AN INVESTIGATION OF CONCURRENT VARIATIONS IN BLOOD OXYGEN SATURATION AND CEREBRAL BLOOD FLOW DURING APNEA

by

JENNIFER SWITTENS

Presented to the Faculty of the Graduate School of

The University of Texas at Arlington in Partial Fulfillment

of the Requirements

for the Degree of

MASTER OF SCIENCE IN BIOMEDICAL ENGINEERING

THE UNIVERSITY OF TEXAS AT ARLINGTON

May 2013

ACKNOWLEDGEMENTS

I would like to extend my heartfelt gratitude and appreciation to Dr. Khosrow Behbehani, Professor and Chair, Department of Bioengineering at UTA. He has been a great mentor and role model, and his support, guidance and patience have had a profound influence over me and assisted me throughout my graduate studies and this research.

I would also like to thank the members of my research group for their continuous support and help in all possible ways during this research. I would like to specially thank Manikandan Ravi (Mani), a wonderful friend and my guide to Matlab, for the continuous help and support provided with the utmost patience in helping me to understand the software and supporting me whenever I tumbled upon it.

My sincere thanks to my parents and sister for understanding and supporting my decisions and being a great motivation to help me in making my dreams come true. And I cannot thank enough my friend and partner Anand Dhanasekharan for being a moral support and always believing and supporting me all through these years.

Last but never the least, my heartfelt praise and gratitude to the Almighty God, for being with me all through the walk of life and showering me with his blessings in all what I do. I surrender this research and all my achievements to his presence.

April 22, 2013

ABSTRACT

AN INVESTIGATION OF CONCURRENT VARIATIONS IN BLOOD OXYGEN SATURATION AND CEREBRAL BLOOD FLOW DURING APNEA

Jennifer Swittens, M.S.

The University of Texas at Arlington, 2013

Supervising Professor: Khosrow Behbehani

Sleep apnea derived from Greek word “apnoia” which means “without air or temporary interruption in breathing”, is a sleep – associated breathing disorder that involves a decrease or complete stop in airflow despite a constant effort to breathe. It is estimated that sleep apnea is prevalent in the US in 18 million people and is approximately 6% of the population.

This thesis aims to study the physiological effects of sleep apnea on cerebral blood flow (CBF) and the percentage oxygen saturation (%SaO2), the effect of duration of apnea episode or a breath hold on CBF and %SaO2 and to derive a relation between CBF and %SaO2.

Two studies were performed, simulated apnea study, using breath hold maneuvers to simulate and apnea episode and the sleep apnea study. Simulated apnea was performed on a group of sixteen volunteers (29±5 yr. and BMI 24.1±4.8, 9M and 7F). Sleep apnea was performed on a group of 10 subjects (50.28±9.60 yr. and BMI 31.33±6.29, 8M and 2F). The cerebral blood flow and percentage oxygen saturation were measured for the two groups of patients. The cerebral blood flow was measured using a transcranial doppler system and the percentage oxygen saturation was measured using a digital pulse oximeter.

For the simulated apnea study, apnea was simulated using breath hold maneuvers and the %SaO2 and CBF was continuously recorded. The breath hold maneuver was repeated 5 times by each subject. The duration of the breath hold (simulated apnea) was variable, depending on the subject's ability to prolong the breath hold. The time interval between consecutive breath hold was fixed at 30s and 90s intervals to model severe and moderate apnea, respectively. Further, the subjects were tested in sitting and supine position for both severe and moderate simulated apnea; the order of these four protocols was randomized. For the sleep apnea study, 8 hour Polysomnography was performed in a sleep lab.

The features extracted from the CBF and %SaO2 waveform were the area under the curve, amplitude of rise, amplitude of drop, time to rise and time to drop. Using these metrics, the physiological variations during both simulated and actual sleep apnea are determined and the results indicate a significant drop in the %SaO2 and significant rise in the CBF waveform. In addition, a significant correlation was obtained for the effect of duration of apnea / breath hold on the CBF and %SaO2. Results also show that there is a significant relation between the %SaO2 and CBF waveforms.

A correlation coefficient of 0.69 with a p value of 0.00015 was obtained for the effect of the duration of breath hold on the area of the CBF waveform in simulated apnea study. A correlation coefficient of 0.70 with a p value of 0.00013 was obtained for the effect of the duration of breath hold on the area of the %SaO2 waveform in simulated apnea study. A correlation coefficient of 0.66 with a p value of 0.0008 was obtained for the effect of the duration of apnea on the area of the CBF waveform in sleep apnea study. A correlation coefficient of 0.67 with a p value of 0.0009 was obtained for the effect of the duration of apnea on the area of the %SaO2 waveform in sleep apnea study. This shows that there is a significant relationship between the duration of apnea / breath hold to the area of the CBF and %SaO2 waveforms.

A correlation coefficient of 0.56 with a p value of 0.007 was obtained for area of %SaO2 vs. area of %CBF in sleep apnea study. A correlation coefficient of 0.66 with a p value of 0.004

was obtained for area of %SaO2 vs. area of CBF in simulated apnea study. This shows that there is a significant relationship between the cerebral blood flow waveform and the percentage oxygen saturation waveform during a breath hold maneuver.

TABLE OF CONTENTS

LIST OF ILLUSTRATIONS

LIST OF TABLES

CHAPTER 1

INTRODUCTION

1.1 Sleep Apnea

1.1.1 Definition

Sleep apnea derived from Greek word “apnoia” which means “without air or temporary interruption in breathing”, is a sleep – associated breathing disorder that involves a decrease or complete stop in airflow despite a constant effort to breathe [1]. This cessation is caused when the muscles relax during sleep, causing tissues at the level of the tongue and/or in the back the throat to collapse and block the upper airway. Thus leading to partial block in breath (hypopneas) and complete block (apneas) that may last from a few seconds to over a minute and may recur a numerous number of times during a single night of sleep [2]. Such events lead to abrupt reductions in blood oxygen saturation levels, with oxygen levels falling as much as 40% or more in severe cases [1].

Due to the falling oxygen levels, the brain alerts the body, by a brief arousal from sleep to restore normal breathing. Since this pattern may occur numerous times in one night, there is a reduced quality of sleep that often produces an excessive level of day-time sleepiness [3]. A common indication to sleep apnea is snoring. Most people with sleep apnea snore loudly and frequently, with periods of silence when their airway is blocked and choking or gasping sounds when their airway opens [1].

A common measurement for sleep apnea is the Apnea-Hypopnea index. This is used to assess the severity, based on the total number of apnea’s and hypopnea’s occurring per hour of sleep. This index is used to classify the severity of the disease with values of Mild 5-15, Moderate 15-30 and Severe >30 [4].

1.1.2 Types of Sleep Apnea

The three main types of apnea are

1. Central Sleep Apnea (CSA)
2. Obstructive Sleep Apnea (OSA)
3. Mixed or complex sleep apnea (CSA and OSA)

Central Sleep apnea defined by the National Institute of Health is a disorder in which your breathing repeatedly stops during sleep, because the brain temporarily stops sending signals to the muscles that controls breathing [5].This form of apnea is more common in people with congestive heart failure.

Obstructive Sleep apnea is the most common form of sleep apnea that occurs when the flow of air decreases or ceases during sleep, due to blocked or narrowed airway because of excessive muscle relaxation in the posterior oropharynx [1] [6] .Figure 1.1 shows the sites of obstruction in obstructive sleep apnea.

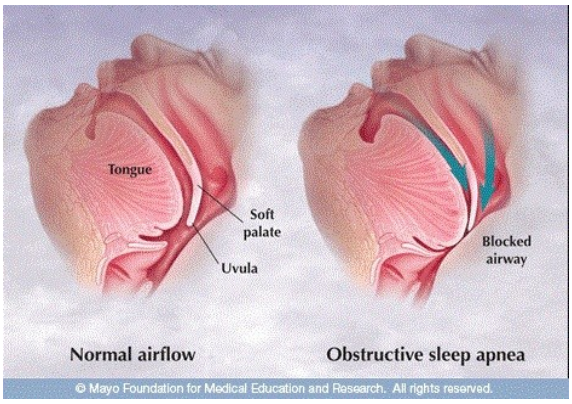


Fig 1.1 Site of obstruction during Obstructive Sleep apnea [36]

Mixed or Complex sleep apnea is a form of apnea that has both obstructive and central sleep apnea and is identified by the emergence of central apnea upon exposure to CPAP when the obstructive apnea events have disappeared [7].

1.1.3 Prevalence and Physiological Effects of Sleep Apnea

It is estimated that Sleep apnea affects more than 18 million Americans. The occurrence rate is approximately 6% in the US [8]. About 24% of men and 9% of women have symptoms of obstructive sleep apnea. It is also estimated that about 2% of children most common at preschool ages have symptoms of obstructive sleep apnea. Additionally about 80-90% of adults with obstructive sleep apnea remain undiagnosed [1, 8].

Sleep apnea adversely affects quality of life. The effects range from agitation to life threatening. Hypertension, depression, change in behavior, developmental and growth problems, learning and memory problems have been associated to sleep apnea [9].

The National Sleep Foundation reports that roughly up to one-third of patients with heart failures also have sleep apnea. High blood pressure, strokes and coronary artery diseases have also been associated with sleep apnea [10]. Recent studies show that obstructive sleep apnea results in degeneration of neurons in the hippocampus that results in various neurocognitive deficits and apoptosis [11]. These recent findings may help in explaining learning and memory impairments and mood disorders related to sleep apnea [11, 12].

Sleep apnea studies have gained importance over the years, as it has affected millions of people in all walks of life. And since sleep is vital to our well being, and is closely linked to serious health and mood problems there is an increase in awareness and need for treatment.

1.1.4 Detection and Treatment of Sleep Apnea

The most commonly used means of detection of sleep apnea is polysomnography (PSG). PSG is a comprehensive recording of physiological changes that occur during sleep. The PSG monitors various biological signals including EEG, EOG, EMG and ECG and various other body functions such as blood oxygen levels, oral and nasal air flow, chest and abdominal movement [13]. These measurements are used to detect apnea and hypopnea.

Treatment of sleep apnea depends on the severity of the disease. For milder cases of sleep apnea, treatments are typically lifestyle changes. For much more serious cases a number

of other treatments such as mouth pieces and breathing devices that help open up a blocked airway may be used. In extreme cases, surgery may be necessary. The most commonly used treatment for obstructive sleep apnea in the Continuous Positive Airway Pressure (CPAP).
CPAP is a device that delivers air through a mask that fits over the nose and the mouth, at a mildest level of pressure that is needed to keep the airway open during sleep.

The most recent treatment approved by the Food and Drug Administration is the Expiratory Positive Airway Pressure. This device is small and single used, placed over each nostril. The device allows air to move in freely, however the exhaled air goes in through the small valves in the device thus increases pressure in the airway and keeps it open. This maybe an option for some who cannot tolerate using CPAP [38, 39].

1.2 Cerebral Blood Flow

1.2.1 Cerebrovascular System

Cerebrovascular system is the system that comprises of the brain and the blood vessels that perfuse the brain. The blood vessels functions as the transport system of blood to and away from various parts of the brain. This system continuously delivers oxygen and nutrients to the brain, which is one of the most demanding organ in the human system. Discontinuities to this supply leads to severe brain tissue damage and results in morbidity.
The human brain receives approximately 15% of the total cardiac output and is delivered through the right and left internal carotid and vertebral arteries as shown in figure 1.2. A profound understanding of the cerebrovascular system is necessary to understand the basis of cerebral blood flow and brain energy metabolism [14] [17].

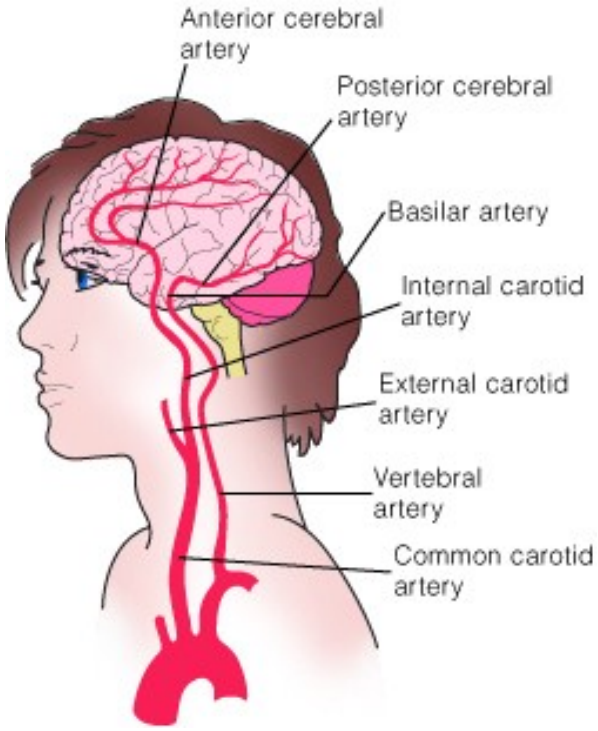


Figure 1.2 Saggital view of the cerebrovascular system [40].

1.2.2 Definition of Cerebral Blood Flow

Cerebral Blood Flow is the amount of blood supplied to the brain. The brain is the most demanding organ that comprises only about 2.5% of the body's weight and approximately receives almost 15% of the blood flowing from the heart. The brain requires 50-54 ml/100 gm of continuous blood supply per minute [14][16]. The internal carotid arteries and its branches form the anterior circulation that supplies the forebrain, cortex, basal ganglia, thalamus and the internal capsule. The vertebral arteries and its branches form the posterior circulation that supplies blood to the posterior cortex, the midbrain and the brainstem [17].

The measure of the velocity and ability of blood to perfuse brain tissues adequately at a given period of time is known as the cerebral blood flow velocity [15]. This depends on various factors, such as viscosity of the blood, dilation of blood vessels, cerebral perfusion pressure and the body's blood pressure [18].

1.2.3 Significance of Cerebral Blood Flow

Cerebral blood flow is a tightly regulated function, so as to meet the metabolic demands of the brain. Cerebral blood flow is important for the delivery of oxygen, maintaining the intracranial pressure and the removal of waste from the brain [19] [20]. Increase in Cerebral blood flow, known as hyperemia results in an increase in the intracranial pressure leading to damage to the delicate brain tissues. Decrease in cerebral blood flow, also known as ischemia reduces the flow of blood to the brain resulting in damage and possible death of brain cells.

Recent studies show that if there is an inadequate supply of blood glucose and oxygen to certain regions of the brain, the neurons and glia cells get injured or die leading to strokes, spinal cord injury and Alzheimer's disease [21]. Further research shows that cerebral blood flow and metabolism decreases and plateaus after maturation, reflecting its association in the growth and metabolism of an individual [22].

1.2.4 Physiological Effects of Sleep Apnea on Cerebral Blood Flow

Since sleep apnea occurs a multiple number of times over a night sleep, oxygen saturation of the blood decreases. Cerebral autoregulation tries to maintain a constant supply of oxygen to the brain and this results in an on and off fluctuation in the blood flow though the arteries. These fluctuations lead to various long and short term effects on cerebral blood flow and the metabolism of the brain. Arterial PO2 and pH decreases and PCO2 increases resulting in various pathological conditions including cardiovascular diseases such as hypertension, heart failure, stroke, cardiac arrhythmias, myocardial ischemia and metabolic dysregulations [24] [25].

Recent studies also link sleep apnea to silent strokes and small lesions in the brain. The researchers found that almost 1/3 of patients with white matter lesions suffered from severe obstructive sleep apnea and almost 91% of the people who have a stroke have obstructive sleep apnea [23] [25].

1.2.5 Detection Methods of Cerebral Blood Flow

Cerebral Blood Flow can be detected by different methods. The most common methods of measurements are the Functional magnetic resonance imaging (FMRI) and Positron emission tomography (PET). These techniques are used to measure regional cerebral blood flow and cerebral perfusion in the brain. However a continuous examination of cerebral hemodynamic is not possible with these techniques due to their poor temporal resolution and, particularly their restricted access in specialized centers in the brain [42]. The other and more recent means of detection is the Transcranial Doppler (TCD) Ultrasonography. TCD measures the velocity of the red blood cells in the arteries (mostly the middle cerebral artery) and provides an index that is directly proportional to the rate of the blood flow. TCD is one of the more powerful and noninvasive tool that have been used to provide significant insight about cerebral blood flow during obstructive sleep apnea [24].

A more recent study shows ultrasound tagged near infrared spectroscopy (UT-NIRS) to be a new real-time noninvasive hybrid technology with a continuous monitoring system for cerebral blood flow [26].

1.3 Arterial Oxygen Saturation

1.3.1 Definition of Arterial Oxygen Saturation

Arterial oxygen saturation is a measure of the percentage of hemoglobin saturated with oxygen in the arteries at the time of measurement. It is expressed in milligrams per liter (ppm) or mgL^{-1} [28]. This is typically expressed in percentage and a range of 96-99 percent saturation in considered normal.

The oxygen we breathe is delivered to the body through blood. The blood carries oxygen in different forms, dissolved in the plasma, combined with hemoglobin and converted into oxyhemoglobin that is required for cellular metabolism. Research shows that only 1.5% of the oxygen is diffused into the plasma and almost 98.5% is combined with hemoglobin that is present in the blood cells.

Within each red blood cell there are about 250 million hemoglobin molecules, and each hemoglobin molecule consists of a globin portion with 4 polypeptide chains, and four heme groups that are comprised of iron pigments. Each of these iron atoms bind to one molecule of oxygen. Thus each hemoglobin molecule can transport up to 4 oxygen molecules. If a hemoglobin molecule carries 4 molecules of oxygen it is 100% saturated, when they carry fewer molecules they are partially saturated. Measuring the number of these oxygen molecules in hemoglobin using various concepts of physics of light and reflectance is knows as oxygen saturation.

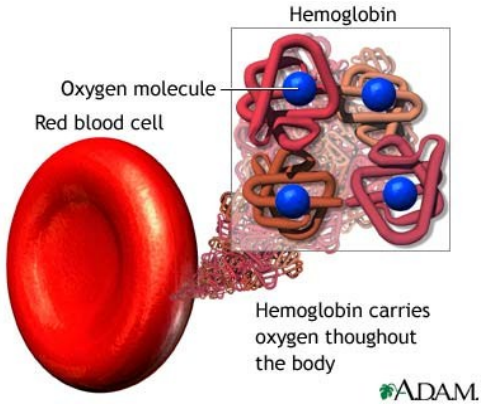


Fig 1.3 Oxyhemoglobin structure [37]

1.3.2 Significance of Arterial Oxygen Saturation

Since oxygen is essential to survive, it is important to know if the blood is carrying enough of it. When oxygen saturation levels in the arteries drop it is known as hypoxemia. Common symptoms of hypoxemia are shortness of breath, increase in blood pressure and heart rate, cold extremities and abnormal heart rhythms [28]. Hypoxemia when left untreated often leads to hypoxia, which is decrease of oxygen in the body tissues. If oxygen saturation levels drop lesser than 95% there is an increased risk of cardiovascular diseases, respiratory diseases, cerebral disorders and various other disorders that affect the quality of life. Respiratory failures usually occur when saturation falls to 90% as the oxygen delivery to the tissues and vital organs is likely to be inadequate at this level.

1.3.3 Physiological Effects of Sleep Apnea on Arterial Oxygen Saturation

Obstructive Sleep Apnea leads to depletion of oxygen in the blood due to the reduction of oxygen in the lungs to replenish them, resulting in a drop in the percentage oxygen saturation. Recent studies have linked OSA to the Immune System, by showing that OSA enhances oxidative stress by reducing the antioxidant capacity of blood [32].

1.3.4 Detection methods of Arterial Oxygen Saturation

There are different ways of measuring arterial oxygen saturation. An oxygen sensor is one of the methods of detection. However this method requires drawing blood for the media to be measured. Recently the most commonly used method of detection is the Pulse Oximetry system. This is a noninvasive technique developed in 1940 by Glenn Allan Millikan [34]. These systems measures and monitors the oxygen saturation of the blood, but was limited to the measurement of ventilation. The Pulse Oximetry systems have an increased usage according to a report by iData Research. The US market for the pulse oximetry monitoring market was over 700 million dollars in 2011 [35]. A CO- Oximeter is used to measure the ventilation of the blood.

1.4 Research Objective and Organization

1.4.1 Aim of the Study

The aim of the study is to determine features that can quantify cerebral blood flow and oxygen saturation variations in sleep apnea and simulated apnea and determine their efficiency in the detection of apnea. In order to attain this goal, this research proposed the following hypothesis.

1. There is a relation between the duration of breath hold or duration of apnea episode with the CBF waveform and %SaO2 waveform
2. There is a relation between the rise in cerebral blood flow and the percentage fall in oxygen saturation.

Testing this hypothesis was done in two parts. The first part was a controlled experiment of simulating sleep apnea, and the second was a sleep study conducted in a sleep lab to evaluate the efficacy of the features and measures.

1.4.2 Significance of the Study

During an apnea episode, the level of oxygen entering the body drops, which results in the drop of oxygen saturation. There is an increase in the partial pressure of carbon di-oxide that stimulates the chemoreceptors in the central and the peripheral nervous system. This triggers the sympathetic nerve activity that increases the arterial blood pressure. The increase in arterial blood pressure causes vasodilation in the cerebral arteries and there is an increase in the cerebral blood flow. This increase in the cerebral blood flow is seen as a rise in the CBF waveform collected during sleep apnea.

Since the brain has a tightly regulated function and both an increase and decrease in the cerebral blood flow affects the intracranial pressure of the brain and may lead to brain tissue damage, it is important to study the changes of the cerebral blood flow during sleep apnea and also compare it to the oxygen saturation changes.

1.4.3 Thesis Organization

The methods proposed in this research investigate the effects on cerebral blood flow and oxygen saturation during sleep apnea and simulated apnea studies. So far the reader has had a brief overview of the important features of this research. The following chapters will specify details on the methodology behind this research. Chapter two describes in detail the transcranial doppler system and the pulse oximetry system used to measure the cerebral blood flow and the oxygen saturation during sleep and simulated apnea. It also describes the experimental setup and the methodology behind the signal processing algorithm, feature extracted and the analysis of data. Chapter three presents the results of the research obtained from statistical analysis. Chapter four discusses the significance and interpretation of the results shown in chapter 3, and also includes the limitations and future work of this research.

CHAPTER 2

METHODS

2.1 Cerebral Blood Flow Velocity Measurement Using Transcranial Doppler System

2.1.1 Principle and Working of Transcranial Doppler System

Transcranial Doppler system is a noninvasive technique that uses a microprocessor controlled, low frequency (2MHz) doppler transducer to measure the velocity of the blood flow through the brain. They work in two modes: Continuous wave and the Pulsed wave mode. The basic principle is based on the Doppler Effect that states, sound waves are reflected by moving targets and the frequencies of the reflected and transmitted wave differ

The principle behind the continuous wave doppler probe is that, the transmission and reception of ultrasound waves are continuous. As explained in Figure 2.1, the transmitter emits ultrasound waves to the blood vessel; the moving blood cells in the vessel scatter the ultrasound back to their receiving transducer, of a slightly different frequency. This difference in frequency is detected and calculated using the formula

$$\Delta f = 2f \frac{V cos\theta}{c} \quad (1)$$

Where,

f is the incident frequency

Vcosθ is the velocity of the target in the direction if the transducer

C is the velocity of the ultrasound.

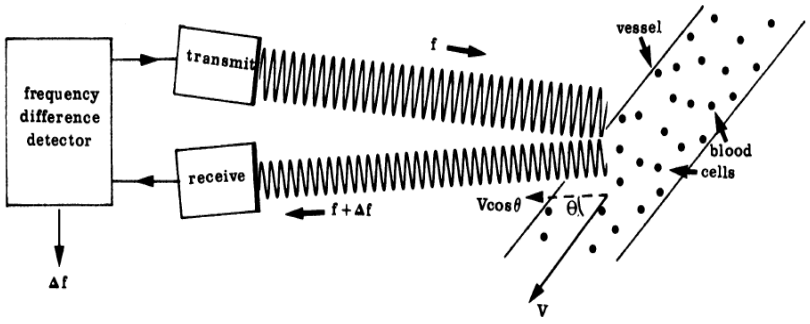


Figure 2.1 Principle of Continuous wave Doppler system [43]

One of the drawbacks of the continuous wave doppler is that it suffers from a lack of range resolution and it is unable to determine the specific position of the target. Meaning that the doppler waveforms would superimpose if there were more than one vessel in the beam and hence are not well suited for color flow images.

These disadvantages are overcome in the pulsed wave Doppler probe; the principle is shown in Figure 2. A short pulse of ultrasound is transmitted towards the blood vessel and after a time delay for the pulse to travel; the scattered echo is sampled for doppler shifts. This method ensures that the doppler signals originate only from the targets moving within the sample volume. The range for the sample volume is determined by the transmit- sample delay time and the shape is defined by the length of the transmitted pulse and the width of the ultrasonic beam.

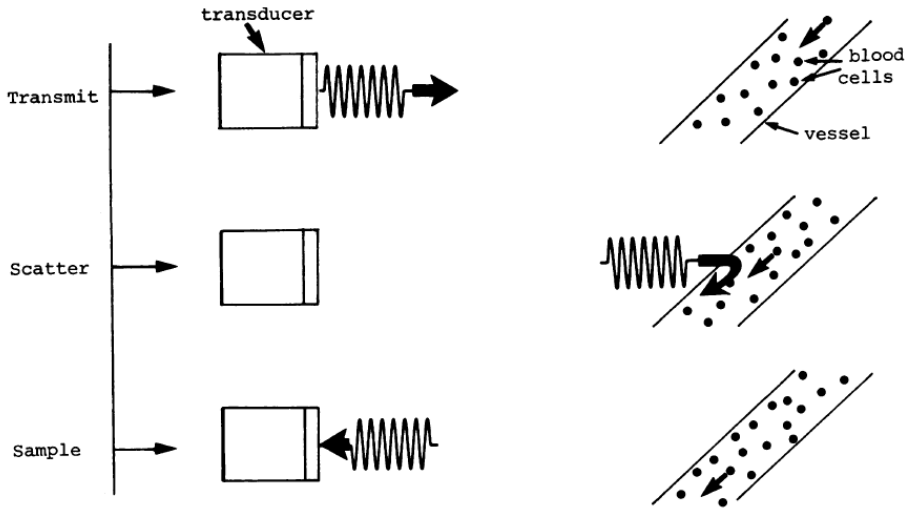


Figure 2.2. Principle of Pulsed wave Doppler system [43]

In this research a Transcranial Doppler is a pulsed ultrasound Doppler. Since the bones of the skull are thick with an average of 6.5mm in men and 7.1mm in women [42], a frequency as low as 2 MHz is used to achieve sufficient bone penetration. This increases tissue penetration however reducing spatial resolution. Therefore even with recent Transcranial duplex scanners the two dimensional B- mode images are of low spatial resolution and hence this method can be used to only measure cerebral blood flow velocity and not absolute volumetric flow.

