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Correlating Heart Rate Variability with Mental Fatigue

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Correlating Heart Rate Variability with Mental Fatigue

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Abstract

The long duration and repetitive nature of watchstanding in the Navy triggers an increase in the mental fatigue which would cause a decline in working memory functions, slowed reaction, poor judgment, and decreased productivity. To minimize the damage caused by fatigue, it is necessary to understand how physiological parameters changes during the fatigue. According to recent researches, heart rate variability (HRV) can be calculated from photoplethysmogram (PPG) to indicate nervous system activity. N-back M-pitch, a cognitive working memory test was utilized to define the level of fatigue. An increase in fatigue was indicated by decrease in the accuracy of the test. In this project, HRV's high frequency area and low frequency area have been found correlated to mental fatigue and change over time as hypothesized.

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Authorship Page

In this Major Qualifying Project of Correlating Mental Fatigue with Physiological Parameters, Yichao Joy Xu put in major effort in designing signal processing algorithms, programming N-back M-pitch psychological test, and analyzing correlation between mental fatigue and physiological parameters. Fangjie Ding put in major effort in designing the low-power PPG sensor. Ningxin Fu documented the biomedical experimental settings while coordinated with data analysis. Sinan Assad assisted with the experiment. In documenting this MQP, Yichao Joy Xu, Fangjie Ding and Ningxin Fu authored the design process of signal processing, hardware implementation and experimental settings, while Sinan Assad contributed in describing project strategy, and discussion. Detailed documentation contribution shares are listed below.

Section	Contributor(s)
Chapter 1: Introduction	NF
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Chapter 4 Alternative Designs	FD, YX, SA
Chapter 5 Methodologies	YX, FD, NF, SA
Chapter 6 Experiment Results	YX, NF
Chapter 7 Methodology Validation Analysis	YX, FD
Chapter 8 Discussion and Conclusion	SA, NF
Chapter 9 Recommendations	NF, FD

Chapter 1: Introduction

Watchstanding in the Navy typically concerns those on a ship that is operating 24 hours a day. During the entire commissioned life of a ship, there will always be sailors on watch to ensure the safe navigation of a ship. Types of watches vary depending on whether the ship is in port or in transition (i.e. away from homeport). Watchstanding is often for security purposes, and operated by an officer of the deck, or a pier sentry. Types of watches can be either operational or engineering-oriented, such as a damage control watch officer, or a status board operator. For purposes of communications, security, and safety, it is necessary to maintain watchstanding even when the ship is in port receiving services. The average duration of a watch in the U.S. Navy is four hours. During this time, sentries must devote full attention to every event regarding the crew, operation, and safety of the ship, as inattention or negligence may result in severe consequences (United States Navy, 1999).

However, due to the long duration and repetitive nature of watchstanding, the alertness of sentries tends to decrease over time. Michael R. Häack, who served with the Naval Security Group, wrote in his book *The Navy*,

> "*I thought my first night of watch standing would last forever. Each time I looked at the clock to make a time entry on the log it was exactly five minute later than it had been the last time I had looked. I thought, 'this will drive me crazy in one watch. What's going to happen to me when I have to do this job full time, day and night?'" (Häack, 2007)*

A decrease in alertness, i.e. mental fatigue, can have various causes, such as sleep deprivation, time-on task, and circadian desynchronosis. Sentries or guards who are on duty for long hours can suffer from the effects of fatigue, which include a decline in working memory functions, slowed thinking and reaction, poor judgment, increased stress and decreased productivity (Cox, unknown). It is possible that these symptoms can lead to accidents, which will result in extensive and unnecessary damages to the ship and possibly crewmembers. Therefore, the problems caused by mental fatigue and the extents to which

fatigue can compromise both physiological and psychological performance have been growing concerns (D. Williams, 1998). In order to prevent or minimize the damage caused by fatigue, it is necessary to understand how to assess the level of fatigue based on measurable physiological parameters.

Over the years, studies have been done to relate fatigue to heart rate variability (HRV), which describes the variation in the time interval between heartbeats. The analysis of HRV has been found to be a reliable and powerful tool in assessing autonomic function (Malik, 1996). The autonomic nervous system (ANS), which can affect the speed and rhythm of the heart, consists of two primary branches: the sympathetic nervous system (SNS), and the parasympathetic nervous system (PNS). SNS can increase the heart rate by sending stimulating chemicals to the heart; in contrast, PNS serves to decrease the heart rate. A popular method of analyzing HRV is to compare the power spectral density (PSD) of HRV data (Yuru Zhong, 2006). There are three main components of HRV in the spectrum: very low frequency (0.003-0.04 Hz; VLF), low frequency (0.04-0.15 Hz; LF), and high frequency (0.15-0.40 Hz; HF). Researches have suggested that the LF component often associates with stress and drowsiness, and has a tendency to increase as subjects become fatigued (Verwey, 1999) (Egelund, 1982). It has also been found that HRV increases when subjects are performing a vigilance task rather than a proofreading task (Ahsberg, 2000).

The goal of this project was to detect and analyze the correlation between fatigue and HRV, which was extracted from the data collected using a non-invasive photoplethysmogram (PPG) sensor. To simulate a psychomotor vigilance task, an auditory memory test called N-back M-pitch was utilized in the study procedures of this project. During the experiment, subjects were instructed to complete a total of 24 sessions of the N-back M-pitch test. Subjects were asked to report whether the auditory stimulus presented one step prior (N=1) had the same or different stimulus duration as the current. The subjects' percent accuracy, which was a direct indication of their alertness, was recorded simultaneously, and so were their PPG signals. After completing the experiment, the results of N-back M-pitch were compared against the spectral analysis of HRV for each subject. We were able to draw conclusions by analyzing the

correlations between HF of HRV, LF of HRV, LF/HF ratio, heart rate, percent accuracy, and average response time.

Chapter 2: Literature Review

2.1 Fatigue - General

When the word *fatigue* comes to mind, people tend to associate it with the feeling of extreme tiredness, weakness, and the need for sleep or rest. In fact, the meaning of fatigue varies from common definitions to psychological and physiological terminologies. Fatigue is considered a nonspecific symptom (Susan Torres-Harding, 2005), because it can be an indicator of various causes or conditions. Examples of this include physiological stress caused by sleep deprivation or heavy muscle exercise, psychological disorders such as depression and anxiety, and medical conditions such as chronic inflammatory conditions. Fatigue may also be a result of unhealthy lifestyles (Peter Manu, 1992), such as irregular sleep patterns, and excessive caffeine intake. Fatigue impairs cognitive performances. In this project, we focus on sleep deprivation as a cause of fatigue, along with extreme tiredness and lack of motivation as symptoms of fatigue.

2.1.1 Circadian Rhythm and Sleep

Humans follow a biological clock with a roughly 24-hour cycle called the circadian rhythm (Myers, 2010). The word circadian, which comes from the Latin *circa* and *diem*, means "about a day". Circadian rhythm includes sleep and wakefulness on a 24-hour cycle, and it is controlled by various external factors such light and internal factors such as body temperature. Light is one of the most common external factors.

Before Edison invented the light bulb, humans used to sleep more and work less (Stanford University, 1999). This is because people used to adjust their circadian rhythm according to the sunlight. When the sun went down, people would start to prepare for sleep, and when the sun came up, people woke up and started their day. Bright light activates the light-sensitive retinal proteins, which trigger signals to the suprachiasmatic nucleus (SCN) in the hypothalamus of the brain. The SCN causes the production of the sleep-inducing hormone *melatonin* to decrease (Myers, 2010). When it is nighttime

with significantly less light present, the light-sensitive retinal proteins stop sending signals to the SCN, allowing more melatonin to be released into the bloodstream, which in turn induces sleep.

Sleep, which is part of our circadian rhythm, has its own biological rhythm. While we are sleeping, we go through a cycle of 5 distinct sleep stages about every 90 minutes (Myers, 2010), which are illustrated in Figure 1 below. During a typical night of sleep, we enter Stage 1 where hallucinations may occur shortly after we fall asleep. Hallucinations are false sensory experiences that occur without a sensory stimulus, such as a falling sensation, in which case our body jerks and we may or may not wake up. After this stage, we relax more deeply and enter Stage 2 of sleep, which lasts for about 20 minutes. We are clearly asleep during this stage, though we could still be awakened by outside stimulus without much difficulty. Next, we go through Stage 3 and the stage of deep sleep, Stage 4. These two stages together last for about 30 minutes, in which we would be hard to wake up (Myers, 2010).

