AN INTERACTIVE, REAL-TIME, HIGH PRECISION AND PORTABLE MONITORING SYSTEM OF OBSTRUCTIVE SLEEP APNEA

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ABSTRACT

Obstructive sleep apnea (OSA) is the most common type of sleep apnea which is defined as the suspension of breathing. OSA is generally caused by complete or partial obstruction of airway during sleep, making the breathing pattern irregular and abnormal for prolonged periods of time. Apnea can contribute to a variety of life threatening medical conditions, and can be deadly if left untreated. Nowadays, out of 18 to 50 million people in the US, most cases remain undiagnosed due to the cost, cumbersome and resource limitations of overnight polysomnography (PSG) at sleep labs. Currently PSG relies on a doctor's experience. In order to improve the medical service efficiency, reduce diagnosis time and ensure a more accurate diagnosis, a quantitative and objective method is needed.

In this dissertation, an innovative method in characterizing bio-signals for detecting epochs of sleep apnea with high accuracy is presented. Three data channels that are related to breath defect; respiratory sound, ECG and SpO_2 are investigated, in order to extract physiological indicators that characterize sleep apnea. An automated

method was used to analyze the respiratory sound to find pauses in breathing. Furthermore, the automated method analyzed ECG to find irregular heartbeats and SpO_2 to find rises and drops. The system consists of three main parts which are signal segmentation, features extraction and features classification. Feature extractions process is based on statistical measures. Features classification process is learned through Support Vector Machines (SVMs) and Neural Network (NN) classifiers. Moreover, a preprocessing technique is carried out to distinguish the R-wave from the other waves of the ECG signal.

The approach presented in this dissertation was tested using downloaded polysomnographic ECG and SpO_2 data from the Physionet database. In addition, to identifying sleep apnea using the acoustic signal of respiration; the characterization of breathing sound was carried by Voice Activity Detection (VAD) algorithm. VAD was used to measure the energy of the acoustic respiratory signal during breath and silence segments. From the experimental results for the three signals, it was concluded that the precision of classifying sleep apnea has an accuracy of 97%. This result offers a clinical reference value for identifying OSA instead of expensive PSG visual scoring method which is commonly used to asses sleep apnea, and could reduce diagnostic time and improve medical service efficiency.

To my loving little family, my husband (Mohammad) and my daughter (Ariaam)

For all of your waiting time

This dissertation would be incomplete without a mention of the support and unconditional love given to me by my husband, who kept my spirits up when the muses failed me since he trusts me more than what I am

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ACRONYMS

OSA	Obstructive Sleep Apnea
CSA	Central Sleep Apnea
SA	Sleep Apnea
ECG	Electrocardiography
SpO_2	Arterial Oxygen Saturation
NN	Neural Network
SVM	Support Vector Machines
PSG	Polysomnography
VAD	Voice Activity Detection
EMG	Electromyography
EEG	Electroencephalography
EOG	Electrooculography
AHI	Apnea-Hypopnea Index
Se	Sensitivity
Sp	Specificity
Acc	Accuracy

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CHAPTER 1: INRTODUCTION

Sleep is the circadian rhythm which is essential for human life. Humans spend approximately one-third of their life to sleep. Sleep is necessary for optimal health, as the person sleeps, his body repairs itself. Blood pressure fluctuates, heart rate slows down, hormone fluctuates, muscles and other tissues relax and repair and the replacement of aging or dead cells occur during sleep. Without sleeping, the humans do not function as well as they can [1].

A sleeping disorder takes place when one cannot sleep, causing the body to lose function. Just as the body's benefits of rest can range from physical to emotional and psychological effects, lack of sleep can damage the body physically, emotionally and psychologically. The 25 year old field of sleep medicine, now is covering 84 kinds of sleep disorders, includes the most common ones such as narcolepsy, insomnia, sleep apnea, and restless leg syndrome [2].

1.1 Research Problem and Scope

Sleep Apnea (SA) is becoming a more common cause of sleepiness in children and adults. It is characterized by abnormal pauses of breathing or abnormally low breath during sleep. These pauses of breathing can range in frequency and duration. The

duration of the pause might be ten to thirty seconds and upwards to as much as four hundred pauses per night in those with severe SA [3].

There are two major types of SA. One type of SA is known as obstructive, which is generally caused by a blockage of the airflow airway. Central sleep apnea (CSA) is the other type of apnea, which occurs when the brain's drive to breathe is reduced. Most cases of CSA are mixed, meaning that it is often along with OSA. However, OSA is more common in the general population than CSA [4].

In fact, SA is not a problem to be taken lightly, since it is associated with a major risk factor of health implications and increased cardiovascular diseases and sudden death. It has been linked to irritability, depression, sexual dysfunction, high blood pressure (hypertension), learning and memory difficulties, in addition to stroke and heart attack.

The most frequent night symptoms of SA can include snoring, nocturnal arousals, sweating and restless sleep. Moreover, like all sleeping disorders, symptoms of sleep apnea do not occur just during the night. Daytime symptoms can range from morning headaches, depression, impaired concentration and excessive sleepiness which cause mortality from traffic and industrial accidents. However, these symptoms are not definitive to detect SA syndrome [5] [6].

Several treatments options for OSA patients include weight loss, positional therapy, oral appliances, surgical procedures and continuous positive airway pressure (CPAP). CPAP is a common and effective treatment especially for patients with moderate to severe OSA. CPAP devices are masks worn during sleep that improves oxygen saturation and reduces sleep fragmentation [7].

1.2 Motivation behind the Research

Nowadays, Polysomnography (PSG) is a standard testing procedure to diagnose OSA. Complete PSG includes the monitoring of the breath airflow, respiratory movement, oxygen saturation (SpO_2), body position, electroencephalography (EEG), electromyography (EMG), electrooculography (EOG), and electrocardiography (ECG). Nevertheless, the whole PSG process is complex, expensive and time consuming procedure due to the need of many physiologic variables using multiple sensors that needs to be attached to the patients [8].

According to the American Academy of Sleep Medicine (AASM), the Apnea-Hypopnea Index (AHI) is used to describe the number of complete and partial apnea events per hour of sleep and it is calculated to assess OSA syndrome severity. OSA severity is usually determined as follows: AHI 5-15 indicates mild, 15-30 indicates moderate and over 30 indicates severe OSA syndrome. Therefore, patients are diagnosed with OSA if they have five or more apnea events per hour of sleep during a full night sleep period [9].

However, new simplified diagnostic methods and continuous screening of OSA is needed, in order to have a major benefit of the treatment on OSA outcomes. In this work, an alternative method to the expensive PSG visual scoring method, which is commonly used today to assess a patient's sleep quality, is provided.

1.3 Potential Contributions of the Research

The aim is to present, an innovative hybrid method in characterizing bio-signals for detecting epochs of sleep apnea with high accuracy. In this regard, in this dissertation, the methods for the automatic processing of different statistical features of three data channels that are related to breath defect; respiratory sound, ECG and SpO_2, in order to extract physiological indicators characteristics of sleep apnea are presented.

A model using the ECG signal features was developed and its effectiveness using the Apnea ECG database was evaluated, using different records available in that database. The model is based on a selective set of RR-interval based features that are given to a Support Vector Machines (SVM) and a Neural Network (NN) for classification. The model was evaluated on three different epoch lengths and two different combination features set scenarios.

From the experimental results, it was concluded that SVM with linear kernel showed the best accuracy with 15 second epoch length.

Moreover, a NN and SVM using SpO_2 measurements obtained from pulse oximetry to predict OSA were developed and validated. The results demonstrated a high performance and an improved accuracy of the SVM.

In addition, to identify sleep apnea using the acoustic signal of respiration; the characterization of breathing sound was carried by Voice Activity Detection (VAD)

algorithm, which is used to measure the energy of the acoustic respiratory signal during breath and silence segments.

From the experimental results for the three signals, it is concluded that the precision of classification of sleep apnea had an accuracy of 97%. This offers a clinical reference value for identifying OSA, and could reduce diagnostic time and improve medical service efficiency.

To sum up, in this research a model of classification was built , to detect and study of how OSA effect oxygen levels in the blood, heart rate variability, and breathing patterns in a patient.

However, the study could be extended to implement the algorithms by developing a system that can capture, measure, record, and analyze the signals related to breath defect in real-time, normally initiated from biomedical sensors, collected by a smartphone device, and transmitted through the cellular and cloud networks, where the medical personnel can be contacted only when there is a negative condition and the patient does not need hospitalization and can be diagnosed and receive feedback at home, which eases follow-up and retesting after treatment.

In chapter 2, a detailed review of earlier studies focusing specifically on the automatic detection methods of OSA is presented. Advantages, drawbacks, and applications for these methods/approaches are also given. Literature results for previous work on OSA detection are summarized at the end of the section.

In chapter 3, a new model for the automatic OSA diagnosis is presented. Three different physiological signals are used; ECG, SpO_2, and the respiratory sound. The work is based on SVM and NN classification using the RR-interbeat interval series in the ECG

signal. In addition, NN and SVM using SpO_2 signal measurements obtained from the pulse oximetry are also investigated. Moreover, respiratory sounds are used to detect abnormalities in breathing or breathing cessations.

In chapter four, the results of the new model and evaluation of the performance of the classification system are presented. Two statistical indicators, Sensitivity (Se) and Specificity (Sp) in addition to the Accuracy (Acc) were used to evaluate the presented model.

The last chapter discusses and summarizes the results. Conclusions and future work are also outlined in this chapter.

CHAPTER 2: LITERATURE SURVEY

2.1 Introduction

A final OSA diagnosis decision is obtained by means of medical examination using complete PSG test at sleep labs, where expert human observer is needed to work overnight, which requires much labor and skills for diagnosis. Currently PSG relies on a doctor's experience. In order to improve medical service efficiency, reduce diagnosis time, and ensure a more accurate diagnosis, a quantitative and objective method is needed. New techniques for SA classification are being developed by bioengineers for comfortable and timely detection, and will assist medical personnel when the resources are insufficient for all patients to be diagnosed immediately.

Much of the current apnea research is ranging from off-line computer-based systems for automatic evaluation of apneas by analyzing different signals stored in PSG records to comprehensive portable real-time devices that enable the patient to be diagnosed and receive feedback at home in order to alert of the apnea event and help the patient to recover.

2.2 Computer Aided Sleep Apnea Detection

Over the past few years most of the related research has focused on presenting methods for the automatic processing of different statistical features of different signals such as thorax and abdomen effort signals, nasal air flow, oxygen saturation, electrical activity of the heart (ECG), and electrical activity of the brain (EEG) for the detection of SA.

The validated database used to assess the detection algorithms in the related research studies is supplied online from the PhysioNet web site [10]. PhysioNet is a database that offers access to a collection of physiological records from healthy subjects and patients with a variety of conditions with major public health implications, including congestive heart failure, sudden cardiac death, gait disorders, sleep apnea, epilepsy, and aging. This website is funded by the National Institute of Biomedical Imaging and Bioengineering (NIBIB) and the National Institute of General Medical Sciences (NIGMS), two institutes of the National Institutes of Health (NIH) [11].

The Apnea Database available in PhysioNet has been created to support such studies. All apneas in the recordings are either obstructive or mixed and it does not contain episodes of pure central apnea or of Cheyne-Stokes respiration. The full overnight polysomnogram recordings are divided into a set of one-minute segments. Each segment is annotated based on visual scoring of disordered breathing during sleep and if at any time during that minute there is evidence of sleep apnea, the segment is classified

as “apnea”; otherwise it was classified as “normal”. Segments containing hypopneas are also classified as apnea [12].

Apnea recordings in the database are varying in length from slightly less than 7 hours to nearly 10 hours each. “The subjects of these recordings were men and women between 27 and 63 years of age (mean: 43.8±10.8 years) with weights between 53 and 135 kg (mean: 86.3±22.2 kg). The sleep recordings originated from 32 subjects (25 men, 7 female) which were recruited for previous studies on healthy volunteers and patients with OSA” [13].

Several studies show that the brain waves signal, Electroencephalogram (EEG), which indicates states of mental activity ranging from concentrated cognitive efforts to sleepiness [14], is able to diagnose SA.

Wavelet transforms and an artificial neural network (ANN) algorithm are applied to the EEG signal in [15] to find a solution to the problem of identifying SA episodes. The EEG signals can be classified into four frequency bands of basis waves, namely as delta (δ), theta (θ), alpha (α) and beta (β). When an episode of SA occurs, the EEG signal shifts above the delta frequency band. Then, sleep EEG activity shifts from a delta wave to theta and alpha waves frequency bands in the range of 4~14 Hz once episode of SA ends. The system’s identification achieved a sensitivity of approximately 69.64% and a specificity of approximately 44.44%. However, even though this study yielded promising initial results, it still requires improvement since the EEG signal characteristic of a SA is easily contaminated by artifacts, therefore, a preprocessor circuit is needed to eliminate EEG signal artifacts and enable the system to recognize SA episodes. The analysis in [16] applies topographic EEG brain mapping to record changes during OSA episodes in

the brain. The results show a clear decrease in the δ power during OSA. Since δ waves are related to learning, it is thought that reduced δ power during OSA episodes can partially cause the OSA patient daytime symptoms, including cognitive deterioration and memory impairments.

Many studies show that detection of OSA can be performed through the Electrocardiogram (ECG) signal due to cyclic variations in the duration of a heartbeat. This consists of bradycardia during apnea followed by tachycardia upon its cessation [13].

