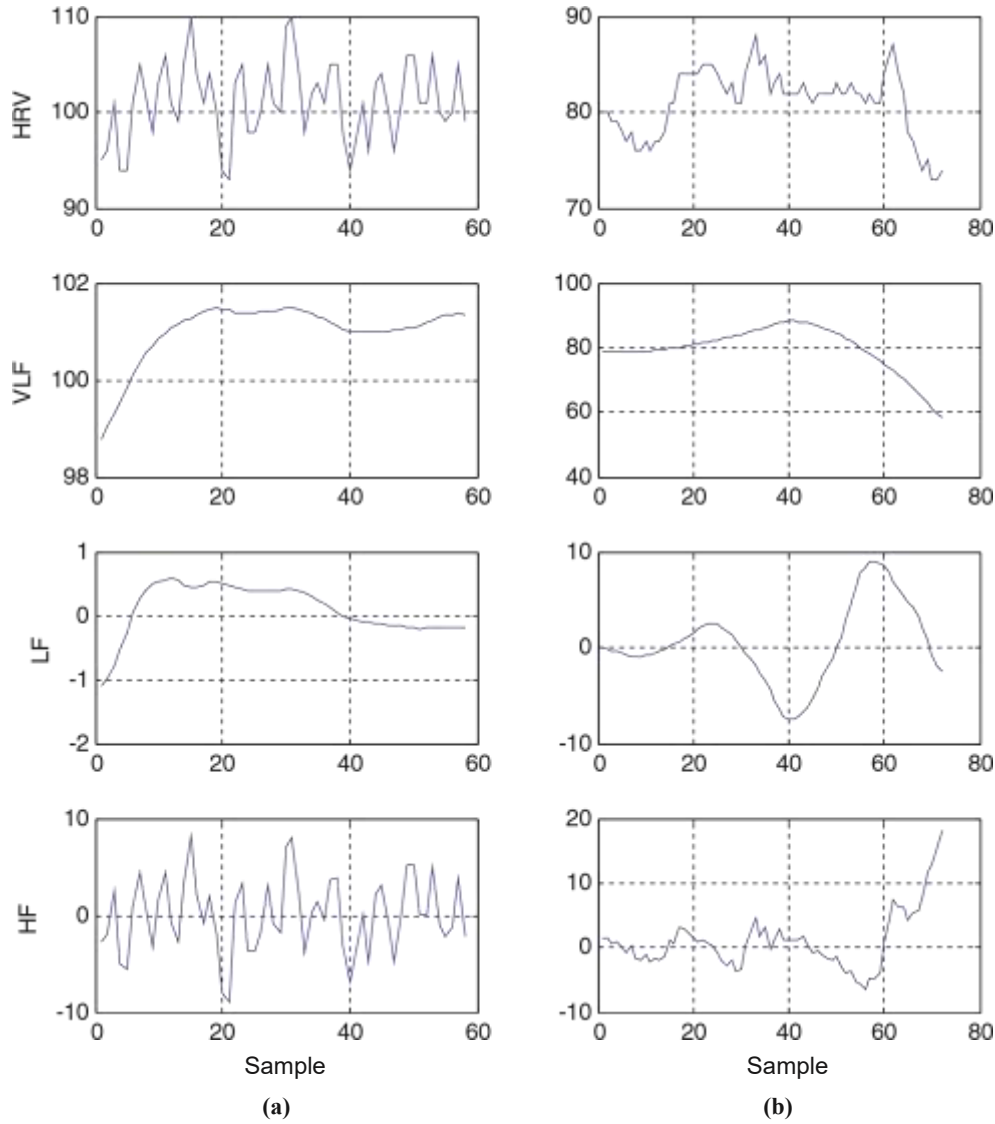


Figure 4. The HRV signal derived from the 1 min episode of a nocturnal ECG record for (a) normal and (b) OSAHS events and their frequency bands separated using wavelet decomposition.

results may vary for signals with different sampling frequencies. In this algorithm, results are obtained for the ECG signal with a sampling frequency of 100 Hz.

After separating the VLF, LF and HF frequency bands of the HRV signal, their powers have been calculated and considered as spectral features. Figure 4 depicts an HRV signal with its related frequency bands for both normal and OSA episodes using the wavelet method explained in this section.