After falling asleep for about an hour, we ascend from the stage of deep sleep back to Stage 3 and 2. After about 30 minutes, we enter a phase characterized by rapid eye movement (REM) sleep. There are many things occurring simultaneously during this stage: our heart rate increases, respiratory rate becomes rapid and irregular, and our eyes move around quickly even behind closed eyelids. Researchers have also found that vivid dreams occur during REM sleep, and if they wake the subjects during or within 3 minutes after a REM sleep stage, the subjects are able to recall the dreams that just occurred in vivid detail.

The sleep cycle repeats itself approximately every 90 minutes. As we can see in Figure 1, Stage 4 disappears after the second cycle of sleep, and REM periods increase as night progresses. By morning, around 20-25% of our typical 8-hour sleep has been REM sleep.

There has always been a question of "How many hours of sleep do we really need?" In fact, the general idea that "everyone needs 8 hours of sleep" is untrue, as the amount of sleep needed by individuals varies considerably. For instance, newborns sleep for two-thirds of their day, while most adults sleep for no more than one-third. Some people find fewer than 6 hours of sleep sufficient, while others sleep for 9 hours or more on a regular basis (Myers, 2010). It has also been found that most adults

will sleep at least 9 hours a night, if they are allowed to sleep unhindered (Coren, 1996). With sufficient amount of sleep, we are able to perform tasks more efficiently and accurately. Without the amount of sleep that our bodies need, we accumulate a sleep debt, which leads to sleep deprivation that affects the efficiency and accuracy of our performance during the day, and cannot be compensated by one marathon sleep (Myers, 2010).
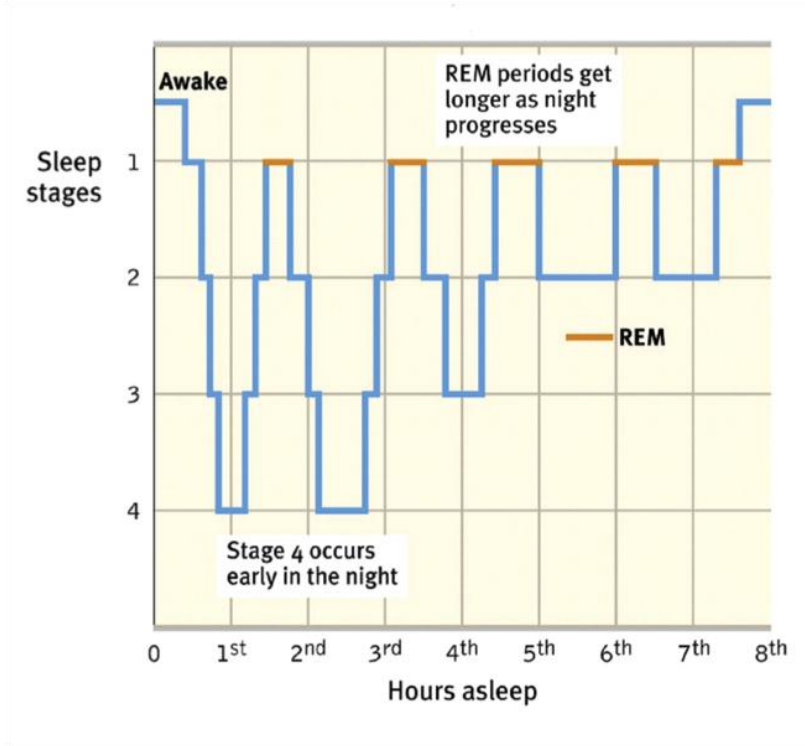
Figure 1 The Stages in a Typical Night's Sleep (Myers, 2010)

2.1.2 Sleep Deprivation and Its Impact

Sleep deprivation has various physiological effects on our bodies, including notable impacts on brain function. It has been found that any amount of sleep deprivation will adversely affect the cognitive performance (The Franklin Institute, 2004). Researchers have also categorized the effects of sleep deprivation into 1) general effects on alertness and attention, and 2) selective effects on certain brain areas and functions (Paula Alhola, 2007).

Decreased alertness and attention could be mediated through lapses, slowed responses, and wake-state instability. Lapses, caused by micro sleeps that have a very short period of sleep-like EEG activity, as well as brief moments of absent-mindedness have been considered the main reason for the decrease in cognitive performance during sleep deprivation. Researchers have also concluded that performance during sleep deprivation is most likely to decrease during long, repetitive, and monotonous tasks that require reaction speed and responsiveness (Paula Alhola, 2007).

According to research evidence on selective effects, sleep deprivation impairs cognitive performance due to interference with the functioning of certain brain areas. In 1993, Horne first suggested that sleep deprivation especially impairs cognitive performances that depend on the prefrontal cortex of the brain. One of these cognitive performances is executive functioning (Horne, 1993). Executive functioning is "the ability to plan and coordinate a willful action in the face of alternatives, to monitor and update action as necessary and suppress distracting material by focusing attention on the task at hand" (K. Jones, 2001). Psychologists D. Norman and T. Shallice have outlined five types of situations in which the executive functions are invoked (D. Norman, 1980):

1. Situations involving decision making

2. Situations involving error correction and troubleshooting

3. Situations where responses are not well-rehearsed

4. Situations that are dangerous or technically difficult

5. Situations requiring overcoming of a strong habitual response or resisting temptation

Studies have also shown that sleep deprivation has a negative impact on working memory tasks. Working memory, which may be considered a more specific term for short-term memory, focuses on the conscious, active processing of incoming information, including auditory and visual-spatial information (Myers, 2010). In one of the studies, the working memory task involved lighting up a sequence of randomly selected pegs, then requiring the subjects to repeat back the lighting sequence. The subjects of the experiment include both sleep deprived and non-sleep deprived individuals. The result has shown that the sleep deprived group responded to the task much faster than the non-sleep deprived group, however,

the sleep deprived group also made significantly more errors than the other group (Kanav Kahol, 2008). Therefore, their study concluded that sleep deprivation increases the number of errors made on working memory tasks.

Another study involved recording EEG during the performance of working memory tasks. The researchers compared data from alert daytime baseline tests with data from tests during a late night of up to 21 hours of sleep deprivation. They found that alertness measured both subjectively and by using EEG decreased with increasing sleep deprivation. They also found that, within 1 hour after participants' normal time of sleep onset, the participants became slower in response and more error prone in working memory tasks.

2.2 Direct Fatigue Assessment

Due to the complex nature of fatigue, its measures are generally multidimensional approaches instead of single questions (e.g. "Are you tired?") (Susan Torres-Harding, 2005). These multidimensional measures assess the level of fatigue based on daily activities, mental and physical performances, and other related characteristics (Ivan Barofsky, 1991). In this section, we will introduce some of the measures and experiments that have been utilized in the past for fatigue assessment.

2.2.1 N-back Task

Introduced by Wayne Kirchner in 1958, the N-back task is a Continuous Performance Task to measure the short-term retention of rapidly changing information (Kirchner, 1958). In general, a Continuous Performance Task measures a person's sustained and selective attention. Sustained attention refers to the capability to maintain focus on continuous stimuli, and selective attention refers to the capability to focus only on selected stimulus and ignore the distractions.

In recent years, researchers have been using variants of the N-back procedure to investigate the neural basis of working memory processes. A typical form of the N-back task requires the participant to monitor a series of stimuli and to signal whenever the current stimulus matches the one that appeared N-

th trials prior to the current one in the series, where n is a defined positive integer (Adrian M. Owen, 2005). The task involves on-line monitoring, updating, and manipulating remembered information. Therefore, the N-back task has been considered an efficient way to assess a number of major processes within working memory.

In the original N-back task conducted by Kirchner in the 1950's, the visual display system included a keyboard with 12 Morse keys numbered 1 to 12 from left to right, and 12 small lights placed directly above each of the 12 keys. Each key corresponded to the light that was placed above it. The lights could turn on one at a time in a random sequence. The inter-stimulus interval between the disappearance of one light and the appearance of another did not vary. The duration of each light could be either 1.5 or 4.5 seconds. However, all lights in a series during the experiment must have the same duration. The subjects were asked to give their responses by pressing the keys. All responses from each subject were recorded and timed by an electronic recording device called SETAR, which also determined whether or not each response was corrected automatically. If the subject gave a correct response, a buzzer would sound; if not, there would be no sound, and the subject could give a second (or third, fourth, etc.) try by pressing other keys if time allowed (Kirchner, 1958).