An ECG-based work presented in [17] explores the application of time varying autoregressive models and KNN linear classifier to evaluate and classify the probability of being in apnea or not during each minute. The classification results demonstrated accuracy higher than 85% depending on power spectral features extracted by the autoregressive models, especially the spectral component in very low frequency which defines the rhythm of apnea-normal respiration. In particular, possible improvement could be done to obtain higher value in accuracy by the extraction of other features of different nature using different time resolutions such as 30s.

The comparison of the different algorithms to identify OSA episodes using different ECG-derived parameters in addition to heart rate variability was the result of a competition conducted in 2000, by an annual IEEE conference (Computers in Cardiology CINC) and PhysioNet. High overall accuracy with several algorithms, “such as ECG pulse energy (MCNAMES and FRASER, 2000), R-wave duration (SHINAR et al., 2000), amplitude of the S component of each QRS complex (MCNAMES and FRASER, 2000), and two used the ECG-derived respiration (EDR) technique (MOODY et al.,

1985) to measure the amplitude modulation of the ECG signal to estimate respiratory activity. These are based on spectral analysis of the R-wave amplitude using power spectral density (PSD) (DE CHAZAL et al., 2000) and of the T-wave amplitude using the discrete harmonic wavelet transform (RAYMOND et al., 2000)" [18].

Arterial oxygen saturation (SpO_2) measured by pulse oximetry can be useful in OSA diagnosis as clinical experience indicates that an apneic event is frequently accompanied by a fall in the SpO_2 signal (oxygen desaturation) [19].

Several studies assess multivariate analysis of the usefulness of SpO_2 in OSA diagnosis [20-24]. Multivariate adaptive regression spilines [20] and linear regression [21] are applied to classify subjects from different oximetric indexes. Classifiers based on quadratic discriminant (QD), linear discriminant (LD), K-nearest neighbors (KNN) and logistic regression (LR) analyses have been also evaluated in the context of OSA diagnosis using spectral and nonlinear features [22]. Additionally, the study carried out by Marcos et al. [23] provids an automated means for interpretation of SpO_2 signals, based on (LD) classifier and the linear combination of spectral and nonlinear features from SpO_2 recordings using principal component analysis (PCA). However, in [24] the best diagnostic performance with an accuracy of 86.3% (89.9% sensitivity and 81.1% specificity) is achieved by radial basis function (RBF) network with spectral and nonlinear features extracted from SpO_2 recordings.

It has been reported that, snoring is a common finding in people with OSA. OSA is generally caused by blocking he airway's airflow. Therefore, the snoring must become due to the vibration of soft tissues when the airflow stimulates the ill structure in the upper airway during sleep [25].

Several snore-based methods have shown to be a promising tool for the detection of SA to avoid a full-night PSG Study at the hospital [26-32]. Snore intensity and intervals calculation [26], linear prediction autoregressive (AR) modeling with a low order is used for spectral envelope estimation, which is closely related to the mechanism of snoring production [27], analyzing pitch and jitter [28], power spectrum analysis [29], time and frequency analysis [30] and formants estimation [31]- [32are used to gather additional data snoring in order to diagnose OSA. Of all methods for diagnosing OSA, the formants estimation method is most widely used. The formants information contains the essential acoustic properties of the upper airway. It is established by studies that there is a correlation between the state of the upper airway and the first formant frequency. A narrower upper airway leads to a higher first formant frequency. Therefore, Andrew et al. [31] - [32] proposed fixed formant frequency thresholds to detect the hypopneic snores which must be higher than that of the typical ones. On the other hand, the effects of the patient's individual differences in some cases, such as narrow upper airway in some females and children or wide upper airway in some males, lead to ineffective snores validation based on fixed thresholds. To address this problem, Zhao et al. [25] set a personalized threshold varying with each individual to distinguish hypopneic formant frequencies from the normal ones. The experimental results show that the proposed detector can achieve 90% sensitivity and 91.67% specificity.

Recently, based on the tracheal breathing sounds recording analysis during sleep, which can be used for respiratory flow estimation and distinguish the changes in breathing pattern recognition of the patient, the study in [33] reports a new fully automatic technology for OSA detection. Different parameters are investigated to

distinguish the breathing level during each individual apnea event, including the total energy of the breath sound segments. After collection of data, each parameter is then fuzzified with a sigmoid function and the fuzzy output of the fuzzy functions are added together to classify the sound signals. The results show high sensitivity and specificity values of more than 90% in differentiating normal respiration from disordered breathing patients.

In the present studies, the researchers provide complementary information with combined different physiological signals, in order to obtain additional information to that provided by classical methods to evaluate sleep quality and detect apnea. In some studies, ECG and SpO_2 data have been bridged to analyze sleep data. As the blood oxygen saturation falls during apnea, the resultant increase in heart rate and blood pressure causes stress and potential injury to the parts of the cardiovascular system [34]. In [35], the authors analyze various feature sets and a combination of classifiers based on the arterial oxygen saturation signal measured by pulse oximetry (SpO_2) and the ECG. In this work, the Bagging with REP Tree classifier achieves sensitivity of 79.75%, specificity of 85.89% and overall accuracy of 84.40%.

Because of the desaturation event that activates the sympathetic nervous system, the relationship between periodic changes in the SpO_2 profile and in the EEG pattern due to apnea events during the night is investigated in [36]. The combined spectral analysis of these two signals achieves 91% sensitivity, 83.3% specificity and 88.5% accuracy in OSA diagnosis.

The first successful preliminary attempts to directly assess the interactions of power spectral of sleep EEG and ECG signals in detecting OSA events is presented in

[37]. Consistency between these two signals over different frequency bands (0-128 Hz) are evaluated before, during and after an OSA terminations event (with/without arousals) in non-REM as well as REM sleep.

2.3 Home-Recording for SA Detection

Nowadays, much of the current apnea research is being done on providing portable devices that monitor those experiencing apnea during the day. The device could act as an inexpensive and convenient way for doctors to diagnose SA patients and as a means for collecting data on apnea sufferers to determine the severity of the condition once diagnosed. More specifically, this may help in the initial assessment of patients with suspected OSA in order to prioritize patients. Patients with utmost need of treatment will go through complete PSG recordings within a sensible time frame; meanwhile those who are free of apnea symptoms will avoid the cumbersome procedure [38].

Various portable monitor devices already exist in the market. ApneaLink^{TM} Plus Home Sleep Apnea Test Device is one of the carriage able in home sleep test diagnostic devices that records up to four channels of information: respiratory effort, pulse, oxygen saturation and nasal flow. The patient can sleep normally while ApneaLink^{TM} Plus monitors his/her sleep, checking breathing patterns and the amount of oxygen in his/her blood and recording possible apneas or other breathing abnormalities [39]. Also, SleepStrip^{TM} may be a simple and effective tool for OSA diagnostic strategy. This device has to be worn for a minimum of five hours of sleep, and the actual device is placed on the individual's face where the two flow sensors (oral and nasal thermistors) are placed in

just below the nose and above the upper lip to capture the breath of individual patient. For all samples combined, sensitivity and specificity values ranges from 80-86% and 57-86% respectively [38].

WM ARES is a home sleep test device that records heart rate, airflow, respiratory effort and oxygen saturation [40]. When the patient wakes up in the morning, after removing the tube from the nose and the tape and sensor from the finger, he/she returns the device to the clinician for analysis. The device contains a detailed record of the patient's personal sleep patterns, which can be downloaded, analyzed and processed in the clinician's computer. The clinician will then identify if the person is suffering from sleep apnea.

In [41], a new screening test for OSA is implemented on a Personal Digital Assistant (PDA) platform to perform the test at home during the patient's nightly rest. The Bluetooth ECG sensor, made by Corscience [42] is integrated into this platform, and the algorithm running on the PDA calculates an index that quantifies the magnitude of the heart beats rate variability power spectrum alterations. After the patient's first night using the device at home, the collection of test results are transmitted directly from the PDA to the hospital via the internet either by a WiFi connection, or by GPRS/UMTS connection. Once the healthcare staffs have evaluated the results, they will notify the patient whether the collected test results are conclusive or not. If the results are conclusive the patient should return the device. If needed; however, the patient may be asked to repeat the test again to collect additional data the following night. However, there is a loss of efficiency in the use of the wireless network because normal ECGs are also sent, which implies a high cost.

The portable device hardware design of an FPGA for home preliminary screening of SA syndromes in [43] stores a combination of three signals data of three sensors, namely the nasal air flow and the thorax and abdomen effort signals of overnight sleep on a Secure Digital card. Later, the sleep specialist at the clinic uses an algorithm for the evaluation and detection of SA. The device is relatively inexpensive and simple to use to diagnose more cases of SA.

Habul et al. [44] developed a diagnostic device for initial test at home that measures three vital signals, namely "the respiratory rate measurement, the oxygen concentration in blood and chest oscillations. The system architecture is divided into 5 parts, the microcontroller, the external communications, data storage, power management, and signal conditioning part. The data will be transmitted wirelessly and stored on the storage device. After the patient has finished sleeping, the next morning he or she can bring the data received on the storage device to a clinic's office, where the physician can interpret the data and determine what the patient's condition is. However, the device will reduce the cost for the patient because the patient does not have to pay for an overnight stay at the sleep center" [44].

In using vision based analysis to diagnose OSA in [45], there has been effective use of two SONY infrared camcorders (DCR-HC-30E) that work together in order to capture 10 video clips from three different angles. General body movement is continuously monitored and updated in a 2D breathing activity template. After collection of video data, offline analysis is used to detect abnormal breathing and to facilitate diagnosis of OSA.

Furthermore, after a careful meta-analysis of literature for twenty-five various tools and devices used to screen and detect SA by Ross et al. [46], it is discovered that only two of these are done at home, all others are performed under supervision in the sleep laboratory. The results show sensitivity values ranging from 78-100% and specificity values ranging from 62-100%. However, the related issues such as reliability, compliance, prices and safety, equipment failure rates are largely ignored.

2.4 Real-Time Systems for Continuous Detection and Screening of Sleep Apnea

Although the systems in [38]-[46] provide home based OSA diagnosis, all of them record the physiological sleep data of patients to memory card. Then, the patient must load these data into medical center computers where physicians use specialized software to analyze the data. Meanwhile, some patient can experience life threatening episodes by not receiving proper feedback notification from a medical center. Hence, to reduce the waiting times, as an alternative proposal to that scenario, the real-time monitoring systems that promotes not only a transmission of physiological data but also a real-time analysis of these data in order to alert of the apnea event and help patients to recover is performed in researches that appear in [47]-[52].

Sechang et al. [47] propose a wireless OSA monitoring system, which enables the patient to be diagnosed and receive feedback at home. The system supports monitoring five different biomedical signals continuously, namely, electrocardiogram with dry electrodes, body position, nasal airflow, abdomen/chest efforts and oxygen saturation. A wireless transmitter unit in the system sends the measured signals from sensors to a

receiver unit with Zigbee communication. The receiver unit, which has two wireless modules, Zigbee and Wi-Fi, receives signals from the transmitter unit and retransmits signals to the remote monitoring system with Zigbee and Wi-Fi communication, respectively.

In [48], the implementation of HealthGear, a real-time monitoring wearable system with a blood oximeter to monitor the pateint's blood oxygen level and pulse is presented. The three main hardware components of HealthGear's include: an oximetry sensor, a data transmission module and a smart phone. The sensor is connected wirelessly via Bluetooth to a smart phone which collects, analyzes and transmits the stored physiological data, and presenting it to the patient in an understandable way. This study addresses with 20 participants how HealthGear manages to acquire, process, store, and display the medical information.

The study in [49] develops a wearable biomedical system embedded in a comfortable glove. The work is based on the photoplethysmographic (PPG) signal coming from a standard SpO_2 wrapped sensor placed in one of the fingers for the continuous monitoring of SA patient at home. The real-time monitoring is performed through the glove communications with an internet gateway connected with a remote station. When the number of SA events crosses a guard level, the alarm is released.

More recent works implement real-time monitoring systems that detect apneic events while the patient is sleeping [50]-[51]. This monitoring system constitutes of SpO_2 values analysis from the Medical, Inc., 4100 Digital Pulse Oximeter. The oximeter uses the Bluetooth serial line profile to send SpO_2 current values every second to the PDA. The classifier of apnea episodes is built using the Bagging method that uses the decision

tree ADTree as base classifier. However, it must be taken into consideration that the classifier has only been trained and tested with the eight records of Apnea-ECG Database from the Physionet website that contain SpO_2 records, and when validated against Apnea-ECG Database, provides an accuracy of 93%. Moreover, the system is limited to the detection of SA, but the proposed system can be used for the detection of a variety of sleep disorders.

Another recent work, Apnea MedAssist [52], is implemented on Android operating system (OS) based smartphones. The smartphone provides initialization, configuration, and synchronization of Bluetooth connectivity to an off-the-shelf one Lead ECG sensor used for recording heart activity on a per 1-min epoch basis. The fully automated processing platform on a Smartphone, which is implemented to process ECG and generate input features for the SVM classifier to recognize OSA events, shows a high degree of accuracy for both home and clinical care applications. However, to increase the accuracy to the ones considered here, more extracted input features from ECG or other biomedical sensors such as SpO_2 can be added.

2.5 Summary

In this section, much of the past and current apnea research, the vital signals features and parameters of the SA automatic detection are introduced. Advantages, drawbacks, and applications for the earlier proposed systems are given. The related work on real-time and continuous monitoring of SA and the analysis is also summarized in this section.