The Transcranial Doppler System used in this research, the Doppler–Box^{TM} by Compumedics USA Inc. Charlotte, North Carolina, meets the requirements of Medical Device Directive 93/42/EEC- Annex II.3. A 2 MHz probe is attached to the front panel of Doppler box. The rear panel consists of the analog output, a power cord and a cord for network connection to the PC, in which the software QL2.4 is run. This data is then passed on to the Data Acquisition (DAQ), acquired using the LabView software and sampled at 1 KHz for further processing in Matlab. The sample volume was adjusted to 12 mm and depth was adjusted according to different subjects. The Doppler Box used is shown in figure 2.3.

Figure 2.3 Front and Rear Panel of the Doppler-Box™

Transcranial Doppler Systems (TCD) is used in the detection of intracranial abnormalities such as hemorrhage, vasospasm, stenosis and various other problems.

2.1.2 Velocity Calculation

The velocity of the blood flow in a vessel is related to velocity by the following equation

$$f_d = \frac{2 * f_t * V * cos\theta}{c} \quad (2)$$

Where,

f_d: Doppler frequency shift (Hz)

c: Speed of sound in tissue (cm/s)

f_t: Transmitted frequency (Hz)

V: Velocity of blood (cm/s)

θ: Angle of insonation (degrees)

Figure 2.4 shows the principle behind calculation of velocity of blood using TCD. If a red blood cell moves with a velocity of V and with an angle of θ, the velocity can be measured by measuring the frequency shift (f_d) of the wave. The transducer measures the frequency shift. Since the other variables in the equation are know, velocity can be calculated by substituting them in the equation.

The angle of insonation (θ) is a critical factor in measuring the velocity of the blood flow. In ideal circumstances, the angle of insonation is 0°. In routine clinical practices, it is preferred to maintain an angle that is relatively small; this may introduce a small and acceptable error in

flow velocity measurements [44]. However when a larger angle is chosen, the error in measurement can be considerably greater [45].

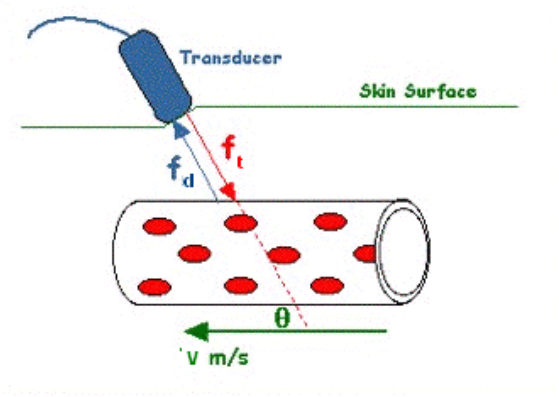


Figure 2.4 Principle behind Velocity calculation of blood flow [40]

2.1.3 Importance of Angle of Insonation

Our intent is to increase the spatial resolution and the signal to noise ratio to get more accurate values of cerebral blood flow velocity. To achieve this, it is important to have a high Doppler frequency. The factors that contribute to achieving high Doppler frequency are:

1. Increase in velocity
2. Increase in frequency
3. Increased alignment of the beam (Angle of Insonation).

Since the velocity is the variable that is being measured and frequency is set to 2 MHz for better insonation, they cannot be adjusted. Leaving angle of insonation the only variable that can achieve higher Doppler frequency. From equation 2 we see that Doppler frequency is directly proportional to the cosine of the angle of insonation in degrees. Hence the smaller angle of insonation, the higher is the value of frequency and vice versa. This is explained in Figure 2.5 below.

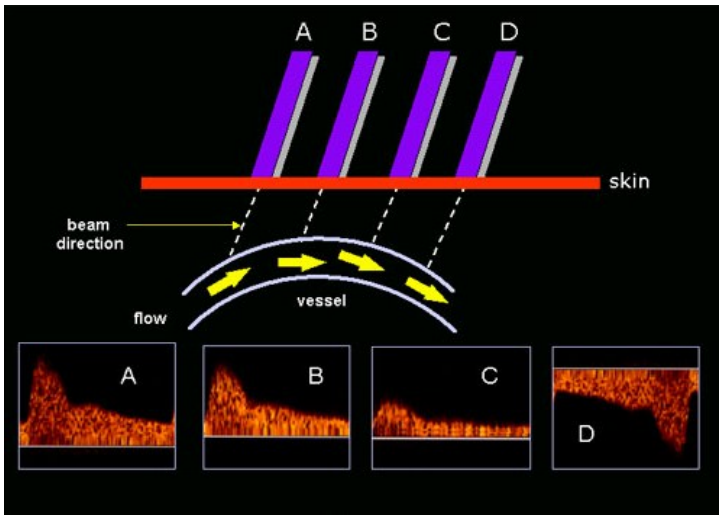


Figure 2.5 Effect of angle of insonation

As seen in figure 2.5 beam direction of transducer A is more aligned to the direction of flow and hence has a higher signal, in comparison to B and C. Beam direction of transducer D is away from the direction of flow and has a negative signal.

Since the penetration of the ultra sound depends on the thickness of the skull, various bone windows, with the thinnest ultrasound barriers, is used to insonate the cerebral arteries and the vertebral arteries. Localization can be achieved by fixing the Doppler probe over the temple by a special headset seen in Figure 2.6. Depth of focus is increased until a bidirectional flow is seen; it is then decreased until a positive signal is seen exclusively, classic flow in a Middle Cerebral Artery. Recent studies show that color flow duplex systems, can display the Doppler information from a number of vessels, improving the identification of the intracranial vessels [45].

Figure 2.6 Headset attached with the Transcranial Doppler ultrasound

2.2 Arterial Oxygen Saturation using Pulse Oximetry

2.2.1 Principle and Working of Pulse Oximeter

The pulse Oximetry is a noninvasive method of measuring the oxygen saturation of a person's hemoglobin in the blood. The principle is based on the absorption characteristics of red and infrared wavelengths in oxygenated and deoxygenated blood. Oxygenated hemoglobin absorbs more infrared light and deoxygenated hemoglobin absorbs more red light, letting the other pass. The wavelengths of the red and infrared are shown in Figure 2.7.

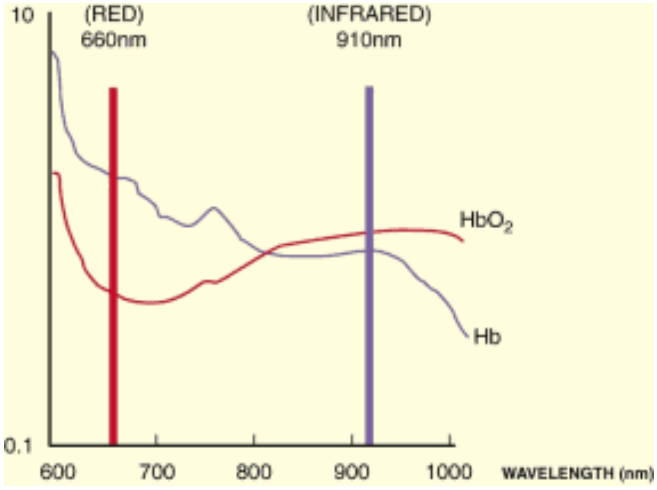


Figure 2.7 Absorption spectra of Hb and HbO_2

The Pulse Oximetry has two methods of sending light, transmission and reflectance. The transmission method has an emitter that emits red and infrared wavelengths through a light-emitting diode (LED), and a photo detector on the opposite side to absorb wavelengths of light with the measuring site sandwiched in between them. The reflectance method has the emitter and the photo detector on the same side of the measuring site. The measuring site is usually a thin part of the human body and can a fingertip or an ear lobe. The emitter passes the red (R) and the infrared (IR) signals through the measuring site and the less absorbed wavelengths are detected at the detector as shown in Figure 2.8.

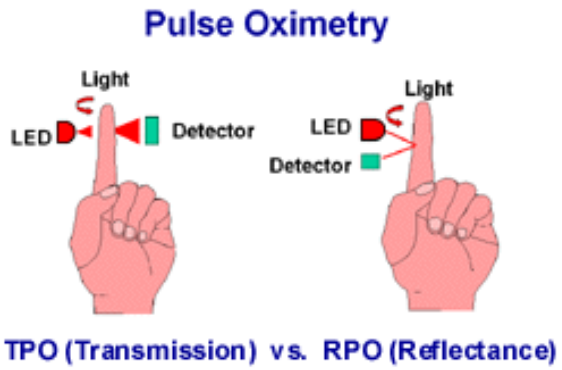


Figure 2.8 Principle of Pulse Oximeter

The R/IR ratio is calculated which is then converted to the oxygen saturation levels. The table below shows a few R/IR values and their corresponding oxygen saturation percentage.

Table 2.1: R/IR ratio for various %SaO2 values

Red by infrared (R/IR)	**Percentage Oxygen Saturation (%SaO2)**
0.5	100%
1.0	82%
2.0	0%

The Pulse Oximeter used in this research is the Nellcor oximax N-600x pulse Oximeter by Covidien, Massachusetts, USA. This provides both the analog output as wells as the PPG

waveform. The analog output is collected from the data port on the rear panel of the pulse Oximeter using a DAQ ground. This output is then fed to the NI CB-68 LP through a cable with a DB 15 connector and open wires that can be screwed into it, The NI CB-68 LP has 68 terminals that is connected to the NI- DAQcard – 6024E. The DAQ card converts the analog signal to digital using LabView 8.6 at a sampling rate of 1000 hertz (1 KHz). The instrumentation setup, NI CB-68 LP and the NI – DAQcard – 6024E is shown in Figure 2.9.

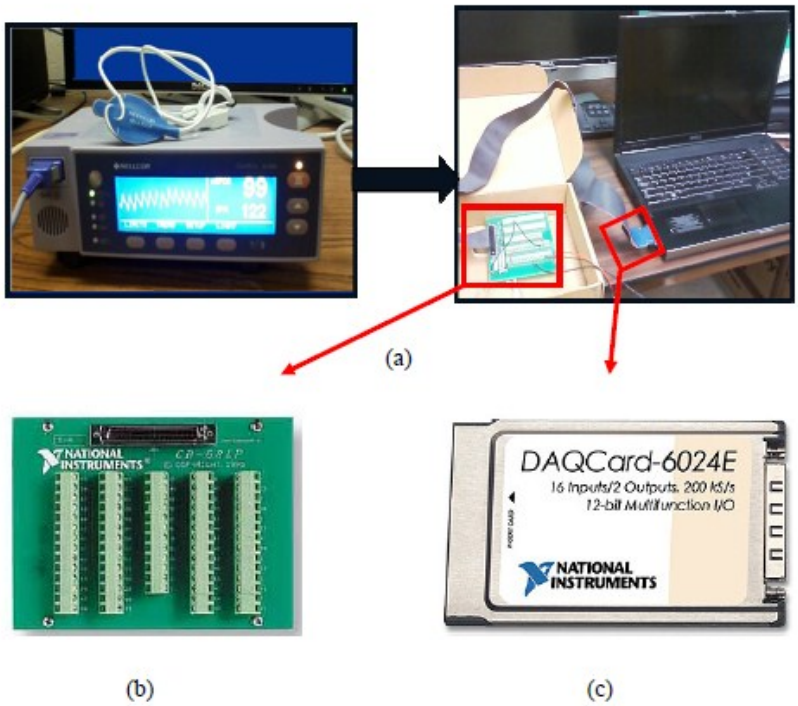


Figure 2.9 Instrumentation setup for the measuring arterial oxygen saturation using Pulse Oximetry

2.2.2 Calibration of the Pulse Oximeter

The principle used to compute the values of arterial SaO2 is the Beer- Lambert law that is shown in equation 3.

$$A = \varepsilon bc \tag{3}$$

Where,

ε = molar absorbtivity with units of L mol^{-1} cm^{-1}

b = path length in cm

c = concentration of compound in solution in mol L^{-1}

The law states that absorbance depends on concentration and the path length. However the Beer Lambert law based on the equation for the pulse oximeters does not take into consideration the multiple scattering of the red blood cells. As a result, instruments based on Beer-Lamberts law tends to give an erroneous value of oxygen saturation .To avoid this, calibration of the pulse Oximetry is necessary.

Calibration of the Nellcor oximax N-600x used in this research is done using a AVL Omni Co-Oximeter. Co Oximetry uses the same principle as in the Pulse Oximetry, but functions in the visible wavelength of light. This is done by taking a small volume of blood, hemolysed by ultrasound and stored in a cuvette. A monochromatic light obtained from a wide bandwidth (500 nm – 700 nm)of light from a tungsten- halogen lamp is shone on the cuvette and is detected by a photodiode. It is then digitized and fed into a microprocessor to calculate different parameters such as Oxyhemoglobin, carboxyhemoglobin and other chromophores using Beer-Lamberts law.

2.3 Experimental Design and Setup

2.3.1 Simulated Sleep Apnea Study

For this research we tested two groups of volunteers. The control group consisted of sixteen healthy volunteers and the patient group consisted of 10 volunteers who were diagnosed with sleep apnea and will be explained in the following sections.

2.3.1.1 Subject Demographics in Simulated Apnea

This includes the first group or the control group. The control group consisted of a health population of 16 volunteers who did not have any known sleep disorder, cardiac, neural or respiratory disorders. These groups of volunteers were chosen from the Bioengineering

department of the University of Texas at Arlington. They were given complete details on the experiment and signed informed consent forms as per the institutional Review board. The Subject demographics of the control group are shown in detail in Table 2.2.

Table 2.2 Subject Demographics for Control Group (Simulated Apnea)

Number of Subjects	Gender	Age (years)	Height(cm)	Weight (kg)	BMI (Kg/m^2)
16	Male – 9 Female - 7	29±4.9	165.9 ± 9.3	67.2 ± 19.3	24.1 ±4.8

2.3.1.2 Experimental Setup in Simulated Apnea

Data recording for simulated apnea not only included Cerebral Blood flow and Arterial Oxygen saturation, but also had measurements for Blood Pressure, End title carbon di-oxide and Electrocardiogram. It also had an on- off switch that was used to generate an event marker. The experimental setup in Simulated Apnea is shown in Figure 2.10.

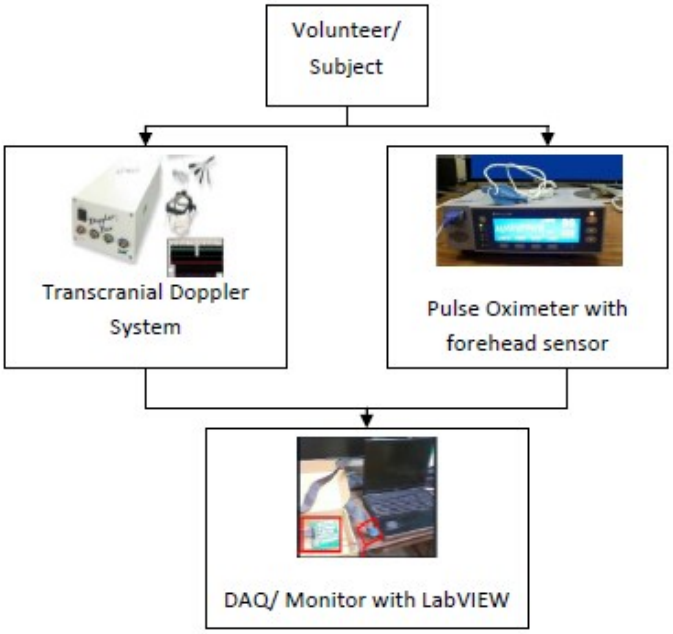
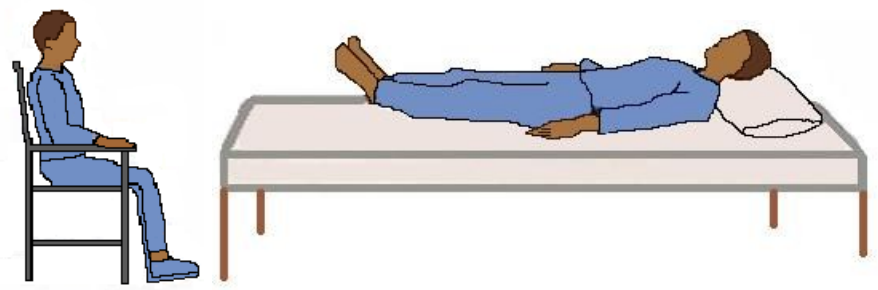


Figure 2.10 Experimental Setup in Simulated Apnea

2.3.1.3 Postures and protocols in Simulated Apnea

Data was collected in two different postures: Sitting and Supine positions.



(a) (b)

Figure 2.11: Postures used in Simulated Apnea (a) Sitting and (b) Supine

Two different protocols namely Protocol A and Protocol B were designed by using breath hold as a method to imitate sleep apnea and measure the impact on cerebral blood flow and arterial oxygen saturation, and were performed in the two different postures explained above. All the four data sets were collected one after another over a period of three hours. They were randomized to eliminate bias in the results.

Protocol A started with 60 seconds of normal breathing in either of the postures. During this initial stage no breath hold maneuver was performed. This was done to obtain baseline data of normal cerebral blood flow and oxygen saturation for the subject. After the baseline data was collected, a nose clip was placed blocking airflow through the nostrils and the subject was asked to hold his/her breathe as long as he/she could. When the subject could no longer hold his/her breath, she was asked to signal by moving a thumb. At the signal the nose clip was removed and the subject resumed normal breathing as the data collection continued. A period of 90 seconds of normal breathing was provided before the next breath hold maneuver was performed. This maneuver continued for a total of five breath holds. Once the five breath hold maneuver was completed, the subject continued normal breathing of 60 seconds prior to ending data collection. A timing diagram for protocol A is shown in figure 2.12.

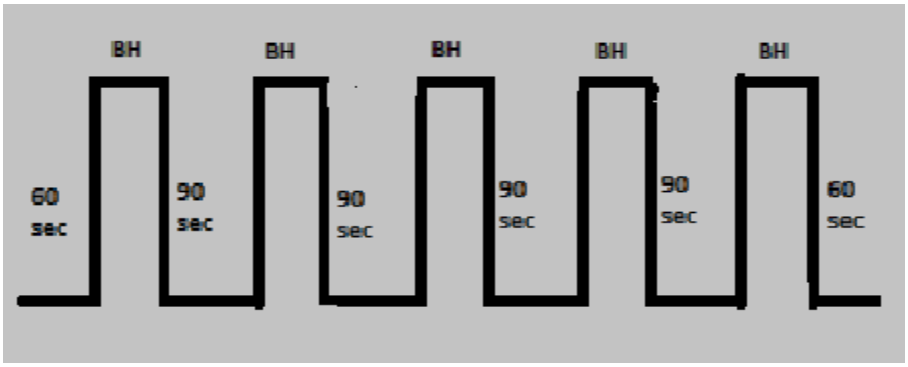


Figure 2.12 Timing diagram for Protocol A

The design of protocol A was to imitate the physiological responses that may be obtained when successive apnea episodes occur with enough time between events, allowing the responses to return back to or near the baseline values.

Protocol B was similar to protocol A, but for the duration between the breath hold maneuvers. Protocol B had 30 second duration in comparison to the 90 second in Protocol A. this was designed to study if the shorter durations lead to an accumulative increase in the physiological responses of the subject. Protocol B better mimics the real Sleep Apnea condition, as sleep apnea occurs frequently over shorter intervals. The timing diagram for Protocol B is shown in figure 2.13.

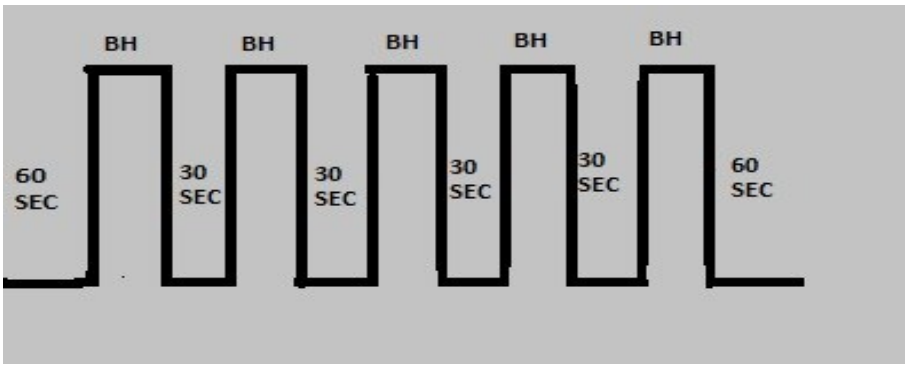


Figure 2.13 Timing diagram for Protocol B

The on and off switch was pressed every time a breath hold maneuver was performed and was fed into the DAQ.

2.3.2 Sleep Apnea Study

This study consisted of the second group or the patient group. This group had a total of 10 subject volunteer who were diagnosed with sleep apnea and no other respiratory diseases. This group consisted of X men and Y women and is described in detail in the following sections.

2.3.2.1 Subject Demographics in Sleep Apnea

This contains the second group or the patient group. The patient group consisted of a 10 volunteers who were diagnosed with sleep apnea but did not have any known cardiac, neural or respiratory disorders. This group of volunteers was chosen from Sleep Consultants, Inc. (Fort Worth, TX). Data was collected for an entire 8 hour night sleep (Polysomnography). They were given complete details on the experiment and signed informed consent forms as per the institutional Review board. The Subject demographics of the patient group are shown in detail in Table 2.3.

Table 2.3 Subject Demographics for Patient Group (Sleep Apnea)

Number of Subjects	Gender	Age (years)	Height(cm)	Weight (kg)	BMI (Kg/m^2)
10	Male – 8 Female - 2	50.28±9.60	173.0 ±13.3	93.7 ± 25.6	31.33 ±6.29

2.3.2.2 Experimental Setup in Sleep Apnea

Data recording was approximately for an 8 hour Polysomnography. The parameters monitored for sleep apnea not only included Cerebral Blood flow and Arterial Oxygen saturation, but also had measurements for Electroencephalogram (EEG), electro-oculogram (EOG), electromyogram(EMG), Blood Pressure, End title carbon di-oxide, movements of leg, chest and abdomen, snoring and a video monitoring of the subject. It also had a synchronization signal that was used to generate an event marker to ensure that there is no time lag between the

Sandman software used by Sleep Consultant, Inc and DAQ monitoring used by us. The experimental setup for Sleep Apnea is shown in Figure 2.14.

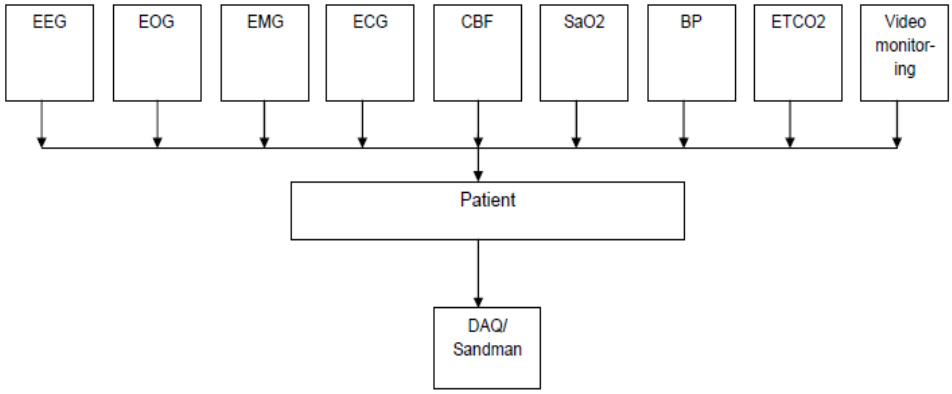


Figure 2.14 Experimental setup for Sleep Apnea

2.3.2.3 Apnea Scoring in Sleep Apnea

Once the 8 hour Polysomnography data is collected, it is scored by a expert sleep lab scorer. Scoring is done to determine the sleep stages and the occurrence of apneas and hypopneas. The data that is scored is the Sandman data and contains the information regarding the time and duration of stages. This is then imported to Matlab and a graphical representation of the stages is created. The stages and the episodes are assigned a value and are generated for the entire period of study. Apnea episodes are scored as 1 and Hypopnea episodes are scored as 4.

2.4 Data Acquisition

2.4.1 Computer- Based Data Acquisition Unit

The analog signals obtained from the various physiological monitoring systems are passed on to the Data Acquisition Unit (DAQ) manufactured by national Instruments (Austin TX). This research used a DAQ 6024E which is a 12 bit, 16 channel, 200kS/s Multifunction DAQ. The analog output from the Doppler-Box^{TM} and the Nellcor Pulse Oximeter are passed on to a connector block that interfaces with the DAQ. The connector block used is the CB-68 LP

and has 64 I/O pins. The DAQ is then interfaced with LabView 8.6. The basic function of the DAQ is to digitize the signals at a given sampling frequency (1000 Hz) and the output is obtained from the LabView software. The DAQ and the Connector block are shown in Figure 2.15.

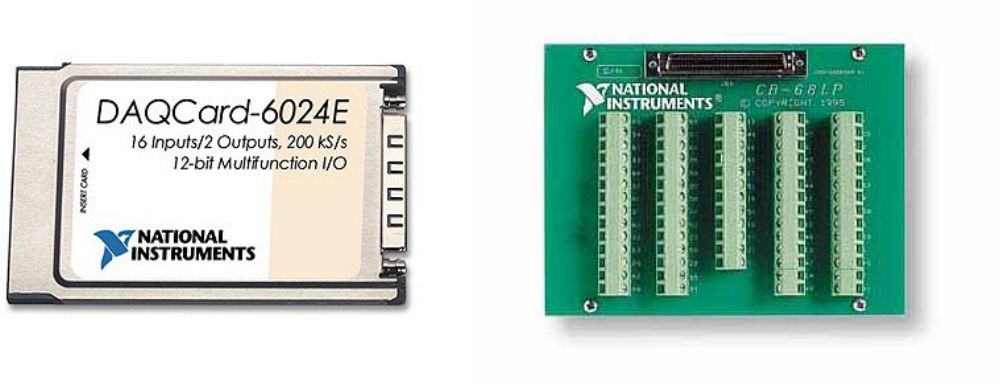


Figure 2.15 Data Acquisition Card (DAQ 6024 E) and the Connector Block (CB-68 LP)

2.5 Data Analysis

The data obtained from the LabView software has to undergo preprocessing, before useful information can be extracted from it. The preprocessing steps include clipping data, filtering, detecting points of interest and feature selection of data. The various preprocessing techniques are explained in detail in this section.

2.5.1 Clip Preparation and Selection

The data obtained from the LabView is in the .lvm format. Data processing is performed using Matlab that accepts both .lvm and .mat files. Data for simulated apnea were directly processed in matlab by using an lvm import function to open .lvm files in matlab. However the data obtained for sleep apnea is long which makes the size of the file to be very large and occupies great amount of memory. To overcome these issues the data obtained from the sleep lab were clipped at their apnea episodes and the normal breathing.

The clipping was performed using a graphic user Interface (GUI) program in matlab developed by Gauri Bhave [46]. Figure 2.16 shows the graphical user interface used for clipping data.