There are four conditions during the experiment defined as follows:

1. No-back: the subject is asked to press the key where the light appears. No-back serves as a control condition, because there is no manipulation of information within working memory (Adrian M. Owen, 2005)

2. One-back: the subject is asked to press the key where the light has just disappeared

3. Two-back: the subject is asked to press the key where the light has disappeared two steps before

4. Three-back: the subject is asked to press the key where the light has disappeared three steps before

The goal of Kirchner's study was to investigate the impact that age has on short-term memory. He found that the older subjects were generally unable to perform as well as the younger subjects. The

older subjects tended to make more random guesses, indicating that they were having trouble keeping up with the trails.

N-back performance tasks test working memory. In a study done by University of Groningen in the Netherlands, researchers found out that individuals have different baseline for working memory and the subjects with a higher score of Raven Progressive Matrices Test, which indicates Intelligence Quotient (IQ), (Raven, 1962) have bigger working memory capacities (Linda Jongman, 1996). Except for the subjects with extremely high Raven score, whose working memory was not impaired by mental fatigue, the subjects' working memory capacities decreased due to mental fatigue. In the case of this project, the working memory capacities could be interpreted by the "Nth" back of information, and thus the performance of N-back experiments could indicate levels of fatigue.

One variant of the N-back is an auditory N-back M-pitch procedure, which has recently been utilized by the Naval Submarine Medical Research Laboratory (NSMRL) to assess cognitive performance. Instead of using a visual display as in the traditional N-back procedure, the NSMRL presented the stimuli as tones with four distinct frequencies (M = 4) and two different durations. The subjects were required to determine whether the stimulus presented N steps prior has the same duration as the current stimulus. The variation in frequency was independent of the variation in duration and was also irrelevant to the task. The performance of the subjects was reflected by the percent of correct responses, and the missed responses were considered incorrect (Michael Qin, 2011).

2.2.2 Drowsiness Estimation by Wierwille and Ellsworth Criteria

The driver drowsiness evaluation by trained raters has been first reported by Wierwille & Elsworth (1994). The experiment re-conducted by Berlin University of Technology had 83 subjects who were asked to drive the simulators for 2 hours. The synchronized close-up video recording of the operators faces have been rated according to the Wierwille drowsiness states by six trained raters using facial information such as facial tone, slow eyelid closure, and mannerisms (rubbing, yawning, nodding, etc.). The study showed that this method was straightforward and reliable (Vöhringer-Kuhnt T., 2004). A

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recent study done by the University of Technology, Sydney also deployed this method, but scaled the level of drowsiness by five descriptors: alert or not drowsy (class 1); slightly drowsy (class 2); moderately drowsy (class 3); significantly drowsy (class 4); and extremely drowsy (class 5) (Khushaba, 2011). However, due to video recording identification being extremely time consuming and no trained raters could be provided, we can only use this method for reference.

2.2.3 Electrooculography

Electrooculography (EOG) is an electrophysiological test of the function of the outer retina and retinal pigment epithelium (RPE) in which the change in the electrical potential between the cornea and the ocular fundus is recorded during successive periods of dark and light adaptation (Brown M, 2006).

EOG measures blink rate (BR), blink duration (BD), long closure rate (LCR), blink amplitude (BA), saccade velocity (SV), saccade rate (SR), and peak saccade velocity (PSV) (T.L. Morris, 1996). Two researchers, T.L. Morris and J.C. Miller, conducted an experiment with ten pilots, who were or used to be active Air Force pilots, to identify the correlation between pilot fatigue and the specific components of eye and eyelid movements. The pilots were partially sleep deprived prior to the experiment, and they were asked to complete a 4-hour sortie in an instrument flight simulator. During the sortie, the performance of each pilot was measured by the flight instruments and was reflected by the error scores. The error scores were calculated simultaneously across altitude, airspeed, heading, and vertical velocity. In conclusion, they found that a number of components of the EOG signal were good predictors of performance changes due to fatigue. Among these components, SR, BA, LCR, BR, and BD were the best predictors of performance decrements, and were also significantly correlated to the error scores.

Another study was conducted with 138 subjects in a driving simulator with 2-hour durations. Subjects were asked to avoid exits and not to speed up above a certain limit. This study revealed an increase in the blinking duration, an increase in the delay in reopening the eyelid, a deceleration of the standardized eyelid closure speed, and an increase in the number of micro sleeps versus lower self-assessment of the alertness level (R. Schleicher, 2008).

2.2.4 Electroencephalography

There are numerous available physiological indicators that can describe a human subject's level of alertness. An EEG signal, consisting of multiple wave forms that have different frequency bands such as Alpha, Beta, Theta, Delta, and Gamma, has been shown to be one of the most predictive and reliable means of measuring mental fatigue (Artaud, 1994).

Many experiments have shown variations in the power spectrum of EEG bands during different phases of mental and physical workloads. Schwarz-Ottersbach and Goldberg noticed increases in delta and theta power magnitude during different attention and reaction tests. Theta had lower power with low attention demands than when this attention-demand was high. They showed a complex "stress EEG pattern" characterized by high Alpha and Delta activity and low Alpha and Beta activity.

35 non-professional, sleep deprived (2 hours below their averages amount of sleep) participants performed a laboratory simulated driving task. The participants were asked to breathe normally and avoiding unnecessary movements while doing two stages of recordings: a) 10-15 min active driving with many road stimuli; b) up to 2 hours monotonous driving with very few stimuli and under 80 km/hr. A 19-channel EEG and EOG, which showed a significant increase in Delta and Theta wave magnitudes over the entire head during transition to fatigue by 22% and 26%, respectively, obtained the recording. Alpha and Beta activity was also found to increase but by a smaller extent by 9% and 5%, respectively (Saroj K.L. LAL, 2002).

An algorithm was developed by Saraj K.L. LAL based on EEG changes to detect different phases of fatigue due to EEG changes reported in prior data (Saroj K.L. LAL, 2002). The results suggested a correlation between previous studies and findings. The previous findings that suggest drivers are at risk of driving in a fatigued state for most of the time during monotonous driving tasks supports their offline testing which shows that truck drivers were in a fatigue state for 60% of the total driving time.

2.3 Photoplethysmography (PPG)

Photoplethysmography (PPG) is a non-invasive optical measurement technique and it is widely used in pulse oximeters. The PPG sensor uses a light source and a photo-detector to measure blood volume changes in the microvascular bed of peripheral tissues. When the light source emits light through the skin, it first reaches the bones and then gets reflected. The photo-detector produces a current source corresponding to the amount of reflected light. For this project, an infrared light emitting diode (LED) was used as the light source and a photo diode was used as the photo detector. A LED is a P-N junction device that emits light when it is forward-biased. A photodiode is a semiconductor light sensor that generates a current proportional to the light intensity it receives. Since a LED only emits light within a specific bandwidth, a matching photo diode for that wavelength is usually used for PPG measurement.

When a raw PPG sensor (a light emitter diode and a photo detector) is placed on the body, for example, on a finger, the emitter emits light into the tissue and the detector will pick up the amount of light that is reflected back from the tissue as shown in Figure 2. There are many different factors that would affect the light after it is sent from the LED and before it is reflected to the detector. The blood volume and the surrounding tissue have the largest impact on the light that gets reflected. The reflected light intensity decreases as the blood volume increases in the region where the diodes are placed. Therefore, as the blood volume varies according to the cardiac output, the reflected light intensity respectively gets affected. In addition, there is another steadier component that is due to the attenuation by tissues and the average amount of blood volume that always remains in the artery. As a result, the raw PPG wave contains an alternating current (AC) component that is superimposed onto a large, quasi-DC (direct current) component (Allen 2007). The amount of AC component is much smaller than the DC component, so some amplification and filtering is needed in order to extract the pulse rate from the raw PPG waveform.
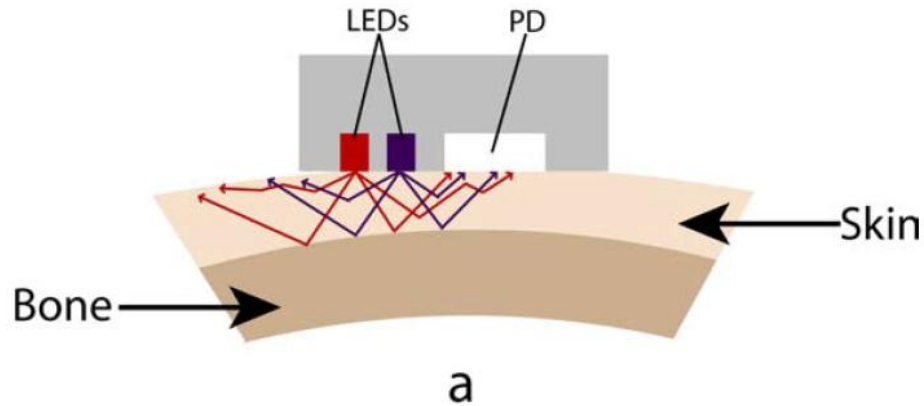
Figure 2 Photoplethysmography

2.4 Heart Rate Variability

The autonomic nervous system (ANS) controls heart rate and rhythms (Malik, 1996). As shown in Figure 3, ANS has two divisions – parasympathetic nervous system (PSNS) and sympathetic nervous system (SNS). PSNS is particularly responsible for the activity stimulus when the body is at rest, and SNS prepares the body for intensive physical activity when facing a threat, also known as fight-on-flight response (Malik, 1996) (Sherwood, 2005).