Table 1 provides a summary of all related work with respect to performance measures, signals employed, technique used, test set and size, decision method chosen to signify if there is an apnea on a specific signal interval or not, whether it is run in real-time, offline or portable, hardware used in the implementation, and more extra features such as the cost.

From such results, it is concluded that most of the approaches make use of the whole signal in order to perform the analysis, and the validation provided by the tests have been performed on the Apnea-ECG Database. Furthermore, the various systems that deal with OSA monitoring it could be categorized, that is, those portable commercially available as well as research proposals into off-line and real-time systems. Off-line systems that help to diagnose SA using the automatic computer analysis on downloaded recorded data. For example, Zhao et al. [25], ApneaLink^{TM} Plus [39], and other portable commercial systems that only record the signals (SpO_2 and airflow) to perform off-line analysis. These systems still have various limitations resulting from the fact that the classification is not performed in the place where the signal is acquired. Real-time systems perform local real-time OSA monitoring. For example, MedAssist [52] can be classified within this category. In general, the diversity of the studies designs and objectives are very high and the methodological rigor of these studies as assessments of diagnostics and monitoring tests is low.

Thus, to enhance the utility of this literature, three offline methods to detect OSA on downloadable recorded data are implemented in this dissertation. The physiological data altogether will be sufficient not only to detect OSA but also understand its pattern.

Table 1 Summary of the literature research works

Research work	Performance [%]			Signal analyzed	Techniques employed	Decision method	Test set & size	Real-time/ Offline/ Portable	Hardware used
	Se	Sp	Acc						
Lin et al. [15] 2006	69.64	44.44	NA	EEG	Wavelet Transforms & ANN	Threshold (delta wave frequency)	slp59 EEG recording from the MIT-BIH sleep database	Offline	NA
Coito et al. [16] 2011	NA	NA	NA	EEG	Wavelet Transforms	Threshold (delta wave power)	15 male patients PSG recording	Offline	NA
Mendez et al. [17] 2007	NA	NA	85	ECG	Bivariate autoregressive model of HRV	KNN linear classifier	70 ECG recording from physionet	Offline	NA
Marcos et al. [24] 2007	89.9	81.1	86.3	SpO_2	Spectral and nonlinear features	Radial basis function classifier	187 subjects PSG recording	Offline	NA
Zhao et al. [25] 2011	90	91.67	NA	Snoring	Formant frequency	Personalized threshold	12 simple snores (7 males, 5 females) and 30 OSA patients (27 males, 3 females)	Online	A non-contact unidirectional microphone placed about 0.3m above the patient's mouth simultaneously with their full PSG study
Yadollahi et al. [33] 2009	90	90	NA	Tracheal breathing	Total energy of the breath sounds segment	fuzzy functions	40 patients	Online	Sony (ECM-77B) Microphone
Xie et al. [35] 2012	79.75	85.89	84.4	Spo_2 and ECG	Features set	Bagging with REP Tree classifier	25 subjects PSG recording	Offline	NA
Alvarez et al. [36] 2009	91	83.3	88.5	Spo_2 and EEG	Spectral analysis	Forward stepwise logistic regression (LR)	148 subjects PSG recording	Offline	NA
Shochat et al. [38] 2002	80-86	57-86	NA	Airflow	NA	NA	402 patients	Online, Portable	oral and nasal thermistors
Wang et al. [45] 2006	NA	NA	NA	Body movement	Video information	A continuously updated 2D breathing activity template	2 subjects	Online	Two SONY infrared camcorders (DCR-HC-30E)
Angius et al. [49] 2008	NA	NA	NA	PPG	Frequency analysis	Guard level (fixed threshold)	20 volunteers	Remote real-time	SpO2wrapped sensor, remote station
Burgos et al. [50,51] 2010	NA	NA	93	SpO_2	Features set	decision tree ADTree classifier	8 records from Physionet	Real-time, portable	Medical, Inc., 4100 Digital Pulse Oximeter, PDA
Bsoul et al. [52] 2011	96	NA	NA	ECG	Features measure	SV classifier	ECG recording from Physionet	Real-time, portable	ECG sensor, smartphone, server

CHAPTER 3: PROPOSED METHODOLOGY

3.1 Introduction

The apnea episode cycle starts when the muscles, that keep airways open in the day, relax at night which causes airway obstruction and pauses in breathing. Those pauses imply to get less oxygen from air and, therefore, a reduction of the oxygen level in the blood. As the blood oxygen saturation falls during apnea, that affects that heart rate and blood pressure [53].

Apnea diagnosis could be achieved by assessing only three data channels measurements that are related to breath defect; respiratory sound, ECG and SpO_2. The system presented in this dissertation consists of three main parts which are signal segmentation, features extraction based on statistical measures and features classification process. Features classification is learned through; Support Vector Machines (SVMs) and Neural Network (NN). The details of the overall methodology shown in Figure 1 are discussed in the subsequent sections.

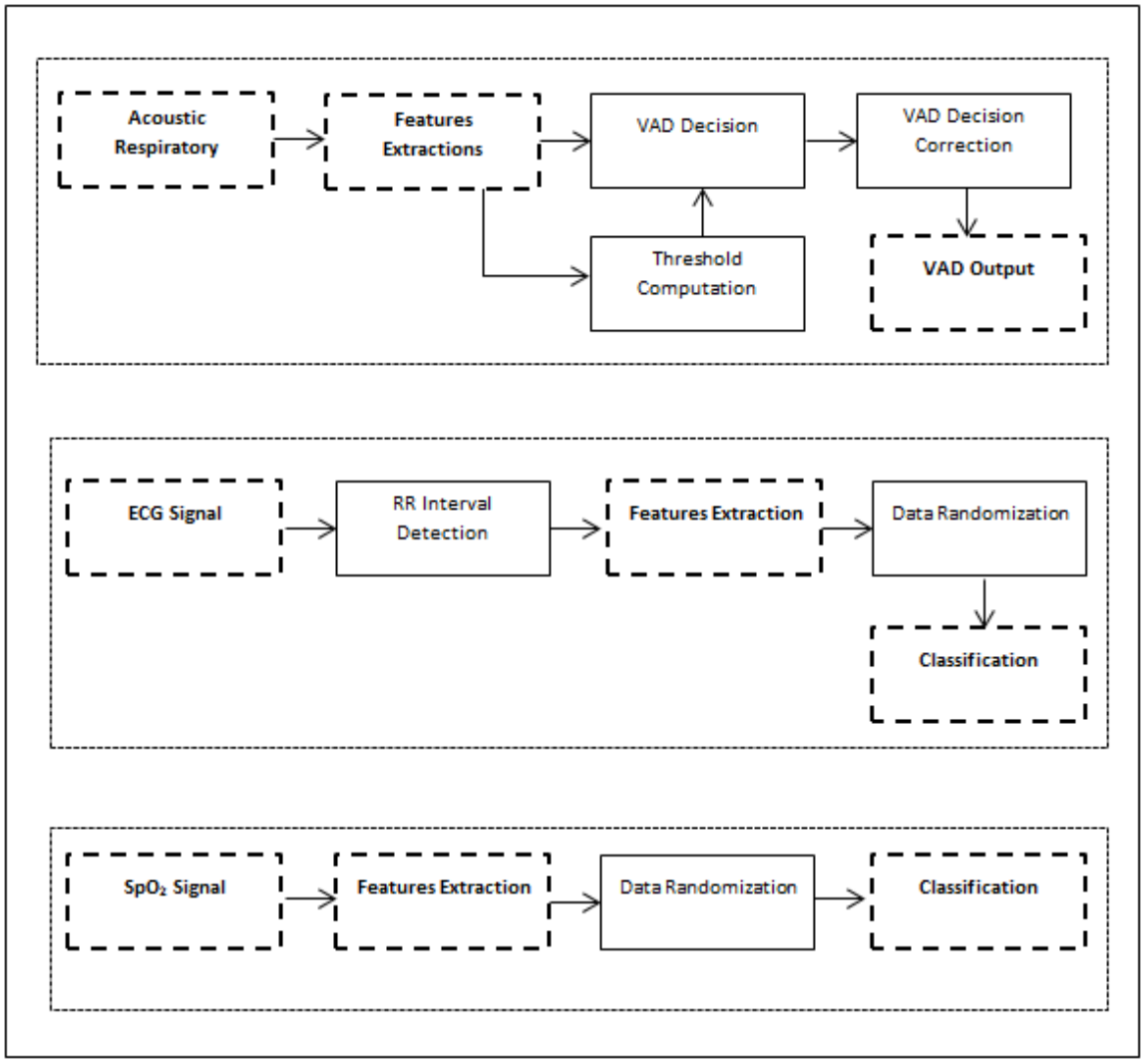

Figure 1 Schematic of the Proposed Methodology

3.2 Analysis of ECG Signal

The electrocardiogram (ECG) is a representation of the electrical activity of the heart; each activity has a distinctive waveform. Normal ECG graph consists of the P wave, QRS complex and the T wave. A small U wave is normally visible in 50-75% in the ECG [54]. Figure 2 shows a waveform representation of the normal ECG signal.

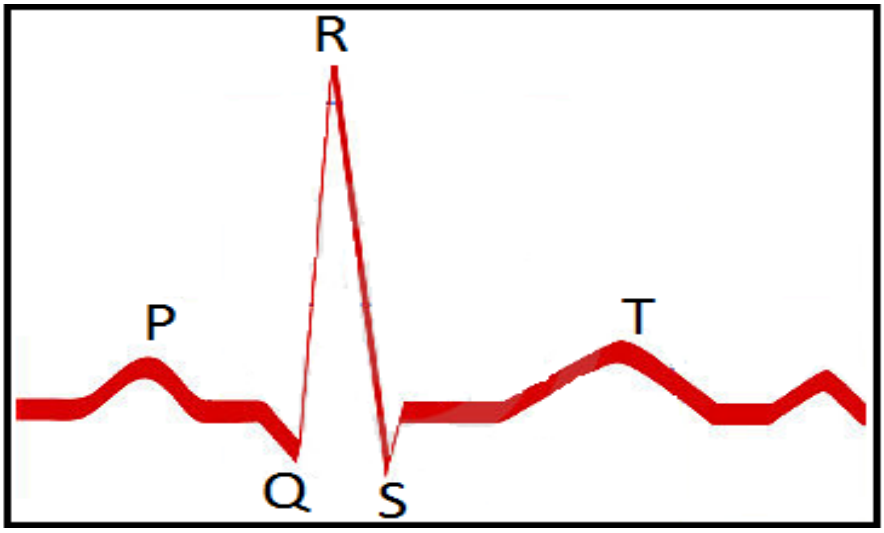

Figure 2 Schematic representation of normal ECG

ECG is considered as one of the most efficient features to detect sleep disorders. Cyclic variations in the duration of a heartbeat, also known as RR intervals (time interval from one R wave to next R wave) of ECG have been reported to be associated with sleep apnea episodes. This consists of bradycardia during apnea followed by tachycardia upon its cessation [13].

According to [54], RR interval time series is generated for each ECG as follows:

$$rr(i) = r(i+1) - r(i), \quad i = 1,2,\dots,n-1. \qquad (3.1)$$

RR-interval is defined as the time interval between two consecutive R peaks.

3.2.1 Data Preparation

To select the data, the ECG records from PhysioNet website [10] which have continuous apnea data for a certain period of time, followed by a regular (normal) data representation for a period of time, or vice versa was chosen. The data preparation was used for training the classifiers.

To give more clarification about data preparation, an example was provided regarding the data selection. In data set1 of record *a03,* to get regular data, the data from 2:27:00.000 to 2:57:00.000, and to get apnea data was chosen, the data from 3:06:00.000 to 3:36:00.000 was chosen. The reason of choosing those periods was because the data at those periods have clear apnea and regular data.

In data set2 of record *b02*, to get apnea data, apnea data from 1:17:00.000 to 1:37:00.000 was chosen, and to get regular data, regular data from 1:57:00.000 to 2:17:00.000 was chosen. Similarly, the reason of choosing those periods was because the data at those periods had clear apnea and regular data, and they are within the same hour.

MATLAB toolset was used in the experiments for signal processing. The data records were imported as MATLAB matrices (.mat) from the Physionet web site.

The next step in the proposed procedure after data selection is data partitioning. In this work, three cases of partitioning were analyzed, as follows:

- *Case* 1. The apnea and regular data were partitioned into 10 second pieces.
- *Case* 2. The apnea and regular data were partitioned into 15 second pieces.
- *Case* 3. The apnea and regular data were partitioned into epochs of 30 second pieces.

Since apnea is defined as a pause in breathing, and can last from a few seconds to minutes (almost >=10 sec); the three above cases to determine the best accuracy that can be achieved were investigated.

3.2.2 Noise Cancellation and R Wave Detection

SA episodes consist of bradycardia during apnea followed by tachycardia upon its cessation, which represent cyclic variations in the duration of a heartbeat, also known as RR intervals of ECG signal [13].

Generally, the ECG-based sleep apnea recognition techniques have two parts: haracteristics extraction, and waveform classification and recognition [55].

The characteristics extraction includes noise cancellation and QRS complex wave detection. The R-wave which has the highest or lowest value in the QRS complex wave is the outstanding characteristics in ECG signal.