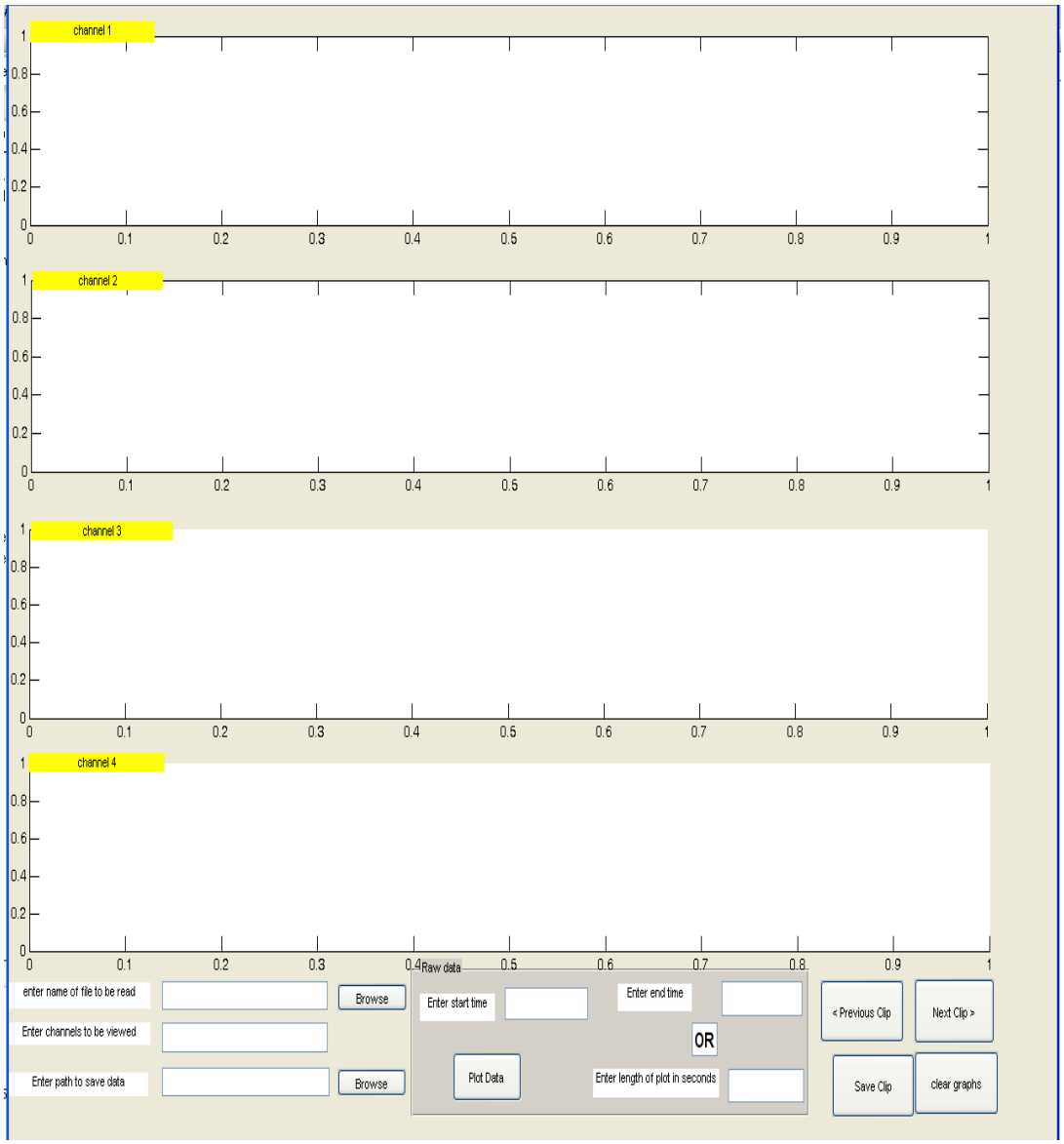


Figure 2.16 Graphic User Interface to clip sleep data

The GUI was designed to open data/ clips, select channels, view previous and next clips, and select start and end data point for clipping. The normal breathing clips are selected such that 5 seconds prior an episode is neglected. This is done to avoid fluctuations in the

signal due to the reason that the physiological parameters do not return to baseline immediately once the subject resumes normal breathing and hence the effect of apnea is seen in the first few seconds of recovery.

The apnea episodes are clipped based on the synchronous signal and the scored event signal (golden standard) obtained from the Sandman system. The length of the clips depends on the duration of the event. However since oxygen saturation and cerebral blood flow do not return back to its rested phase, even though the scored event is completed, the clips are extended to include them.

2.5.2 Feature Extraction for %SaO2 waveform

Oxygen saturation is the measure of the amount of oxygen bound to hemoglobin in the blood. During a breath hold maneuver, a drop in the percentage oxygen saturation is noticed. This can be related to the physiological changes that occur in the body, that is the decrease of oxygen molecules that are bound to the hemoglobin in the blood.

To obtain the physiological effect of the breath hold maneuver on the percentage oxygen saturation waveform, five major features were extracted. The features extracted are the Area, Amplitude of drop, Amplitude of rise, Time to drop and Time to rise.

Area of the %SaO2 waveform explains the changes in the amount of oxygen in the blood at that given time.

The other metrics such as the amplitude of drop and rise and the time to drop and rise explain the changes to the amount of oxygen present in one molecule of hemoglobin in the blood during the breath hold maneuver.

The raw data obtained from LabVIEW is imported into Matlab and is first filtered using a FIR – non causal zero phase digital filter. This is achieved by using an inbuilt function in Matlab known as filtfilt. Several designed features are then extracted from the filtered waveform to conduct statistical analysis. The steps involved in feature extraction are shown in Figure 2.17.

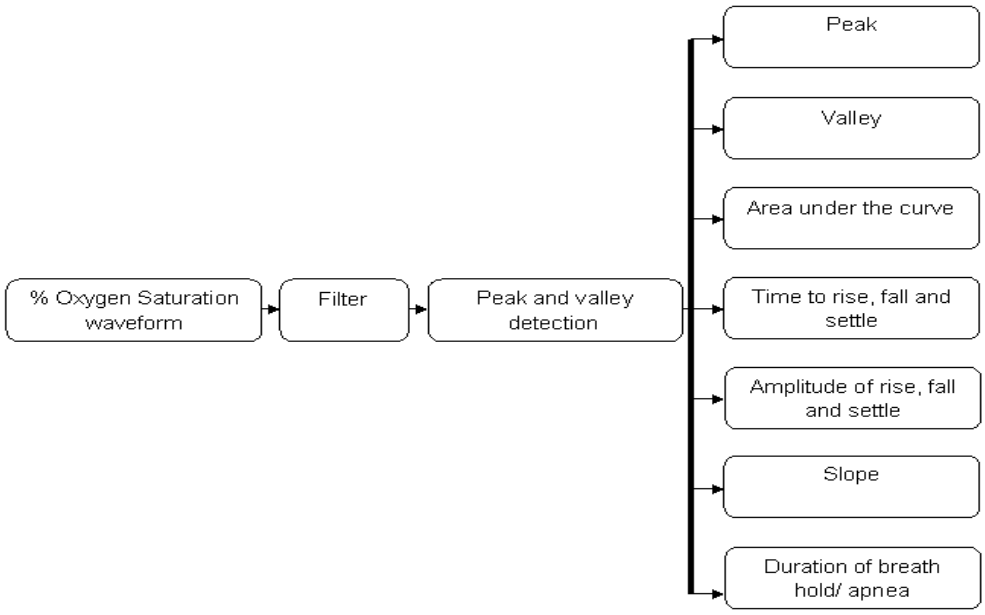


Figure 2.17 Flowchart depicting steps in Feature Extraction for the % SaO2 waveform

2.5.2.1 Simulated Apnea

Figure 2.18 shows the percentage oxygen saturation waveform during simulated apnea. Initially it is seen that the percentage of oxygen saturation is constant at 98%. The green block represents the start and stop of breath hold. The percentage oxygen saturation then starts dropping after a delay of a few seconds from the start of the breath hold. Similarly it is seen that it returns to baseline, after a delay from the stop of breath hold. These changes in the waveform contribute to the change in the physiological response as an effect of apnea.

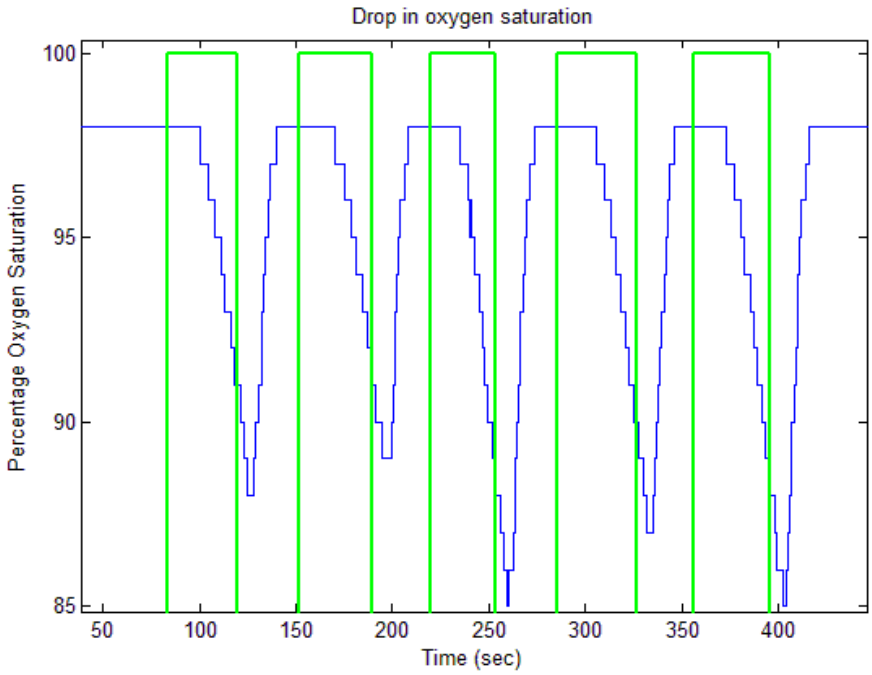


Figure 2.18 Drop of Percentage Oxygen Saturation waveform during simulated apnea

The peak, valley and settling point is detected using peak-valley detection function known as 'findpeaks' and 'findvalleys' which is developed in the Matlab environment. This function returns the local maxima and local minima of the waveform. This is specifically done by comparing each element in the data set with its neighboring values. If the element is the largest/smallest in the comparison they are stored in a max or min array. Thus returning the peak and valleys of the entire waveform. This array of peaks is then reduced to select the desired peak, valley and settling points. The Matlab program for this peak detection and feature selection can be found in appendix A. The features such as area, time to drop, time to rise, amplitude of drop, amplitude of rise and duration of breath hold are then extracted once the desired points are obtained. Figure 2.19 shows the desired points and the various features extracted from the waveform.

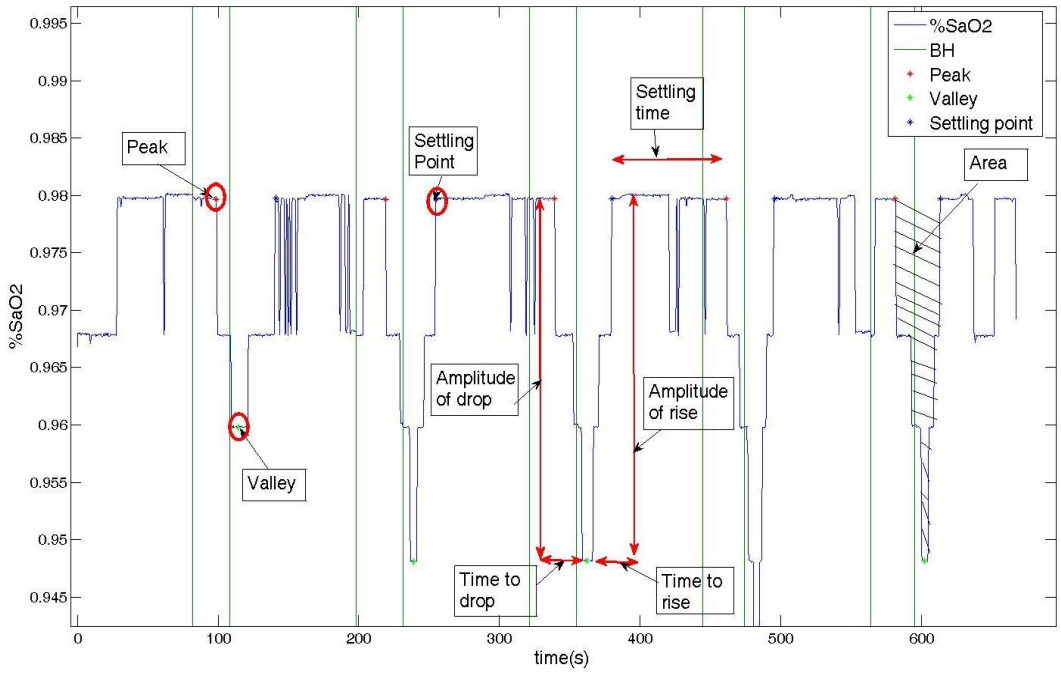


Figure: 2.19 Desired points and Features extracted from %SaO2 waveform during simulated apnea

2.5.2.2 Sleep Apnea

Figure 2.20 shows the percentage oxygen saturation in an apnea episode clip taken from the Sleep apnea data. The clips are obtained from a GUI explained in section 2.5.1. Desired points (peak, valley and settling point) and features (area, amplitude of drop, amplitude of rise, time to drop and time to rise) are extracted from the waveform similar to the simulated apnea, and are processed in Matlab. Figure 2.20 shows the desired points and the features extracted from the %SaO2 waveform during sleep apnea. The Matlab program for the peak detection and feature extraction can be found in appendix B.

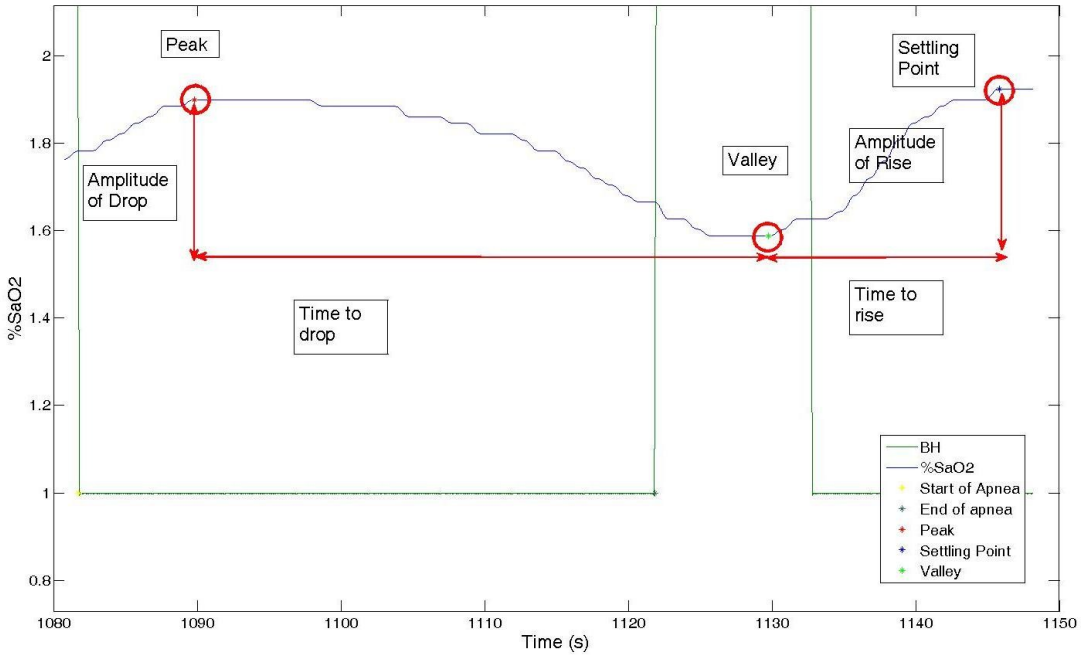


Figure 2.20 Desire points and features extracted from %SaO2 waveform during sleep apnea

2.5.3 Feature Extraction of CBF waveform

Feature extraction of the cerebral blood flow waveform followed similar steps as in the percentage oxygen saturation. Figure 2.21 shows the cerebral blood flow waveform obtained from the Transcranial Doppler system. The raw data was imported into Matlab and is first filtered using a FIR – non causal zero phase digital filter. Several designed features that reflected the response of the cerebral blood flow due to apnea are extracted from the filtered waveform to conduct statistical analysis. The steps involved in feature extraction for the Cerebral Blood Flow waveform are shown in Figure 2.22.

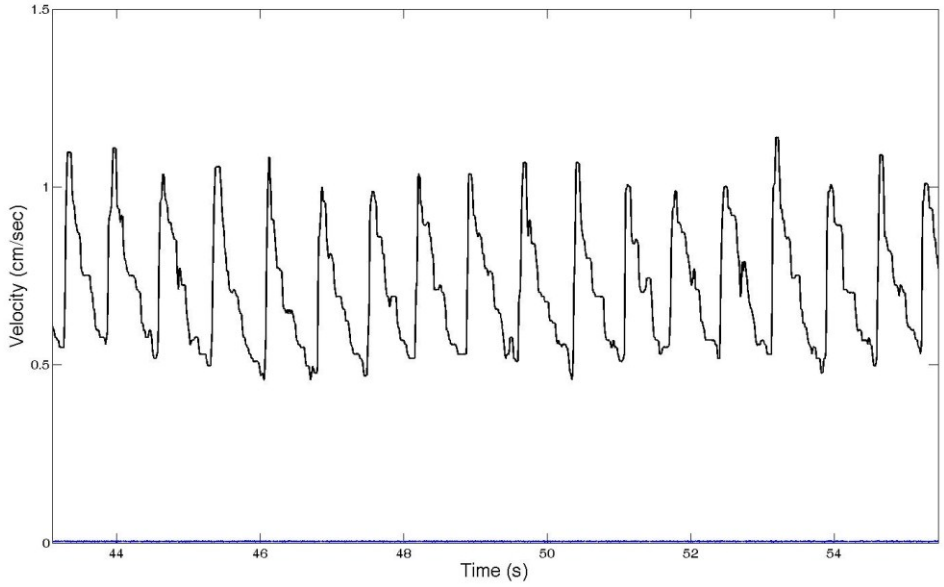


Figure 2.21 Sample of Cerebral Blood Flow waveform collected

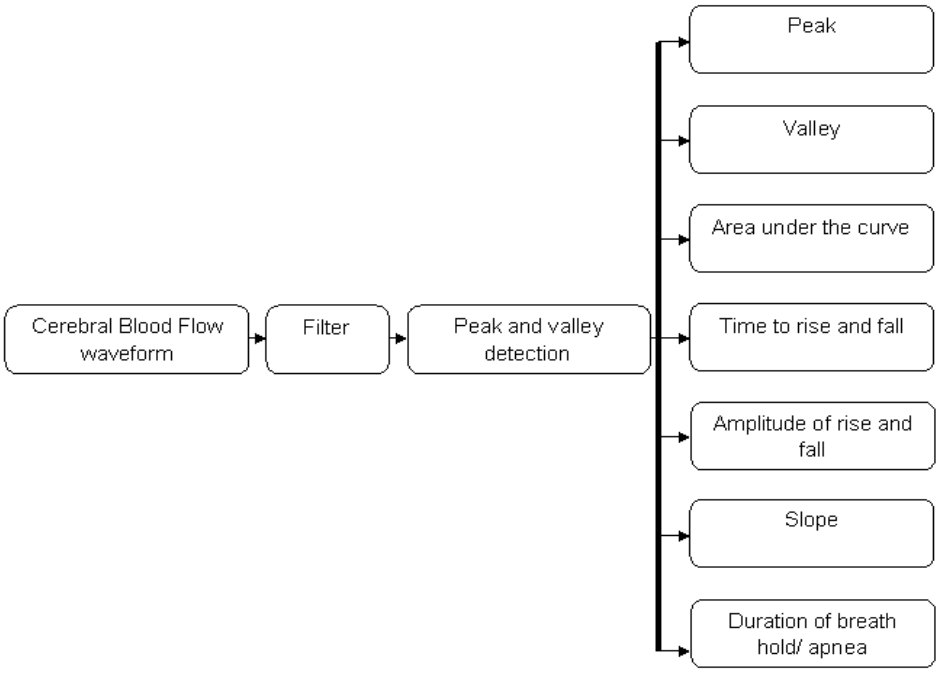


Figure 2.22 Flowchart depicting steps in Feature Extraction for the Cerebral Blood Flow waveform

The first feature that was extracted was the area under the curve. The cerebral blood flow velocity increases at the start of the breath hold and returns to its baseline at the end of the breath hold. The area of this change in velocity was calculated for each of the breath hold maneuvers. The number of area points for each breath hold duration depends on the length of the breath hold and the heart rate of the subject. The area under the velocity curve is an integration of velocity over time. Hence, if an assumption can be made that the diameter and the mechanical property of the middle cerebral artery remains the same throughout the given pulse, the area under the curve will be proportional to the volume of the blood flowing through the artery.

The second set of features that was extracted was the amplitude of the rise and drop. This relates to the amount of blood that flows through the MCA at a particular time. During a breath hold maneuver the cerebral blood flow increases from its baseline in a continuous fashion. It returns to its baseline at the end of the maneuver. This can attributed to the fact that there is an increase in the amount of blood flowing through the brain due to cerebral auto regulation during an apnea episode.

The next set of features that was extracted was the time to rise and drop of the waveform. This time span represents the rate at which the blood is flowing in the MCA i.e. the heart rate, as each pulse of the CBFV represents the heart beat. When this is compared with the area under the curve and velocity trend, it will show if the changes is due to the change in heart rate or the volume of flow or both.

2.5.3.1 Simulated Apnea

Figure 2.22 shows the cerebral blood flow waveform during simulated apnea. The green block represents the start and stop of breath hold. The cerebral blood flow velocity starts rising at the start of breath but attains its maximum only after the breath hold maneuver is stopped. It is also seen that it returns to baseline, after a delay from the stop of breath hold.

These changes in the waveform contribute to the change in the physiological response as an effect of apnea and make interesting feature detection.

The peak and valley points are detected using the peak-valley detection function known as 'findpeaks' and 'findvalleys' which is developed in the Matlab environment. The start point is taken to be the peak just after start of the breath hold. The features such as the area, amplitude of drop, amplitude of rise, time to drop and time to rise are then extracted once the peak, valley and start points are obtained. The algorithm for the peak detection and feature selection is provided in appendix C. Figure 2.22 shows the desired points and the various features extracted from the waveform.

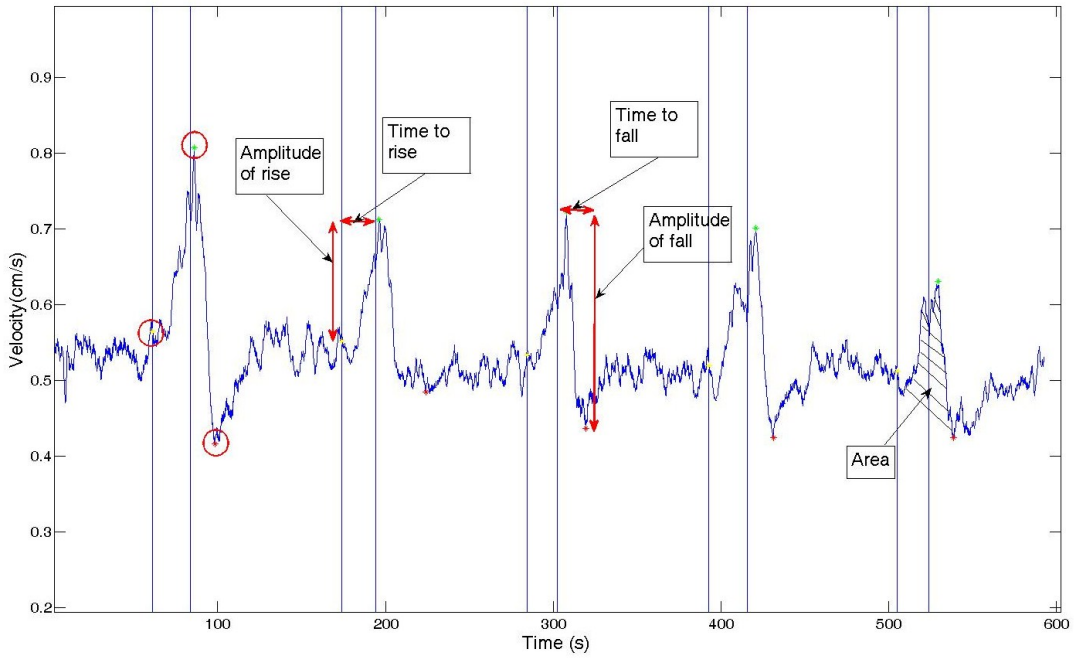


Figure: 2.23 Desired points and the features extracted from CBF waveform during simulated apnea

2.5.3.2 Sleep Apnea

Figure 2.23 shows the cerebral blood flow velocity waveform in an apnea episode clip taken from the Sleep apnea data. The clips are obtained from a GUI explained in section 2.5.1. Features such as the area, amplitude of drop, amplitude of rise, time to drop and time to rise

are extracted from the waveform , and are processed in Matlab. The Matlab program for the peak detection and feature extraction can be found in appendix D.

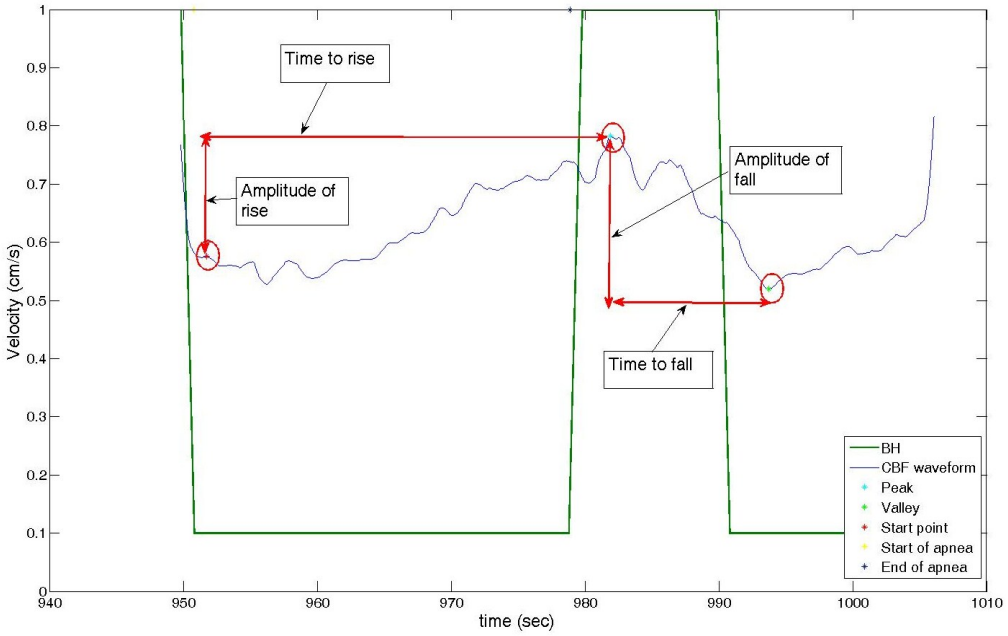


Figure 2.24 Features extracted from CBF waveform during sleep apnea

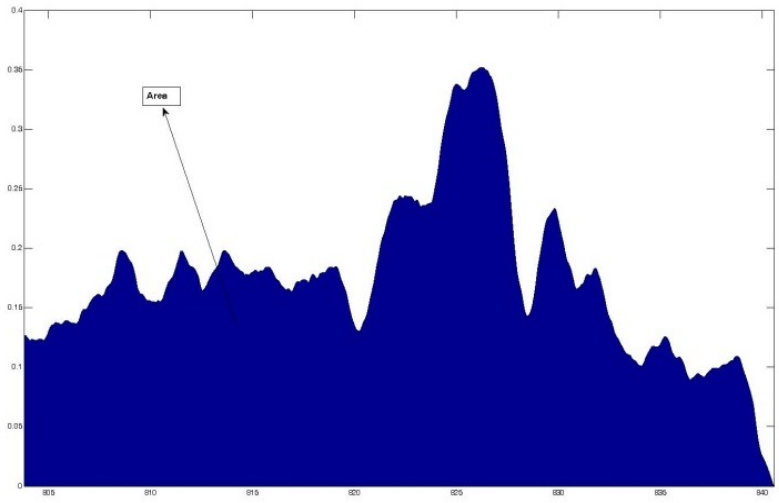


Figure 2.25 Clip of the Area extracted from CBF waveform during sleep apnea

2.5.4 Export to Excel

When all parameters were obtained, they were written into Microsoft Excel using the Matlab inbuilt functions 'xlswrite'.This is a simple function that exports or writes a matrix M to an Excel file. The matrix data is always written to the first worksheet in the file and starts at cell A1 and does not over write previous data. This can be found in the last section of programs in appendices A-D.