Parasympathetic postganglionic fibers influencing the heart rate lead from the brain and release acetylcholine as neurotransmitter (Sherwood, 2005). The muscarinic acetylcholine receptors respond with an increase K+ conductance in cell membrane that suggests a slow diastolic depolarization (Malik, 1996). The sympathetic postganglionic fibers release norepinephrine, which activates ß-adrenergic receptors and results in increases in ICal (Internal calcium ion concentration) and acceleration of slow diastolic depolarization (Malik, 1996).

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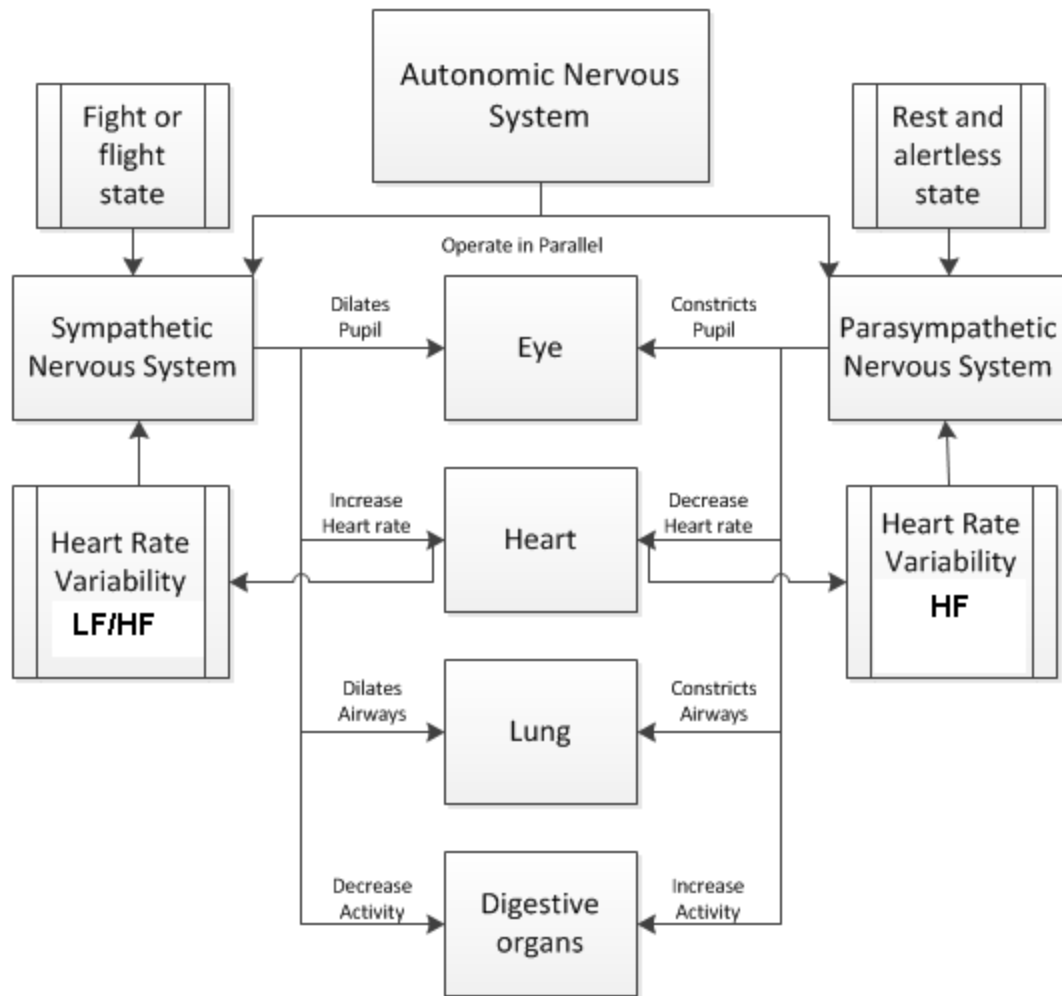
Figure 3 Autonomous Nervous System influences on different organs (Sherwood, 2005)

The variations in heart rate could be analyzed in both time domain and frequency domain. In the time domain, global descriptive statistics such as standard deviation of the heart rate could be used to characterize the distribution of heart rates. In the frequency domain, the heart rate needs to be modeled into periodic patterns to extract specific frequency by the power spectrum density (Gary G. Berntson, 1997) (Malik, 1996). The spectral power on certain frequency bands such as the low and high frequency regions could then be quantified by calculating the area under the spectral density function (Gary G. Berntson, 1997). Data processing procedures may include preliminary processing such as artifact canceling, peak-to-peak interval fetching and periodic heart rate justification (Gary G. Berntson, 1997).

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The low-frequency (LF) components of the HRV between 0.04Hz and 0.15Hz and the high-frequency (HF) components between 0.15Hz and 0.45Hz are influenced by SNS and PSNS, respectively. The vagus nerve controls the parasympathetic innervation of the heart and lowers the heart rate. Vagal activity contributes to most of the high-frequency components (Malik, 1996). Equations (1) and (2) are commonly employed to mirror the Sympathetic Nervous Activity (SNA) and Parasympathetic Nervous Activity (PNA) (Ayumi Tsuchida, 2009).

$$SNA = LF \qquad (1)$$

$$PNA = LF \text{ and } HF \qquad (2)$$

It has been shown that in the supine position, the power spectrum of the heart rate shows dominant spectral amplitudes in the HF region, and they are indicative of the PNA. In the upright position, the lower frequency region has the larger power while the HF region decreases; thus, in this case the SNA is dominant (Bruce Pomeranz, 1985). Sympathetic stimulations increase the brain activity and alertness while parasympathetic stimulation presents no effect on brain (Sherwood, 2005). Therefore, decreasing SNA and increasing PNA impair cognitive performances. Thus, as shown in previous studies, HRV should be used as one of the legitimate physiological parameters to be correlated with the psychological cognitive performance (Kanav Kahol, 2008). Furthermore, a recent study has shown that the LF components decrease over the course of the fatigue-inducing tasks, while HF components increase. This further explains the necessity to analyze HRV as a representation for physiological indicator of mental fatigue (Yvonne Tran, 2009).