The noise cancellation technique used in this work is the traditional "Pan and Tompkins" algorithm [56] modified with the use of adaptive filter to preprocess the signal to reduce interference. The resulting digital signal passes successively through a sequence of processing steps as follows: noise cancellation using adaptive filtering, signal slope detection, squaring, windowing and RR-wave interval calculation.

1) Adaptive filtering: The Least Mean Square adaptive algorithm is one of the most robust techniques used to reduce any random noise signal interfaced to the ECG. A step size of 0.8×10^{-5} and filter length of 10^6 can be used to cancel any noise added to the recorded ECG. Figure 3 shows an ECG waveform with a lot of random noise included.

2) Signal Slope Detection: A differentiator is used to detect and provide the QRS complex slope waveform information. A five point derivative is used with the following transfer function:

$$H(z) = (1/8T)(-z^{-2} - 2z^{-1} + 2z^{1} + z^{2} \qquad (3.2)$$

The difference equation is:

$$y(nT) = \left(\frac{1}{8T}\right)[-x(nT - 2T) - 2x(nT - T) + 2x(nT + T) + x(nT + 2T)] \qquad (3.3)$$

3) Squaring: The point by point squaring function is described by the following equation:

$$y(nT) = [x(nT)]^2 \qquad (3.4)$$

This results in positive data points and also performs nonlinear amplification of the differentiated ECG frequencies.

4) Windowing: Additional waveform features are calculated by a moving-window integration equation given by:

$$y(nT) = \left(\frac{1}{N}\right)[x(nT - (N-1)T) + x(nT - (N-2)T) \ldots . + x(nT)] \qquad (3.5)$$

Where N is the number of samples in the width of the integration window. For a sample, a rate of 200, a window of 30 samples wide (150 ms) is used.

5) RR wave interval calculation: Automatically adjustable thresholds to float over the noise are applied to the integrated wave form. The applied sets of thresholds are calculated from:

$$SPK = 0.125\ PEAK + 0.875\ SPK \qquad (3.6)$$

(if PEAK is the signal peak)

$$NPK = 0.125\ PEAK + 0.875\ NPK \qquad (3.7)$$

(if PEAK is the noise peak)

$$THRESHOLD\ 1 = NPK + 0.25(SPK - NPK) \qquad (3.8)$$

$$THRESHOLD\ 2 = 0.5\ THRESHOLD\ 1 \qquad (3.9)$$

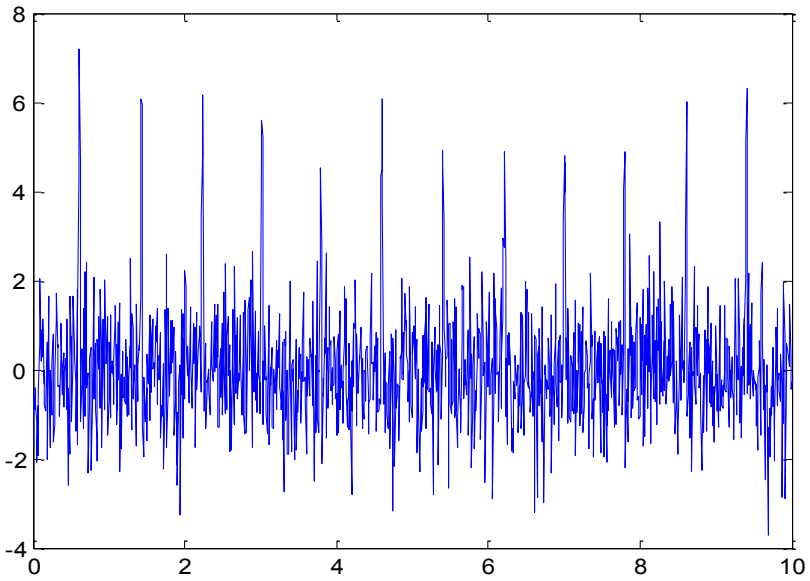

Figure 3 An ECG waveform with noise

In the above equations, all the variables refer to the integration waveform: *PEAK* is the overall peak, *SPK* is the running estimate of the signal peak, *NPK* is the running estimate of the noise peak, *THRESHOLD*1 is the first threshold applied, and *THRESHOLD*2 is the second threshold applied. Every time a peak is recognized, a QRS complex is identified in the filtered and integrated waveform. The RR average is then given by taking the mean of the eight most recent consecutive RR intervals. Figure 4 shows the detection of R-peaks and intervals.

$$RR_{AVERAGE} = 0.125(RR_{n-7} + RR_{n-6} + \cdots + RR_n) \qquad (3.10)$$

3.2.3 Feature Extractions

The implemented technique relies on an effective combination of ECG signal features which is a novel hybrid of features extracted from [13] and [57]. According to [54], the following most effective ECG features for apnea detection are calculated:

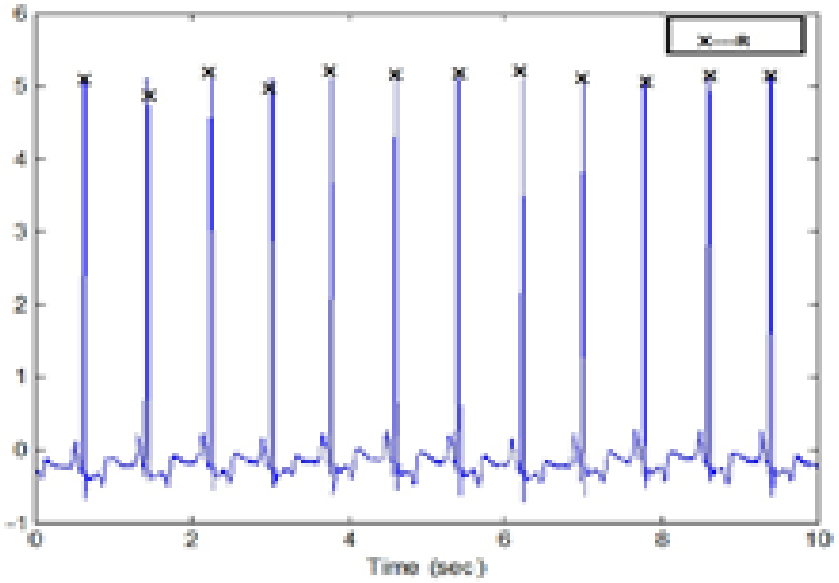

Figure 4 Detection of R-Peaks and Intervals

- Mean epoch of recording RR-interval.
- Standard deviation of the epoch and recording RR-interval.
- The NN50 measure (variant 1), defined as the number of pairs of adjacent RR-intervals where the first RR-interval exceeds the second RR-interval by more than 50 ms.
- The NN50 measure (variant 2), defined as the number of pairs of adjacent RR-intervals where the second RR-interval exceeds the first RR interval by more than 50 ms.

- Two pNN50 measures, defined as each NN50 measure divided by the total number of RR-intervals.
- The SDSD measures, defined as the standard deviation of the differences between adjacent RR- intervals.
- The RMSSD measures, defined as the square root of the mean of the sum of the squares of differences between adjacent RR- intervals.
- Median of RR-intervals.
- Inter-quartile range, defined as difference between 75^{th} and 25^{th} percentiles of the RR-interval value distribution.
- Mean absolute deviation values, defined as mean of absolute values obtained by the subtraction of the mean RR-interval values from all the RR-interval values in an epoch.

The first seven features are proposed by Chazal et al. [13], while the three latter features are proposed by Yilmaz et al. [57], who claims that RR interval mean, standard deviation, and range are sensitive to outliers, and thus classification performance deteriorates when only these features are included.

The implemented hybrid technique includes a combination of the most effective set of RR-interval based features of the ECG signal for classification. The classification results confirm the improved accuracy compared to the two above techniques.

3.2.4 Data Randomization

In this step, the apnea and non-apnea data were separated. Then training data and testing data were separated, with 80% for the training and 20% for the testing, then with different percentage with 50% for the training and 50% for the testing.

A MATLAB built-in function (*rand*) was used to determine whether a feature set in 10s (or 15s or 30s) of data belongs to test group or rule creation group. If '*rand*' was larger than 0.2, then the 10s data will belong to rule creation group, otherwise it will belong to testing group. After the signals are separated, the training for SVM, then for NN is performed to evaluate the performance with different classification techniques.

3.2.5 Support Vector Machines

Support Vector Machines (SVMs) as a classification (also known as supervised learning) method was used in order to investigate apneic epoch detection.

SVMs are learning methods, which aim to find the optimal separating plane that analyze data and recognize pattern used for regression analysis.

In SVM, P data is classified to which class it belongs, by points with a $(P-1)$ dimensional hyper plane, which is called a linear classifier. The optimal hyper plane that separates the clusters of vectors is found by SVM modeling. The cases with one category of the target variable are on one side of the plane and cases with the other category are on the other side of the plane. Figure 5 illustrates the working principle of SVM.

A good separation between the two possible classes is achieved by building a maximal margin hyper plane. The margin maximizes the distance between the classes and the nearest data point of each class. In general, the larger the margin is, the lower the generalization error of the classifier [54].

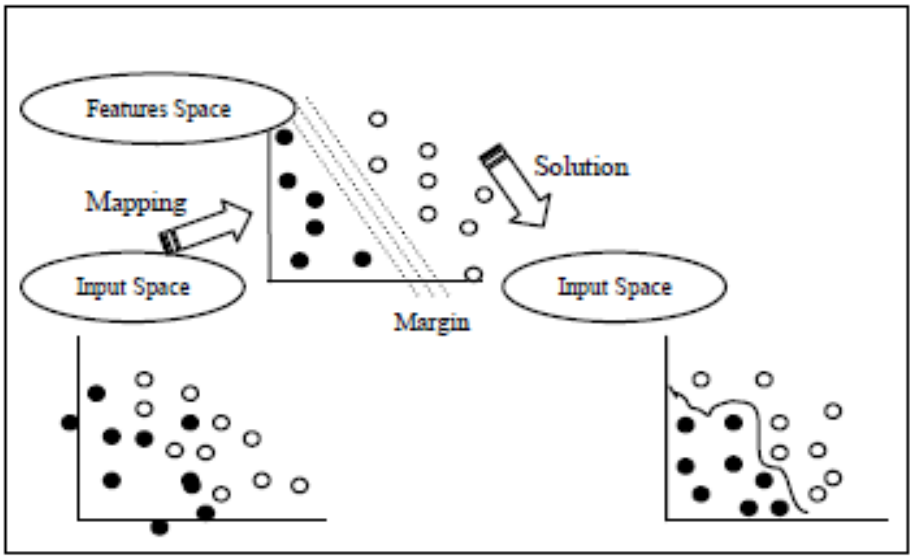

Figure 5 The SVM Algorithm [58]

In addition, SVMs handles the separation by a linear kernel function to map the data into a different space with a hyper plane. SVM gives the flexibility for the choice of the kernel. Linear, polynomial and radial can be taken as an example for a kernel function.

The choice of a kernel depends on the problem that needs to be solved. Polynomial kernels are well suited for problems where all the training data is normalized, and it allows to model feature conjunctions up to the order of the polynomial. Radial basis functions allow picking out circles (or hyperplanes). In contrast, the linear kernel, allows only picking out lines (or hyperplanes) [58].

Different kernel function to map the training data into kernel space is used in the proposed implementation. In the optimization process, a method called sequential minimal optimization is used to find the separating hyperplane.

3.2.6 Multi-Layer Networks Classifier

In this work, a neural network (NN) as a classifier to identify the diagnostic performance of OSA was applied using ECG features.

A neural network is used to perform a pattern classification task. NNs classifiers have been proven to be extremely helpful in assisting medical specialties in clinical diagnosis [59].

The NN described in this study is based on three layers feed-forward neural network learned with back-propagation algorithm; an input layer, an output layer, and a hidden layer. The hidden layer consists of a direct connection between the input and the output layer.

The ECG features act as inputs to a neural network, and the diagnosis of OSA is the target. This is achieved by presenting previously recorded inputs to a neural network and then tuning it to produce the desired target outputs. This process is called neural network training. Network parameters are adjusted through training by attempting to minimize the error between the target (t) and the actual (y) network output values. This error is expressed as the mean square error [60]:

$$E = \frac{1}{N}\sum_{n=1}^{N}\left\|t_n - y_n\right\|^2 \qquad (3.11)$$

where N is the number of samples in the training set. Since the output space must be divided into two regions: OSA positive and OSA negative, using a single output node is suggested.

3.3 Analysis of SpO_2 Signal

SpO_2 is the amount of oxygen being carried by the red blood cells in the blood. SpO_2 goes up and down according to how well a person is breathing and how well the blood is being pumped around the body [61].

SpO_2 measured by pulse oximetry can be useful in OSA diagnosis. Significant changes can be found in patients affected by OSA because of the recurrent episodes of apnea, which are frequently accompanied by oxygen desaturations [62].

3.3.1 Features Extraction

In the work, the SpO_2 signals were saved to separate files and processed off-line by an automated system, which was developed using MATLAB to compute two of the common oximetric indices and one nonlinear metric. These three features are detailed as follows, respectively:

1) Delta index (Δ index): This is a common measure to detect the apneic events by measuring SpO_2 variability. Levy et al. [62] calculates Δ index as the sum of the absolute variations between two successive points, divided by the number of intervals. It is usually computed for 12-sec. intervals.

2) Oxygen desaturation indices of 3% (ODI3): This measure is obtained by calculating the number of times per hour with values of SpO_2 greater than or equal to 3% from the baseline. The baseline is set initially as the mean level in the first 3 minutes of recording [63].