Apart from the spectral analysis of the HRV signal, the estimated EDR sequence is also analysed to detect the respiration changes in OSA. The PSD of this signal, which is done directly by the FFT method, is also calculated for each 1 min episode and used as a feature in further analysis. Figure 5 shows the extracted EDR signal and the PSD for both normal and OSA episodes. Consequently, four spectral features from the HRV and EDR signals are extracted.

These spectral features consist of the power of the VLF, LF and HF frequency bands of the HRV as well as the power of the EDR signal for both OSA and normal episodes.

3.2.2. Bispectral analysis. For decades, spectral analysis was the main tool for digital signal processing. Spectral analysis provides useful information concerning Gaussian signals. However, while dealing with non-Gaussian signals these tools fail and it is necessary to look beyond the conventional autocorrelation sequence. HOS is the spectral representation of higher order statistics (moments and cumulants of third order and beyond). Thus, this approach enables us to detect deviations from Gaussianity, linearity, stationarity and the presence of phase relations. Since most biomedical signals are of a non-Gaussian, non-linear and non-stationary nature, this approach can result in useful information.

A higher order spectrum is defined as the spectral representation of higher order cumulants of a random process, and it is called Bispectrum for third order cumulants (Chua *et al* 2010). A third order cumulant for a zero-mean random process $x(n)$ is equal to its third order moment defined as follows:

$$c_3(\tau_1, \tau_2) = E\{x(k) x(k + \tau_1) x^*(k + \tau_2)\} \quad (1)$$

The Bispectrum is a 2D Fourier transform of the third order cumulant:

$$B(f_1, f_2) = \sum_{\tau_1=-\infty}^{+\infty} \sum_{\tau_2=-\infty}^{+\infty} c_3(\tau_1, \tau_2) \exp[-j2\pi \tau_1 f_1 - j2\pi \tau_2 f_2] \quad (2)$$

In practice, discrete forms of a random process are available and limited samples of the random process are accessible. Thus, the Bispectrum is estimated from these finite samples. It has been shown that the Bispectrum of a non-Gaussian signal, $x(n)$ can be defined in terms of its Fourier transform as follows (Chua *et al* 2010):

$$B(f_1, f_2) = E\{X(f_1) X(f_2) X^*(f_1 + f_2)\} \quad (3)$$

where $X(f)$ is the Fourier transform of the random process $x(n)$, and $E\{\cdot\}$ stands for the expectation operation. It is observable that the Bispectrum of a random process is a function of two frequencies. The frequency band can be normalized using the Nyquist frequency to map it between 0 and 1. The Bispectrum illustrates the relation between f_1, f_2 and $f_1 + f_2$ frequencies of the random process. As a result of non-linear interaction between harmonic components, phase coupling occurs. Three harmonics with the frequencies of f_k and phase ϕ_k for $k = 1, 2, 3$ are quadratic phases coupled if $f_3 = f_1 + f_2$ and $\phi_3 = \phi_1 + \phi_2$. When signal passes through a quadratic system, quadratic phase coupling (QPC) occurs. Bispectrum can detect these QPCs. When there is a relation between these three frequencies the Bispectrum would possess a non-zero value, and if they are completely random-phase, the Bispectrum would be zero. Figure 6(a) illustrates the contour plot of the Bispectrum for normal and OSA episodes of HRV and EDR. As assumed, the Bispectrum of HRV and EDR signals contain phase coupling information. Both HRV and EDR signals depict highly non-Gaussian and non-linear information in which this information varies significantly between normal and OSA episodes. Phase coupling in the normal episodes of HRV are concentrated in high frequencies and low frequencies while this information for OSA episodes of HRV is observable in the middle frequencies. In addition, in normal episodes of HRV the vast majority of frequencies exhibit QPCs, but in the OSA episodes the amount of frequencies with QPC is in decline as indicated