2.6 Statistical Analysis

Statistical Analysis is performed to obtain significance of the extracted features. This was compared in 3 different ways.

1. Comparison of features (peak, valley, amplitude of drop and rise, time to drop and rise and area) with the duration of breath hold or apnea episode.
2. Comparison of features (peak, valley, amplitude of drop and rise, time to drop and rise and area) among %SaO2 and CBF waveforms.
3. Comparison of features (peak, valley, amplitude of drop and rise, time to drop and rise and area) among sleep and simulated apnea.

   The various features which were compared are explained in the sections above. Statistical software in Minitab and excel were used to apply proper statistical testing outlined below.

2.6.1 Correlations

Correlation is a statistical tool that shows whether and how strongly, pairs of variables are related. This is measured in terms of correlation coefficient whose values range between -1 and +1. Correlations were performed on the features in the three different comparison explained above. The significance of each correlation is obtained using a T-statistic in excel.

The significance of correlation is obtained using the following equation.

$$\boldsymbol{Significance\ of\ \rho = Td}(|\mathbf{Ts}|, \boldsymbol{df}, \mathbf{p}) \quad (4)$$

Where,

ρ is the correlation

Td is the t distribution of the correlation ρ

Ts is the t statistic of the Pearson correlation ρ, and is calculated using the equation

$$\boldsymbol{Ts} = \frac{\rho}{S_\rho} \quad \textbf{(5)}$$

Sρ is the standard error of the sampling distribution

df is the degree of freedom

And p is the number of tails, 2 for a two tailed test.

2.6.2 Analysis of Variance (ANOVA)

For multiple comparisons of features ANOVA was used. In this test, observed variances were separated in to different groups based on their sources including inter-subject variations. One way ANOVA is used to test differences among two or more independent groups. The study used one-way ANOVA to test the differences among the features (peak, valley, amplitude of drop and rise, time to drop and rise and area) with duration of breath hold or apnea episode, comparisons among %SaO2 and CBF waveforms and also comparisons among sleep and simulated apnea.

CHAPTER 3

RESULTS

This chapter describes the results obtained from the comparisons of various features derived from the percentage oxygen saturation and cerebral blood flow waveforms of this study. Table 3.1 shows a summary of the various features as defined in detail in Chapter 2.

Table 3.1: Summary of Features Extracted

No	Features Extracted from %SaO2 and CBF waveforms
1	Area Under the Curve
2	Amplitude of Rise
3	Amplitude of drop
4	Time to rise
5	Time to drop
6	Duration of breath hold / apnea*

*in this research breath hold maneuvers were used to represent apnea episodes in healthy subjects and is explained in more detail in Section 2.3 of this thesis.

The results are explained in two major sections. First results from the simulated apnea study and second from the sleep apnea study. Statistical tools such as ANOVA and correlations are performed using software's, minitab and excel to make the following comparisons on each of these studies.

i. Relation between the CBF features and the %SaO2 features.

ii. Effect of the apnea or breath hold episode to the features extracted shown in table 3.1.

3.1 Simulated Sleep Apnea Study

3.1.1 Average and Standard deviation of the Cerebral Blood Flow waveform features

In this section we will present the average and standard deviation of the features obtained in the cerebral blood flow waveform. Also statistical comparison, ANOVA is performed on the means of each of the features obtained.

Figure 3.1 shows the average and standard deviation of the Area under the curve of the cerebral blood flow waveform. ANOVA shows that a p-value of <0.05 is obtained for the comparison of the average made across the four protocols as well as across the five breath hold maneuvers.

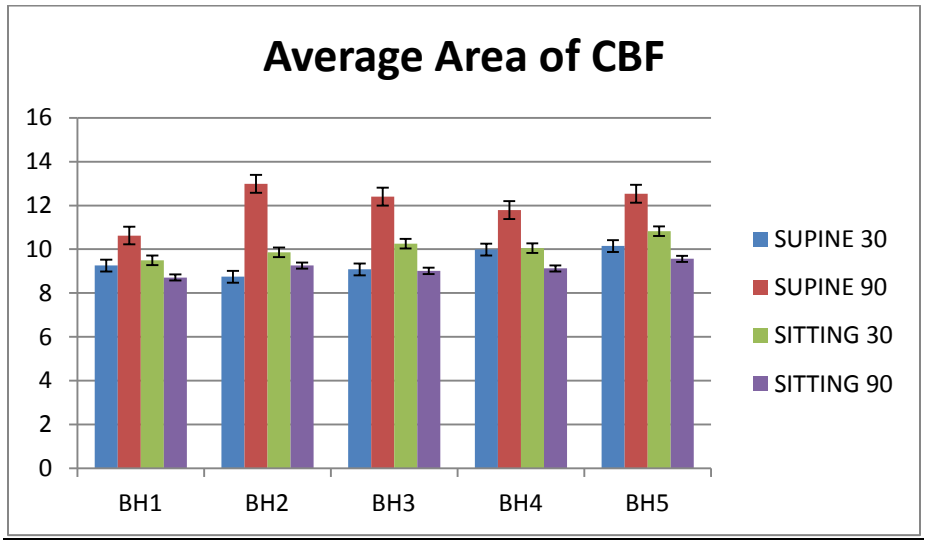


Figure 3.1 Average values of Area under the curve of the CBF waveform for simulated apnea study

Figure 3.2 shows the average and standard deviation of the Amplitude of rise of the cerebral blood flow waveform. ANOVA shows that a p-value of <0.05 is obtained for the comparison of the average made across the four protocols as well as across the five breath hold maneuvers.

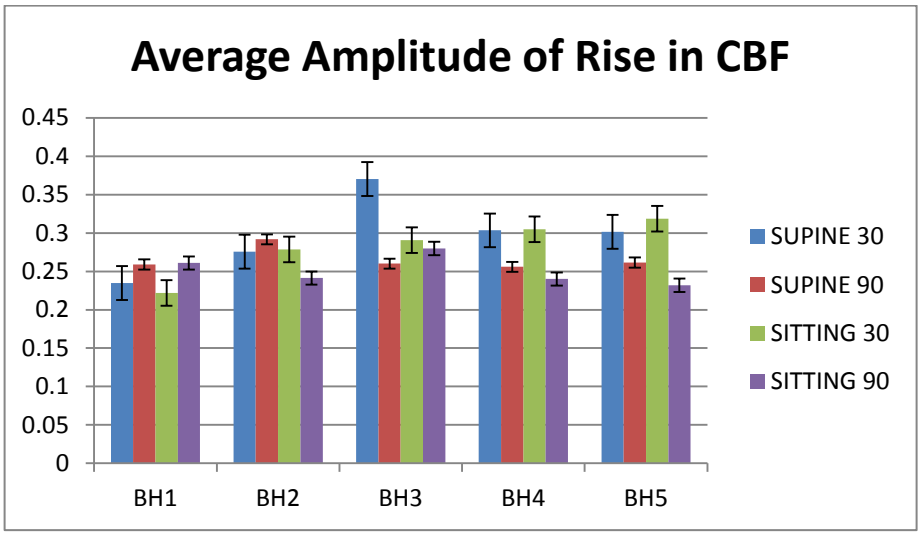


Figure 3.2 Average values of Amplitude of rise of the CBF waveform for simulated apnea study

Figure 3.3 shows the average and standard deviation of the Time to rise of the cerebral blood flow waveform. ANOVA shows that a p-value of <0.05 is obtained for the comparison of the average made across the four protocols as well as across the five breath hold maneuvers.

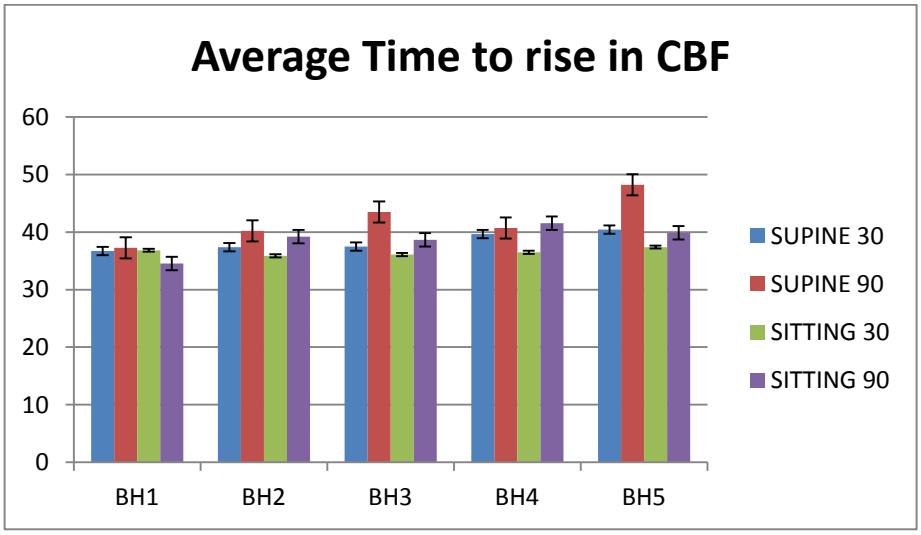


Figure 3.3 Average values of Time to rise of the CBF waveform for simulated apnea study

3.1.2 Effect of duration of breath hold on CBF waveform features

In this section, data obtained from the cerebral blood flow waveform during simulated apnea is analyzed. Comparisons are made in order to investigate the relationship between the proposed features shown in table 3.1 extracted from the CBF waveform with the duration of breath hold. An ANOVA is performed to obtain the significance of the comparison. Correlation coefficients are computed for the significant comparisons. The significance of each correlation coefficient is obtained using a t- test in excel and is explained in section 2.6.1 of this thesis.

A Post- Hoc analysis is performed to obtain the significance of the correlation coefficients across the four different protocols (Supine 90, Supine 30, Sitting 90 and Sitting 30).

3.1.2.1 Area vs. duration of breath hold

An ANOVA is performed to obtain the significance of the comparison of the area under the curve versus the duration of breath hold. A p value of less than 0.05 is obtained for the comparison of the means.

Figure 3.4 shows the correlation coefficient for the comparison of the area under the curve of the cerebral blood flow waveform and the duration of breath hold. Statistical significance of the correlation coefficients was calculated using a t-test and is explained in section 2.6.1. A p-value less than 0.05 were obtained for each of the correlation coefficients proving that these correlations are statistically significant. This also shows that there is a strong relationship between the area under the curve and the duration of breath hold in the cerebral blood flow waveform obtained.

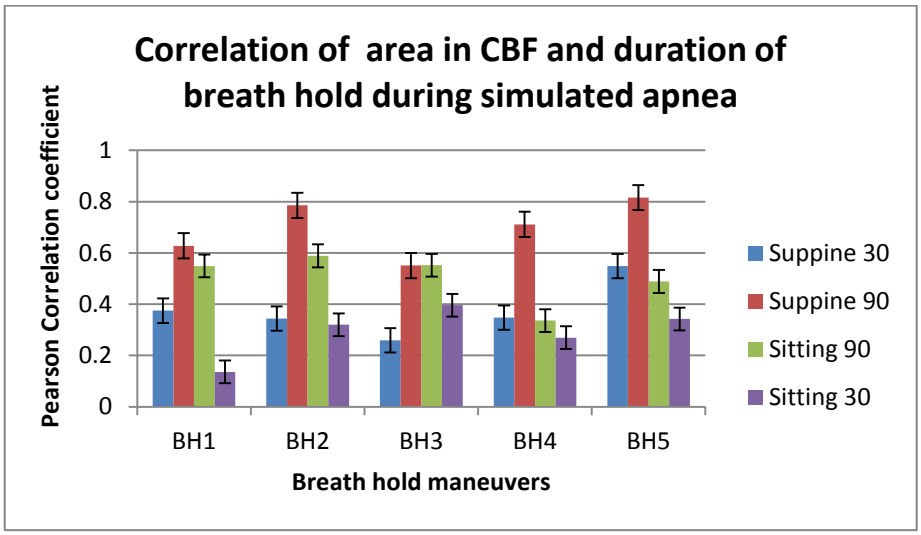


Figure 3.4 Correlation of area and duration of breath hold (BH) maneuvers 1 to 5 in the cerebral blood flow waveform during simulated sleep apnea (p-value <0.05)

An ANOVA was performed for the correlation coefficients across the four different protocols (Supine 90, Supine 30, Sitting 90 and Sitting 30), and was found to be statistically significant . Post Hoc analysis was performed to see the significance of correlations across the four protocols individually and the results are shown in table 3.2. Significance level of P<0.05 are noted with an asterisk.

Table 3.2 Post hoc analysis on the correlation between the area and duration of breath hold in the cerebral blood flow waveform

Protocol versus Protocol
Supine 30 and Supine 90 *
Supine 30 and Sitting 90
Supine 30 and Sitting 30
Supine 90 and Sitting 90 *
Supine 90 and Sitting 30 *
Sitting 90 and Sitting 30 *

*indicates significance p-value less than 0.05

3.1.2.2 Amplitude of rise vs. duration of breath hold

An ANOVA is performed to obtain the significance of the comparison of the amplitude of rise versus the duration of breath hold. A p value of less than 0.05 is obtained for the comparison of the means.

Figure 3.5 shows the correlation coefficient for the comparison of the amplitude of rise and the duration of breath hold. Statistical significance of the correlation coefficients was calculated using t-test. A p-value less than 0.05 resulted for the correlation coefficients obtained for the Supine 90 and Sitting 90 protocols. However a p value of greater than 0.05 was obtained for the Sitting 30 and Supine 30 protocols.

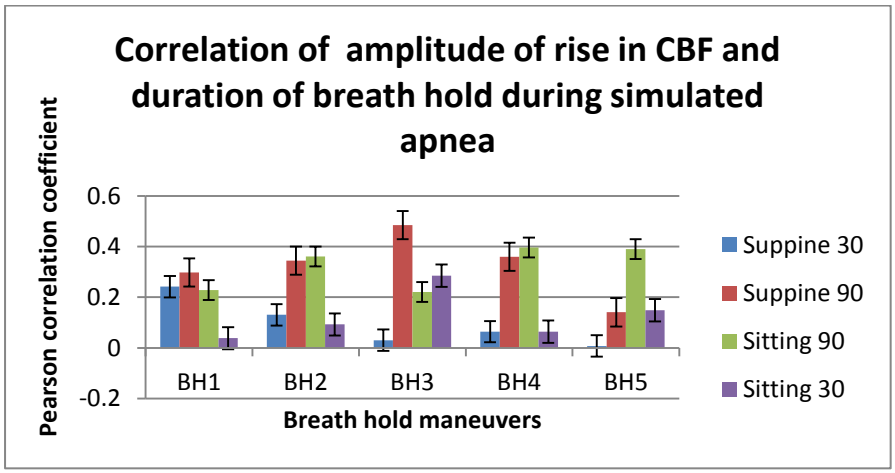


Figure 3.5 Correlation of the amplitude of the rise and duration of breath hold (BH) maneuvers1 to 5 in the cerebral blood flow waveform during simulated sleep apnea (p-value <0.05)

The results obtained from the post hoc analysis across protocols are shown in Table 3.3.

Table 3.3 Post hoc analysis on the correlation between the amplitude of rise and duration of breath hold in the cerebral blood flow waveform

Protocol versus Protocol
Supine 30 and Supine 90
Supine 30 and Sitting 90
Supine 30 and Sitting 30
Supine 90 and Sitting 90 *
Supine 90 and Sitting 30
Sitting 90 and Sitting 30

*indicates significance p-value less than 0.05

3.1.2.3 Time to rise vs. duration of breath hold

An ANOVA is performed to obtain the significance of the comparison of the time tof rise versus the duration of breath hold. A p value of less than 0.05 is obtained for the comparison of the means.

Figure 3.6 shows the correlation coefficient of the comparison of the time to rise and the duration of breath hold. Statistical significance of the correlation coefficients was calculated using t-test. A p-value less than 0.05 for each of the correlation coefficients was obtained.

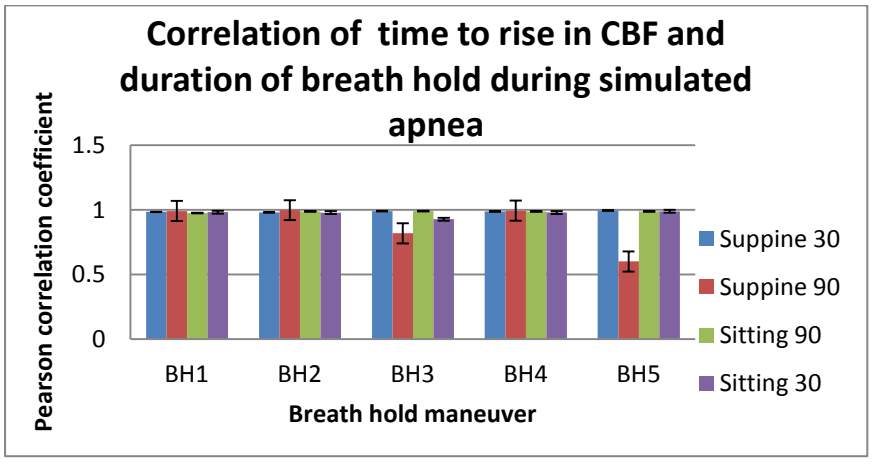


Figure 3.6 Correlation of the time to rise and duration of breath hold (BH) maneuvers 1 to 5 in the cerebral blood flow waveform during simulated sleep apnea (p-value <0.05)

An ANOVA was also performed for the correlation coefficients across the four different protocols (Supine 90, Supine 30, Sitting 90 and Sitting 30), and was found to be statistically significant. A post hoc analysis on the correlations across the four protocols was obtained and is shown in table 3.4.

Table 3.4 Post hoc analysis on the correlation between time to rise and duration of breath hold in the cerebral blood flow waveform across the 4 protocols

Protocol versus Protocol
Supine 30 and Supine 90 *
Supine 30 and Sitting 90 *
Supine 30 and Sitting 30 *
Supine 90 and Sitting 90 *
Supine 90 and Sitting 30 *
Sitting 90 and Sitting 30 *

*indicates significance p-value less than 0.05

Table 3.5 summarizes section 3.1.2 by showing the significant comparisons of the effect of breath hold on the cerebral blood flow features (table 3.1).

Table 3.5 Summary of statistical analysis of the effect of breath hold on cerebral blood flow features

Protocol versus Protocol	**Features**		
	Area Under Curve	**Amplitude of rise**	**Time to rise**
Supine 30 and Supine 90	*		*
Supine 30 and Sitting 90			*
Supine 30 and Sitting 30			*
Supine 90 and Sitting 90	*	*	*
Supine 90 and Sitting 30	*		*
Sitting 90 and Sitting 30	*		*

*indicates significance p-value less than 0.05

3.1.3 Average and Standard deviation of the %SaO2 waveform features

In this section we will present the average and standard deviation of the features obtained in the percentage oxygen saturation waveform. Also statistical comparison, ANOVA is performed on the means of each of the features obtained.

Figure 3.7 shows the average and standard deviation of the Area under the curve of the percentage oxygen saturation waveform. ANOVA shows that a p-value of <0.05 is obtained for the comparison of the average made across the four protocols as well as across the five breath hold maneuvers.

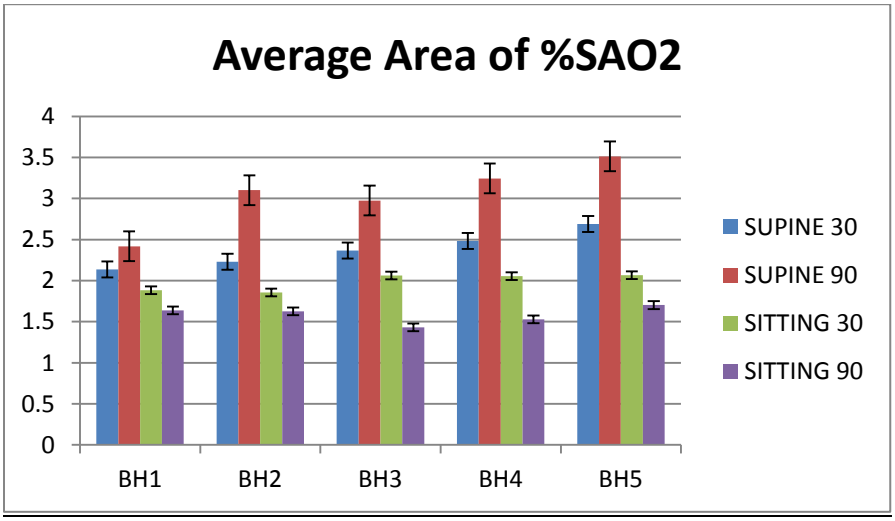


Figure 3.7 Average values of Area under the curve of the %SaO2 waveform for simulated apnea study

Figure 3.8 shows the average and standard deviation of the Amplitude of drop of the percentage oxygen saturation waveform. ANOVA shows that a p-value of <0.05 is obtained for the comparison of the average made across the four protocols as well as across the five breath hold maneuvers.

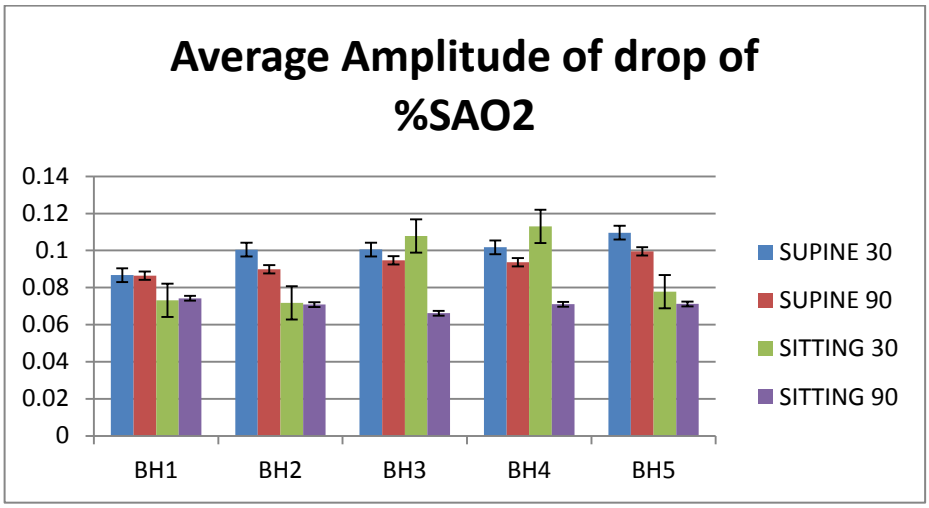


Figure 3.8 Average values of Amplitude of drop of the %SaO2 waveform for simulated apnea study

Figure 3.9 shows the average and standard deviation of the amplitude of rise of the percentage oxygen saturation waveform. ANOVA shows that a p-value of <0.05 is obtained for the comparison of the average made across the four protocols as well as across the five breath hold maneuvers.

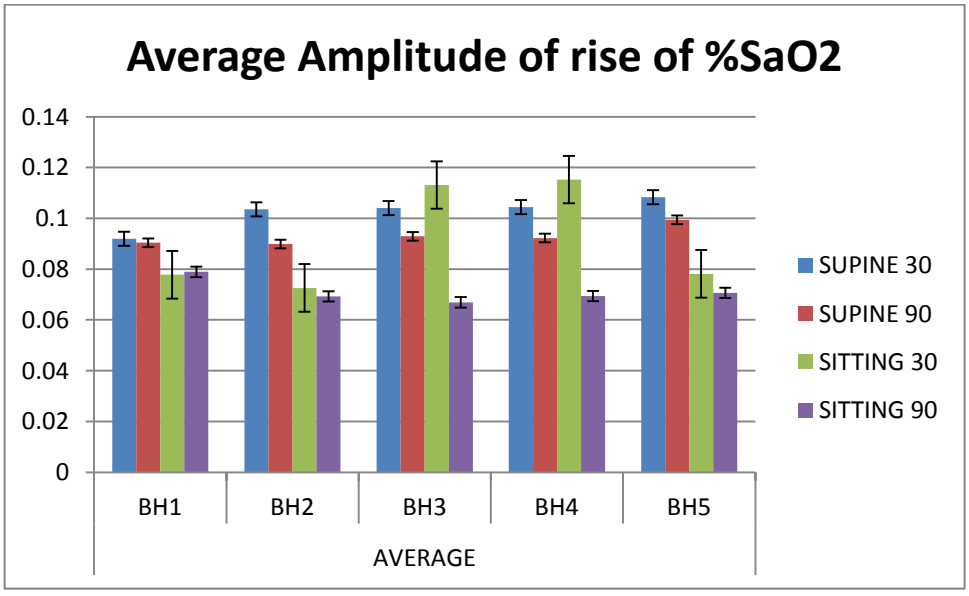


Figure 3.9 Average values of Amplitude of rise of the %SaO2 waveform for simulated apnea study

3.1.4 Effect of duration of breath hold on %SaO2 waveform features

This section explains the analysis made to obtain a relationship between the extracted features derived from the percentage oxygen saturation waveform shown in Table 3.1 with the duration of breath hold during the simulated apnea study. The analysis is performed in three different steps.

1. An ANOVA to obtain the significance of comparison between the duration of breath hold and the extracted features of percentage oxygen saturation waveform .
2. Calculation of the Pearson correlation coefficient between the duration of breath hold and the extracted features.
3. Significance of the Pearson correlation coefficient using a t-test.
4. Post Hoc analysis of correlation coefficients across the four protocols.

The results obtained from the ANOVA showed that the features area, amplitude of drop and time to drop did not vary from one breath hold to another for a given protocol. The p values obtained for this comparison were all greater than 0.05, showing that the comparisons made are not statistically significant.

3.1.4.1 Area vs. duration of breath hold

An ANOVA is performed to obtain the significance of the comparison of the area under the curve versus the duration of breath hold. A p value of less than 0.05 is obtained for the comparison of the means.