3) Central tendency measure with radius 0.5 (CTM50): This measure is applied in [63]. CTM50 is computed by selecting a circular region of radius 0.5 around the origin, counting the number of points that fall within the radius, and dividing by the total number of points. Given N data points from a time series, N-2 would be the total number of points in the scatter plot. Hence, CTM50 can be computed as [64]:

$$CTM = \frac{\sum_{i=1}^{N-2} \delta(d_i)}{N-2} \qquad (3.12)$$

Where,

$$\delta(d_i) = \begin{cases} 1 & if \left[(x_{i+2} - x_{i+1})^2 + (x_{i+1} - x_i)^2 \right]^{1/2} < 0.5 \\ 0 & otherwise \end{cases} \qquad (3.13)$$

3.3.2 Classification

The three SpO_2 features act as inputs to a NN, and the diagnosis of OSA is the target. Also, other classification using SVM is conducted in order to evaluate the better working classifier.

3.4 Analysis of Respiratory Signal

The characterization of breathing sound is carried by Voice Activity Detection (VAD) algorithm, which is used to measure the energy of the acoustic respiratory signal during breath and breath hold.

3.4.1 VAD-The Principle

In this work, the VAD algorithm [65] was employed to detect the presence or absence of apnea on real breathing signals is described.

Voice Activity Detector plays an important role in speech processing techniques such as speech coding [66], speech enhancement, and speech recognition [67]. Other examples include cellular radio systems (GSM and CDMA based) [65], hands-free telephony [68], VoIP applications and echo cancellation.

VAD relies on measurement of features from speech which yield highly in differentiating between voiced and unvoiced segments, where the regions of voice information within a given audio signal are referred to as 'voice-active' segments and the pauses between talking are called 'silence' or 'voice-inactive' segments. Therefore, the performance trade-offs of VAD algorithm are made by maximizing the detection rate of active speech while minimizing the false detection rate of inactive segments [69].

The most important part in VAD classifier is feature extraction, from which different regions in the audio signal can be separated. Common features used in the VAD detection process are cepstral coefficient [70], spectral entropy [65], zero-crossing rate [66, 71], least square periodicity measure [72], and average magnitude difference function [73]. Another important and widely used feature in this regard is signal energy, which is presented in this work, and compared with the dynamically calculated threshold.

3.4.2 Apnea Detection Using VAD Based-Energy

The assumptions on the VAD algorithm used here is that the speech is quasi-stationary and its spectral quickly changes over short periods like 20-30ms. The

background noise is relatively stationary and changes very slowly with time. In addition, the energy of the active speech level is usually higher than background noise energy [74].

In the first step, the respiratory signal was filtered to remove the undesired low frequency components. Then, the power with different window sizes of the Fast Fourier Transform (FFT) was calculated for the filtered signal [75].

Let x(t) be the input signal samples, and X(n) be Fast Fourier Transform (FFT) samples. The VAD algorithm begins with the energy computation within the smallest integer range of frequency values n1 and n2:

$$Energy = \sum_{n=n1}^{n2} |X(n)|^2 \qquad (3.14)$$

The energy of the signal is computed in two window frames; short window and long window for every window number i:

$$E_{short}(i) = \emptyset_{short} E_{nergy} + (1 - \emptyset_{short}) E_{short}(i) \qquad (3.15)$$

$$E_{long}(i) = \emptyset_{long} E_{nergy} + \left(1 - \emptyset_{long}\right) E_{long}(i) \qquad (3.16)$$

The number of frames used is N/L, where N represents the number of samples in the signal and L represents the window size in the frequency domain. The coefficients φ_{short} and φ_{long} refer to the window-length factors, where φ_{short} = 1/16, and φ_{long} = 1/128, and L= 528 are used in this study.

At this point, since VAD aims to differentiate voice and silence, where silence is mostly referring to background noise, the noise level at every frame

needs to be computed. For this purpose, a threshold THR value needs to be determined for comparing the signal value against noise:

$$THR = \frac{K_f}{1-\varphi_{long}} + M \qquad (3.17)$$

In the above formulation, Kf is the K-th frame and M is a margin value that can be considered to separate voice and silence in the event that noise level is flat.

The VAD technique eventually makes a decision by comparing every frame of the signal energy against the THR value. It is important to note that transitional periods from active voice to silence may also affect the decision. Based on the above steps and discussions, the decision on the VAD identifier (ID) values was made as follows:

$$\text{VAD- ID} = \begin{cases} 1, \text{ if } Energy > THR \\ 1, \text{ if } Energy \leq THR \text{ and in transitional period} \\ 0, \text{ if } Energy \leq THR \text{ and not in transitional period} \end{cases} \qquad (3.18)$$

The outcome of the VAD technique is the separated speech and silence phases which can be fine-tuned for identifying breath versus breathing cessations for apnea detection.

A second threshold (Tr) that would be used to decide whether a silence phase corresponds to apnea or not is proposed. According to the sleep apnea literature, a breathing cessation (silence) of 15 seconds or more would be classified as apnea, as shown below:

$$\text{If} \quad (\text{VAD-IDj} == 0) \text{ and } (\text{TVAD-IDj} \geq 15\text{Sec}) \Rightarrow$$
$$\text{VAD-IDj is a SA event period} \qquad (3.19)$$

In the above relationship, TVAD-IDj corresponds to the duration of silence phase j detected by the VAD technique.

3.5 Summary

In this chapter, three data channels that are related to breath defect; respiratory sound, ECG and SpO_2 were investigated, in order to extract physiological indicators that characterize sleep apnea. An automated method was used to analyze the respiratory sound to find pauses in breathing. Furthermore, it analyzes ECG to find irregular heartbeats and SpO_2 to find rises and drops.

CHAPTER 4: TESTING PROCEDURE AND RESULTS

The effectiveness of the ECG and SpO_2 methodology is evaluated using the Apnea-ECG database, using different records available in that database in PhysioNet website [10]. Respiratory signal analysis is evaluated from recorded breathing for human subjects.

To evaluate the performance of the classification system, two statistical indicators, Sensitivity (*Se*) and Specificity (*Sp*) in addition to the Accuracy (*Acc*) were used. The sensitivity of a test is the percentage of patients in the OSA positive group correctly diagnosed, whereas the specificity is the percentage of subjects in the OSA negative group correctly classified by the test.

4.1 ECG Testing

The database used in this study is available from the PhysioNet web site [10]. The Apnea-ECG Database contains 70 recordings, containing a single continuous ECG signal varying in length of approximately 8 hours duration. The sampling frequency of ECG signal is 100 Hz, with 16-bit resolution, and one

sample bit representing 5μV [13]. Figure 6 shows a sample ECG signal from PhysioNet.

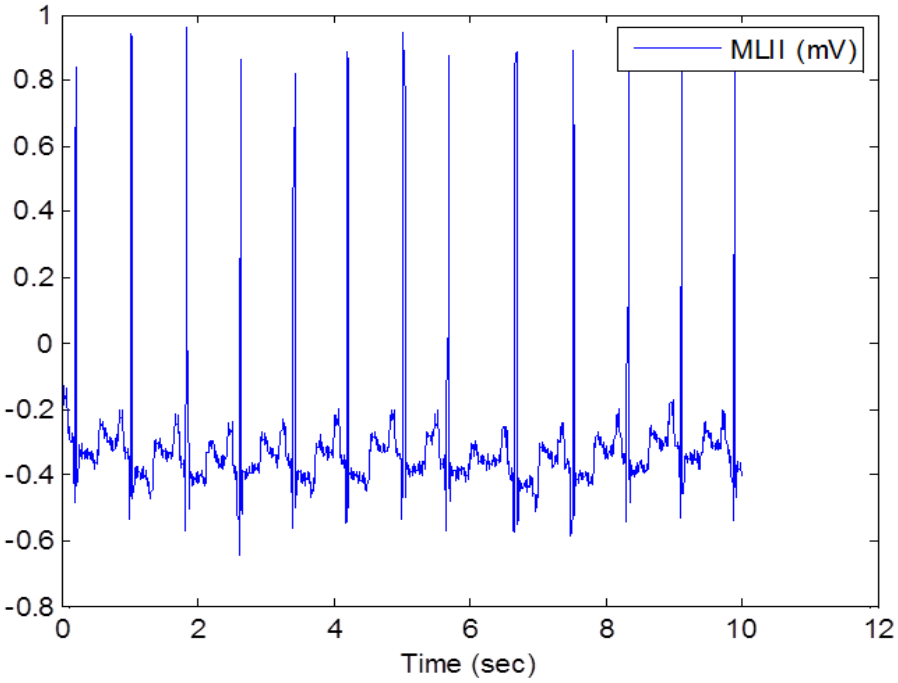

Figure 6 ECG signal from PhysioNet [10]

The Database is scored by physicians by dividing the recordings into a set of one-minute segments. The segment is classified as "apnea", if at any time during that minute there is an evidence of SA on the basis of respiration and oxygen saturation, otherwise it is classified as "normal" [13].

4.1.1 ECG Classification with SVM

In this section, an automated classification algorithm is presented which processes short duration epochs of the electrocardiogram (ECG) data. The automated classification algorithm is based on support vector machines (SVM) and has been trained and tested on sleep apnea recordings from subjects with and without OSA.

The effectiveness of the model is evaluated using the Apnea-ECG database, using different records available in that database.

Table 2, 3 and 4 show the classification results for the three cases mentioned in the data partitioning step. The model is based on a linear kernel SVM using various RR-interval features of the ECG signal. The training data and testing data were separated, with 80% for the training and 20% for the testing. The program repeats the training and classification process for 50 times to take the average value.

Two scenarios in the experiment were used: the whole combination of the features, and every two separate features.

1) All Features:

The three cases used here are: (*i*) 10 seconds data partitioning, (*ii*) 15 seconds, and (*iii*) 30 seconds. The accuracy of the approach is 86.1%, 97.8%, and 95%, respectively.

From Table 3, SVM with linear kernel using 15 second epochs shows the best classification accuracy with high successful rate of correct prediction.

1) Every Two Separate Features:

The 15 sec data are used in this analysis as the classification achieved the highest accuracy with 15 sec. The analysis randomly selected 80% of normal data and selected 20% of apnea data.

Table 2 10 sec. (Accuracy is 86.1%)

Input\Output	***Regular***	***Apnea***
Regular	**97.2%**	2.78%
Apnea	25%	**75%**

Table 3 15 sec. (Accuracy is 97.8%)

Input\Output	***Regular***	***Apnea***
Regular	**99.2%**	0.80%
Apnea	3.5%	**96.5%**

Table 4 30 sec. (Accuracy is 95%)

Input\Output	***Regular***	***Apnea***
Regular	**100%**	0%
Apnea	10%	**90%**

Table 5 shows the classification accuracy results for every two combination features set. From the table, it is concluded that the best two features combination are 25 and 75 percentiles of RR interval with mean absolute value feature with a high degree of accuracy, has an accuracy of 97.1%.

Table 5 Classification Accuracy of every two combination features

	Mean value of RR-interval	Standard deviation of RR-interval	NN50 variant 1	NN50 variant 2	pNN50-1 values	pNN50-2 values	SDSD	RMSSD	Median of RR interval	25 and 75 percentiles of RR interval	Mean absolute value
Mean value of RR-interval		70.4	59.4	52.1	55.9	55.1	73.9	65.6	64.3	93.6	90.6
Standard deviation of RR-interval	69.0		63.7	65.1	45.7	53.9	50.6	60.3	64.3	96.8	91.8
NN50 variant1	57.4	63.3		55.9	60.4	62.7	62.0	59.8	59.4	93.7	89.7
NN50 variant2	57.8	64.0	57.8		61.3	56.4	61.6	60.3	59.1	94.8	90.8
pNN50-1 values	52.8	48.0	61.0	56.5		51.6	49.8	49.1	62.8	95.8	89.8
pNN50-2 values	54.1	49.5	62.4	59.5	47.6		54. 3	46.3	63.3	91.8	90.8
SDSD	71.1	46.8	61.7	61.4	49.4	49.5		60.4	67.4	95.0	91.0
RMSSD	61.6	57.8	58.0	61.6	47.9	49.8	59.2		66.9	96.1	90.1
Median of RR interval	60.7	65.1	56.0	62.6	59.3	54.5	67.3	61.9		87.2	91.2
25 and 75 percentiles of RR interval	94.9	96.7	95.2	94.6	95.0	91.2	94.2	96.8	88.6		97.1
Mean absolute value	93.1	82.3	95.1	90.1	88.1	87.0	92.6	90.2	91.6	93.1	

Moreover, further analysis was performed using different kernel and different percentages of training and testing are shown in Table 6.

Table 6 SVM Performance Evaluation

Percentage of training set	Percentage of testing set	kernal function	Sensitivity	Specificity	Accuracy
80%	20%	Kernel	98.8%	96.9%	**97.8%**
50%	50%	Kernel	98.3%	96%	**97.1%**
50%	50%	Rbf	93%	94.3%	**93.6%**

4.1.2 ECG Classification with NN

The NN classifier described in this study is based on multi-layers feed-forward neural network learned with back-propagation algorithm; an input layer with 11 nodes which represents the features, an output layer with one node which represents the binary classification, and different models were performed which are varying in the number of hidden layers, the types of the hidden layers and the number of nodes. The carried analysis randomly selected 50% of the data set for the training and 50% of the data set for the testing. The results are shown in the Table 7. From the Table 7, the two hidden layers with *tansig* function and purelin function show the best classification accuracy with high successful rate of correct prediction.