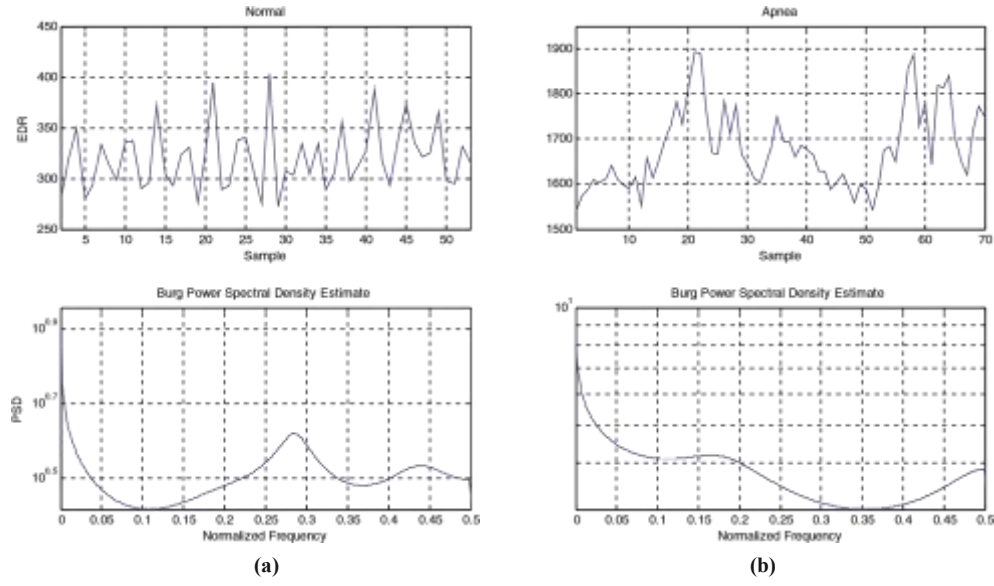


Figure 5. EDR signals derived from the 1 min episode of a nocturnal ECG record and their estimated PSD for (a) normal and (b) OSAHS events.

in the contour plot of the Bispectrum. Similarly, the occurrence of phase coupling between the various frequency components of the EDR signal differs in normal and OSA episodes. Observed QPCs for normal EDR signals are concentrated in the middle frequencies and the EDR of OSA episodes has phase couplings in high and low frequencies. In the same way, it can be seen that there are more QPCs in normal episodes. Figure 6(b) illustrates the distinct variations between the normal and OSA episodes of HRV and EDR signals. Even though these plots cannot be used as a measure for automatic detection, it is possible to derive features from them to quantify the features of Bispectrum plots and build a useful feature vector for automatic separation.

Recent studies suggested various features as a measure to assist the separation between normal and abnormal samples of biomedical signals using bispectral analysis. Chua *et al* (2010) presented several features which have been used in previous studies. Assuming there is no bispectral aliasing, the Bispectrum of a real signal is completely definable in a non-redundant area of $0 \leq f_2 \leq f_1 \leq f_1 + f_2 \leq 1$ due to symmetry of these plots. The following features have been calculated from the Bispectrum of HRV and EDR signals.

- The mean magnitude of the Bispectrum:

$$M_{ave} = \frac{1}{L} \sum_{\Omega} |B(f_1, f_2)| \quad (4)$$

where Ω denotes the non-redundant region and L is the number of points within this region.

- The two weighted centers of the Bispectrum:

$$f_{mz} = \frac{\sum_{\Omega} i B(i, j)}{\sum_{\Omega} B(i, j)} \quad (5)$$

Bispectrum of the HRV signal for a normal episode

$\times 10^4$

Bispectrum of the EDR signal for a normal episode

$\times 10^5$

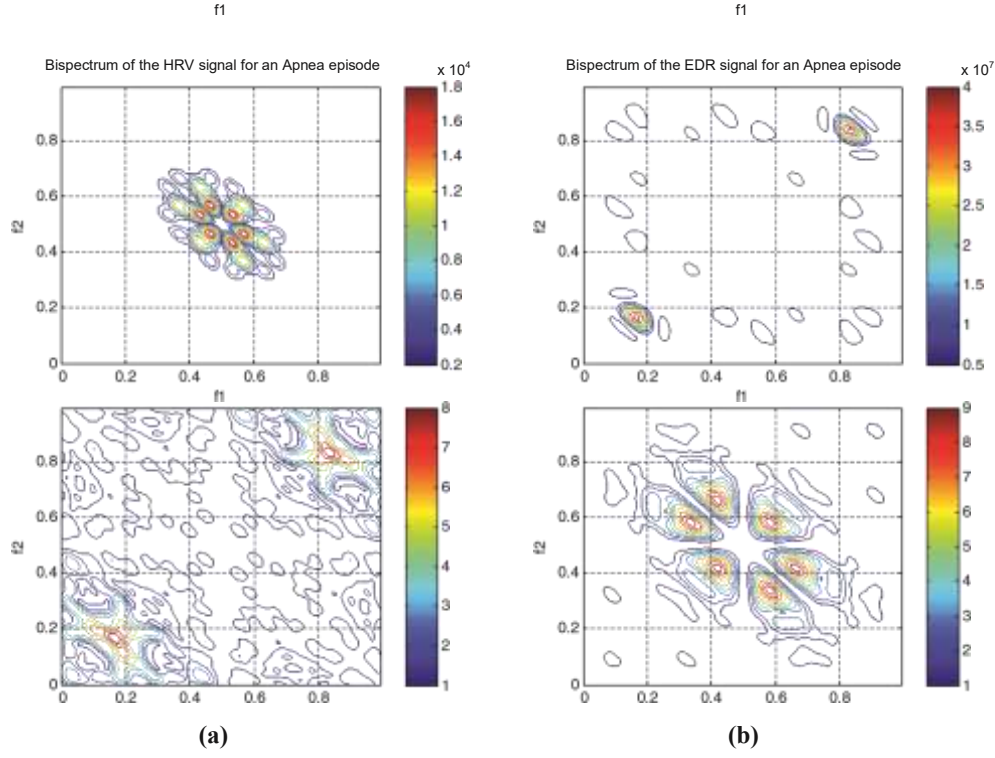


Figure 6. The contour plots for HRV and EDR signals for normal and OSA events. (a) The Bispectrum plot of a normal HRV illustrates numerous QPCs between frequencies and the highest QPCs are concentrated in the higher and lower frequencies. But in an OSA event, the bispectrum of HRV has more zero values and QPCs occur in the middle frequencies. (b) For the EDR signal there are more QPCs in normal episodes and they are concentrated in central frequencies. For the EDR signals derived from OSA episodes QPCs are in higher and lower frequencies.

$$f_{2m} = \frac{\sum_j B(i, j, \omega)}{\sum_{\Omega} B(i, j, \omega)} \quad (6)$$

where i, j are the frequency bin indexes in the depicted region.

- Entropies have been used to detect regularity or irregularity in biological signals. Two types of normalized bispectral entropy (P_1) and normalized squared bispectral entropy (P_2) are presented respectively as follows:

$$P_1 = -\sum_i p_i \log p_i \quad (7)$$

where

$$p_i = \frac{1}{\sum_{\Omega} B(f_i, f_2)} \quad (8)$$

$$P_2 = -\sum_n p_n \log p_n \quad (9)$$

where

$$P_n = \frac{\sum_{\Omega} B(f_1, f_2)^2}{\sum_{\Omega} B(f_1, f_2)} \quad (10)$$

Furthermore, there are several features related to the moments of the bispectral plots that have been used in bispectral analysis.

- The sum of logarithmic amplitudes of the bispectrum:

$$H_1 = \sum_{\Omega} \log(|B(f_1, f_2)|) \quad (11)$$

- The sum of logarithmic amplitudes of diagonal elements in the bispectrum:

$$H_2 = \sum_{\Omega} \log(|B(f_k, f_k)|) \quad (12)$$

- The first-order spectral moment of amplitudes of diagonal elements in the bispectrum:

$$H_3 = \sum_{k=1}^N k \log(|B(f_k, f_k)|) \quad (13)$$

- The second-order spectral moment of amplitudes of diagonal elements in the bispectrum:

$$H_4 = \sum_{k=1}^N (-k - H_3)^2 \log(|B(f_k, f_k)|) \quad (14)$$

3.3. Statistical analysis of extracted features

For both HRV and EDR signals, features defined in the previous section are calculated. A feature vector consists of two sets of HRV and EDR features and each of these vectors contains spectral and bispectral measures. HRV feature sets contain 12 features and EDR sets contain 10 features. To investigate the convenience of these features in discriminating normal and OSA episodes, a two-sample Kolmogorov–Smirnov test (KS-test) is applied to determine the significance of features for normal and OSA episodes. The two-sample Kolmogorov–Smirnov test compares the distributions of each feature sample in the two classes to evaluate its significance. The null hypothesis for this test is the consideration that two vectors have the same distribution. The result is h is 1 if the test rejects the null hypothesis at the 5% significance level; otherwise it is 0. The KS-test resulted in the rejection of the null hypothesis with a significance level of <0.0001 for all features, and it demonstrated that the extracted feature vector differs significantly between normal and OSA episodes.