2.5. Discrete-Time Fourier Transform and Power Spectrum Estimation

2.5.1 Discrete-Time Fourier Transform

Physical signals and mathematical functions can be represented with respect to time and frequency. In the time domain, any signal or function can be visualized using a time domain graph, which shows how the signal or function progresses over time. Figure 4 below shows the time domain

representation of a cosine wave with a frequency of 4Hz over 1 second. Its frequency can be determined by counting how many repetitive cycles there are within 1 second. Clearly, there are 4 repetitions per second, indicating that the frequency is 4Hz.
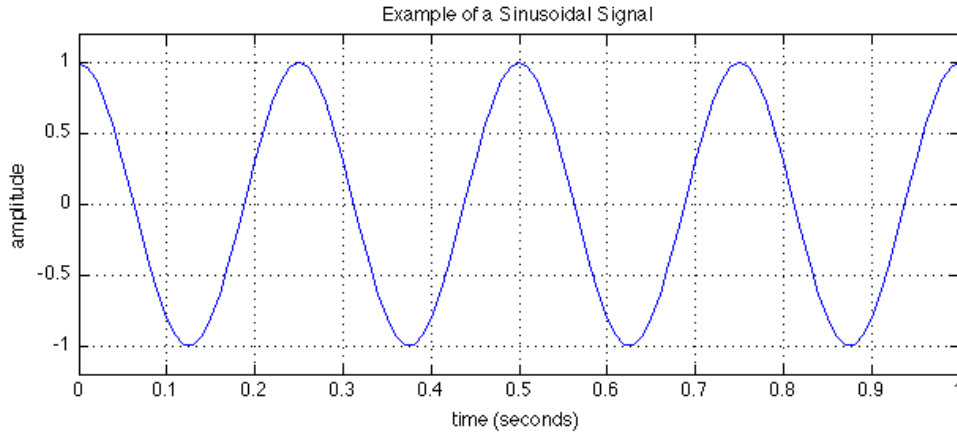
Figure 4 Example of a Sinusoidal Signal of 4Hz

In the case of discrete time, a signal may be obtained by sampling from a continuous-time signal. For instance, the sinusoidal signal shown in Figure 4 can be expressed as

$$x[n] = A\cos(2\pi f n + \theta), \qquad -\infty < n < \infty$$

where A is the amplitude of the sinusoid (A = 1), f is the frequency in Hertz (f = 4), θ is the phase in radians (θ = 0), and n is an integer variable, indicating the sample number. Figure 5 below shows the discrete representation of the same sinusoidal signal. Each stem represents a sample, and if all the stems are connected, the resulting waveform will look approximately the same to the waveform shown in Figure 4. It is important to note that the signal is undefined between successive samples (John G. Proakis, 2007).
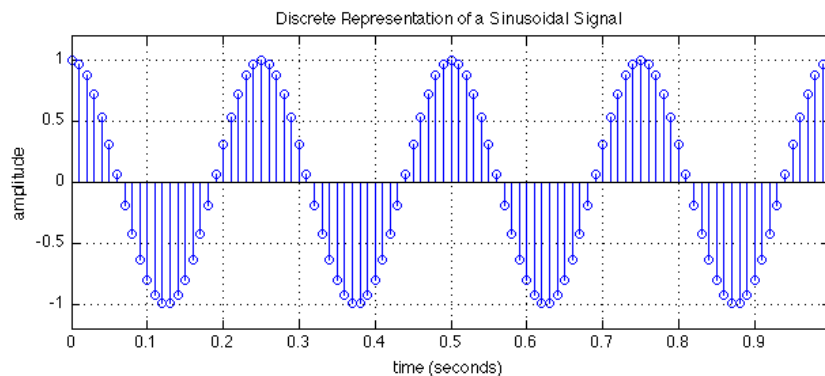
Figure 5 Example of a Discrete-Time Sinusoidal Signal

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When a signal is described in the frequency domain, its graph shows how much of the signal lies within each frequency band over a range of frequencies. For instance, Figure 6 shows the frequency domain representation of the signal given in Figure 4. Since the only frequency component is at 4Hz, there is a spike located at 4Hz, and another one at -4Hz due to complex symmetry.
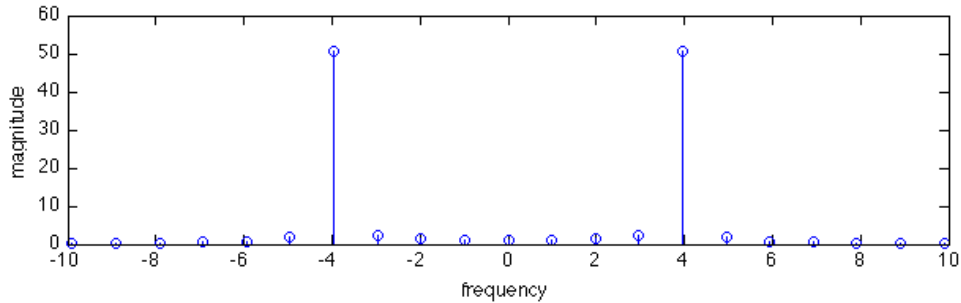
Figure 6 Frequency Domain Representation of a 4Hz Sinusoidal Signal

Any given signal can be converted between time and frequency with a pair of mathematical operators, namely, a transform. A popular mathematical operation with many applications is called the Fourier transform. Fourier transform guarantees that any signal can be expressed as a function of time, as well as a function of frequency. The discrete-time Fourier transform (DTFT) is a specific form of Fourier analysis. As such, DTFT requires a discrete-time function, which is often obtained by sampling a continuous signal. By definition, the Fourier transform of a discrete-time function $x[n]$ is

$$X(f) = \int_{-\infty}^{\infty} x[n]e^{-j2\pi fn}dn,$$

Whose inverse Fourier transforms is

$$x[n] = \int_{-\infty}^{\infty} X(f)e^{j2\pi fn}df.$$

2.5.2 Power Spectrum Estimation

When there are random fluctuations (i.e. noise) in a signal, it is a necessary procedure to eliminate the effect caused by noise as much as possible. To do so, one should characterize the signal from a statistical viewpoint. When signals are stationary over time, the longer the recording of the data,

the better the accuracy of the estimate. On the other hand, if signals are non-stationary over time, one cannot extract the estimate based on a long recording of data. Instead, the length of the data should be determined by the rapidity of the variations of the signals in time (John G. Proakis, 2007).

The energy of a signal is defined as the integral of the signal squared, which is the same as the energy measured in frequency (C. Richard Johnson Jr., 2011)

$$E = \int_{-\infty}^{\infty} |X(f)|^2 df.$$

The power (the average of the energy) of the discrete-time signal is

$$P(x) = \lim_{N \to \infty} \frac{1}{T} \int_{-T/2}^{T/2} |x[n]|^2 dn.$$

Given a signal with an infinite duration, the energy of the signal is also infinite. Thus, the signal does not possess a closed-form Fourier transform expression. One way of measuring and analyzing such signals is by the amount of power within various frequency bands. Power spectral density (PSD) is a positive real function, which has units of power per Hz. PSD provides measures the power distribution of a signal across frequencies, and is helpful in identifying periodicities. If x(t) is a stationary random process, its autocorrelation function is defined as

$$\gamma_{xx}(\tau) = avg[x^*(t)x(t+\tau)]$$

Using the Wiener-Khintchine theorem, the PSD of the stationary random process is the Fourier transform of the autocorrelation, which is

$$\Gamma_{xx}(f) = \int_{-\infty}^{\infty} \gamma_{xx}(\tau) e^{-j2\pi f \tau} d\tau.$$

The time-average autocorrelation can be expressed as

$$R_{xx}(\tau) = \frac{1}{2T_0} \int_{-T_0}^{T_0} x^*(t)x(t+\tau) dt,$$

where $2T_0$ is the interval. Its corresponding PSD, known as the correlogram, is defined as

$$P_{xx}(f) = \int_{-\infty}^{\infty} R_{xx}(\tau) e^{-j2\pi f \tau} d\tau = \frac{1}{2T_0} \left| \int_{-T_0}^{T_0} x(t) e^{-j2\pi f \tau} dt \right|^2.$$

Now, let n be the discrete sample index, and let N be the total number of samples of the signal, the estimate PSD is

$$P_{xx}(f) = \frac{1}{N} \left| \sum_{n=0}^{N-1} x[n] e^{-j2\pi f n} \right|^2 = \frac{1}{N} |X(f)|^2,$$

where $X(f)$ is the Fourier transform of the sampled signal x[n]. The equation shown above is called the periodogram, which was originally introduced by Arthur Schuster in 1898 to detect "hidden periodicities". Periodogram can be considered as a smoothed PSD if a proper window to reduce sidelobes is used (John G. Proakis, 2007).