Figure 3.10 shows the correlation coefficient of the area under the curve of the %SaO2 waveform and the duration of breath hold. A p-value less than 0.05 were obtained for each of the correlation coefficients, showing that the correlations are statistically significant and that there is a strong relationship between the area under the curve and the duration of breath hold in the %SaO2 waveform.

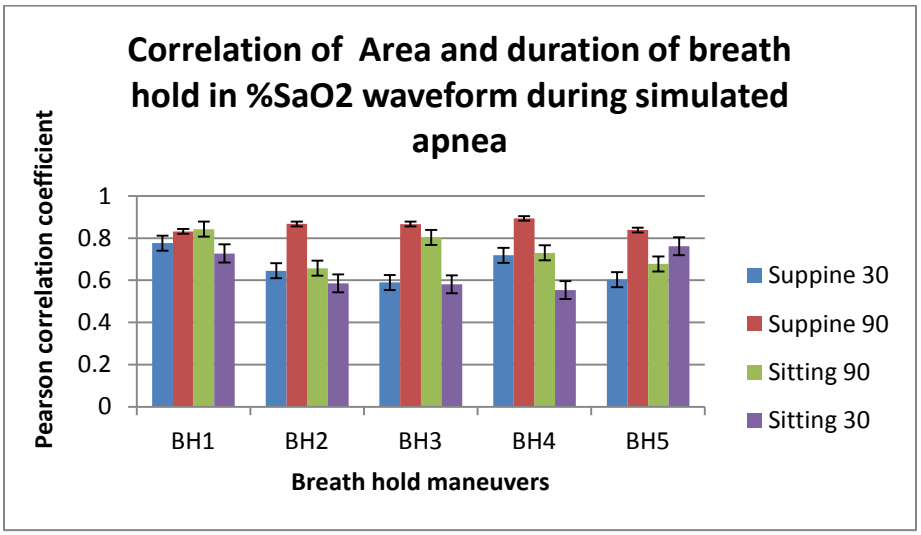


Figure 3.10 Correlation of the area of the %SaO2 waveform and duration of breath hold (BH) maneuvers 1 to 5 during simulated sleep apnea (p-value <0.05)

An ANOVA was also performed for the correlation coefficients across the four different protocols (Supine 90, Supine 30, Sitting 90 and Sitting 30), and was found to be statistically significant. Post hoc analysis was performed to see the significance of correlations across the four protocols individually and the results are shown in table 3.6.

Table 3.6 Post hoc analysis on the correlation between area of the %SaO2 waveform and duration of breath hold across the 4 protocols

Protocol versus Protocol
Supine 30 and Supine 90 *
Supine 30 and Sitting 90
Supine 30 and Sitting 30
Supine 90 and Sitting 90
Supine 90 and Sitting 30 *
Sitting 90 and Sitting 30

3.1.4.2 Amplitude of drop vs. duration of breath hold

An ANOVA is performed to obtain the significance of the comparison of the amplitude of drop versus the duration of breath hold. A p value of less than 0.05 is obtained for the comparison of the means.

Figure 3.11 shows the correlation coefficient for the comparison of the amplitude of drop of the %SaO2 waveform and the duration of breath hold. A p-value less than 0.05 were obtained for each of the correlation coefficients obtained.

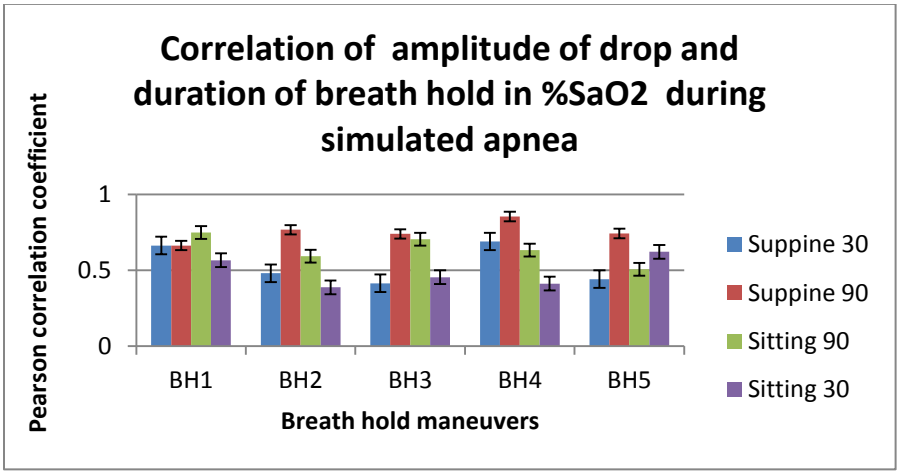


Figure 3.11 Correlation of the amplitude of drop of the %SaO2 waveform and duration of breath hold (BH) maneuvers 1 to 5 during simulated sleep apnea (p-value <0.05)

An ANOVA was performed for the correlation coefficients across the four different protocols (Supine 90, Supine 30, Sitting 90 and Sitting 30), and was found to be statistically significant. Further analysis is performed using post hoc analysis and the significance of correlations across the four protocols individually is obtained and is shown in table 3.7.

Table 3.7 Post hoc analysis on the correlation between amplitude of drop of the %SaO2 waveform and duration of breath hold across the 4 protocols

Protocol versus Protocol
Supine 30 and Supine 90 *
Supine 30 and Sitting 90
Supine 30 and Sitting 30
Supine 90 and Sitting 90
Supine 90 and Sitting 30 *
Sitting 90 and Sitting 30

3.1.4.3 Amplitude of rise vs. duration of breath hold

An ANOVA is performed to obtain the significance of the comparison of amplitude of rise versus the duration of breath hold. A p value of less than 0.05 is obtained for the comparison of the means.

Figure 3.12 shows the correlation coefficient for the comparison of the amplitude of rise of the %SaO2 waveform and the duration of breath hold. A p-value less than 0.05 were obtained for each of the correlation coefficients obtained.

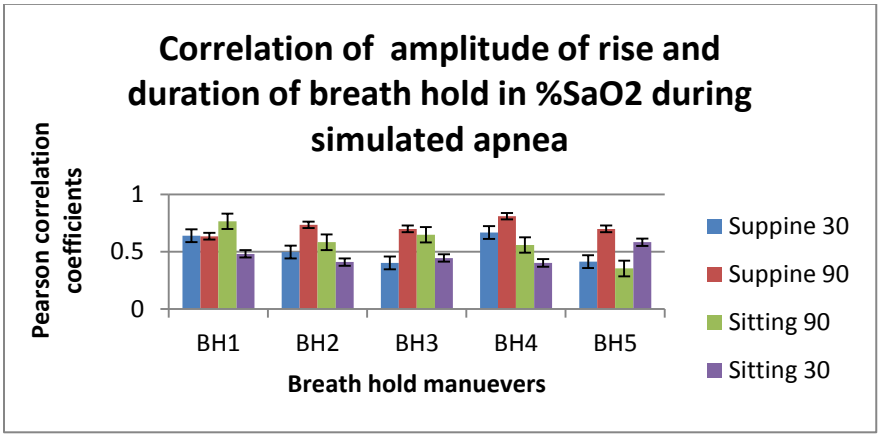


Figure 3.12 Correlation of the amplitude of rise in the %SaO2 waveform and duration of breath hold (BH) maneuvers 1 to 5 during simulated sleep apnea (p-value <0.05)

An ANOVA was also performed for the correlation coefficients across the four different protocols (Supine 90, Supine 30, Sitting 90 and Sitting 30), and was found to be statistically significant. Further analysis was performed using post hoc in Matlab, to obtain the significance of the correlations across the protocols individually. The results are shown in Table 3.8.

Table 3.8 Post hoc analysis on the correlation between amplitude of rise in the %SaO2 waveform and duration of breath hold across the 4 protocols

Protocol versus Protocol
Supine 30 and Supine 90
Supine 30 and Sitting 90
Supine 30 and Sitting 30
Supine 90 and Sitting 90
Supine 90 and Sitting 30 *
Sitting 90 and Sitting 30

Table 3.9 summarizes section 3.1.4 by showing the significant comparisons of the effect of breath hold on the percentage oxygen saturation features (table 3.1).

Table 3.9 Summary of statistical analysis of the effect of breath hold on the percentage oxygen saturation features

Protocol versus Protocol	**Features**		
	Area Under Curve	**Amplitude of drop**	**Amplitude of rise**
Supine 30 and Supine 90	*	*	
Supine 30 and Sitting 90			
Supine 30 and Sitting 30			
Supine 90 and Sitting 90			
Supine 90 and Sitting 30	*	*	*
Sitting 90 and Sitting 30			

*indicates significance p-value less than 0.05

3.1.5 Relationship between the features of CBF and features of %SaO2 waveform

This section, discusses the results obtained of the statistical analysis performed to investigate the relationship between the features obtained from the cerebral blood flow and percentage oxygen saturation waveform (Table 3.1). From Figures 2.19 and 2.22 we see that percentage oxygen saturation drops during the breath hold maneuver and cerebral blood flow

rises during breath hold maneuver. Hence comparison is made on the corresponding features from both of the waveforms to analyze if there is a correlation or dependence on the two data sets. The results are shown below.

3.1.5.1 Area of CBF vs. Area of %SaO2

Figure 3.7 shows the correlation coefficients between the area under the curve in the CBF waveform and the area under the curve in the %SaO2 waveform. Statistical significance of the correlation coefficients was calculated using a t-test. A p-value less than 0.05 were obtained for each of the correlation coefficients obtained

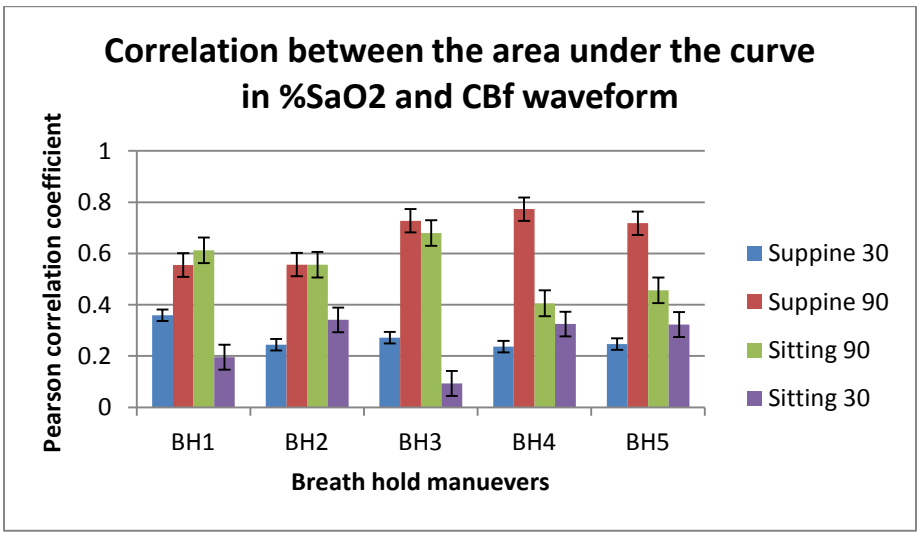


Figure 3.13 Correlation of the area under the curve in %SaO2 and CBF (p-value<0.05)

An ANOVA was also performed for the correlation coefficients across the four different protocols (Supine 30, Supine 90, Sitting 90 and Sitting 30) and was found to be statistically significant. Further analysis using post hoc shows the individual significance of the correlations across the four protocols and is recorded in table 3.10.

Table 3.10 Post hoc analysis on the correlation between area under the curve in the percentage oxygen saturation waveform and cerebral blood flow waveform across the 4 protocols

Protocol versus Protocol
Supine 30 and Supine 90 *
Supine 30 and Sitting 90 *
Supine 30 and Sitting 30
Supine 90 and Sitting 90
Supine 90 and Sitting 30 *
Sitting 90 and Sitting 30 *

3.1.5.2 Time to rise in CBF vs. Time to drop in %SaO2

The mean and standard deviation is calculated for the time to rise of the cerebral blood flow and the time to drop in the percentage oxygen saturation waveform. A t-test is performed to obtain the statistical significance of the means of this comparison. Table 3.11 shows the average and standard deviation values of these features for the five breath hold maneuvers across the four different protocols and also shows the statistical significance of the comparison.

Table 3.11 Average, Standard deviation and Level of significance of the time to rise in CBF vs. the time to drop in %SaO2

Simulated apnea Protocols		**BH1**		**BH2**		**BH3**		**BH4**		**BH5**	
		Time to drop in %SaO2	**Time to rise in CBF**	**Time to drop in %SaO2**	**Time to rise in CBF**	**Time to drop in %SaO2**	**Time to rise in CBF**	**Time to drop in %SaO2**	**Time to rise in CBF**	**Time to drop in %SaO2**	**Time to rise in CBF**
Supine 30	**Average**	27.65	36.69	27.23	37.36	27.68	37.46	29.23	39.64	28.85	40.41
	Stdev	15.28	16.30	19.42	19.94	16.71	23.42	21.78	21.94	16.60	27.79
	p-value	*		*		*		*		*	
Supine 90	**Average**	28.19	37.27	32.10	40.19	30.06	43.46	34.37	40.69	33.20	48.18
	Stdev	15.28	16.30	19.42	19.94	16.71	23.42	21.78	21.94	16.60	27.79
	p-value	*		*		*		*		*	
Sitting 30	**Average**	27.35	36.83	28.45	35.84	23.90	36.11	24.66	36.47	26.92	37.39
	Stdev	11.89	9.93	9.41	8.29	11.17	8.22	8.86	8.12	12.34	8.40
	p-value	*		*		*		*		*	
Sitting 90	**Average**	27.08	34.51	30.45	39.22	29.88	38.64	29.50	41.54	28.54	39.87
	Stdev	10.73	10.51	12.27	12.18	13.77	11.94	16.23	14.23	11.01	11.94
	p-value	*		*		*		*		*	

*p-value is less than 0.05 and is significant

Figure 3.14 shows the correlation coefficients of the comparison between the time to rise in the CBF waveform with the time to drop in the %SaO2 waveform. Statistical significance of the correlation coefficients was calculated using a t-test. A p-value less than 0.05 was obtained for each of the correlation coefficients obtained.

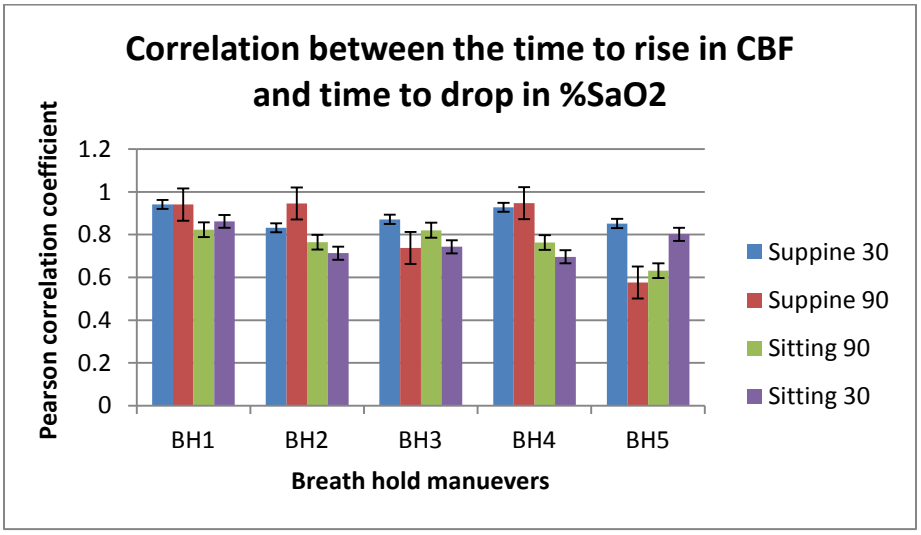


Figure 3.14 Correlation of the time to rise in CBF and time to drop in %SaO2 (p-value<0.05)

An ANOVA was also performed for the correlation coefficients across the four different protocols (Supine 90, Supine 30, Sitting 90 and Sitting 30), and was found to be statistically significant. Further analysis using post hoc is performed and the results are shown in table 3.12.

Table 3.12 Post hoc analysis on the correlation between time to rise in CBF waveform and time to drop in %SaO2 waveform across the 4 protocols

Protocol versus Protocol
Supine 30 and Supine 90 *
Supine 30 and Sitting 90 *
Supine 30 and Sitting 30 *
Supine 90 and Sitting 90 *
Supine 90 and Sitting 30 *
Sitting 90 and Sitting 30 *

Table 3.13 summarizes section 3.1.5 by showing the relation between the cerebral blood flow and the percentage oxygen saturation waveforms.

Table 3.13 Summary of statistical analysis of the correlation between the features obtained with duration of breath hold in the percentage oxygen saturation waveform

Protocol versus Protocol	**Features**	
	Area Under Curve of CBF vs. Area under Curve of %SaO2	**Time to rise in CBF vs. Time to drop in %SaO2**
Supine 30 and Supine 90	*	*
Supine 30 and Sitting 90	*	*
Supine 30 and Sitting 30		*
Supine 90 and Sitting 90		*
Supine 90 and Sitting 30	*	*
Sitting 90 and Sitting 30	*	*

*indicates significance p-value less than 0.05

3.2 Sleep Apnea Study

A sleep apnea study was carried out to compare the results with the simulated apnea study. The demographics of subjects and the methods used are explained in detail Chapter 2 of this thesis. The sleep data was clipped to obtain apnea episodes and the features selected are explained in detail in section 2.5 of this thesis. Statistical Analysis is performed to compare the extracted features derived from the percentage oxygen saturation and cerebral blood flow waveforms (Table 3.1) with the duration of apnea. As explained earlier in this chapter, severity of sleep apnea is usually indicated by the frequency of apnea episodes occurring over a period of sleep. However, it is also important to investigate the relation between the duration of each apnea episode to the level of physiological response. Hence analysis is performed to obtain a relationship between the features obtained from the cerebral blood flow waveforms and the oxygen saturation waveform to the duration of the apnea episode. Also analysis is performed to

obtain a relationship between the cerebral blood flow waveform and percentage oxygen saturation waveform.

3.2.1 Average and Standard deviation of the CBF waveform features during sleep apnea

Table 3.14 shows the average and standard deviation of the features obtained in the cerebral blood flow waveform during the sleep apnea study.

Table 3.14: Average and Standard deviation for the CBF features during sleep apnea

Features of CBF in Sleep apnea	**Average**	**Standard Deviation**
Area	9.4904	2.5
Amplitude of drop	0.2486	0.08
Amplitude of rise	0.1706	0.07
Time to drop	15.29	6.5
Time to rise	29.95	10.8

3.2.2 Effect of duration of apnea episode on CBF waveform features

The extracted features shown in table 3.1, obtained from the cerebral blood flow waveform are compared to the duration of the apnea episode. Statistical Analysis is performed in two steps.

1. ANOVA on the features that are being compared
2. Calculation of the correlation coefficient of the features with the duration of apnea.
3. Measure significance of the correlation coefficient using a t-test.

An ANOVA is performed to obtain the significance of the comparison of the area under the curve, amplitude of drop, amplitude of rise, time to drop and time to rise with the duration of the apnea event . A p value of less than 0.05 is obtained for the comparison of the means.

Figure 3.15 shows the correlation coefficients of the area under the curve, amplitude of drop, amplitude of rise, time to drop and time to rise when compared to the duration of the apnea event.

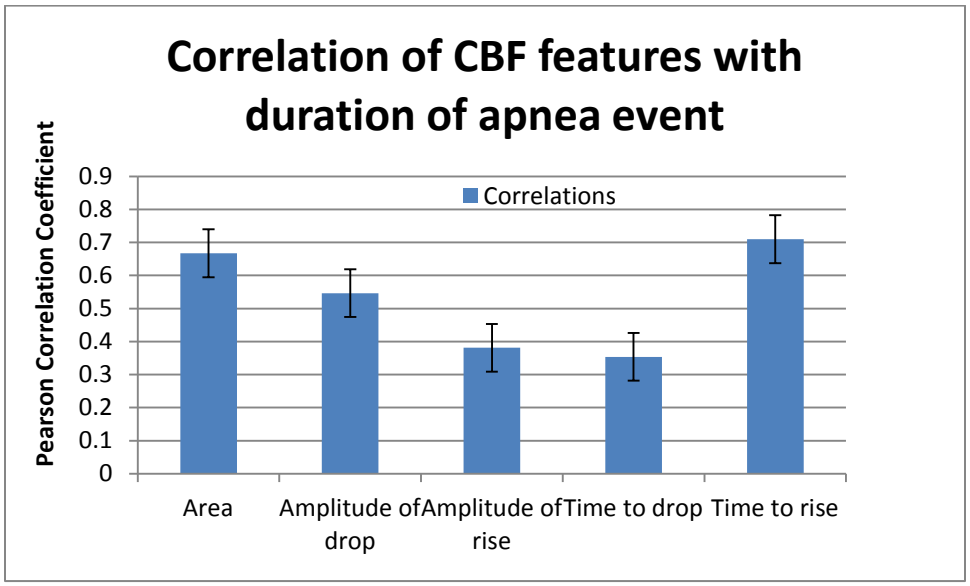


Figure 3.15 Correlation of the cerebral blood flow features with the duration of apnea event in Sleep Apnea study

Statistical significance of the correlation coefficient was calculated using TTEST. Table 3.15 shows the significant correlations.

Table 3.15 Significance of correlations between duration of apnea and CBF features

Correlation of duration of apnea with CBF features
Area under curve *
Amplitude of drop *
Amplitude of rise *
Time to drop*
Time to rise *

*significant feature with p-value less than 0.05

This shows that there is a strong relation between the area, amplitude of rise and drop and the time to rise of the cerebral blood flow waveform to the duration of apnea episode.

3.2.3 Average and Standard deviation of the %SaO2 waveform features during sleep apnea

Table 3.16 shows the average and standard deviation of the features obtained in the percentage oxygen saturation waveform during the sleep apnea study.

Table 3.16: Average and Standard deviation for the %SaO2 features during sleep apnea

Features of CBF in Sleep apnea	Average	Standard Deviation
Area	3.75	2.03
Amplitude of drop	0.22	0.08
Amplitude of rise	0.22	0.08
Time to drop	26.3	7.86
Time to rise	12.28	3.18

3.2.4 Effect of duration of apnea episode on %SaO2 waveform features

The percentage oxygen saturation waveform is analyzed similar to the cerebral blood flow waveform in section 3.2.2. Analysis of the waveform includes calculating the correlation coefficient between the duration of sleep apnea episode and the extracted. Further analysis is performed to obtain the significance of the correlation coefficient using a t-test.

An ANOVA is performed to obtain the significance of the comparison of the area under the curve, amplitude of drop, amplitude of rise, time to drop and time to rise with the duration of the apnea event . A p value of less than 0.05 is obtained for the comparison of the means.

Figure 3.16 shows the correlation coefficients obtained for the comparisons between the duration of apnea with the features obtained from the percentage oxygen saturation waveform during sleep apnea.

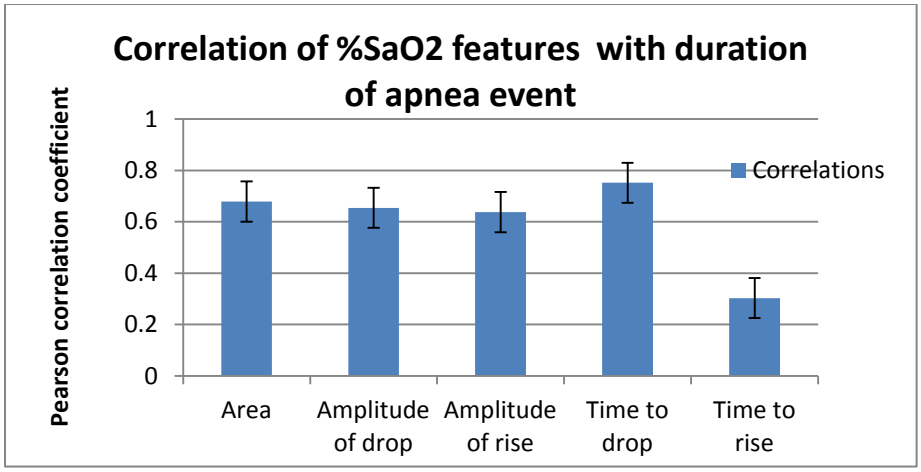


Figure 3.16 Correlation of duration of apnea event and features obtained from %SaO2 waveform

Statistical significance of the correlation coefficient was calculated using a t-test. Table 3.17 shows the significant correlations.

Table 3.17 Significance of correlations between duration of apnea and %SaO2 features

Correlation of duration of apnea with %SaO2 features
Area under curve *
Amplitude of drop *
Amplitude of rise *
Time to drop *
Time to rise

*significant feature with p-value less than 0.05

This shows that there is a significant relation between the area, amplitude of rise and drop and the time to drop of the percentage oxygen saturation waveform to the duration of apnea episode.

3.2.5 Relationship between the features of %SaO2 and CBF waveform

To investigate the relationship between cerebral blood flow and oxygen saturation during sleep apnea, the features obtained from the waveform are compared with each other. Analysis is performed to obtain the correlation of the features obtained in the cerebral blood flow waveform with the features obtained from the oxygen saturation waveform. A t-test is performed to obtain the significance of the obtained correlations.

Figure 3.17 shows the scatter plot of the area under the curve of percentage oxygen saturation waveform versus the area under the curve of the cerebral blood flow waveform. The correlation coefficient obtained for this comparison was 0.56 and was found to be significant. This result shows that there is a strong relationship between the area under the curve of the percentage oxygen saturation waveform and area under the curve for the cerebral blood flow waveform. Regression analysis was performed on the data and a regression line was fitted and is shown in the figure along with its equation. The regression analyses show R to be 0.549 and

R square to be 0.3022. It is also noted that the regression value is significant with a p value of less than 0.05.

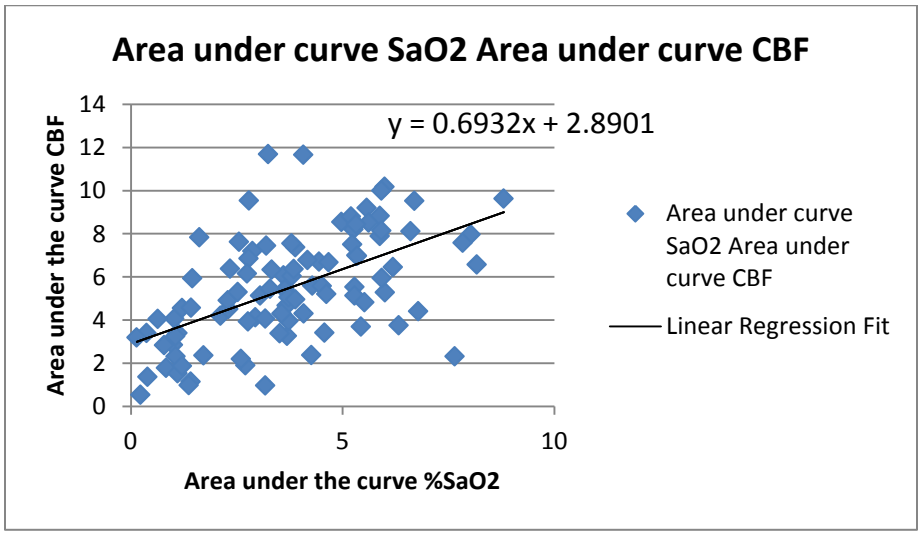


Figure 3.17 Scatter plot – Area of CBF versus Area of %SaO2

Figure 3.18 shows the scatter plot of the amplitude of rise in CBF waveform versus the amplitude of drop in the %SaO2 waveform. The correlation coefficient obtained for this comparison was 0.46 and is found to be statistically significant .This result shows that there is a strong relationship between the amplitude of rise in cerebral blood flow waveform and amplitude of drop in percentage oxygen saturation waveform. Regression analysis was performed on the data and a regression line was fitted and is shown in the figure along with its equation. The regression analyses show R to be 0.456 and R square to be 0.2086. It is also noted that the regression value is significant with a p value of less than 0.05.