3.4. Classification

The last step of the proposed method is the automatic classification of episodes. For automatic classification of normal and apnea subjects an LS-SVM classifier has been used. The SVM classifier was developed by Cortes and Vapnik (1995) and has since been widely used for machine learning techniques. Using a kernel function, the SVM maps input space to a higher space and through solving a quadratic set of optimization equations in the feature space, the SVM finds the optimal hyper-plane in which the best separation performance is given.

The optimal hyper-plane for a classic binary SVM is developed through the following optimization problem:

$$\begin{aligned} \min_{w, \xi} & \frac{1}{2} \|w\|^2 + C \sum_{i=1}^N \xi_i \quad (15) \\ \text{Subject to: } & y_i (w^T \phi(x_i) + w_0) \geq 1 - \xi_i, \xi_i \geq 0 \text{ for } i = 1, \dots, N \end{aligned}$$

where x_i is the input vector of the pattern for the i th example and y_i is the corresponding target output, $\phi(x_i)$ is the kernel function which maps input space into a higher dimensional space, w is the weight vector of the optimal hyper-plane, C is the regularization parameter, and ξ_i are slack variables for the SVM.

However, as mentioned before this optimization problem leads to a quadratic set of equations which require a high computational cost. Recently, Suykens developed a new version of the SVM classifier by reformulating it and this is called the LS-SVM (Van Gestel *et al* 2002). In order to solve the required optimization problem, unlike a conventional SVM, the LS-SVM results in a linear set of equations. The optimization problem for the LS-SVM is as follows:

$$\min_{w, \xi} \frac{1}{2} \|w\|^2 + \frac{C}{2} \sum_{i=1}^N \xi_i^2 \quad (16)$$

$$\text{Subject to: } y_i (w^T \phi(x_i) + w_0) = 1 - \xi_i$$

$$\text{For } i = 1, \dots, N$$

In an LS-SVM classifier, the inequality equations are converted into equality equations where the value on the right hand side is considered more as a target value than a threshold value. These modifications result in the simplification of the problem.

4. Results

The implementation of the proposed method was done in the MATLAB environment. For the implementation of the LS-SVM classifier the LS-SVMlab1.8 toolbox developed by Pelckmans *et al* (2002) was used. For the evaluation of this method, 16479 one-minute episodes were extracted from 35 patients in the database. Of these episodes, 9966 were from normal ECG records, while the other episodes were from records during OSA occurrence. The HRV and EDR signals of each episode were calculated using the result of their R peak detection algorithm. In addition, three frequency bands of HRV signal were reconstructed. Therefore, 22 features that have been described were extracted from each episode.

All feature vectors have been normalized for each subject prior to classification to be within $[-1, +1]$. This normalization prevented the feature vectors from having big feature variances. To prevent the classifier from being patient dependent, data randomization had been done before training. This was done in order to select episodes randomly from all of the patients. To assess the classifier performance, a 10-fold cross-validation technique was carried out over 13000 episodes (6500 normal episodes and 6500 apnea episodes). This technique evaluates the classifier performance by dividing the data into 10 separate parts and training it with nine parts while testing it with the other part. Therefore, this process took place 10 times so that

Table 1. The obtained results for the OSA detection of the 35 subjects of the independent test data.

Record	Number of non-apnea episodes	Number of apnea episodes	Accuracy (%)	Record	Number of non-apnea episodes	Number of apnea episodes	Accuracy (%)
x01	149	375	91.6	x19	81	407	94.47
x02	261	209	90.42	x20	250	264	93
x03	454	12	99.14	x21	391	120	93.54
x04	483	0	97.93	x22	481	2	87.16
x05	190	316	95.26	x23	409	119	97.54
x06	451	0	88.78	x24	429	1	95.58
x07	270	240	93.73	x25	220	291	96.82
x08	194	324	95.95	x26	177	344	96.35
x09	342	167	95.87	x27	11	488	95.79
x10	415	96	96.28	x28	62	434	90.73
x11	445	13	97.6	x29	471	0	93.21
x12	471	57	96.78	x30	186	326	93.4
x13	215	292	93.69	x31	42	516	94.62
x14	52	439	93.69	x32	114	425	91.5
x15	299	200	95.19	x33	471	3	91.56
x16	451	65	93.61	x34	472	4	93.7
x17	400	1	92.77	x35	484	0	97.31
x18	458	2	96.09	Total	10602	6177	94.12

each part was used independently for testing. The results were obtained from an average of these steps.