Figure 7 below shows the PSD estimate of the same signal defined in Figure 4 using periodogram. As expected, the total power of the signal is centered at 4Hz, which is the only frequency component of the signal. The estimate of the PSD is computed and graphed in MATLAB using periodogram (The MathWorks).
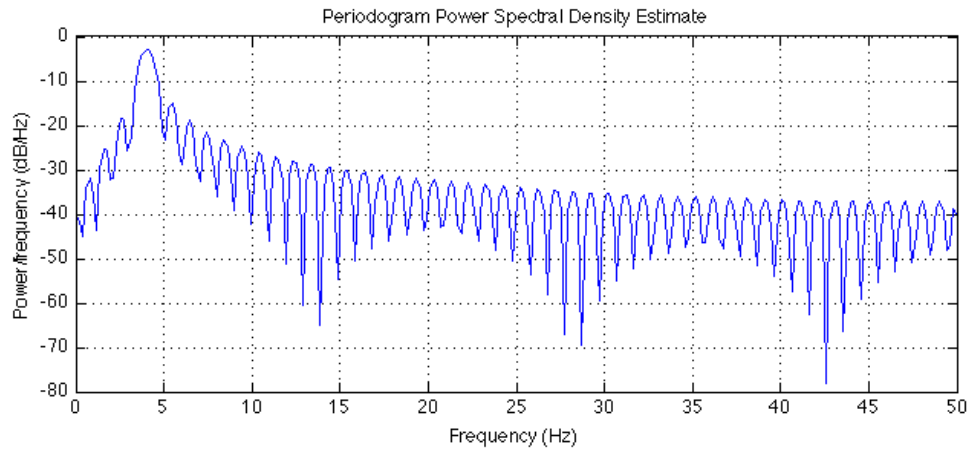
Figure 7 Periodogram PSD Estimate of a Sinusoidal Signal of 4Hz

Another approach to PSD estimation is called the Welch's method, which was introduced in 1967 by P. D. Welch. This method is based on the concept of periodogram estimation. There were several modifications made. First, Welch allowed the data segments to overlap; second, he windowed the data segments prior to computing the periodogram (John G. Proakis, 2007). Welch's method is an improvement on the original periodogram estimation. It reduces the noise power and reduces variance in the power spectrum at a cost of reduced frequency resolution due to overlapping of the data segments. The overlapping is necessary, because most window functions cause information loss at the edges, and overlapping can be used to compensate for the loss. Figure 8 shows the PSD estimate of the signal shown

in Figure 4 using the pwelch function in MATLAB. By default, the signal is divided into 8 segments with

50% overlap (The MathWorks).
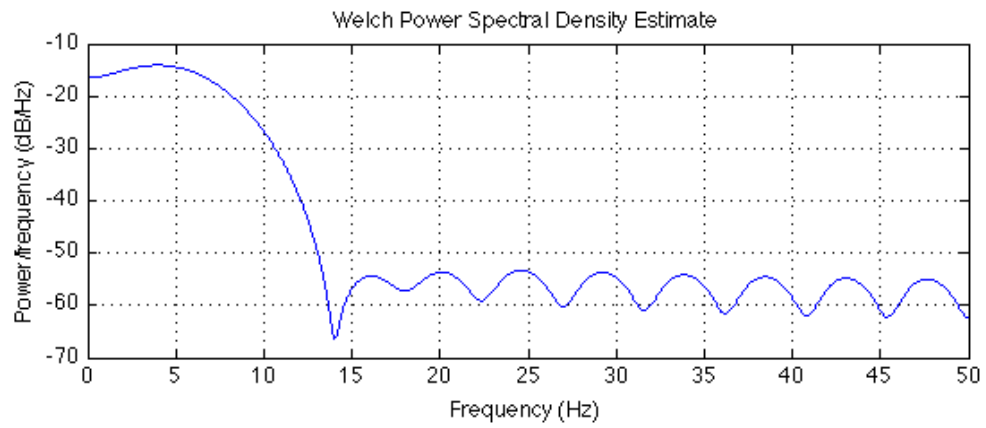
Figure 8 Welch PSD Estimate of a Sinusoidal of 4Hz

Chapter 3 Project Strategy

3.1 Project Approach

The main objective of this MQP was to design a system that can ultimately find the correlation between psychological fatigue signs and physiological parameters. In order to accomplish this task, the psychological fatigue level was measured using N-Back M-Pitch stimulus-response program, generated by our team, whereas the heart rate was monitored simultaneously using a pulse oximeter sensor that was also developed by our team. The current methods utilize the photoplethysmograph (PPG) signal for Heart Rate Variability (HRV) analysis in an offline mode, including time-domain and frequency-domain analysis. Eventually, the power spectrum of the PPG heart rate duration variability can be used to indicate the severity of fatigue and, in future applications, for fatigue detection systems in advance to its occurrence.

3.2 Initial Client Statement

Michael Qin, Ph.D from the Naval Submarine Medical Research Laboratory (NSMRL), Groton, Connecticut, was considered the sole client for this project. He has provided our MQP team with the following initial client statement:

Watchstanding, which lasts for long periods of time, is a regular status in the Navy, and it typically concerns those on a ship that is operating 24 hours a day. Sailors, for instance, stay on watch duty for continuous hours to ensure the safe navigation of the ship. Keeping watch is often for security purposes and operated by an officer of the deck, or a pier sentry, and this is why it is critical for those on duty to keep alert and not to be fatigued where awareness level is on the line. Other purposes include communications, security, and safety, it is also necessary to maintain watch even when the ship is in port receiving services. The shift duration for keeping watch in the Navy is usually four hours. During this

time, sentries must devote their full attention to every event regarding the crew, operation, and safety of the ship, as inattention or negligence may result in severe consequences (United States Navy, 1999).

From the initial client statement above, the MQP group identified client's objectives and needs. It was also the bottom line to investigate in more-detail topics through gathering more information through literature search, client interviews and brainstorming, in order to develop a final statement based on engineering point of view to fulfill the client's goals. The client wanted to measure the fatigue level using a physiological input data through a pulse oximeter device. By analyzing these PPG data, which were recorded simultaneously with N-Back M-Pitch memory tasks, in an offline procedure to approve or reject the hypothesis that there is a direct relationship between fatigue and HRV. Desired system outputs should be including fatigue level assessment by means of accuracy percentage of the N-Back M-Pitch task over time, coordinated with HRV by means of power density over time.

3.3 Objectives

The objectives were created by the MQP team based on the interviews that were held with the client and the advisors and user requirements. A list of design objectives and sub-objectives were ranked due to their importance and limited to the ultimate goal of this project in a pairwise comparison chart (PCC) summarized, Table 1. This helped to determine the priority that should be focused on during the design stage. The objectives were listed in the first row and first column in the same order, and each row element was compared to a corresponding column elements. Row elements were assigned a score of 1 if considered more important than column feature, 0 if considered less important and 0.5 if equally valued. An (x) is assigned for the same row and column entry.

Project objectives were evaluated and ranked according to these points
1- Safety: The physiological meter device should be non-invasive and should have no sharp edges that might harm the subject or the user who will be putting it on. The device should also prevent any feedback current that might cause electrical shock.

2- Reliability: The system should provide accurate results. These results should give an indication whether or not there is a correlation between the power spectrum of heart beating rate and fatigue assessment tests. The device should be providing precise results over the whole course of experimenting days.

3- Ease of Use: The device should have convenient user instructions when conducting the experiments on subjects with a software interface to input the acquired data to computer. The sensors should have minimal weight and comfortable to wear by the subjects.

5- Synchronization: During conducting the memory N-Back M-Pitch fatigue assessment tasks, it is very important to have the data recorded simultaneously to best evaluate the correlation between fatigue and HRV.

6- Real time analysis: In order to detect fatigue, the physiological parameter, heart rate, should be analyzed so that it alerts the subjects every time he/she goes into a fatigue state.

Table 1 Objective assessment in pairwise comparison chat

	Safe	Reliability	Ease of Use	Sync	Real-Time	Total
Safe	****	0	0	0	1	1
Reliability	1	****	1	0.5	1	3.5
Ease of Use	1	0	****	0	1	2
Sync	1	0.5	1	****	1	3.5
Real-Time	0	0	0	0	****	0

The last table indicates that the reliability and synchronization are the most important and critical features in the experiment design. Inaccurate results come out of the device will lead to wrong calculations and it may produce inaccurate conclusions. It was also necessary to design a device that would be able to correlate the changes in the data obtained from the PPG sensor with the results of the N-

Back M-Pitch memory tasks. In order to do that, the PPG signals must be recorded simultaneously during the N-Back M-Pitch testing.

Although device safety is important, there was no risk of electrical shock due to the battery operated hardware or USB operated circuit (~5 Volts) and so this would ensure electrical safety. Also, there were no sharp edges on the device that might be considered dangerous to subjects.

Real time analysis scored zero, because it is not necessary to find the correlation between the fatigue psychological parameter and physiological HRV instantaneously while recording the data for this project. For future applications that require fatigue detection, this feature will have a higher priority.

3.4 Constraints

The major design constraints, that could limit the implementation of the design project, were identified as follows:

1- Expense: The project was funded by the client for the device implementation and subjects recruiting which was limited to $100 per subject.