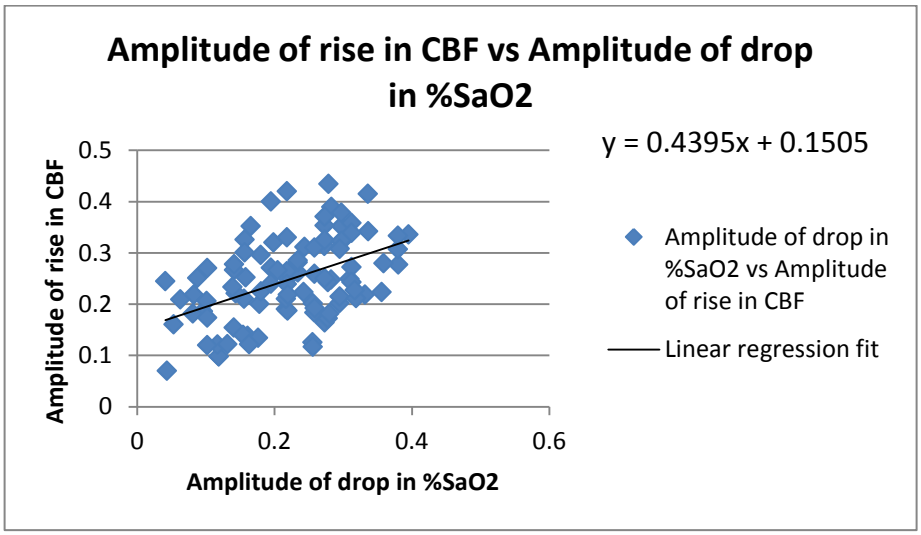


Figure 3.18 Scatter plot - Amplitude of rise in CBF versus Amplitude of drop in %SaO2

Figure 3.19 shows the scatter plot of the comparison made on the time to drop in the %SaO2 waveform versus time to rise in CBF waveform. The correlation coefficient obtained for this comparison was 0.47 and is found to be statistically significant .This result shows that there is a strong relationship between the amplitude of rise in cerebral blood flow waveform and amplitude of drop in percentage oxygen saturation waveform. Regression analysis was performed on the data and a regression line was fitted and is shown in the figure along with its equation. The regression analyses show R to be 0.462 and R square to be 0.213. It is also noted that the regression value is significant with a p value of less than 0.05.

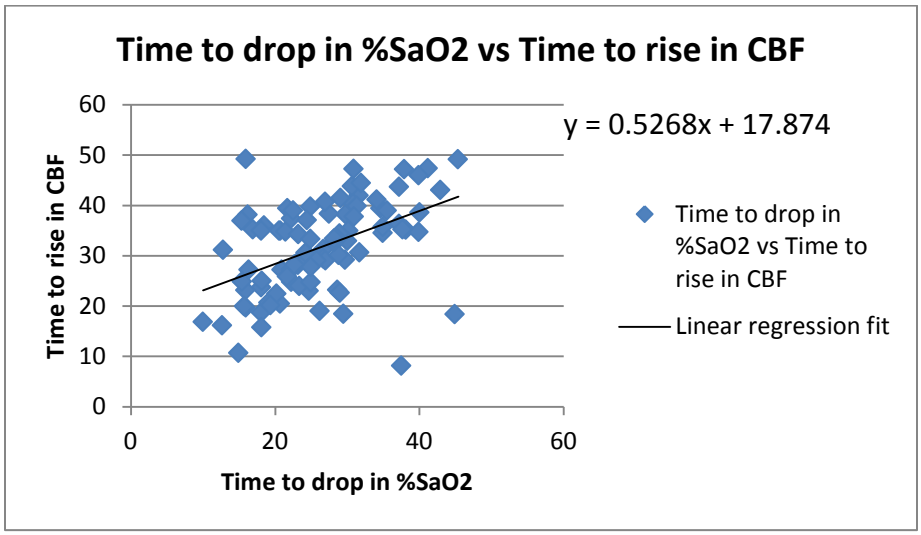


Figure 3.19 Scatter plot - Time to rise in CBF versus Time to drop in %SaO2

Table 3.18 shows the mean, standard deviation of the comparison of the time to drop in %SaO2 and time to rise in CBF and also shows the statistical significance of the comparison using a t-test.

Table 3.18 Mean, Standard deviation and the level of significance of the time to rise in CBF vs. the time to drop in %SaO2.

Sleep Apnea	Time to drop in SaO2	Time to rise in CBF
Average	26.31	31.73
Standard deviation	7.86	8.85
Significance	*	

*p-value is less than 0.05 and is significant

Figure 3.20 shows the correlation coefficients of the comparisons made among the features of %SaO2 and CBF waveforms. Statistical analysis is performed on the correlation coefficients using a t-test. A p-value of lesser than 0.05 was obtained on all correlations coefficient obtained when compared among the features, thus making the correlations statistically significant.

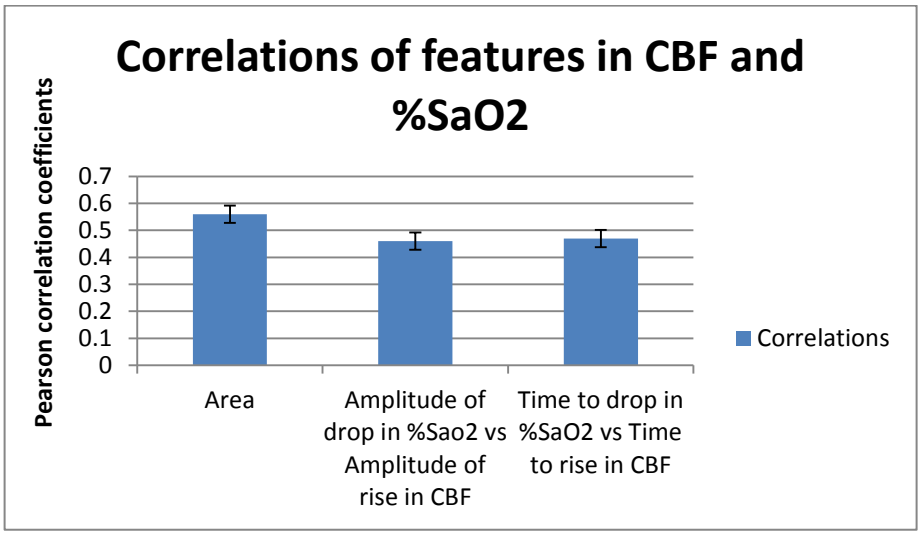


Figure 3.20 Correlation of the Area, Amplitude of drop and rise and time to drop and rise in percentage oxygen saturation waveform and cerebral blood flow velocity waveform during sleep apnea

3.3 Simulated Apnea versus Sleep Apnea Study

This section shows the comparisons performed on the cerebral features for the simulated apnea and sleep apnea study. The average and standard deviation of the features are calculated and a t-test is performed to obtain the level of significance of the comparison of the features.

Table 3.19 shows the average, standard deviation and the level of significance for the comparison of the area under the curve of the CBF waveform in simulated apnea study to the area under the curve of the CBF waveform in sleep apnea study.

Table 3.19 Average, Standard deviation and level of significance of the area under the curve of the CBF waveform in simulated and sleep apnea studies

	Simulated Apnea	Breath hold maneuvers	Average	Standard Deviation	Significance when compared with sleep apnea
Simulated Apnea	Supine 30	BH1	9.259	5.346	* **P value <0.05 and is significant**
		BH2	8.748	4.275	
		BH3	9.038	5.066	
		BH4	9.987	6.087	
		BH5	10.149	5.184	
	Supine 90	BH1	10.627	5.876	
		BH2	12.983	7.115	
		BH3	12.398	8.793	
		BH4	11.787	7.064	
		BH5	12.535	8.168	
	Sitting 30	BH1	8.713	4.463	
		BH2	9.259	5.707	
		BH3	9.015	5.437	
		BH4	9.125	5.473	
		BH5	9.565	4.509	
	Sitting 90	BH1	9.492	6.618	
		BH2	9.858	6.479	
		BH3	10.250	6.267	
		BH4	10.056	8.124	
		BH5	10.826	7.109	
Sleep Apnea	-	-	5.409	2.523	

Table 3.20 shows the average, standard deviation and the level of significance for the comparison of the amplitude of rise of the CBF waveform in simulated apnea study to the amplitude of rise of the CBF waveform in sleep apnea study.

Table 3.20 Average, Standard deviation and level of significance of the amplitude of rise of the CBF waveform in simulated and sleep apnea studies

	Simulated Apnea	Breath hold maneuvers	Average	Standard Deviation	Significance when compared with sleep apnea
Simulated Apnea	Supine 30	BH1	0.2348	0.1026	* **P value <0.05 and is significant**
		BH2	0.2758	0.1433	
		BH3	0.3702	0.1948	
		BH4	0.3034	0.1525	
		BH5	0.3013	0.1461	
	Supine 90	BH1	0.2589	0.1246	
		BH2	0.2917	0.1610	
		BH3	0.2601	0.1378	
		BH4	0.2559	0.1291	
		BH5	0.2616	0.1385	
	Sitting 30	BH1	0.2218	0.0982	
		BH2	0.2785	0.1519	
		BH3	0.2906	0.1600	
		BH4	0.3048	0.1756	
		BH5	0.3187	0.2018	
	Sitting 90	BH1	0.2609	0.1557	
		BH2	0.2413	0.1442	
		BH3	0.2798	0.1502	
		BH4	0.2400	0.1188	
		BH5	0.2318	0.1064	
Sleep Apnea	-	-	0.170794	0.079581	

Table 3.21 shows the average, standard deviation and the level of significance for the comparison of the time to rise of the CBF waveform in simulated apnea study to the time to rise of the CBF waveform in sleep apnea study.

Table 3.21 Average, Standard deviation and level of significance of the time to rise of the CBF waveform in simulated and sleep apnea studies

	Simulated Apnea	Breath hold maneuvers	Average	Standard Deviation	Significance when compared with sleep apnea
Simulated Apnea	Supine 30	BH1	36.694	13.500	* **P value <0.05 and is significant**
		BH2	37.359	10.053	
		BH3	37.463	11.837	
		BH4	39.640	12.552	
		BH5	40.408	11.817	
	Supine 90	BH1	37.270	16.300	
		BH2	40.194	19.942	
		BH3	43.462	23.421	
		BH4	40.688	21.935	
		BH5	48.179	27.791	
	Sitting 30	BH1	36.833	9.934	
		BH2	35.842	8.292	
		BH3	36.107	8.232	
		BH4	36.465	8.114	
		BH5	37.390	8.403	
	Sitting 90	BH1	34.514	10.505	
		BH2	39.219	12.781	
		BH3	38.642	11.930	
		BH4	41.535	14.235	
		BH5	39.871	11.903	
Sleep Apnea	-	-	29.903	5.490	

CHAPTER 4

DISCUSSION AND CONCLUSION

In this chapter, we discuss the interpretation and significance of results presented in the previous chapter. Section 4.1 discusses the results obtained when comparisons are made on features during the simulated apnea study explained in section 3.2 of the thesis. Section 4.2 explains the results obtained when comparisons are made among features in the sleep apnea study explained in section 3.4 of the thesis. Section 4.3 compares the results of the simulated apnea study with the results obtained in the sleep apnea study. Sections 4.4 conclude the thesis and 4.5 discusses the limitations of the study and the future work that can be performed.

The features and comparisons of features can shed light into various physiological changes occurring during sleep apnea and delineate a possible relation between oxygen saturation and cerebral blood flow changes during sleep apnea.

4.1 Simulated Apnea

This section discusses the results obtained during the simulated apnea study. The features extracted from the CBF waveform are the area under the curve, amplitude of drop, amplitude of rise, time to drop, time to rise and duration of breath hold. The features extracted from the %SaO2 waveform are the area under the curve, amplitude of drop, amplitude of rise, time to drop and time to rise. The intent of using these features is explained in detail in Chapter 2 of this thesis.

4.1.1 Effect of duration of breath hold on CBF features during simulated apnea study

Comparisons were made between the extracted features, area, amplitude of drop, amplitude of rise, time to drop and time to rise of the cerebral blood flow waveform to the duration of breath hold in the cerebral blood flow waveform. Features area, amplitude of rise and time to rise of the cerebral blood flow waveform were found to be significant with a p value

of less than 0.05 and are correlated with the duration of breath hold. The Pearson correlation coefficients were calculated for these significant features and the level of significance of the correlation coefficient was obtained. Post Hoc analysis was performed to obtain the significance of the features across the protocols. The effect of breath hold on each of the significant feature is explained in detail below.

4.1.1.1 Effect of breath hold duration on Area of the CBF waveform

The area of the CBF waveform was correlated with the duration of breath hold. Correlation coefficients of 0.69 and 0.50 were obtained for the Supine 90 and Sitting 90 protocols respectively and statistical tests prove them to be significant (pvalue<0.05). A correlation coefficient of 0.5 is considered to be a reasonable correlation. This suggests that the volume of blood flowing through the middle cerebral artery (MCA) is dependent to the duration of the breath hold maneuver. A weaker correlation coefficient with values 0.37 and 0.29 are obtained for the Supine 30 and Sitting 30 protocols respectively. However statistical test shows that nonetheless, the weak correlation coefficient is statistically significant. This may suggest that a greater frequency of breath hold may reduce the covariation of the CBF area with the duration of breath hold.

Statistical analysis show that when comparisons are made across the Supine 90, Sitting 30 and Sitting 90 protocols, the correlation between the area and the duration of breath hold are found to be significant. This shows that there is statistically a 95% chance that the posture and the frequency of the breath hold have an effect on the changes seen in the area of the CBF with respect to the baseline.

4.1.1.2 Effect of breath hold duration on amplitude of rise in CBF waveform

The amplitude of rise in the CBF waveform was correlated with the duration of breath hold. Low correlation coefficients of 0.32 and 0.31 were obtained for the Supine 90 and Sitting 90 protocols respectively. However statistical tests show that nonetheless, the weak correlation coefficient is statistically significant. This suggests that the amount of blood flowing through the

MCA has a low but significant dependency on the duration of breath hold. Supine 30 and Sitting 30 protocols had a low correlation coefficient and was not significant to the duration of the breath hold.

Statistical analysis shows that when comparisons are made across the protocols, the correlation between the amplitude of rise and duration of breath hold is found to be significant only at the Supine 90 and Sitting 90 protocols. This may suggest that for a lower frequency of the breath hold maneuver, a stronger covariance of the Amplitude of rise and duration of breath hold in CBF results.

4.1.1.3 Effect of breath hold duration on the time to rise in CBF waveform

The time to rise in the CBF waveform is correlated with the duration of the breath hold maneuver. A correlation coefficient of 0.98, 0.88, 0.98 and 0.97 is obtained for all the Supine 30, Supine 90, Sitting 90 and Sitting 30 protocols. This shows that there is a strong correlation between the duration of breath hold and the time it takes for the blood to flow through the MCA. This result suggests that as long as the breath hold continues, the volume of blood flow through the MCA continues to rise. However there is no significance of the time taken for the rise in blood to flow to return back to the baseline, at the end of the breath hold maneuver that is represented by the time to drop in the cerebral blood flow waveform.

Statistical analysis shows that when comparisons are made across the Supine 90, Supine 30, Sitting 90 and Sitting 30 protocols the correlation between the time to rise and duration of breath hold is found to be significant at all the protocols. This suggests that the posture or frequency of apnea did not affect the covariation of the apnea duration and time to rise of CBF.

From the analysis seen in section 3.1.1 we can conclude that the volume of blood flowing through the MCA rises significantly during the breath hold. Also, it is noticed that the posture and frequency have a 95% chance to impact the effect of duration of breath hold with

the area and the time to rise in the cerebral blood flow waveform. The posture and frequency have an effect on the amplitude of rise only in the Supine 90 and Sitting 90 protocols.

4.1.2 Effect of duration of breath hold on %SaO2 features in simulated apnea study

Comparisons were made between the duration of breath hold and the extracted features area, time to drop, time to rise, amplitude of drop and amplitude of rise, of the percentage oxygen saturation waveform. Features area, amplitude of drop and amplitude of rise were found to be significant and are correlated to the duration of breath hold. The Pearson correlation coefficients were calculated for these significant features and the level of significance of the correlation coefficient was obtained. Post Hoc analysis was performed to obtain the significance of the features across the protocols. The effect of breath hold on each of the significant feature is explained in detail below.

4.1.2.1 Effect of breath hold duration on area of the %SaO2 waveform

The area of the %SaO2 waveform was correlated with the duration of breath hold. Correlation coefficients of 0.85, 0.74, 0.64 and 0.66 were obtained for the Supine 90, Sitting 90, Sitting 30 and Supine 30 protocols respectively and statistical tests prove them to be significant. This suggests that the level of drop in oxygen saturation in the blood is directly correlated to the duration of the breath hold maneuver. That is a longer breath hold maneuver results in a higher drop in oxygen saturation.

Statistical analysis show that when comparisons are made across the Supine 90, Sitting 30 and Supine 30 protocols, the correlation between the area and the duration of breath hold are found to be significant. This shows that there is statistically a 95% chance that the supine posture and the frequency of the breath hold would have an effect on the changes seen in the area of the %SaO2.

4.1.2.2 Effect of breath hold duration on amplitude of drop in %SaO2 waveform

The amplitude of drop in the %SaO2 waveform was correlated with the duration of breath hold. Correlation coefficients of 0.75 and 0.64 were obtained for the Supine 90 and

Sitting 90 protocols respectively and statistical tests prove them to be significant. This suggests that the drop in oxygen saturation in the blood is highly dependent to the duration of the breath hold maneuver. A weaker correlation coefficient with values of 0.53 and 0.48 were obtained for the Supine 30 and Sitting 30 protocols respectively. However statistical test shows that nonetheless the weak correlation coefficient, it is proved to be significant. This may suggest that a greater frequency of breath hold may reduce the covariation of the %SaO2 amplitude of drop with the duration of breath hold.

Statistical analysis show that when comparisons are made across the Supine 90, Sitting 30 and Supine 30 protocols, the correlation between the amplitude of drop and the duration of breath hold are found to be significant. A few reasons could be that the chest wall inhibits the lungs to expand or that the soft palate collapses and inhibits airflow into the lungs. The frequency of the breath hold also is noted to have an effect on the changes seen in the area of the %SaO2. Statistically a 95 % chance is seen for a 30 sec breath hold maneuver to have an effect on the amplitude of drop in the %SaO2 waveform. Greater the frequency of breath hold, a greater covariance is seen between the area and duration of breath hold in %saO2.

4.1.2.3 Effect of breath hold duration on amplitude of rise in %SaO2 waveform

The amplitude of rise in the %SaO2 waveform was correlated with the duration of breath hold. Correlation coefficients of 0.71 and 0.58 were obtained for the Supine 90 and Sitting 90 protocols and statistical tests prove them to be significant. This suggests that the changes in oxygen saturation in the blood after the end of the breath hold protocol is dependent to the duration of the breath hold maneuver. A weaker correlation coefficient with values of 0.52 and 0.46 were obtained for the Supine 30 and Sitting 30 protocols respectively. However statistical test shows that nonetheless the weak correlation coefficient, it is proved to be significant. This may suggest that a greater frequency of breath hold may reduce the covariation of the %SaO2 amplitude of drop with the duration of breath hold.

Statistical analysis show that when comparisons are made across the protocols, for Supine 90 and Sitting 30, the correlation between the amplitude of rise and the duration of breath hold are found to be significant. This shows that the posture and frequency do not have an effect on the amplitude of rise in %SaO2 waveform.

4.1.3 Relationship between CBF and %SaO2 features during simulated apnea

Comparisons were made between the extracted features, area, amplitude of drop, amplitude of rise, time to drop and time to rise of the cerebral blood flow waveform to the area, amplitude of drop, amplitude of rise, time to drop and time to rise of the %SaO2 waveforms.

Correlation between area of the CBF waveform to the area of the %SaO2 waveform were found to be significant. The correlation coefficient of 0.66 and 0.54 were obtained for the Supine 90 and Sitting 90 protocols respectively. This suggests that the increase in the volume of blood flowing through the MCA is highly interrelated to the drop in the oxygen saturation during a breath hold maneuver. A weaker correlation coefficient with values of 0.27 and 0.25 were obtained for the Supine 30 and Sitting 30 protocols respectively. However statistical test shows that nonetheless the weak correlation coefficient, it is proved to be significant. This may suggest that a greater frequency of breath hold may reduce the covariation of the area of the CBF waveform to the area of the %SaO2 waveform.

Statistical analysis show that when comparisons are made across the Supine 30, Supine 90, Sitting 30 and Sitting 90 protocols, the correlation between the area of the CBF and the area of the %SaO2 are found to be significant. This shows that there is a 95% chance that the posture and the frequency of the breath hold have an effect on the changes seen in the area of the CBF and the area of the %SaO2.

The next set of correlation calculation is made between the time to rise in CBF and the time to drop in the %SaO2 waveform. Figure 3.8 shows that a correlation coefficient of 0.82, 0.88, 0.76 and 0.76 are obtained for the supine 90, supine 30, sitting 90 and sitting 30 protocols respectively. This shows that there is a strong relationship between the time taken for the blood

to flow through the MCA and the time taken for the oxygen saturation of the blood to drop during a breath hold maneuver.

Statistical analysis is performed on the comparison of the time to rise in CBF to the time to drop in %SaO2 and is explained in detail in section 3.1.5.2. This comparison shows that there is a significant difference between the time to drop in %SaO2 and the time to rise in CBF across the 5 breath holds and in all four protocols. This could relate to the physiological responses that occur in the brain during a breath hold episode. As oxygen saturation decreases, the blood pressure increases that in turn increases the intracranial pressure. In order to maintain the intracranial pressure the blood vessels dilate and increase the blood flow.

Statistical analysis show that when comparisons are made across the Supine 30, Supine 90, Sitting 30 and Sitting 90 protocols, the correlation between the time to rise in the CBF waveform and the time to drop in the %SaO2 waveform are found to be significant. This shows that there is a 95% chance that the posture and the frequency of the breath hold have an effect on the changes seen in the time to rise in CBF and the time to drop in the %SaO2. This relation can used to predict the volume of blood flowing through the MCA from the level of oxygen saturation during a breath hold maneuver.

4.2 Sleep Apnea

This section discusses the results obtained during the sleep apnea study. The sleep apnea study was conducted to examine the changes in the response of CBF and %SaO2 due to actual sleep apnea. Further we compared these response to those obtained to the simulated apnea study. The methods and features used during this study are explained in Chapter 2 of this thesis.

4.2.1 Effect of duration of apnea episode on CBF features

Comparisons were made between the extracted features, area, amplitude of rise, amplitude of drop, time to rise and time to drop of the cerebral blood flow waveform to the duration of apnea episode in the CBF waveform. The Pearson correlation coefficients were

obtained for each of the features to the duration of apnea episode. Correlation coefficients 0.66, 0.54 and 0.70 were obtained for the area, amplitude of drop and time to rise of the CBF waveform respectively and statistical test show that they are significant with a p value of less than 0.05.

A lower correlation coefficient 0.38 and 0.35 were obtained for the amplitude of rise and time to drop respectively. However statistical test shows that nonetheless the weak correlation coefficient, it is proved to be significant. This suggests that the volume of blood flow and the time taken by blood to flow through the MCA is strongly related to the duration of apnea episode. That is for a longer apnea episode, the volume of blood flowing through the MCA will be greater.

4.2.2 Effect of duration of apnea episode on %SaO2 features

Comparisons were made between the extracted features, area, amplitude of drop, amplitude of rise, time to drop and time to rise of the percentage oxygen saturation waveform to the duration of apnea episode in the %SaO2 waveform. The Pearson correlation coefficients were obtained for each of the features to the duration of the apnea episode. Correlation coefficients of greater than 0.67, 0.65, 0.63 and 0.75 were obtained for area, amplitude of drop, amplitude of rise and time to drop of the %SaO2 waveform respectively and statistical test prove them to be significant with a p value of less than 0.05.

This suggests that the level of drop in oxygen saturation in the blood is strongly related to the duration of an apnea episode. That is for a longer apnea episode the drop in oxygen saturation is going to be greater, since the blood does not receive oxygen due to the difficulty in breathing during sleep. Time to rise has a lower correlation coefficient of 0.3 and is not significant.

4.2.3 Relation between the features of the %SaO2 waveform and the CBF waveform

Comparisons are made between the features extracted from the %SaO2 waveform to the features extracted from the CBF waveform. The area under the curve of the CBF is

correlated with the area under the curve of %SaO2 waveform. A pearson correlation coefficient of 0.56 is obtained and is found to be significant. This suggests that there is a significant relation between the rise in the volume of blood flow through the MCA and the drop in the percentage oxygen saturation during an apnea episode. This relation is brought about the linear equation shown in figure 3.11. The equation is fitted to the data and provides an estimate of the relationship among the two variables, Area of CBF and Area of %SaO2.

Comparisons were made between the amplitude of rise in CBF to the amplitude of drop in %SaO2. A pearson correlation coefficient of 0.46 is obtained. Though the correlation coefficient is considered to be weak, a level of significance $p<0.05$ is obtained, that shows that the correlation between the amplitude of rise in CBF and the amplitude of drop in %SaO2 is significant. This suggests that the rise in volume of blood flowing through the MCA is related to the drop in oxygen saturation during a sleep apnea episode. This relation is brought about the linear equation shown in figure 3.12. The equation is fitted to the data and provides an estimate of the relationship among the two variables, amplitude of rise in CBF and amplitude of drop in %SaO2.

The last set of comparisons was made between the time to rise in CBF versus the time to drop in %SaO2 waveform. A pearson correlation coefficient of 0.47 was obtained and found to be significant with a p value of less than 0.05. This suggests that the time taken for blood to flow through the MCA is significantly correlated with the time it takes for the oxygen saturation to drop during a apnea episode.

From the analysis above, we can conclude that there is a significant relationship between the duration of the apnea episode with the velocity of blood flowing through the MCA and the changes in oxygen saturation levels during an apnea episode. Also a significant relationship can be obtained between the area, amplitude of drop and time to drop of the percentage oxygen saturation waveform with the area, amplitude of rise and time to rise in the cerebral blood flow waveform.

4.3 Simulated apnea vs. Sleep apnea

In this section, we compare the results obtained from the simulated apnea study seen in section 3.1 with the sleep apnea study seen in section 3.2 of this thesis.