For evaluating the proposed method, three measures of accuracy, sensitivity and specificity were used (Rangayyan 2001). Given these facts, the average of the 10-fold cross validation resulted in an accuracy of 95.57%, a sensitivity and specificity of 98.64% and 92.48% for minute-by-minute classification. In order to have an independent analysis of the proposed method, 35 additional records available in the apnea-ECG database were used as test data. The independent evaluation of our proposed algorithm resulted in an accuracy of 94.12% and a sensitivity and specificity of 93.46% and 94.79% respectively in OSA episode detection. The results of classification for the test data are illustrated in table 1 for each subject. Table 1 illustrates a high accuracy in the discrimination of OSA episodes from normal ones in the independent test. The obtained results demonstrate that the proposed methodology presents a better performance than with other existing approaches.

5. Discussion

Since the annual challenge of PhysioNet for Computers in Cardiology in 2000, many studies participated regarding OSA detection (Drinnan *et al* 2000, Schrader *et al* 2000, Stein and Domitovich 2000, Raymond *et al* 2000). In various previous studies, several examples of time domain and/or spectral domain analysis were done on HRV and EDR signals, and the best results for OSA detection were reported by Khandoker *et al* (2009). They achieved an accuracy of 94.84% in apnea episode detection. Table 2 presents a summary of the classification performances of various methods as well as our proposed algorithm for the

detection of OSA episodes. In the previous studies, ECG-based apnea detection algorithms were limited to the use of parameters derived from HRV and/or EDR signals in which conventional spectral

Table 2. A comparison of the proposed algorithm with previous methods.

Author	Number of extracted features	Method	Accuracy	Sensitivity	Specificity
de Chazal <i>et al</i> (2003)	84	Time domain and PSD features of HRV and EDR signals with LD and QD classifiers	90%	86.4%	92.3%
Khandoker <i>et al</i> (2009)	45	Two-stage feed-forward neural network model using wavelet features from ECG signals	94.84%	—	—
Mendez <i>et al</i> (2009)	72	Sleep apnea screening by autoregressive models from a single ECG lead	88%	85%	90%
Gubbi <i>et al</i> (2012)	510	Wavelet packet analysis of short-term ECG signals	91.08%	91.02%	91.09%
Bsoul <i>et al</i> (2011)	111	Time and spectral features of HRV and EDR with subject independent SVC	91.16%	89.12%	92.35%
Nguyen <i>et al</i> (2014)	72	Recurrence quantification of HRV signal	85.26%	83.47%	86.37
This method	22	Bispectral and spectral analysis of HRV and EDR signals	95.57%	98.64%	92.51%

and time domain analysis and their non-linear and non-Gaussian nature had been neglected. In addition, a lot of the information embedded in the ECG signal was discarded. Whereas an HRV signal exhibits non-Gaussian and non-stationary behavior (Obayya and Abou-Chadi 2009, Peng *et al* 2011, Mohebbi and Ghassemian 2012), analyzing the non-linear activities of the ECG rhythm by utilizing the ability of high order statistic techniques in revealing hidden details of these rhythms could improve the detection of an OSA occurrence.

Therefore in this study, we concentrated on the HRV and EDR signals which can be taken as an indicator of the coordination of cardio-respiratory rhythms during an OSA occurrence and tried to disclose the non-Gaussian and non-linear characteristics of these signals. In order to manifest this information, the bispectrum of these signals was utilized to reveal the quadratic phase coupling between the various frequency components of signals. Our results demonstrated that in the case of normal episodes a highly non-linear coupling between frequency components does exist and at the instance of apnea such phase coupling will start to reduce. This interaction between frequencies can be related to the non-linearities present in the signal and its generating system. During normal rhythm, the bispectrum is expected to achieve large values due to the coherency of the electrical signal of the heart, and the phase coupling effect between various frequency components will be large. But when an OSA occurs, a loss in the synchronized rhythm of the heart causes different parts of it to contract at different times and there is no consistent pattern to such regularity. As a result the bispectrum plot reflects these irregularities by the increasing non-linearity between frequencies and the occurrence of the QPC starts to vanish.