2- Regulatory Requirements: The MQP group had to design a device in compliance with Food and Drug Administration (FDA) regulations and to be approved by the Institutional Review Board at WPI.

3- Time line: The project was limited to four terms starting from September 2011 to May 2012.

3.5 Revised Client Statement

Based on the weighted objectives, the MQP team has re-written the client statement to better identify the final aims of the project. The following is the revised client statement:

The goal of this project is to collect and analyze the data from the PPG sensor and N-back M-Pitch task to find a correlation between fatigue and HRV, which can be extracted from the data collected non-

invasively and analyzed afterwards. To simulate a psychomotor vigilance task, the auditory memory test, N-back M-pitch, was utilized for the experiment in this project. The experiment takes place through two days where the subjects are not allowed to sleep, and should complete a total of 24 sessions of the N-back M-pitch task. The instructions require subjects to report whether the auditory stimulus presented N steps prior had the same or different stimulus duration as the current. The subjects' low percentage of accuracy is a direct indication of their fatigue level. This task should be conducted while simultaneous PPG signal measurement is taking place. After completing the experiment, the accuracy scores can be compared with the variation in heart beating rate of the subjects. Based on that, conclusions can be drawn by analyzing the correlation between level of fatigue and the HRV data.

Chapter 4 Alternative Designs

4.1 Instrumentation

4.1.1 Sensor Input

An alternative design for the sensor input is to use a light dependent resistor (LDR) instead of a photodiode as shown in Figure 9. A LDR is a light sensor whose resistance varies when the light intensity changes. As the light intensity increases, a LDR's resistance decreases. In order to digitize the PPG signal, the resistance must be converted to a voltage. The easiest way to do the conversion is to use a voltage divider as shown in Figure 10. We did not use LDR for our final design because we were not able to find any commercial integrated PPG sensor using LDRs.
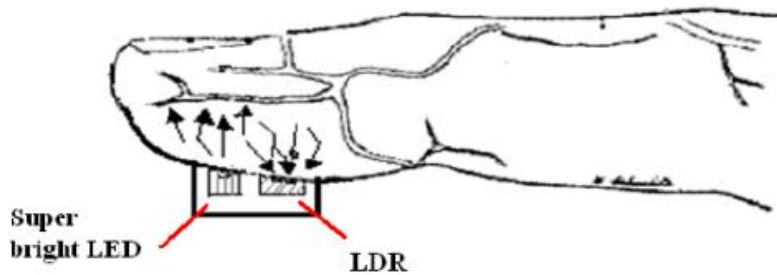
Figure 9 Alternative Design for Sensor Input
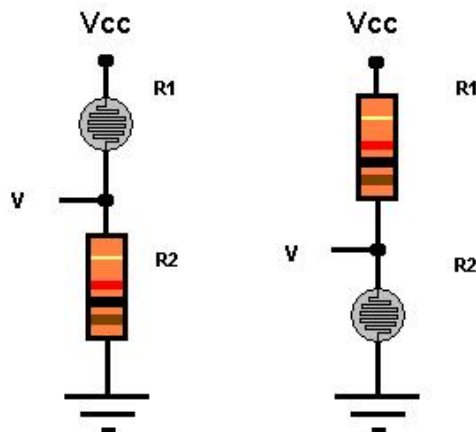
Figure 10 Sample LDR Circuit

4.1.2 Analog Filtering Circuit

An alternative design for the analog filtering circuit is to use other configurations such as the Chebyshev filter. A comparison of magnitude response between Butterworth low pass filter and Chebyshev low pass filter is shown in Figure 11. Chebyshev filter has a sharper cut-off frequency ("roll off "on Figure 11) than Butterworth filter, but ripples exit over the pass band. On the other hand, Butterworth filter has an almost flat magnitude response over the pass band, but the "roll off" is not as sharp as Chebyshev. Common circuit configurations for Chebyshev low pass filter is shown in Figure 12. Although Chebyshev has better performance over the stop band, ripples over the pass band would affect the signal strength. For this reason, we decided to choose Butterworth over Chebyshev.
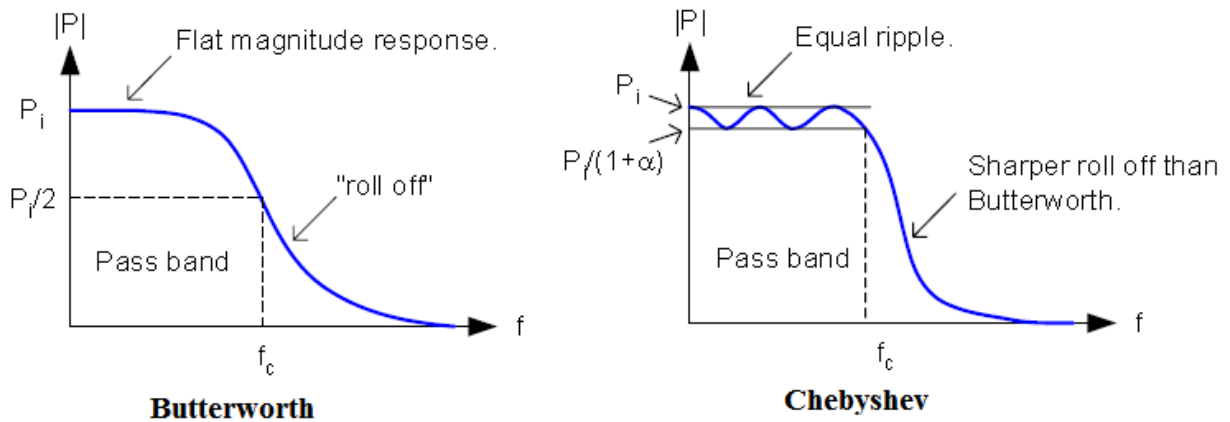
Figure 11 Comparison between Butterworth and Chebyshev Lowpass Filters
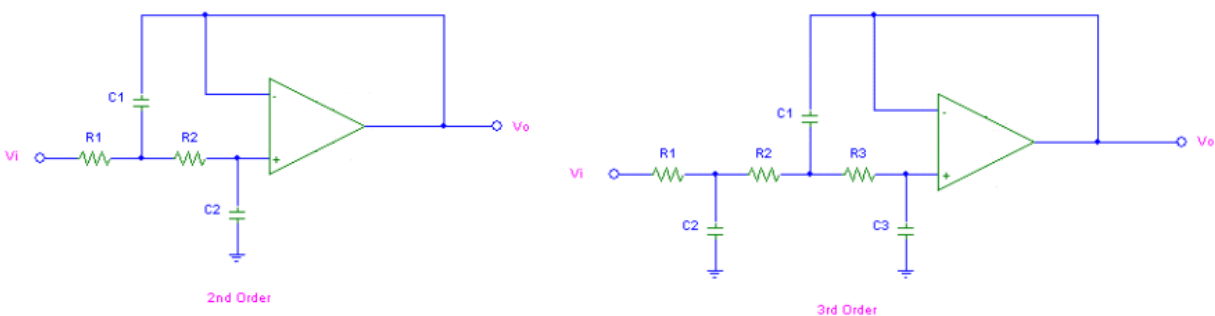
Figure 12 Circuit Configuration of 2nd and 3rd Order Chebyshev Lowpass Filters

4.1.3 Automatic Gain Control Circuit

Automatic gain control (AGC) is an adaptive circuit used in many pulse oximeters. The voltage level from the average output signal is fed back and the gain is adjusted to an appropriate level for a voltage range of input signals. One way of implementing the AGC circuit is shown in Figure 13. Output signal from the current-to-voltage converter is taken into a low-pass filter which has a very small cut-off frequency such as 0.2 Hz. The low-pass filter extracts the DC component of the input signal, and then this DC signal is taken into a differential amplifier. The output of the differential amplifier could be calculated using the following equation:

$$V_{OUT} = Gain \times (V_{ref} - V_{dc})$$

The output signal from the differential amplifier is used drive the infrared LED. When the input DC signal is small, the signal used to drive the LED is large. When the input DC signal is large, the signal used to drive the LED is small. We did not implement the AGC circuit because it would increase the total circuit area and our current design already satisfied the needs for this project.
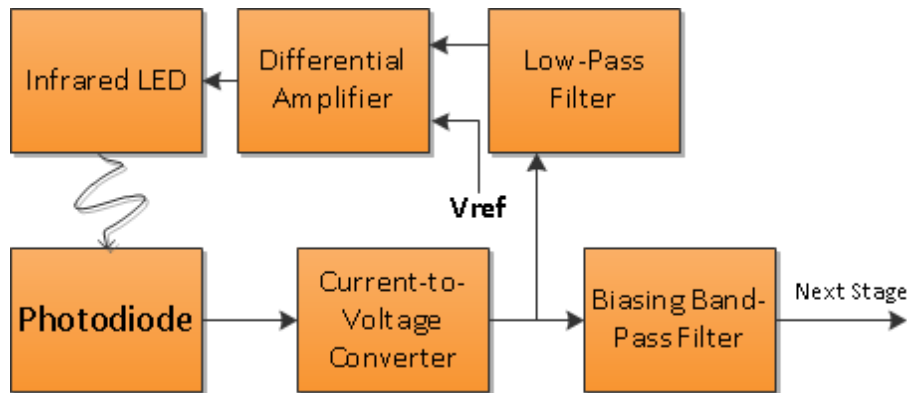
Figure 13 Block Diagram for AGC Implementation