4.3.1 Cerebral Blood Flow

The extracted features area, amplitude of rise, amplitude of drop, time to rise and time to drop were compared to the duration of breath hold in simulated apnea and duration of apnea episode in the sleep apnea study. Table 4.1 shows the significant features obtained for correlations between the features and the duration of breath hold/ apnea episode.

Table 4.1 Simulated apnea vs. Sleep apnea for CBF waveform

Comparison	Simulated Apnea Study		Sleep Apnea study	
Duration of breath hold / apnea episode vs. Features	Features	Protocols	Features	Protocols
	Area *	Supine 90, Sitting 30 and Sitting 90	Area *	N/A
	Amplitude of rise *	Supine 90 and Sitting 90	Amplitude of rise*	N/A
	Time to rise *	Supine 90, Supine 30, Sitting 90 and Sitting 30	Time to rise *	N/A
	Amplitude of drop	N/A	Amplitude of drop *	N/A
	Time to drop	N/A	Time to drop *	N/A

*significant feature with p-value less than 0.05

It is seen that the correlations for all extracted features with the duration of apnea episode were found to be significant in the sleep apnea study. However only correlations between the area, amplitude of rise and time to rise with the duration of the breath hold are significant in the simulated apnea study. It could be due to the fact that the sleep apnea study was performed on a group of individuals between the ages of 50 to 60 and who were previously diagnosed with sleep apnea, and simulated apnea was performed on a group of individuals between the ages of 29 to 33, and had no prior prognosis of difficulty in breathing. The age plays an important factor, as it is known that there is a decline in physiological metabolism with increased age.

Section 3.3 shows the statistical comparison of the means of the CBF features area, amplitude of rise and time to rise during simulated and sleep apnea. It is noted that the mean of the features in the simulated apnea study is greater than that of the sleep apnea study. This could be related to the subject population in the simulated and sleep apnea studies. The simulated apnea study was performed on a group of healthy individuals with no prior diagnosis of apnea and between the age of 29 and 32. However the sleep apnea study was performed on a group of patients with apnea or strongly suspected to have apnea and between the age of 59 and 64. The physiological condition of the sleep apnea subjects were comparatively weak and could have an effect to the mean of the features obtained.

4.3.2 Percentage Oxygen Saturation

The extracted features area, amplitude of rise, amplitude of drop, time to rise and time to drop were compared to the duration of breath hold in simulated apnea and duration of apnea episode in the sleep apnea study. Table 4.2 shows the significant features obtained for correlations between the features and the duration of breath hold/ apnea episode.

Table 4.2 Simulated apnea vs. Sleep apnea for %SaO2 waveform

Comparison	Simulated Apnea Study		Sleep Apnea study	
	Features	Protocols	Features	Protocols
Duration of breath hold / apnea episode vs. Features	Area *	Supine 90, Sitting 30 and Supine 30	Area *	N/A
	Amplitude of rise *	Supine 90 and Sitting 30	Amplitude of rise*	N/A
	Time to rise	N/A	Time to rise	N/A
	Amplitude of drop*	Supine 90, Sitting 30 and Supine 30	Amplitude of drop *	N/A
	Time to drop	N/A	Time to drop *	N/A

*significant feature with p-value less than 0.05

It is seen that the correlations for all area, amplitude of drop, amplitude of rise and time to drop with the duration of apnea episode were found to be significant in the sleep apnea study. However only correlations between the area, amplitude of rise and amplitude of drop with the duration of the breath hold are significant in the simulated apnea study. Non- significance of

time to rise is expected, and can be classified as the physiological robustness of the body. It could be due to the fact that the sleep apnea study was performed on a group of individuals between the ages of 50 to 60 and who were previously diagnosed with sleep apnea, and simulated apnea was performed on a group of individuals between the ages of 29 to 33, and had no prior prognosis of difficulty in breathing. The age plays an important factor, as it is known that there is a decline in physiological metabolism with increased age.

4.3.3 CBF vs. %SaO2

The extracted features area, amplitude of rise and time to rise of the CBF is compared to the area, amplitude of drop and time to drop of the %SaO2 waveform respectively. Correlations were calculated and is explained in detail in sections 4.1.3 and 4.2.3 of this chapter. It is seen that a significant relationship can be obtained between the rise in velocity of blood flow and the drop in oxygen saturation during an apnea episode as well as a breath hold maneuver. This suggests that both in simulated and sleep apnea study we see a significant relationship between the CBFV and the %SaO2.

The means of the time to rise in CBF waveform is compared to the means of the time to drop in %SaO2 and are explained in detail in sections

Thus a model can be created to measure the cerebral blood flow velocity with the percentage oxygen saturation.

4.4 Conclusion

From the results and discussions presented in chapter 3 and 4 for simulated apnea, it has been observed that there is a significant correlation between the duration of the breath hold and the area, amplitude of rise and time to rise of the cerebral blood flow waveform. Also, significant correlation coefficients are obtained between duration of breath hold and the %SaO2 features, area, amplitude of drop and amplitude of rise. A significant correlation is obtained between the area of the CBF to the area of the %SaO2 waveform and the time to rise in CBF to the time to drop in %SaO2 waveform. This shows that the duration of a breath hold maneuver

is an important feature that strongly covaries with the physiological changes (rise in cerebral blood flow and drop in oxygen saturation) in the body and that there is a significant relationship between the cerebral blood flow waveform and the percentage oxygen saturation waveform during a breath hold maneuver.

Similarly from the results and discussions presented in chapter 3 and 4 for actual sleep apnea , it has been observed that there is a significant correlation between the duration of apnea episode and the area, amplitude of rise, amplitude of drop, time to rise and time to drop of the cerebral blood flow waveform. Also, significant correlation coefficients are obtained between apnea episode and the %SaO2 features, area, time to rise, time to drop, amplitude of drop and amplitude of rise. A significant correlation is obtained between the area of the CBF to the area of the %SaO2 waveform, amplitude of drop in %SaO2 to the amplitude of rise in CBF and the time to rise in CBF to the time to drop in %SaO2 waveform. This shows that the duration of an apnea episode is an important feature that strongly covaries with the physiological changes (rise in cerebral blood flow and drop in oxygen saturation) in the body and that there is a significant relationship between the cerebral blood flow waveform and the percentage oxygen saturation waveform during an apnea episode.

4.5 Limitations of the study and Future Work

Feature detection of the cerebral blood flow waveform was found to be challenging as the cerebral blood flow waveform is a very noisy signal and is prone to motion artifacts due to the placement of probe and subject movement during sleep. Due to this, there is a loss in signal in the waveform. Though a filter is applied to remove the noisy artifact, there are still a few abrupt variations seen in the waveform. This affects the peak and valley detection in the cerebral blood flow waveform, thus affecting the features obtained.

This study has discussed a possible relation between the cerebral blood flow and the percentage oxygen saturation. Future work includes noise reduction in the cerebral blood flow waveform, age matching between the simulated apnea and sleep apnea groups, creating a

method of estimating the cerebral blood flow velocity features from the %SaO2 features, and developing a method to diagnose sleep apnea with more simplistic measurement techniques.

APPENDIX A

MATLAB CODE FOR FEATURE EXTRACTION IN %SAO2 WAVEFORM DURING SIMULATED APNEA

%To obtain the name of the file for excel

```
[fname, pathname] = uigetfile('*.lvm', 'Select a .lvm file','MultiSelect','on');
% for z=1:4
filename = fullfile(pathname, fname);
```

%Importing the file

```
result=lvm_import(filename);
savedata=result.Segment1.data;
X=savedata(:,1);
Y=savedata(:,2);
Z = savedata(:,6);
thr=0.005;

current1=0;
current2=0;
current3=0;
current4=0;
current5=0;
current6=0;
current7=0;
current8=0;
current9=0;
current10=0;
current11=0;
current12=0;
current13=0;
current14=0;
current15=0;
current16=0;
current17=0;
current18=0;
current19=0;
current20=0;
current21=0;
current32=0;
timestamps=0;
timestamps2=0;
timestamps22=0;
timestampes=0;
timestampes1=0;
setvalue=zeros(1,5);
setts=zeros(1,5);
abc1=0;
abc2=0;
abc3=0;
abc4=0;
abc5=0;
dips=0;
dipes=0;
finalvalleyset1=0;
```

```
finalvalleyset2=0;
finalvalleyset3=0;
finalvalleyset4=0;
finalvalleyset5=0;
finalvalset1=0;
finalvalset2=0;
finalvalset3=0;
finalvalset4=0;
finalvalset5=0;
```

%Smoothing the waveform

```
width=499;
yy =filtfilt(ones(width,1)/width,1,Y);
```

%% Finding Peaks

```
L=findpeaks(X,yy,0.00000000005,0,10,1,1);
%  figure;
%  plot(X,yy);
peak=L(:,2);%time of the plot after findpeak function
value=L(:,3);%value of the plot after find peak function
%  hold on
%  plot(peak,value,'r*');
```

%Finding the time and the corresponding peak of the %Sao2 waveform.

```
for i=2:length(value)
   G=value(i-1)-value(i);
   if G>thr
      dip=value(i-1);
      timestamp=peak(i-1);
      timestamps=[current1 timestamp];
         dips=[current2 dip];
   end
   current1=timestamps;
   current2=dips;
end
for i=2:length(value)
   M=value(i)-value(i-1);
   if M>thr
      dipe=value(i-1);
      timestampe=peak(i-1);
      timestampes1=[current10 timestampe];
         dipes=[current11 dipe];
   end
   current10=timestampes1;
   current11=dipes;
end
timestampes=timestampes1(2:length(timestampes1));
```

%% Finding the time x-axis of the switch signal(breath hold signal)

```
for i=2:length(Z)
   H=Z(i)-Z(i-1);
   if H>1
      timestamp2=X(i-1);
      timestamps2=[current3 timestamp2];
      end
   current3=timestamps2;

end
for i=2:length(Z)
   H1=Z(i)-Z(i-1);
   if H1<-1
      timestamp22=X(i-1);
      timestamps22=[current32 timestamp22];
      end
   current32=timestamps22;

end
```

%% Finding the final peaks corresponding time and values
%Corresponding time

```
for i=1:length(timestamps)
   if timestamps(i)>timestamps2(2)
      abc1=[current4 timestamps(i)];
   end
   if timestamps(i)>timestamps2(3)
      abc2=[current5 timestamps(i)];
   end
   if timestamps(i)>timestamps2(4)
      abc3=[current6 timestamps(i)];
   end
   if timestamps(i)>timestamps2(5)
      abc4=[current7 timestamps(i)];
   end
   if timestamps(i)>timestamps2(6)
      abc5=[current8 timestamps(i)];
   end
   current4=abc1;
   current5=abc2;
   current6=abc3;
   current7=abc4;
   current8=abc5;
end
finalvalues=[abc1(2) abc2(2) abc3(2) abc4(2) abc5(2)];
```

%Finding the final peaks

```
for i=1:length(finalvalues)
   ind(i)=find(peak==finalvalues(i));
end
```

```
finalpeak=[value(ind(1)) value(ind(2)) value(ind(3)) value(ind(4)) value(ind(5))];
```

%% Finding Valley

```
J=findvalleys(X,yy,0.00000000005,0,10,1,1);
valley=J(:,2);
val=J(:,3);
def1=find(valley > finalvalues(1));%def- valleys between two set of time values(final values)
def2=find(valley > finalvalues(2));
def3=find(valley > finalvalues(3));
def4=find(valley > finalvalues(4));
def5=find(valley > finalvalues(5));
def5final=def5(1)+100;
mat1=val(def1(1):def2(1));
matty1=valley(def1(1):def2(1));
mat2=val(def2(1):def3(1));
matty2=valley(def2(1):def3(1));
mat3=val(def3(1):def4(1));
matty3=valley(def3(1):def4(1));
mat4=val(def4(1):def5(1));
matty4=valley(def4(1):def5(1));
mat5=val(def5(1):def5final);
matty5=valley(def5(1):def5final);

for i=1:length(mat1)

   mi=min(mat1)+0.004;
   if mat1(i)<mi
      finalvalleyset1=[current12 mat1(i)];
      finalvalset1=[current13 matty1(i)];
   end
   current12=finalvalleyset1;
   current13=finalvalset1;

end
for i=1:length(mat2)

   mi2=min(mat2)+0.004;
   if mat2(i)<mi2
      finalvalleyset2=[current14 mat2(i)];
      finalvalset2=[current15 matty2(i)];
   end
   current14=finalvalleyset2;
   current15=finalvalset2;

end
for i=1:length(mat3)

   mi=min(mat3)+0.004;
   if mat3(i)<mi
      finalvalleyset3=[current16 mat3(i)];
      finalvalset3=[current17 matty3(i)];
```

```
    end
    current16=finalvalleyset3;
    current17=finalvalset3;

end
for i=1:length(mat4)

    mi=min(mat4)+0.004;
    if mat4(i)<mi
        finalvalleyset4=[current18 mat4(i)];
        finalvalset4=[current19 matty4(i)];
    end
    current18=finalvalleyset4;
    current19=finalvalset4;

end
for i=1:length(mat5)

    mi=min(mat5)+0.004;
    if mat5(i)<mi
        finalvalleyset5=[current20 mat5(i)];
        finalvalset5=[current21 matty5(i)];
    end
    current20=finalvalleyset5;
    current21=finalvalset5;

end
finalvalset1=finalvalset1(finalvalset1~=0);
finalvalset2=finalvalset2(finalvalset2~=0);
finalvalset3=finalvalset3(finalvalset3~=0);
finalvalset4=finalvalset4(finalvalset4~=0);
finalvalset5=finalvalset5(finalvalset5~=0);
finalvalleyset1=finalvalleyset1(finalvalleyset1~=0);
finalvalleyset2=finalvalleyset2(finalvalleyset2~=0);
finalvalleyset3=finalvalleyset3(finalvalleyset3~=0);
finalvalleyset4=finalvalleyset4(finalvalleyset4~=0);
finalvalleyset5=finalvalleyset5(finalvalleyset5~=0);
finalvalley=[median(finalvalleyset1) median(finalvalleyset2) median(finalvalleyset3)
median(finalvalleyset4) median(finalvalleyset5)];
finalval=[median(finalvalset1) median(finalvalset2) median(finalvalset3) median(finalvalset4)
median(finalvalset5)];
timestamps3=finalval+40;
if length(finalvalset1)==1
    valleytimediff(1)=0;
else
    valleytimediff(1)=finalvalset1(length(finalvalset1))-finalvalset1(1);
end
if length(finalvalset2)==1
    valleytimediff(2)=0;
else
    valleytimediff(2)=finalvalset2(length(finalvalset2))-finalvalset2(1);
end
```

```
if length(finalvalset3)==1
   valleytimediff(3)=0;
else
   valleytimediff(3)=finalvalset3(length(finalvalset3))-finalvalset3(1);
end
if length(finalvalset4)==1
   valleytimediff(4)=0;
else
   valleytimediff(4)=finalvalset4(length(finalvalset4))-finalvalset4(1);
end
if length(finalvalset5)==1
   valleytimediff(5)=0;
else
   valleytimediff(5)=finalvalset5(length(finalvalset5))-finalvalset5(1);
end
```

%% Finding the peak point before the settling point.

```
for i=1:length(timestampes)
   for j=1:5
   if timestampes(i)<timestamps3(j)
      setvalue(j)=dipes(i);
      setts(j)=timestampes(i);
   end
   end

end
```

%% Finding the settling point(ts)

```
setfinalts=zeros(1,5);
setfinalvalue=zeros(1,5);

for i=1:5
   [r,c]=find(L==setts(i));
   setfinalts(i)=L(r+1,c);
   setfinalvalue(i)=L(r+1,c+1);
end
```

%% Plotting

```
figure;
plot(X,yy,X,Z);
axis([0 700 0.80 1.02])
hold on
plot(finalvalues,finalpeak,'r*');
hold on
plot(finalval,finalvalley,'g*')%finalvalley- the valleys of the plot, finalval- the time corresponding
to the valleys in the plot.
hold on
plot(setfinalts,setfinalvalue,'b*');
% hold on
```

```
%
plot(finalvalset1,finalvalleyset1,'y*',finalvalset2,finalvalleyset2,'y*',finalvalset3,finalvalleyset3,'y*',f
inalvalset4,finalvalleyset4,'y*',finalvalset5,finalvalleyset5,'y*');
```

%% Plotting the area

```
for i=1:5
   clipbh=yy(finalvalues(i)*1000:setfinalts(i)*1000);
   timebh=X(finalvalues(i)*1000:setfinalts(i)*1000);
if finalpeak(i)<=setfinalvalue(i)
   clipbh=clipbh-finalpeak(i);
elseif finalpeak(i)>setfinalvalue(i)
   clipbh=clipbh-setfinalvalue(i);
end
clipbh=-clipbh;
areal(i)=trapz(timebh,clipbh);
end
% figure;
% plot(timebh,clipbh);
```

%% Displaying all features

```
htdrop=finalpeak-finalvalley;                %S1
htrise=setfinalvalue-finalvalley;            %S2
switchtimestamp=timestamps2(2:6);
switchtopeaktime=finalvalues-switchtimestamp;   %T1
timedrop=finalval-finalvalues;               %T2
timerise=setfinalts-finalval;                %T3
valleytime=valleytimediff;
peaktime=zeros(1,4);
for i=1:4
   peaktime(i)=finalvalues(i+1)-setfinalts(i);
end
areaucurve=areal;
durationofbh=timestamps22(2:6)-timestamps2(2:6);

display(htdrop);
display(htrise);
display(switchtopeaktime);
display(timedrop);
display(timerise);
display(valleytime);
display(peaktime);
display(areaucurve);
display(durationofbh);
display(finalpeak);
display(finalvalues);
display(finalvalley);
display(finalval);
```

%% Writing to Excel

```
arrhtdrop=num2cell(htdrop);
arrhtrise=num2cell(htrise);
arrswitchtopeaktime=num2cell(switchtopeaktime);
arrtimedrop=num2cell(timedrop);
arrtimerise=num2cell(timerise);
arrvalleytime=num2cell(valleytime);
arrpeaktime=num2cell(peaktime);
arrareaucurve=num2cell(areaucurve);
arrdurationofbh=num2cell(durationofbh);
arrfinalpeak=num2cell(finalpeak);
arrfinalvalues=num2cell(finalvalues);
arrfinalvalley=num2cell(finalvalley);
arrfinalval=num2cell(finalval);
fn = ('D:\jennie\files\Book1.xlsx');
 [num,txt,raw] = xlsread(fn);
 S = size(raw);
 starting_line = S(1) + 1;
 newraw = cell(S(1)+13,S(2));
 for i = 1:S(1)
    newraw(i,:) = raw(i,:);
 end
newraw(starting_line,1) = cellstr(fname{z});
newraw(starting_line+1,1) = cellstr('htdrop');
newraw(starting_line+2,1) = cellstr('htrise');
newraw(starting_line+3,1) = cellstr('swtopktime');
newraw(starting_line+4,1) = cellstr('timedrop');
newraw(starting_line+5,1) = cellstr('timerise');
newraw(starting_line+6,1) = cellstr('valleytime');
newraw(starting_line+7,1) = cellstr('peaktime');
newraw(starting_line+8,1) = cellstr('areaucurve');
newraw(starting_line+9,1) = cellstr('durationofbh');
newraw(starting_line+10,1) = cellstr('finalpeak');
newraw(starting_line+11,1) = cellstr('finalvalues');
newraw(starting_line+12,1) = cellstr('finalvalley');
newraw(starting_line+13,1) = cellstr('finalval');
newraw(starting_line+1,2:6)= arrhtdrop;
newraw(starting_line+2,2:6)= arrhtrise;
newraw(starting_line+3,2:6)= arrswitchtopeaktime;
newraw(starting_line+4,2:6)= arrtimedrop;
newraw(starting_line+5,2:6)= arrtimerise;
newraw(starting_line+6,2:6)= arrvalleytime;
newraw(starting_line+7,2:5)= arrpeaktime;
newraw(starting_line+8,2:6)= arrareaucurve;
newraw(starting_line+9,2:6)= arrdurationofbh;
newraw(starting_line+10,2:6)= arrfinalpeak;
newraw(starting_line+11,2:6)= arrfinalvalues;
newraw(starting_line+12,2:6)= arrfinalvalley;
newraw(starting_line+13,2:6)= arrfinalval;
xlswrite(fn,newraw);
fprintf(1,'\n  The above results have been added to the file %s.\n\n\n', fn);

end
```

APPENDIX B

MATLAB CODE FOR FEATURE EXTRACTION IN %SAO2 WAVEFORM DURING SLEEP APNEA

. **%To obtain the name of the file for excel**

```
[fname, pathname] = uigetfile('*.mat', 'Select a .mat file');

filename = fullfile(pathname, fname);
Importing the file
load(filename);
X=savedata(:,1);
Y=savedata(:,12);
Z=savedata(:,15);
thr=0.005;
Smoothing the waveform
width=499;
yy =filtfilt(ones(width,1)/width,1,Y);
current1=0;
current2=0;
current3=0;
current4=0;
current5=0;
current6=0;
current7=0;
current8=0;
current9=0;
current10=0;
```

% Finding Peaks

```
L=findpeaks(X,yy,0.00000000005,0,10,1,1);
 peaktime=L(:,2);%time of the plot after findpeak function
peakvalue=L(:,3);%value of the plot after find peak function
 % Finding the time x-axis of the event signal(apnea scored signal)
for i=2:(length(Z)-1)
   H=round(Z(i));
   I=round(Z(i+1));
   G=round(Z(i-1));
   if H==1
     if I==2
         tsr=X(i);
         timestampsrise=[current1 tsr];
         current1=timestampsrise;
      elseif G==2
         tsf=X(i-1);
         timestampsfall=[current2 tsf];
         current2=timestampsfall;
      end

   end
end

this was done to overwrite if a different clip is chosen other than the usual
ones.
timestamprise=timestampsrise(2); % change if need to take second rise
```

```
timestampfall=timestampsfall(2);% change if need to take second fall


if round(Z(length(Z)))==1 && length(timestampsrise)==1
   timestamprise=X(length(Z));
end
if round(Z(1))==1
  timestampfall=X(1);
end

% Finding the peak

for i=1:length(peakvalue)
   if peaktime(i)>timestampfall && peaktime(i)<=timestamprise
      temppeakvalue=[current3 peakvalue(i)];
      temppeaktime=[current4 peaktime(i)];
      current3=temppeakvalue;
      current4=temppeaktime;
   end
end
finalpeakvalue=max(temppeakvalue);
for i=1:length(temppeakvalue)
   ind=find(temppeakvalue==finalpeakvalue);
end
finalpeaktime=temppeaktime(ind);

% Finding Valleys

J=findvalleys(X,yy,0.00000000005,0,10,1,1);
valleytime=J(:,2);
valleyvalue=J(:,3);

% Finding the settling point

for i=1:length(valleyvalue)
   if valleytime(i)>timestamprise
      temp1valleytime=[current5 valleytime(i)];
      temp1valleyvalue=[current6 valleyvalue(i)];
      current5=temp1valleytime;
      current6=temp1valleyvalue;
   end
end
settlingpointvalue=max(temp1valleyvalue);
for i=1:length(temp1valleyvalue)
   index=find(temp1valleyvalue==settlingpointvalue);
end
settlingpointtime=temp1valleytime(index(1));

% Finding valleypoint

for i=1:length(valleyvalue)
   if valleytime(i)>finalpeaktime && valleytime(i)<=settlingpointtime
```

```
        mat1value=[current7 valleyvalue(i)];
        mat1time=[current8 valleytime(i)];
        current7=mat1value;
        current8=mat1time;
    end
end
mat1value=mat1value(2:length(mat1value));
mat1time=mat1time(2:length(mat1time));
for i=1:length(mat1value)

    mi=min(mat1value)+0.005;
    if mat1value(i)<mi
        finalvalleysetvalues=[current9 mat1value(i)];
        finalvalleysettimes=[current10 mat1time(i)];
        current9=finalvalleysetvalues;
        current10=finalvalleysettimes;
    end

end

finalvalleysetvalues=finalvalleysetvalues(2:length(finalvalleysetvalues));
finalvalleysettimes=finalvalleysettimes(2:length(finalvalleysettimes));
finalvalleyvalue=median(finalvalleysetvalues);
finalvalleytime=median(finalvalleysettimes);
valleytimediff=finalvalleysettimes(length(finalvalleysettimes))-finalvalleysettimes(1);

   % Plotting
 figure;
 plot(X,Z);
 hold on
 plot(X,yy);
 hold on
 plot(valleytime,valleyvalue,'c*');
 hold on
 plot(timestampfall,1,'y*',timestamprise,1,'y*');
 hold on
 plot(finalpeaktime,finalpeakvalue,'r*');
 hold on
 plot(settlingpointtime,settlingpointvalue,'b*');
 hold on
 plot(finalvalleytime,finalvalleyvalue,'g*');

 % Plotting the area

if finalpeakvalue<=settlingpointvalue
    mat1value=mat1value-finalpeakvalue;
elseif finalpeakvalue>settlingpointvalue
    mat1value=mat1value-settlingpointvalue;
end
mat1value=-mat1value;
areal=trapz(mat1time,mat1value);
```

```
figure;
plot(mat1time,mat1value);
```

% Displaying all features

```
htdrop=finalpeakvalue-finalvalleyvalue;                %S1
htrise=settlingpointvalue-finalvalleyvalue;            %S2
switchtimestamp=timestamps2(2:6);
switchtopeaktime=finalpeaktime-timestampfall;   %T1
timedrop=abs(finalpeaktime-finalvalleytime);              %T2
timerise=settlingpointtime-finalvalleytime;               %T3
valleytime=valleytimediff;
areaucurve=areal;
durationofevent=timestamprise-timestampfall;

display(htdrop);
display(htrise);
display(switchtopeaktime);
display(timedrop);
display(timerise);
display(valleytime);
display(areaucurve);
display(durationofevent);
display(finalpeak);
display(finalvalues);
display(finalvalley);
display(finalval);
```

% Writing to Excel

```
arrhtdrop=num2cell(htdrop);
arrhtrise=num2cell(htrise);
arrswitchtopeaktime=num2cell(switchtopeaktime);
arrtimedrop=num2cell(timedrop);
arrtimerise=num2cell(timerise);
arrvalleytime=num2cell(valleytime);
arrareaucurve=num2cell(areaucurve);
arrdurationofevent=num2cell(durationofevent);
arrfinalpeak=num2cell(finalpeak);
arrfinalvalues=num2cell(finalvalues);
arrfinalvalley=num2cell(finalvalley);
arrfinalval=num2cell(finalval);

fn = ('D:\jennie\files\Book1.xlsx');
 [num,txt,raw] = xlsread(fn);
 S = size(raw);
 starting_line = S(1) + 1;
 newraw = cell(S(1)+13,S(2));
 for i = 1:S(1)
    newraw(i,:) = raw(i,:);
 end
newraw(starting_line,1) = cellstr(fname);
```

```
newraw(starting_line+1,1) = cellstr('htdrop');
newraw(starting_line+2,1) = cellstr('htrise');
newraw(starting_line+3,1) = cellstr('swtopktime');
newraw(starting_line+4,1) = cellstr('timedrop');
newraw(starting_line+5,1) = cellstr('timerise');
newraw(starting_line+6,1) = cellstr('valleytime');
newraw(starting_line+7,1) = cellstr('areaucurve');
newraw(starting_line+8,1) = cellstr('durationofbh');
newraw(starting_line+9,1) = cellstr('finalpeak');
newraw(starting_line+10,1) = cellstr('finalvalues');
newraw(starting_line+11,1) = cellstr('finalvalley');
newraw(starting_line+12,1) = cellstr('finalval');
newraw(starting_line+1,2)= arrhtdrop;
newraw(starting_line+2,2)= arrhtrise;
newraw(starting_line+3,2)= arrswitchtopeaktime;
newraw(starting_line+4,2)= arrtimedrop;
newraw(starting_line+5,2)= arrtimerise;
newraw(starting_line+6,2)= arrvalleytime;
newraw(starting_line+7,2)= arrareaucurve;
newraw(starting_line+8,2)= arrdurationofevent;
newraw(starting_line+9,2)= arrfinalpeak;
newraw(starting_line+10,2)= arrfinalvalues;
newraw(starting_line+11,2)= arrfinalvalley;
newraw(starting_line+12,2)= arrfinalval;

xlswrite(fn,newraw);
fprintf(1,'\n  The above results have been added to the file %s.\n\n\n', fn);
```