4.2 SpO_2 Testing

The Apnea-ECG Database contains 8 recordings with SpO_2 signals. These recordings have varying length from slightly less than 7 hours to nearly 10 hours each.

Figure 7 depicts a common OSA negative subject, and Figure 8 shows a SpO_2 record with OSA positive subject. However, diagnosis of the disease is not evident by visual inspection.

Figure 7 SpO_2 record with OSA positive subject [10]

Table 7 NN Performance Evaluation

Number of Hidden layers	Hidden layers transfer functions	Number of nodes in hidden layers	Sensitivity	Specificity	Accuracy
1	Tansig	2	94%	83.4%	**88.7%**
2	tansig, purelin	2, 2	95.4%	89.1%	**92.2%**
3	tansig, tansig, purelin	2, 2, 2	85.5%	81.8%	**83.6%**
1	Purelin	2	89%	92.7%	**90.8%**
2	purelin, logsig	2, 2	75.9%	64.4%	**70.1%**
3	Purelin,tansig, tansig	2, 2, 2	58.2%	74.4%	**66.3%**
1	Logsig	2	64%	80.6%	**72.3%**
2	Logsig, tansig	2, 2	89.5%	75%	**82.2%**
3	Logsig, tansig, tansig	2, 2, 2	64.9%	71%	**67.9%**
3	Logsig, purelin, tansig	2, 2, 2	78%	75.9%	**76.9%**

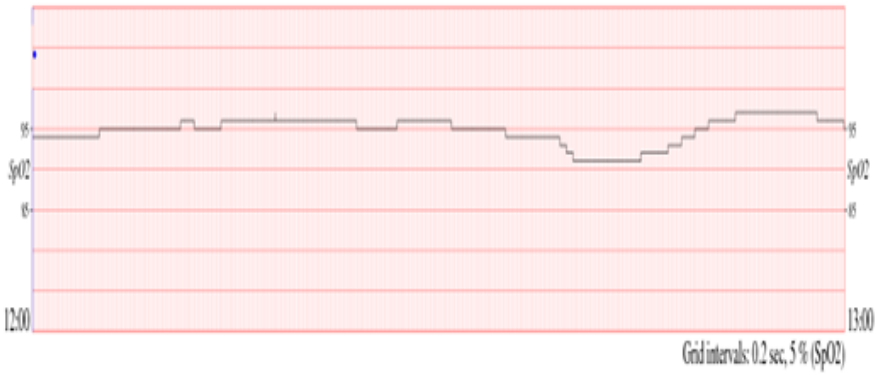

Figure 8 SpO_2 record with OSA negative subject [10]

4.2.1 SpO_2 Classification with NN

In the initial experiment, a total of 114 data sets (45 with a positive diagnosis of OSA and 69 with a negative diagnosis of OSA) were used. Validation was done with the same training dataset, and test dataset has been set to 13% of the original data. With these settings, the input vectors and target vectors were randomly divided into two sets as follows:

- 87% of the data sets were used for training and validation.
- The last 13% of the data sets were used as a completely independent test of network generalization.

The training set with 99 samples was used to train the network. In the training phase, the *Purelin* linear transfer function has been used as an activation function of the output layer of the network (for improving error derivative) [59]. Since the output space must be divided into two regions: OSA positive and OSA negative, a single output node was used. *Hardlim* function was applied [59] to test the data to improve the output of the network in the validation and testing phases. Table 8 shows the performance results with the initial 114 data sets. Figure 9 and Figure 10 show the confusion matrix for training and testing set classification, respectively.

Table 8 Classification Performance with initial total of 114 data sets

A total of Data sets	Percentage of training set	Percentage of testing set	Hidden layers Activation functions	Number of nodes in hidden layers	Sensitivity	Specificity	Accuracy
114 (45 positive, 69 negative)	87%	13%	Purelin	3	91.5%	74%	**82.7%**

The Confusion matrix shows the total percent of correctly classified cases and the total percent of misclassified cases.

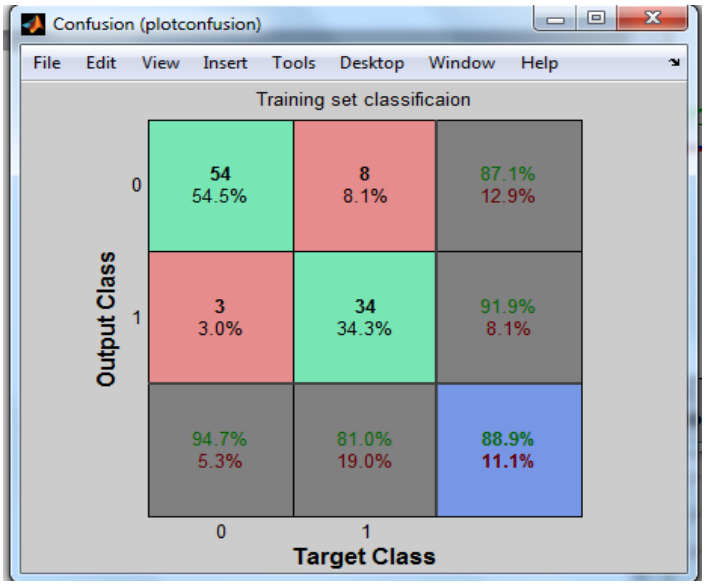

Figure 9 Confusion matrix for training set classification

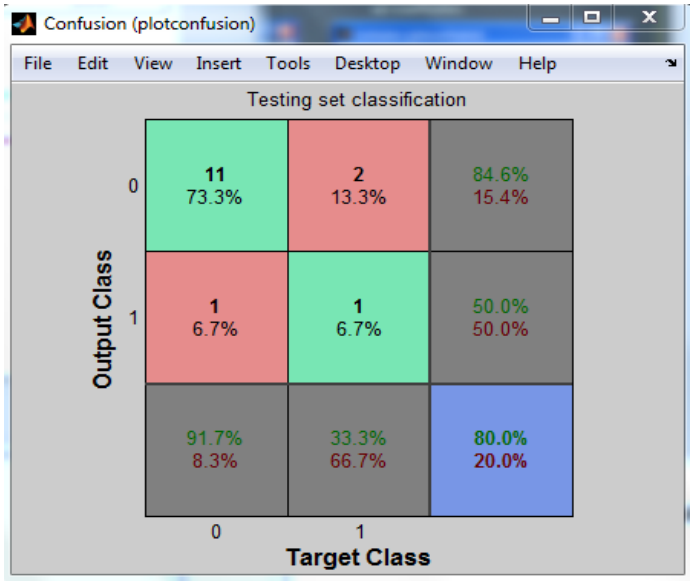

Figure 10 Confusion matrix for testing set classification

Then, the work was enhanced using a larger dataset to achieve better generalization and reliability of the test. A total of 1000 dataset, different combination of the hidden layers activation functions and different percentage of training and testing data were used. The results are shown in Table 9.

Table 9 Classification with larger data sets and different settings

A total of Data sets	Percentage of training set	Percentage of testing set	Hidden layers Activation functions	Number of nodes in hidden layers	Sensitivity	Specificity	Accuracy
1000 (410 positive, 590 negative)	87%	13%	Purelin	3	96.3%	87.5%	**91.9%**
	60%	40%			95.8%	86.6%	**91.2%**
	50%	50%			95.5%	86.7%	**91.1%**
	40%	60%			95.5%	84%	**89.7%**
	50%	50%	Purelin, Purelin	3, 3	71.2%	65.8%	**68.5%**
	50%	50%	Purelin, Tansig	3, 1	63%	66.8%	**64.9%**

4.2.2 SpO_2 Classification with SVM

The model based on a linear kernel SVM function to map the training data into kernel space using 3 features of the SpO_2 signal was used. In the optimization process, a method called sequential minimal optimization was used to find the separating hyperplane. The analysis randomly selected 50% for the training set and 50% for the testing set. The results are shown in the Table 10.

Table 10 Classification with SVM

A total of Data sets	Percentage of training set	Percentage of testing set	Kernel function	Sensitivity	Specificity	Accuracy
1000 (410 positive, 590 negative)	50%	50%	linear	98.6%	96.9%	**97.7%**

4.3 Respiratory Signal Testing

MATLAB environment was used to test the methodology on various samples of breathing signals during breathing and breath hold in 50 normal people. The volunteers were asked to breath 20 cycles. They were asked to hold their breath before, during and after the 20 cycles.

The human respiratory signal was given to the classification system as the input, and the coding was developed in such a way that it calculates the fundamental feature of the respiratory signal, which is the energy. The threshold was then applied to the extracted energy feature and the binary decision was made. VAD=1 is declared if the energy feature exceeds the threshold. Otherwise, VAD=0 is for no breath or when silence (cessations of breathing) is present.

4.3.1 Respiratory Signal Segmentation

Figure 11 shows the results obtained from the segmentation technique of the input signal which splits the acoustic signal of respiration into silence and voiced phases. The

start point and end point of a respiratory signal which contains breathing phases is determined in this work. Hence, the apnea events that are silence phases lasting 15s or longer can be detected.

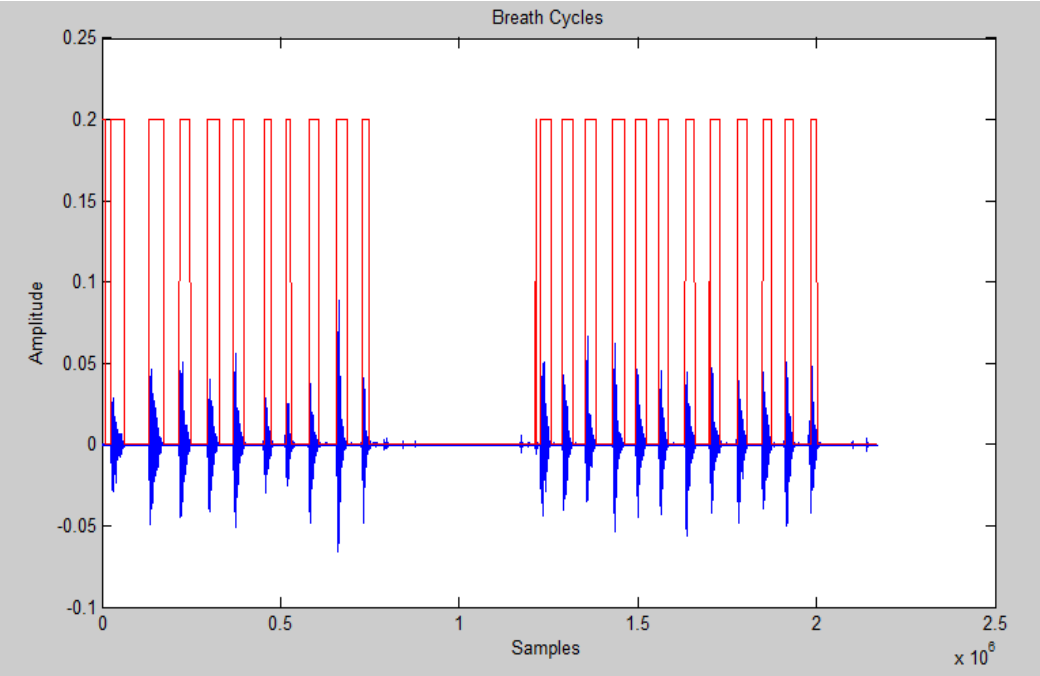

Figure 11 Segmentation acoustic signal of breath using VAD

4.4 Power Analysis

In this section, power analysis is performed in order to estimate the sample size for the experiment and test the alternative hypothesis.

From the experimental results of SVM and NN, it is concluded that SVM classification accuracy outperformed the NN classification accuracy. In this regard, power analysis is used to prove the hypothesis.

The power of a statistical test is the probability that the test will reject the null hypothesis when the null hypothesis is false by confirming the alternative hypothesis when the alternative hypothesis is true [74]. Therefore, two opposing hypotheses could be stated as follows:

1. Null Hypothesis Ho (same, equal, no diff, and no change)
2. Alternate Hypothesis Ha (complement of Ha)

Conclusion of the test will be: Either Accept Ho or Reject Ho.

There are 3 types of tests:

1. Right-tailed test (greater than)
2. Left-tailed test (less than)
3. Two-tailed test (not equal to)

The type of the test used is stated in Ha. The type of the test indicates what the researcher suspects or wishes to show.

The statistical Hypothesis for our work is as follows:

$$\text{Ho} \rightarrow \mu_{SVM} = \mu_{NN} \qquad (4.1)$$

$$\text{Ha} \rightarrow \mu_{SVM} > \mu_{NN} \qquad (4.2)$$

Where μ_{SVM} is the accuracy of SVM classifier and μ_{NN} is the accuracy of NN classifier. In other words, the accuracy of the SVM classifier was higher than the accuracy of NN of the used data set.

The difference significance is determined by the Level of Significance (α) used. Commonly used either α: 5% (0.05) OR 1% (0.01).

To determine the sample size (n) needed, decide on the three parameters:

1. The level of significance (1% or 5%) to use: **(α)**
2. The **required power (80%)** of the test
3. **Effect size (d)**

Based on the work of Cohen [74], the author justifies the levels of effect sizes in Table 11 as a large set using t-test on Means calculation; the effect size will be "d".