In order to quantify these phase couplings between various frequencies, several features from the bispectrum plots were calculated. The combination of these bispectral features and four spectral features led to an efficient 22-dimension feature vector. To assess classification

performance these feature sets were fed into an LS-SVM classifier with a radial base function (RBF) kernel. The performance of our approach had been studied on a database of nocturnal ECGs recorded from normal and OSA individuals. To assess the performance of the classifier

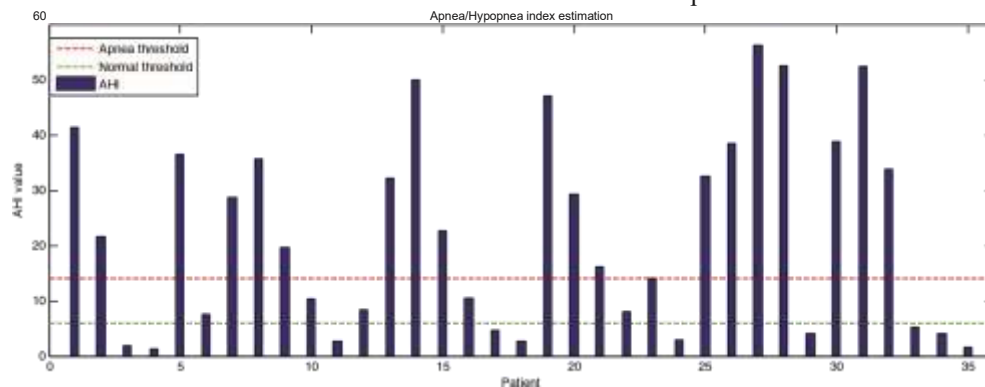


Figure 7. The calculated AHI for the test data of the patients using the proposed method.

and prevent it from being subject-dependent, data randomization and 10-fold cross-validation was performed. Using this method, over 95% of the 1 min episodes extracted from the database were correctly classified based on the spectral and bispectral information of their respective HRV and EDR signals.

It is worth mentioning, as can be seen in table 2, that our presented method produced a minute-by-minute classification with a better accuracy than the performing algorithms published before using a smaller set of features. This is due to the extraction of favorable features that are appropriate to the desired application of apnea detection. In addition, we have used an independent test database for evaluating the performance of our proposed method in discriminating OSA and normal episodes. The high accuracy obtained shows that the proposed method can be used as an efficient tool in OSA detection.

In addition to minute-by-minute episode classification, and in order to give a sense of how useful the methodology is as a screening tool, the AHI was calculated for the test data of each patient. The per-subject estimated AHI is presented in figure 7. The results demonstrated that our algorithm is able to detect all of the patients with clear occurrence of sleep apnea ($AHI \geq 15$). However, there is a small difference between the AHI value presented in the database and the one estimated here. This variation arises from the slight difference in the calculated AHI using minute-by-minute OSA episode detection and the actual definition of AHI. The real AHI is represented by the number of apnea events per hour of sleep. In our method we have calculated the number of 1 min apnea episodes per hour. So as there may be more than one event of OSA in a 1 min segment of ECG, the value of calculated AHI differs mildly from its real value. However, this difference does not affect the results of the method and the algorithm can correctly reveal all the patients who suffer from severe sleep apnea.

To sum up, the originality of this study lies mainly in the application of bispectral features in OSA detection. Our observation proves that the bispectrum analysis of HRV and EDR yields fundamental information on the physiologic processes that can be used to develop simple and fast sleep apnea screening methods. It may, therefore, become an easy, inexpensive and non-invasive technique for the clinical diagnosis of OSA supplementing the conventional method of PSG surveillance.

6. Conclusion

The presented method produces an accurate minute-by-minute classification of OSA episodes. The main advantage of the algorithm described in the present paper is the high performance (better than the previous algorithms presented in literature) but with a smaller feature space. The feature set includes higher-order statistics based on the bispectrum of HRV and EDR signals alongside several spectral features. The main reason is that our method effectively exploits the difference in the non-Gaussian and non-linear dynamical information of HRV and EDR data during normal and apnea episodes. This makes the whole system particularly suited for home screening devices based on one lead ECG signal. A patient suspected of OSA can easily be identified and directed to a sleep center for standard clinical evaluation. Experimental results have shown that based on the proposed features, the LS-SVM classifier achieves a better classification performance than the previously proposed methods. Independent testing has shown that the apneic and normal subjects could be completely separated with a 100% success rate and achieve a 1 min episode classification rate of over 95% accuracy. The high performance of the proposed method both in terms of sensitivity and specificity (98.64%, and 92.51% respectively) confirms the possibility of developing reliable and fast home screenings for sleep apnea patients in a very simple way using only data obtainable from the ECG signal.

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