APPENDIX C

MATLAB CODE FOR FEATURE EXTRACTION IN CBF WAVEFORM DURING SIMULATED APNEA

```
%To obtain the name of the file for excel
[fname, pathname] = uigetfile('*.lvm', 'Select a .lvm file','MultiSelect','on');
for z=1:4
filename = fullfile(pathname, fname{z});

%Importing the file
result=lvm_import(filename);
savedata=result.Segment1.data;
X=savedata(:,1);
Y=savedata(:,7);
Z = savedata(:,6);
thr=0.005;

%Smoothing the waveform
width=1000;
yy =filtfilt(ones(width,1)/width,1,Y);
% figure;
% plot(X,yy);
% hold on
% plot(X,Z);
current1=0;
current2=0;
current3=0;
current4=0;
current5=0;
current6=0;
current7=0;
 current8=0;

%% Finding Valleys
L=findvalleys(X,yy,0.00000000005,0,10,1,1);
%  figure;
%  plot(X,yy);
valleytime=L(:,2);%time of the plot after findpeak function
valleyvalue=L(:,3);%value of the plot after find peak function
% hold on
%  plot(valleytime,valleyvalue,'r*');
%  hold on
%  plot(X,Z);

 %% Finding Peaks
 K=findpeaks(X,yy,0.00000000005,0,10,1,1);
%  figure;
%  plot(X,yy);
peaktime=K(:,2);%time of the plot after findpeak function
peakvalue=K(:,3);%value of the plot after find peak function
% hold on
%  plot(peaktime,peakvalue,'g*');
%  hold on
%  plot(X,Z);
```

```
 %% Finding the time x-axis of the switch signal(breath hold signal)
for i=2:length(Z)
   H=Z(i)-Z(i-1);
   if H>1
      timestamp2=X(i-1);
      timestampsrise=[current1 timestamp2];
      current1=timestampsrise;
      end


end
timestampsrise=timestampsrise(2:6);
for i=2:length(Z)
   H1=Z(i)-Z(i-1);
   if H1<-1
      timestamp22=X(i-1);
      timestampsfall=[current2 timestamp22];
      current2=timestampsfall;
      end


end
timestampsfall=timestampsfall(2:6);

 %% Finding the highest point(peak) of CBF
 for j=1:4
 current3=0;
 current4=0;
  for i=1:length(peaktime)
if peaktime(i)>timestampsfall(j) && peaktime(i)<timestampsrise(j+1)
mat1time=[current3 peaktime(i)]; %mat1 is the peak times within the switch times
mat1value=[current4 peakvalue(i)];
current3=mat1time;
current4=mat1value;
end
 end
 mat1time=mat1time(2:length(mat1time));
 mat1value=mat1value(2:length(mat1value));
 finalpeakvalue=max(mat1value);

 %Finding the final peaks

ind=find(finalpeakvalue==mat1value);

finalpeaktime=mat1time(ind);
finalpeakvalues=[current5 finalpeakvalue];
current5=finalpeakvalues;
finalpeaktimes=[current6 finalpeaktime];
current6=finalpeaktimes;
 end

 %Finding the last peak
```

```
 current3=0;
 current4=0;
 for i=1:length(peaktime)
 if peaktime(i)>timestampsfall(5)
    mat1time=[current3 peaktime(i)]; %mat1 is the peak times within the switch times
mat1value=[current4 peakvalue(i)];
current3=mat1time;
current4=mat1value;
 end
 end
finalpeakvalues(6)=max(mat1value);
ind=find(finalpeakvalues(6)==mat1value);
finalpeaktimes(6)=mat1time(ind);
finalpeaktimes=finalpeaktimes(2:6);
finalpeakvalues=finalpeakvalues(2:6);
%% Finding lowest point of CBF
for j=1:5
    current5=0;
 current6=0;

  for i=1:length(valleytime)
if valleytime(i)>timestampsfall(j) && valleytime(i)<timestampsfall(j)+30
mat2time=[current5 valleytime(i)]; %mat2 is the valley times within the switch times
mat2value=[current6 valleyvalue(i)];
current5=mat2time;
current6=mat2value;
end
 end
 mat2time=mat2time(2:length(mat2time));
 mat2value=mat2value(2:length(mat2value));
 finalvalleyvalue=min(mat2value);
 ind=find(finalvalleyvalue==mat2value);
finalvalleytime=mat2time(ind);
finalvalleyvalues=[current7 finalvalleyvalue];
current7=finalvalleyvalues;
finalvalleytimes=[current8 finalvalleytime];
current8=finalvalleytimes;
 end
 finalvalleytimes=finalvalleytimes(2:6);
 finalvalleyvalues=finalvalleyvalues(2:6);
 %% Finding yellow point
for i=1:5
    yellowpointind(i)=find(timestampsrise(i)==X);
    yellowpointval(i)=yy(yellowpointind(i));
    yellowpointtime(i)=X(yellowpointind(i));
end
 figure;
 plot(X,yy);
 hold on
 plot(finalpeaktimes,finalpeakvalues,'*g');
 hold on
```

```
 plot(finalvalleytimes, finalvalleyvalues,'*r');
 hold on
 plot(X,Z);
 hold on
 plot(yellowpointtime,yellowpointval,'*y');
 %% Plotting the area
for i=1:5
    clipbh=yy(yellowpointtime(i)*1000:finalvalleytimes(i)*1000);
    timebh=X(yellowpointtime(i)*1000:finalvalleytimes(i)*1000);
if yellowpointval(i)<=finalvalleyvalues(i)
    clipbh=clipbh-yellowpointval(i);
elseif yellowpointval(i)>finalvalleyvalues(i)
    clipbh=clipbh-finalvalleyvalues(i);
end

areal(i)=trapz(timebh,clipbh);
end
% figure;
% area(timebh,clipbh);
 %% Displaying all features

 htdrop=finalpeakvalues-finalvalleyvalues;
 htrise=abs(finalvalleyvalues(1:4)-yellowpointval(2:5));
 switchtopeaktime=abs(yellowpointval-finalpeakvalues);
 timedrop=abs(finalpeaktimes-finalvalleytimes);
 timerise=abs(finalvalleytimes(1:4)-yellowpointtime(2:5));
 durationofbh=timestampsfall-timestampsrise;
 areaucurve=areal;
 display(htdrop);
 display(htrise);
 display(switchtopeaktime);
 display(timedrop);
 display(timerise);
 display(areaucurve);
 display(durationofbh);
  display(finalpeakvalues);
 display(finalpeaktimes);
 display(finalvalleyvalues);
 display(finalvalleytimes);

 % Writing to Excel

arrhtdrop=num2cell(htdrop);
arrhtrise=num2cell(htrise);
arrswitchtopeaktime=num2cell(switchtopeaktime);
arrtimedrop=num2cell(timedrop);
arrtimerise=num2cell(timerise);
arrareaucurve=num2cell(areaucurve);
arrdurationofbh=num2cell(durationofbh);
arrfinalpeakvalues=num2cell(finalpeakvalues);
arrfinalpeaktimes=num2cell(finalpeaktimes);
arrfinalvalleyvalues=num2cell(finalvalleyvalues);
```

```
arrfinalvalleytimes=num2cell(finalvalleytimes);

fn = ('D:\jennie\files\Book1.xlsx');
 [num,txt,raw] = xlsread(fn);
 S = size(raw);
 starting_line = S(1) + 1;
 newraw = cell(S(1)+11,S(2));
 for i = 1:S(1)
    newraw(i,:) = raw(i,:);
 end
newraw(starting_line,1) = cellstr(fname{z});
newraw(starting_line+1,1) = cellstr('htdrop');
newraw(starting_line+2,1) = cellstr('htrise');
newraw(starting_line+3,1) = cellstr('swtopktime');
newraw(starting_line+4,1) = cellstr('timedrop');
newraw(starting_line+5,1) = cellstr('timerise');
newraw(starting_line+6,1) = cellstr('areaucurve');
newraw(starting_line+7,1) = cellstr('durationofbh');
newraw(starting_line+8,1) = cellstr('finalpeakvalues');
newraw(starting_line+9,1) = cellstr('finalpeaktimes');
newraw(starting_line+10,1) = cellstr('finalvalleyvalues');
newraw(starting_line+11,1) = cellstr('finalvalleytimes');
newraw(starting_line+1,2:6)= arrhtdrop;
newraw(starting_line+2,2:5)= arrhtrise;
newraw(starting_line+3,2:6)= arrswitchtopeaktime;
newraw(starting_line+4,2:6)= arrtimedrop;
newraw(starting_line+5,2:5)= arrtimerise;
newraw(starting_line+6,2:6)= arrareaucurve;
newraw(starting_line+7,2:6)= arrdurationofbh;
newraw(starting_line+8,2:6)= arrfinalpeakvalues;
newraw(starting_line+9,2:6)= arrfinalpeaktimes;
newraw(starting_line+10,2:6)= arrfinalvalleyvalues;
newraw(starting_line+11,2:6)= arrfinalvalleytimes;

xlswrite(fn,newraw);
fprintf(1,'\n  The above results have been added to the file %s.\n\n\n', fn);
end
%
% %
```

APPENDIX D

MATLAB CODE FOR FEATURE EXTRACTION IN CBF WAVEFORM DURING SLEEP APNEA

```
%To obtain the name of the file for excel

[fname, pathname] = uigetfile('*.mat', 'Select a .mat file','MultiSelect','on');
 for z=1:4
filename = fullfile(pathname, fname{z});
Importing the file
load(filename);
X=savedata(:,1);
Y=savedata(:,7);
Z=savedata(:,15);
Z=z*0.1;
thr=0.005;
Smoothing the waveform
width=1000;
yy =filtfilt(ones(width,1)/width,1,Y);
current1=0;
current2=0;
current3=0;
current4=0;
current5=0;
current6=0;

% Finding Valleys
L=findvalleys(X,yy,0.00000000005,0,10,1,1);
valleytime=L(:,2);%time of the plot after findpeak function
valleyvalue=L(:,3);%value of the plot after find peak function

 % Finding Peaks
 K=findpeaks(X,yy,0.00000000005,0,10,1,1);
peaktime=K(:,2);%time of the plot after findpeak function
peakvalue=K(:,3);%value of the plot after find peak function

  % Finding the time x-axis of the event signal(apnea scored signal)
for i=2:(length(Z)-1)
   H=round(Z(i));
   I=round(Z(i+1));
   G=round(Z(i-1));
   if H==1
     if I==2
         tsr=X(i);
         timestampsrise=[current1 tsr];
         current1=timestampsrise;
      elseif G==2
         tsf=X(i-1);
         timestampsfall=[current2 tsf];
         current2=timestampsfall;
      end

   end
end

%% this was done to overwrite if a different clip is chosen other than the usual
```

ones.

```
timestamprise=timestampsrise(2); % change if need to take second rise
timestampfall=timestampsfall(2);% change if need to take second fall


if round(Z(length(Z)))==1 && length(timestampsrise)==1
   timestamprise=X(length(Z));
end
if round(Z(1))==1
  timestampfall=X(1);
end
% Finding the maximum peak of the signal

finalpeakvalue=max(peakvalue);
for i=1:length(peakvalue)
   ind=find(peakvalue==finalpeakvalue);
end
finalpeaktime=peaktime(ind);

% Finding the minimum valley of the clip/ Signal
 for i=1:length(valleytime)
if valleytime(i)>finalpeaktime;
mat2time=[current3 valleytime(i)]; %mat2 is the valley times within the switch times
mat2value=[current4 valleyvalue(i)];
current3=mat2time;
current4=mat2value;
end
 end
 mat2value=mat2value(2:length(mat2value));
 mat2time=mat2time(2:length(mat2time));
finalvalleyvalue=min(mat2value);
for i=1:length(valleyvalue)
  index=find(valleyvalue==finalvalleyvalue);
end
finalvalleytime=valleytime(index);

% Finding redpoint
redpointtime=peaktime(1);
redpointvalue=peakvalue(1);

% Plotting the area
for i=1:length(X)
   if X(i)>=redpointtime && X(i)<finalvalleytime
      mat1value=[current5 yy(i)];
      mat1time=[current6 X(i)];
   current5=mat1value;
   current6=mat1time;
   end
end
clipbh=mat1value(2:length(mat1value));
timebh=mat1time(2:length(mat1time));
```

```
if redpointvalue<=finalvalleyvalue
   clipbh=clipbh-redpointvalue;
elseif redpointvalue>finalvalleyvalue
   clipbh=clipbh-finalvalleyvalue;
end

areal=trapz(timebh,clipbh);

figure;
area(timebh,clipbh);
% Plotting
figure;
 plot(X,Z*0.1);
 hold on
 plot(X,yy);
hold on
plot(finalpeaktime,finalpeakvalue,'c*');
hold on
plot(finalvalleytime,finalvalleyvalue,'g*');
hold on
plot(redpointtime,redpointvalue,'r*');
hold on
plot(timestampfall,1,'y*',timestamprise,1,'y*');
```

% Displaying all features

```
htdrop=finalpeakvalue-finalvalleyvalue;                %S1
htrise=finalpeakvalue-redpointvalue;            %S2
switchtimestamp=timestamps2(2:6);
switchtopeaktime=abs(finalpeaktime-timestampfall);   %T1
timedrop=abs(finalpeaktime-finalvalleytime);              %T2
timerise=abs(redpointtime-finalpeaktime);              %T3
valleytime=valleytimediff;
areaucurve=areal;
durationofevent=timestamprise-timestampfall;

display(htdrop);
display(htrise);
display(switchtopeaktime);
display(timedrop);
display(timerise);
display(valleytime);
display(areaucurve);
display(durationofevent);
display(finalpeak);
display(finalvalues);
display(finalvalley);
display(finalval);
% Writing to Excel
arrhtdrop=num2cell(htdrop);
arrhtrise=num2cell(htrise);
```

```
arrswitchtopeaktime=num2cell(switchtopeaktime);
arrtimedrop=num2cell(timedrop);
arrtimerise=num2cell(timerise);
arrvalleytime=num2cell(valleytime);
arrareaucurve=num2cell(areaucurve);
arrdurationofevent=num2cell(durationofevent);
arrfinalpeak=num2cell(finalpeak);
arrfinalvalues=num2cell(finalvalues);
arrfinalvalley=num2cell(finalvalley);
arrfinalval=num2cell(finalval);

fn = ('D:\jennie\files\Book1.xlsx');
 [num,txt,raw] = xlsread(fn);
 S = size(raw);
 starting_line = S(1) + 1;
 newraw = cell(S(1)+13,S(2));
 for i = 1:S(1)
    newraw(i,:) = raw(i,:);
 end
newraw(starting_line,1) = cellstr(fname{z});
newraw(starting_line,2) = cellstr('htdrop');
newraw(starting_line,3) = cellstr('htrise');
newraw(starting_line,4) = cellstr('swtopktime');
newraw(starting_line,5) = cellstr('timedrop');
newraw(starting_line,6) = cellstr('timerise');
% newraw(starting_line+6,1) = cellstr('valleytime');
newraw(starting_line,7) = cellstr('areaucurve');
newraw(starting_line,8) = cellstr('durationofbh');
newraw(starting_line+9,1) = cellstr('finalpeak');
newraw(starting_line+10,1) = cellstr('finalvalues');
newraw(starting_line+11,1) = cellstr('finalvalley');
newraw(starting_line+12,1) = cellstr('finalval');
newraw(starting_line,2)= arrhtdrop;
newraw(starting_line,3)= arrhtrise;
newraw(starting_line,4)= arrswitchtopeaktime;
newraw(starting_line,5)= arrtimedrop;
newraw(starting_line,6)= arrtimerise;
newraw(starting_line+6,2)= arrvalleytime;
newraw(starting_line,7)= arrareaucurve;
newraw(starting_line,8)= arrdurationofevent;
newraw(starting_line+9,2)= arrfinalpeak;
newraw(starting_line+10,2)= arrfinalvalues;
newraw(starting_line+11,2)= arrfinalvalley;
newraw(starting_line+12,2)= arrfinalval;

xlswrite(fn,newraw);
fprintf(1,'\n  The above results have been added to the file %s.\n\n\n', fn);

 end
```

REFERENCES

1. James E. Gangwisch, S. B. H., Bernadette Boden-Albala, Ruud M. Buijs, Felix Kreier, Thomas G. Pickering, Andrew G. Rundle, Gary K. Zammit, and Dolores Malaspina. Short Sleep Duration as a Risk Factor for Hypertension: Analyses of the First National Health and Nutrition Examination Survey. Hypertension 47: 833-839, 2006.
2. TERRY Young, Paul E. Peppard and Daniel J. Gottlieb. Epidemiology of Obstructive Sleep Apnea A Population Health Perspective. American Journal of Respiratory and Critical Care Medicine. 165: 1217-1239, 2002
3. Terry Young, Mari Palta, Jerome Dempsey, James Skatrud, Steven Weber and Safwan Badr. The Occurrence of Sleep-Disordered Breathing among Middle-Aged Adults. N Engl J Med. 328: 1230-1235, 1993
4. Guilleminault, C., Tilkian, A., & Dement, W. C. (1976). The sleep apnea syndromes. Annual review of medicine, 27(1), 465-484.
5. Eckert DJ, Jordan AS, Merchia P, Malhotra A. Central sleep apnea: pathophysiology and treatment. Chest. 2007;131:595-607
6. Kasai T, Bradley TD. Obstructive sleep apnea and heart failure: pathophysiologic and therapeutic implications. J Am Coll Cardiol. 2011;57:119-127
7. Gay, P. C. (2008). Complex sleep apnea: it really is a disease. Journal of clinical sleep medicine: JCSM: official publication of the American Academy of Sleep Medicine, 4(5), 403.
8. Veldi, M., Aluoja, A., & Vasar, V. (2005). Sleep quality and more common sleep-related problems in medical students. Sleep medicine, 6(3), 269.

9. Mulgrew AT, Fox N, Ayas NT, Ryan CF. Diagnosis and initial management of obstructive sleep apnea without polysomnography: a randomized validation study. Ann Intern Med. 2007 Feb 6;146(3):157-66.
10. Barclay L., Patients with obstructive sleep apnea have less gray matter, Medscape news,Nov. 21, 2002.
11. Simon J. Fung, MingChu Xi, JianHua Zhang, Sharon Sampogna, Michael H. Chase, Apnea produces excitotoxic hippocampal synapses and neuronal apoptosis, Experimental Neurology, Volume 238, Issue 2, December 2012, Pages 107-113, ISSN 0014-4886, 10.1016/j.expneurol.2012.08.006.
12. Rechtschaffen, A. & Kales, A. (Eds.) (1968). A manual of standardized terminology, techniques, and scoring system for sleep stages of human subjects. Washington D.C.: Public Health Service, U.S. Government Printing Service
13. Walters, FJM. 1998. "Intracranial Pressure and Cerebral Blood Flow." Physiology. Issue 8, Article 4. Accessed January 4, 2007.
14. Tolias C and Sgouros S. 2006. "Initial Evaluation and Management of CNS Injury." Emedicine.com. Accessed January 4, 2007.
15. Kety, S. S. (1956). Human cerebral blood flow and oxygen consumption as related to aging. Journal of chronic diseases, 3(5), 478-486.
16. Purves D, Augustine GJ, Fitzpatrick D, et al., editors. Neuroscience. 2nd edition. Sunderland (MA): Sinauer Associates; 2001. The Blood Supply of the Brain and Spinal Cord. Available from: http://www.ncbi.nlm.nih.gov/books/NBK11042/
17. Kandel E.R., Schwartz, J.H., Jessell, T.M. 2000. Principles of Neural Science, 4th ed., McGraw-Hill, New York. p.1305
18. Orlando Regional Healthcare, Education and Development. 2004. "Overview of Adult Traumatic Brain Injuries." Accessed 2008-01-16.

19. Singh J and Stock A. 2006. "Head Trauma." Emedicine.com. Accessed January 4, 2007.
20. Neurovascular coupling in the normal brain and in hypertension, stroke, and Alzheimer disease. Helene Girouard, Costantino Iadecola J Appl Physiol. 2006 January; 100(1): 328–335. doi: 10.1152/japplphysiol.00966.2005
21. Clarke DD, Sokoloff L. Age and Development Influence Cerebral Energy Metabolism. In: Siegel GJ, Agranoff BW, Albers RW, et al., editors. Basic Neurochemistry: Molecular, Cellular and Medical Aspects. 6th edition. Philadelphia: Lippincott-Raven; 1999.
22. American Heart Association (2012, February 1). Sleep apnea linked to silent strokes, small lesions in brain. ScienceDaily. Retrieved April 16, 2013, from
23. J Am Heart Assoc. 2012; 1: e000091 originally published August 13, 2012, doi: 10.1161/JAHA.111.000091
24. Zauner, A., & Muizelaar, J. P. (1997). Brain metabolism and cerebral blood flow. Head Injury, 89-99.
25. Journal Article 2012 1541-6933 Neurocritical Care 17 1 10.1007/s12028-012-9720-2 A New Technology for Detecting Cerebral Blood Flow: A Comparative Study of Ultrasound Tagged NIRS and 133Xe-SPECT http://dx.doi.org/10.1007/s12028-012-9720-2 Humana Press Inc 2012-08-01
26. Dimich, I., Singh, P. P., Adell, A., Hendler, M., Sonnenklar, N., & Jhaveri, M. (1991). Evaluation of oxygen saturation monitoring by pulse oximetry in neonates in the delivery system. Canadian journal of anaesthesia, 38(8), 985-988.
27. West, John B. (1977). Pulmonary Pathophysiology: The Essentials. Williams & Wilkins. pp. 22. ISBN 0-683-08936-6.

28. Bitterman, N. (2004). "CNS oxygen toxicity". Undersea and Hyperbaric Medicine **31** (1): 63–72. PMID 15233161. Retrieved 29 April 2008.Clark & Thom 2003, p. 376.
29. Oxygen toxicity.S. G. Jenkinson New Horiz. 1993 November; 1(4): 504–511.
30. James E Sinex, Pulse oximetry: Principles and limitations, The American Journal of Emergency Medicine, Volume 17, Issue 1, January 1999, Pages 59-66, ISSN 0735-6757, 10.1016/S0735-6757(99)90019-0.
31. Millikan G. A. (1942). "The oximeter: an instrument for measuring continuously oxygen-saturation of arterial blood in man". Rev. Sci. Instrum **13** (10): 434–444.doi:10.1063/1.1769941.
32. U.S. Market for Patient Monitoring Equipment. i Data Research. May 2012
33. Sylvia. S. Mader, Inquiry into Life, 8th edition. Copyright © 1997. The McGraw-Hill Companies, Inc. All rights reserved.
34. Walsh JK, Griffin KS, Forst EH, et al. A convenient expiratory positive airway pressure nasal device for the treatment of sleep apnea in patients non-adherent with continuous positive airway pressure. Sleep Med 2011;12:147-52.
35. Kryger MH, Berry RB, Massie CA. Long term use of a nasal expiratory positive airway pressure (EPAP) device as a treatment for obstructive sleep apnea. J Clin Sleep Med 2011:7:5:449-453.
36. Easton JD, Albers GW, Caplan LR, et al. Discussion: Reconsideration of TIA terminology and definitions. Neurology. 2004; 62 (supplement): S29-S34.
37. Els, T., Daffertshofer, M., Schroeck, H., Kuschinsky, W., & Hennerici, M. (1999). Comparison of transcranial Doppler flow velocity and cerebral blood flow during focal ischemia in rabbits. Ultrasound in medicine & biology, 25(6), 933-938.
38. Ross, M. D., Lee, K. A., & Castle, W. M. (1976). Skull thickness of Black and White races. South African medical journal= Suid-Afrikaanse tydskrif vir geneeskunde, 50(16), 635.

39. Atkinson, P., & Wells, P. N. (1977). Pulse-Doppler ultrasound and its clinical application. The Yale Journal of Biology and Medicine, 50(4), 367.
40. Operating Instructions – Doppler Box – DWL Compumedics Germany
41. Hallam, M. J., Reid, J. M., & Cooperberg, P. L. (1989). Color-flow Doppler and conventional duplex scanning of the carotid bifurcation: prospective, double-blind, correlative study. American Journal of Roentgenology, 152(5), 1101-1105.
42. Bhave, G. (2010). A Study Of The Physiological Effects Of Sleep Apnea On Cerebral Blood Flow Velocity.
43. Lupetin AR, Davis DA, Beckman I, Dash N. Transcranial Doppler sonography, I: principles, technique, and normal appearances. Radiographics 1995;15:179–191
44. Eicke BM, Tegeler CH, Dalley G, Myers LG. Angle correction in transcranial Doppler sonography. J Neuroimaging 1994;4:29–33
45. Santalucia P, Feldmann E. The basic transcranial Doppler examination: technique and anatomy. In: Babikian VL, Wechsler LR, eds. Transcranial Doppler Ultrasonography 2nd ed. Boston, Mass: Butterworth Heidemann; 1999;13–31

BIOGRAPHICAL INFORMATION

Jennifer Swittens was born in a small town in Jabalpur, Madhya Pradesh, India on June 21st, 1989, to a Engineer father and a science-teacher mother. She completed her high school education at St. Patrick's Anglo Indian School in Chennai. She had a keen interest in cultural activities and represented her school as the cultural secretary. Her interest in medical sciences and the engineering behind it, led her to pursue her dreams of becoming a Biomedical Engineer. She completed her bachelor of engineering at Jerusalem College of Engineering affiliated to Anna University. She excelled and graduated as a Biomedical Engineer on May of 2010. She continued to pursue her studies and joined as a graduate student in the Bioengineering program in University of Texas at Arlington. She chose Bioinstrumentation as her major that led her to opt for a thesis in the instrumentation track.

Her interest in medical devices brought about an opportunity to work as an Intern for St. Jude Medical, a leading manufacturer of Neuro-modulation products in the Texas area. She completed two semesters as an intern and was offered a full time Manufacturing Engineer position on January 2013.

She is currently is working on Sleep apnea as her Master's Degree thesis and is working as a Manufacturing Engineer for St. Jude medical. She hopes to one day be a part of a great medical device invention.