Table 11 Effect size values

	Effect size Index	Small	**Medium**	Large
t-test on Means	***D***	0.20	**0.50**	0.80
t-test on Correlations	*R*	0.10	0.30	0.50
F-test ANOVA	*F*	0.10	0.25	0.40
F-test regression	f^2	0.02	0.15	0.35
Chi-Square Test	*W*	0.10	0.30	0.50

Sample size (n) = $\frac{2(Zcrit+Zp)^2}{d^2}$ (4.3)

Where,

Zcrit = the unit normal curve deviate for α (for α = 0.05 and one-tailed test,

Zcrit = 1.645)

Zp = the unit normal curve deviate for power (for power = 0.80, Zp = 0.842)

d is the effect size, 0.50 is selected from the above table

When all the above values applied in sample size equation, n will be 57. Then, the following parameters are computed in order to make the decision of the hypothesis.

Mean $(\overline{X}) = \frac{\sum x}{n}$ = 97.1052632 (4.4)

Variance $(\sigma^2) = \frac{\sum(x-\bar{x})^2}{n}$ =23.2382707 (4.5)

Standard Deviation $(\sigma) = \sqrt[2]{\sigma^2}$ = 4.82060895 (4.6)

Degree of freedom (d.f) = n-1 = 56 (4.7)

Confidence Level (1-α) = 95% (4.8)

Significance (α) = 5% (4.9)

Critical t = TINV (α ,d.f) = 2.00324072 (4.10)

Standard Error (Sx) = $\frac{\sigma}{\sqrt{n}}$ = 0.63850525 (4.11)

Lower limit = $\overline{X}$ - Critical t * Sx = 0.63850525 (4.12)

Upper limit = $\overline{X}$ + Critical t * Sx = 98.3843429 (4.13)

Hypothesis (Ho) = 92.88 (4.14)

t value = $\frac{X-Ho}{Sx}$ = 6.61742896 (4.15)

p value = TDIST (t value, d.f, 1) = 7.4029E-09 (4.16)

Reject null with = (1-p) = 0.99999999 (4.17)

To make decision or conclusion: Use p value and Level of Significance,

If p value ≤ Level of Significance (Probability Ho is True is Low) → Reject Ho

(4.18)

In our test: **P < α**

7.4029E-9 < 0.05 which improve Reject Ho and Accept Ha.

4.5 Summary

Using the power analysis reveals that a sample set of 57 is sufficient to prove that SVM procedures better efficiency than NN. The used sample is sufficient to prove the stated hypothesis with a high degree of accuracy and confidence.

CHAPTER 5: CONCLUSIONS

This dissertation presented methods for the automatic processing of different statistical features of different bio-signals which are: oxygen saturation (SpO_2), the bioelectrical activity of the heart (ECG) and acoustic respiratory signal for the detection of Sleep Apnea.

A model was further developed using the ECG signal features and an evaluation of its effectiveness on the Apnea ECG database was carried, using different records available in database. The model is based on a selective set of RR-interval based features that are given to different classifiers such as SVM and NN for classification. The model was evaluated using three different epoch lengths and two different combination features set scenarios.

From the experimental results, it is concluded that SVM with linear kernel showed better accuracy with 15 second epoch length with more than 97% than NN with accuracy 92%. Moreover, the classification was developed and validated using SpO_2 measurements obtained from pulse oximetry to predict OSA. The results have demonstrated a high performance and an improved accuracy of the SVM with 97.7% and less accuracy with NN with 91%.

Moreover, this work sought to determine the effectiveness of VAD based - energy in distinguishing the apnea in breathing signal. The provided respiratory signal was classified successfully with the help of the formulated algorithm with more than 96% accuracy. However, in order to detect sleep apnea in real-time, the algorithm could be improved and adjusted by adding calibration procedures to run on an FPGA [75].

5.1 Future Work

It is planned to incorporate this work into a real-time monitoring system of sleep data. A preliminary design is shown in Figure 12. The study could be extended to implement the presented algorithms by developing a system that can capture, measure, record, and analyze the signals related to breath defect in real-time, normally initiated from biomedical sensors, collected by smartphone device, and transmitted through the cellular and cloud networks. This provides a system for medical personnel to be contacted only when there is a negative condition and the patient does not need hospitalization and can be diagnosed and receive feedback at home. As a result of the implementation, follow-up and retesting after treatment is easily achieved. Furthermore, an implementation of a cloud application is expected to keep health information with personal information (like sleep habits and daily activities) in the individual's records, which will offer access to a large pool of sleep data for further investigations.

The presented framework will establish a simple and helpful at-home OSA screening system, while keeping in mind the cost, efficiency, the portability as well as the comfortability of the patient.

In addition to the nighttime data collection, the system offers daytime data collection through continuously monitoring of the person's lifestyle and habits that factor into the condition of his/her sleep and could be vital signs to derive meaningful physiological parameters of interest. It could allow the user to keep track of the day by asking him/her to enter the data in different ways, such as filling out a quick survey form available on our application. Some of the patterns that could be monitored and logged throughout the day include eating heavy or light meals, drinking alcohol, exercising frequency, and lifestyle such as smoking and sleeping schedule.

This research direction of accumulating patients' data will augment the efforts in this challenging field through providing benchmark data that can be used by researchers to enhance their used mechanisms and tools.

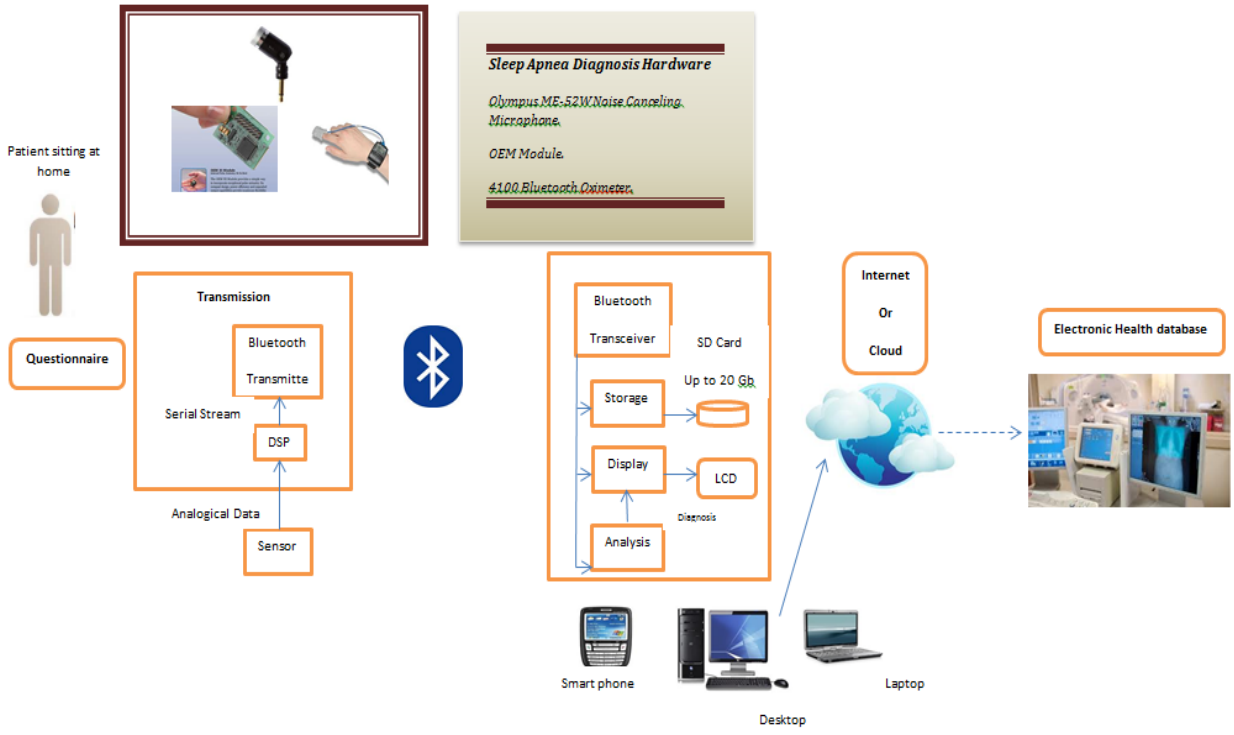

Figure 12 System Framework Implementation

REFERENCES

[1] W. Mendelson, Human Sleep: Research and Clinical Care. Plenum Medical Book Company, New York and London.

[2] Sleep Disorder Overview. www.neurologychannel.com. Date retrieved 11/21/2012.

[3] Sleep Disorders Guide. www.sleepdisordersguide.com. Date retrieved 9/10/2012.

[4] S. Isa, M. Fanany, W. Jatmiko and A. Arymurthy, "Sleep Apnea Detection from ECG Signal, Analysis on Optimal Features, Principal Components, and Nonlinearity," in Proceedings of the 5th IEEE International Conference on Bioinformatics and Biomedical Engineering (iCBBE), pp. 1-4, May 2011.

[5] N. Israel, A. Tarasiuk, and Y. Zigel,"Nocturnal Sound Analysis for the Diagnosis of Obstructive Sleep Apnea," in Proceedings of the 32nd IEEE International Conference on Engineering in Medicine and Biology Society (EMBS 2010), pp. 6146-6149, Sep. 2010.

[6] A. Yilmaz, and T. Dundar, "Home Recording for Pre-Phase Sleep Apnea Diagnosis by Holter Recorder Using MMC Memory," in proceedings of the 2010 IEEE International Conference on Virtual Environments Human-Computer Interfaces and Measurement Systems (VECIMS), pp. 126-129, Sep. 2010.

[7] "Choosing a CPAP," American Sleep Apnea Association, www.sleepapnea.org/resources/pubs/cpap/htm. Date retrieved 7/4/2012.

[8] D. Baraglia et al.,"Automated sleep scoring and sleep apnea detection in children," in proceedings of SPIE 6039, 2005.

[9] P. Chazal, C. Heneghan, and W. Mcnicholas," Multimodal detection of sleep apnoea using electrocardiogram and oximetry signals," Philosophical Transactions of The Royal Society A: Mathematical, Physical and Engineering Sciences, vol. 367, no. 1887, pp. 369-389, 2009.

[10] PhysioNet, The Research Resource for Complex Physiologic Signals, http://www.physionet.org/. Date retrieved 8/15/2011.

[11] T. Penzel, GB. Moody, RG. Mark, AL. Goldberger, and JH. Peter, "The Apnea-ECG Database," Computers in Cardiology 2000., vol. 27, pp. 255–258, Sep. 2000.

[12] P. de Chazal, R. Reilly, and C. Heneghan, "Automatic Sleep Apnoea Detection using Measures of Amplitude and Heart Rate Variability from the Electrocardiogram," in Proceedings of the 16th IEEE International Conference in Pattern Recognition., vol. 1, pp. 775–778, 2002.

[13] P. Chazal, T. Penzel, and C. Heneghan, "Automated Detection of Obstructive Sleep Apnoea at Different Time Scales Using the Electrocardiogram," Institute of Physics Publishing., vol. 25, no. 4, pp. 967–983, Aug. 2004.

[14] D. Liu, Z. Pang, and S. Lloyd, "A Neural Network Method for Detection of Obstructive Sleep Apnea and Narcolepsy Based on Pupil Size and EEG," in IEEE Transactions on Neural Networks., vol. 19, no. 2, pp.308–318, 2008.

[15] R. Lin, R. Lee, C. Tseng, H. Zhou, C. Chao, and J. Jiang, "A New Approach for Identifying Sleep Apnea Syndrome Using Wavelet Transform and Neural Networks," Biomedical Engineering: Applications, Basis & Communications., vol. 18, no. 3, pp. 138–143,2006.

[16] A. Coito, D. Belo, T. Paiva, and J. Sanches, "Topographic EEG brain mapping before, during and after Obstructive Sleep Apnea Episodes," In 2011 IEEE International Symposium on Biomedical Imaging: From Nano to Macro., pp. 1860–1863, 2011.

[17] M. Mendez, D. Ruini, O. Villantieri, M. Matteucci, T. Penzel, and A. Bianchi, "Detection of Sleep Apnea from Surface ECG Based on Features Extracted by an Autoregressive Model," in Proceedings of the IEEE International Conference on Engineering in Medicine and Biology Society (EMBS 2007), pp. 6105-6108, Aug. 2007.

[18] T. Penzel, J. McNames, A. Murray, P. Chazal, G. Moody, and B. Raymond, "Systematic comparison of different algorithms for apnoea detection based on electrocardiogram recordings," Medical & Biological Engineering & Computing Journal, vol. 40, no. 4, pp. 402–407, Jul. 2002.

[19] M. Canosa, E. Hernandez, and V. Moret, "Intelligent Diagnosis of Sleep Apnea Syndrome," In IEEE Engineering in Medicine and Biology Magazine., vol. 23, no. 2, pp. 72–81, 2004.

[20] U. Magalang, J. Dmochowski, S. Veeramachaneni, A. Draw, M. Mador, A. El-Solh, and B. Grant, "Prediction of the apnea-hypopnea index from overnight pulse oximetry," Chest, vol. 124, pp. 1694−1701, 2003.

[21] L. Olson, A. Ambrogetti, and S. G. Gyulay, "Prediction of sleep-disordered breathing by unattended overnight oximetry," J. Sleep Res., vol. 8, pp.51−55, 1999.

[22] J. Marcos, R. Hornero, D. Álvarez, F. del Campo, and C. Zamarón, "Assessment of four statistical pattern recognition techniques to assist in obstructive sleep apnoea diagnosis from nocturnal oximetry," Med. Eng. Phys., vol. 31, pp. 971–978, 2009.

[23] J. Marcos, R. Hornero, D. Álvarez, F. del Campo, and M. Aboy, "Automated detection of obstructive sleep apnoea syndrome from oxygen saturation recordings using linear discriminant analysis," Medical & Biological Engineering & Computing, vol. 48, pp. 895–902, 2010.

[24] J. Marcos, R. Hornero, D. Alvarez, F. Campo, and M. Lopez, "Applying Neural Network Classifiers in the Diagnosis of the Obstructive Sleep Apnea Syndrome from Nocturnal Pulse Oximetric Recordings," in Proceedings of the 29th IEEE Annual International Conference on Engineering in Medicine and Biology Society (IEMBS 2007), pp. 5174–5177, 2007.

[25] Y. Zhao, H. Zhang, W. Liu, and S. Ding, "A snoring Detector for OSAHS based on Patient's Individual Personality," In 3rd International Conference in Awareness Science and Technology (iCAST)., pp. 24-27, 2011.

[26] Y. Hsu, M. Chen, C. Cheng, et al. "Development of a portable device for home monitoring of snoring", in Proceedings of 2005 IEEE International Conference on Systems, Man and CybernetiCS, vol. 3, pp. 176-180, Oct. 2005.

[27] M. Cavusoglu, M. Kamasla, T. Ciloglu, and Y. Serinagaoglu, "Spectral envelope analysis of snoring signals", in Proceedings of the 6th International Conference on Biomedical Engineering, vol.3, pp. 473-477, Feb. 2008.

[28] J. Soler, R. Jane, A. Fiz, and J. Morera, "Pitch analysis in snoring signals from simple snorers and patients with Obstructive Sleep Apnea", In 24th International

Conference of the IEEE Biomedical Engineering SOCiety, vol. 2, pp. 1527-1528, Oct. 2002.

[29] J. Fiz, J. Abad, R. Jane, et al., "Acoustic analysis of snoring sound in patients with simple snoring and obstructive sleep apnea", European Respiratory Journal, vol. 9, pp. 2365-2370, 1996.

[30] A. Yadollahi, and Z. Moussavi, "Automatic breath and snore sounds classification from tracheal and ambient sounds recordings", Medical Engineering and Physics, vol. 32, pp. 985-990, Nov. 2010.

[31] K. Andrew, S. Tong, et al. "Could formant frequencies of snore signals be an alternative means for the diagnosis of obstructive sleep apnea?", Sleep Medicine, vol. 9, pp. 894-898, Dec. 2008.

[32] K. Andrew, T. Koh, E. Baey, et al., "Speech-like analysis of snore signals for the detection of obstructive sleep apnea", In International Conference on Biomedical and Pharmaceutical Engineering 2006 (ICBPE 2006), pp. 99-103, Dec. 2006.

[33] A. Yadollahi, and Z. Moussavi, “Acoustic Obstructive Sleep Apnea Detection”, In Proceedings of IEEE Conference on Engineering in Medicine and Biology Society (EMBC 2009), pp. 7110-7113, Sep. 2009.

[34] T. Micsik, S. Benedek, and Z. Benyo, “A novel Method for the Detection of Apnea and Hypopnea Events in Respiration Signals”, IEEE Transactions on Biomedical Engineering, vol. 49, no. 9, pp. 936-942, Sep. 2002.

[35] B. Xie, and H. Minn, “Real Time Sleep Apnea Detection by Classifier Combination,” in IEEE Transactions on Information Technology in Biomedicine, vol. 16, no. 3, pp. 469-477, May. 2012.

[36] D. Alvarez, R. Hornero, J. Marcos, F. Campo, and M. Lopez, "Spectral Analysis of Electroencephalogram and Oximetric Signals in Obstructive Sleep Apnea Diagnosis," in Proceedings of the 31st IEEE International Conference on Engineering in Medicine and Biology Society (EMBS 2009), pp. 400-403, Sep. 2009.

[37] H. Khandoker,K. Karmaker, and M. Palaniswami, "Analysis of coherence between Sleep EEG and ECG Signals during and after Obstructive Sleep Apnea Events," In Proceeedings of 30th IEEE International Conference on Engineering in Medicine and Biology Society (EMBS 2008), pp. 3876-3879, 2008.

[38] T. Shochat, N. Hadas, M. Kerkhofs, et al., "The SleepStrip™: an apnoea screener for the early detection of sleep apnoea syndrome," European Respiratory Journal, vol. 19, pp. 121-126, 2002.

[39] www.resmed.com. Date retrieved 10/19/2012.

[40] M. Stuart,"Sleep apnea devices: the changing of the guard," START-UP journal, vol. 15, no. 10, pp. 1-8, Oct. 2010.

[41] A. Otero, S. Dapena, P. Felix, J. Presedo, and M. Tarasco, "A Low Cost Screening Test for Obstructive Sleep Apnea that can be Performed at the Patient's Home," In Proceedings of the 6th IEEE International Symposium on Intelligent Signal Processing, pp. 199-204, Aug 2009.

[42] Corscience GmbH & Co. http://www.corscience.es.

[43] K. Al-Ashmount, H. Hamed, and A. Morsy, "FPGA-based Sleep Apnea Screening Device for Home Monitoring," In Proceedings of 28th IEEE International Conference on Engineering in Medicine and Biology Society (EMBS 2006), pp. 5948-5951, 2006.

[44] M. Habul, R. Hallmark, A. Kotlyanskiy, P. Parejk, and R. Kamoua, "Sleep Apnea Diagnosis Device," In Proceedings of 2011 IEEE Long Island conference in Systems, Applications and Technology (LISAT), pp. 1-5, 2011.

[45] C. Wang, A. Ahmed, and A. Hunter, "Vision Analysis in Detecting Abnormal Breathing Activity in application to Diagnosis of Obstructive Sleep Apnoea," In Proceedings of the 28th IEEE International Conference on Engineering in Medicine and Biology Society (EMBS 2006), pp. 4469-4473, 2006.

[46] S. Ross, I. Sheinhait, H. Katherine, et al., "Systematic review and meta-analysis of the literature regarding the diagnosis of sleep apnea," Sleep Journal, vo. 23, no. 4, pp. 519-532, 2000.

[47] O. Sechang, K. Hyeokjun, and V. Vijay, "Ubiquitous Health Monitoring System for Diagnosis of Sleep Apnea With Zigbee Network and Wireless LAN," Journal of nanotechnology in engineering and medicine, vol. 2, no. 2, 2011.

[48] N. Oliver, and F. Mangas, "HealthGear: Automatic Sleep Apnea Detection and monitoring with a mobile phone ," Journal of Communications, vol. 2, no. 2, pp. 1-9, March 2007.

[49] G. Angius, and L. Raffo, "A sleep apnoea keeper in a wearable device for continuous detection and screening during daily life," Computers in Cardiology, pp. 433-436, 2008.

[50] A. Burgos, A. Goni, A. Illarramendi, and J. Bermudez, "Real-Time Detection of Apneas on a PDA," IEEE Transactions on Information Technology in Biomedicine, vol. 14, no. 4, pp. 995-1002, July 2010.

[51] A. Goni, A. Burgos, L. Dranca, et al., "Architecture, cost-model and customization of real-time monitoring systems based on mobile biological sensor data-streams," Computer Methods and Programs in Biomedicine, vol. 96, no. 2, pp. 141-157, May 2009.

[52] M. Bsoul, H. Minn, and L. Tamil, "Apnea MedAssist: Real-time Sleep Apnea Monitor Using Single-Lead ECG," IEEE Transactions on Information Technology in Biomedicine, vol. 15, no. 3, pp. 416-427, May 2011.

[53] A. Goni, J. Rodriguez, A. Burgos, and A. Illarramendi, "Real-Time Monitoring of Mobile Biological Sensor Data-Streams: Architecture and Cost-Model," International Conference on Mobile Data Management Workshops, pp. 97-105, 2008.

[54] S. Isa, M. Fanany, W. Jatmiko and A. Murini, "Feature and Model Selection on Automatic Sleep Apnea Detection Using ECG," in International Conference on Computer Science and Information Systems, ICACSIS 2010, pp. 357-362, 2010.

[55] R. Lee, I. Chou, C. Lai, M. Liu and M. Chiu, "A novel QRS detection algorithm applied to the analysis for heart rate variability of patients with sleep apnea," Biomedical Engineering Applications, Basis & Communications, vol. 17, no. 5, pp. 44-48, Oct. 2005.

[56] J. Pan and W. Tompkins, "A real-Time QRS Detection Algorithm," in IEEE Transactions on Biomedical Engineering, vol. BME-32, no. 3, pp. 230-236, Mar. 1985.

[57] B. Yilmaz, M. Asyali, E. Arikan, S. Yektin and F. Ozgen, "Sleep Stage and Obstructive Apneaic Epoch Classification Using Single-Lead ECG," in Biomedical Engineering Online, vol. 9, 2010.

[58] A. Jain, P. Flynn and A. Ross, "Handbook of Biometrics," Springer, New York, 2008.

[59] A. El-Solh, M. Mador, E. Brock, D. Shucard, M. Abdul-Khoudoud and B. Grant, "Validity of Neural Network in Sleep Apnea," Sleep journal, vol. 22, no. 1, pp. 105-111, 1999.

[60] J. Marcos, R. Hornero, D. Alvarez, F. Campo and Miguel Lopez, "Applying Neural Network Classifiers in the Diagnosis of the Obstructive Sleep Apnea Syndrome from Nocturnal Pulse Oximetric Recordings," in Proceedings of the 29th IEEE International Conference on Engineering in Medicine and Biology Society (EMBS 2007), pp. 5174-5177, Aug. 2007.

[61] What is SpO_2. http://www.neann.com/spo_2.htm.

[62] J. Marcos, R. Hornero, D. Alvarez, F. Campo, C. Zamrron and M. Lopez, "Single Layer Network Classifiers to Assist in the Detection of Obstructive Sleep Apnea Syndrome from Oximetry Data," in Proceedings of the 30th IEEE International Conference on Engineering in Medicine and Biology Society (EMBS 2008), pp. 1651-1654, Aug. 2008.

[63] D. Alvarez, R. Hornero, D. Abasolo, F. Campo and C. Zamarron, "Nonlinear Characteristics of Blood Oxygen Saturation from Nocturnal Oximetry for Obstructive Sleep Apnoea Detection," Institute of Physics Publishing, vol. 27, no. 4, pp. 399-412, Apr. 2006.

[64] J. Jeong, J. Gore and B. Peterson, "A Method for Determinism in Short Time Series, and its Application to Stationary EEG," in IEEE Transactions on Biomedical Engineering, vol. 49, no. 11, pp. 1374-1379, Nov. 2002.

[65] ETSI 126 094 V3.0.0 (2000-01), 3G TS 26.094 version 3.0.0 Release 1999, Universal Mobile Telecommunications System (UMTS), Mandatory Speech Codec speech processing functions AMR speech codec; Voice Activity Detector (VAD), 2000.

[66] S. McClellan, J. Gibson,"Spectral entropy: An alternative indicator for rate allocation," In IEEE International Conference on Acoustics, Speech, Signal Processing, pp. 201-204, Apr. 1994.

[67] B. Atal, L. Rabiner, "A Pattern Recognition Approach to Voiced-Unvoiced-Silence Classification with Applications to Speech Recognition," IEEE Transactions on Acoustics, Speech, Signal Processing, vol. 24, no. 3, pp. 201-212, June 1976.

[68] A. Benyassine, E. Shlomot, and H. Su, "ITU-T recommendation G.729 annex B: A silence compression scheme for use with G.729 optimized for V.70 digital simultaneous voice and data application," IEEE Communications Magazine, vol. 35, no. 9, 1997.

[69] E. Verteletskaya, K. Sakhnov, "Voice Activity Detection for Speech Enhancement Applications," ACTA Polytechnica, vol. 50, no. 4, pp. 100-105, 2010.

[70] J. Haigh, and J. Mason, "Robust Voice Activity Detection Using Cepstral Features, "In Proceedings of IEEE Region 10 Conference on Computer, Communication, Control and Power Engineering (TENCON'93), vol. 3, pp. 321-324, 1993, Beijing.

[71] A. Sangwan, C. MC, H. Jamadagni, et al., "VAD Techniques for Real-Time Speech Transmission on the Internet," In Proceedings of 5th IEEE International

Conference on High-Speed Networks and Multimedia Communications, pp. 46-50, 2002.

[72] Tanyer, and H. Ozer, "Voice Activity Detection in Nonstationary Gaussian Noise," In Proceedings of International Conference on Signal Processing (ICSP'98), pp. 1620-1623, 1998.

[73] M. Orlandi, A. Santarelli, and D. Falavigna, "Maximum Likelihood Endpoint Detection with Time Domain Features," In Proceedings of 8th European Conference on Speech Communication and Technology (eurospeech 2003), pp. 1757-1760, 2003, Geneva.

[74] J. Cohen, Statistical Power Analysis for the Behavioral Sciences, Hillsdale, NJ: Lawrence Earlbaum ciates, 1988.

[75] B. Marinkovic, M. Gillette, and T. Ning, "FPGA Implementation of Respiration Signal Classification Using a Soft-Core Processor," In Proceedings of the IEEE 31st Annual Northeast Bioengineering Conference, pp. 54-55, April 2005.