4.1.4 Clamp Circuit

An alternative design for biasing an op-amp is implementing a clamp circuit. A clamp circuit is used to prevent a signal from exceeding a certain defined voltage level by shifting its DC value. It is useful for shifting the biasing voltage level of the op-amp in order to fully utilize the voltage range of the analog-to-digital converter. Figure 14 shows configuration of a positive unbiased clamping circuit. During

the negative cycle of the input signal, the diode is forward biased. It conducts and charges the capacitor to the maximum positive value of the input signal. During the positive cycle of the input signal, the diode is reverse biased. It does not conduct and the output voltage is therefore equal to the voltage stored in the capacitor plus the original input voltage. Since the constant biasing voltage we implemented already satisfied our needs for signal processing, clamp circuit was not necessary.
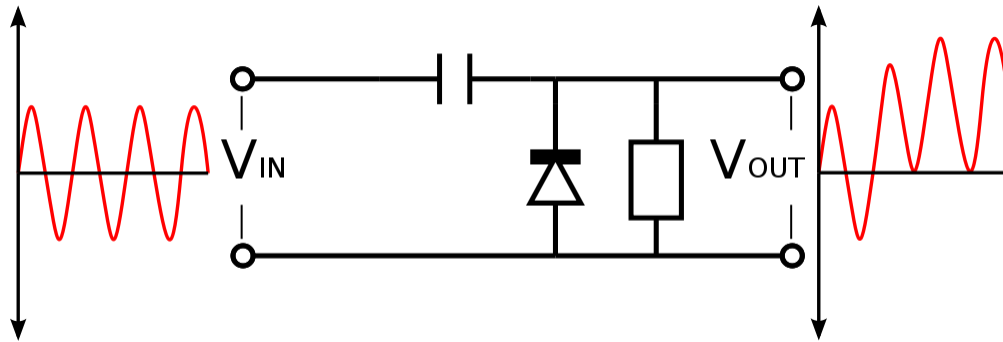
Figure 14 Positive Unbiased Clamping Circuit

4.1.5 Serial Port Transmission

An alternative design for serial port transmission is to use a serial-to-USB adapter other than Texas Instrument's ez430. The baud rate for the one we used is only 9600 bps which greatly restricted the sampling frequency for data recording. Another serial-to-USB adapter we can use is FTDI's Basic as shown in Figure 15. It has a configurable baud rate from 2400 to 115200 bps. Since the current sampling rate already satisfied the signal processing requirement for heart rate variability, we used TI's ez430 serial-to-USB adapter throughout the entire project.

Figure 15 FTDI Basic Serial to USB adapter

4.1.6 Analog to Digital Conversion

An alternative design for digitizing the analog PPG signal is to use an external ADC with higher bit resolution. We might get more precise PPG data by using another ADC, but since the current 10-bit ADC is able to capture all the peaks during the N-back experiment without any misses, another ADC was not necessary.

4.1.7 SpO$_2$ Channel Support

Since the DCM02 sensor we used contains a red LED for SpO$_2$ measurement, it is possible to add a second channel to the ADC to get SpO$_2$ information by adding a sample-and-hold circuit (Figure 16) for each of the LEDs and use only one photodiode. There are two reasons why we did not add this feature: there is no obvious change in SpO$_2$ for a healthy person and the goal of this project was to correlate mental fatigue with only heart rate variability.
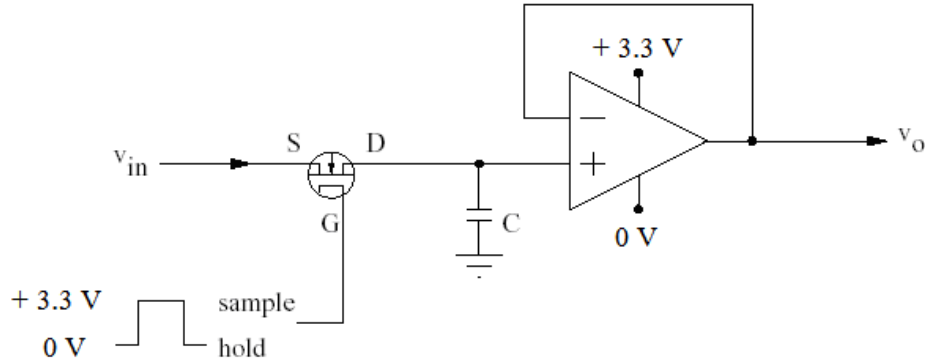
Figure 16 Sample-and-hold Circuit

4.2 Algorithms

4.2.1 Peak detection algorithms

Other than the dynamic range peak detection algorithm designed in this project, the alternative designs include amplitude threshold method and differentiation threshold method. It is necessary for amplitude threshold method to include several stages of filters to remove low frequency components. It also requires a rectification process to determine an appropriate range. We have tried this method prior to final design decision. However, as the filters caused start-up transient, this alternative algorithm is unable to detect the first and last couple heart beats.

Differentiation threshold method uses the fact that the rising edge of a peak has the highest derivative and its turning point has zero derivatives. The algorithms use this method to detect the two rising and falling edges and find the zero crossing as the peak. This method also requires the signal to be as clean as possible which makes the filtering stages necessary, and start-up transient unavoidable. Furthermore, both threshold and filtering compromise the ability of real-time processing. Thus, the dynamic range method was used in our final design.

4.2.2 Periodical Heart Rate Determination

As an alternative design to interpolation, directly up-sampled instantaneous heart rate was one of the alternates; low-pass filtered instantaneous heart rate was the other. After getting the non-periodical heart rates, in order to get reliable heart rate variability, we need to make heart rates periodical and higher in frequencies. As the useful information of HRV-PSD falls into the range of 0-1Hz, it is safe to select 4Hz as the heart rate sampling frequency to make the Nyquist frequency of 2Hz sufficient for desired accuracy and resolution. In order to get the instantaneous heart rate, we designed the testing algorithm to have the entire PPG peak-to-peak interval equals to its corresponding heart rate. The sampling frequency was at its original 75Hz. We then down sample the data into 4Hz to make the instantaneous heart rate. However, this instantaneous heart rate has sharp edges every time heart rate changes, which would create inaccurate high power in the heart rate variability PSD. Thus, a low pass filter is needed to smooth the steps. This "with-filter" version of periodical heart rate determination method improves the accuracy of the heart rate variability PSD. However, when an abnormal heart rate was detected due to motion artifacts, both alternative methods would not be able to remove the abnormalities without affecting the HRV-PSD. Thus, an interpolation method was selected.

4.2.3 Other Alternative Algorithm Designs

Other than the Welch method used in the final design, Fast Fourier Transform could be used to estimate the band power. Comparing the two, Welch program use fewer samples to calculate band power, while Fast Fourier Transform may have higher definition in distinguishing narrow bands. This project only requires area under the curve integration for HRV PSD analysis. Thus using Welch method better fits the efficiency requirements.

Area under the curve calculation could be alternatively calculated by rectangular estimation, trapezoidal estimation and Simpson's rule estimation. All of the three methods have been tested (as shown as part of analysis), and it was found that rectangular estimation has the lowest accuracy, while Simon's rule fluctuates in accuracy and trapezoidal rule showed the best accuracy and stability.

Power spectrum estimation was performed every 2 minutes. Alternatively, we may estimate the PSD in a 2-min window, with variable step sizes. We performed analysis on varying the step sizes. It was found that HRV PSD's high frequency regions and low frequency regions fluctuate throughout the tests. Therefore the final design used the 2 minutes window for PSD estimation and 4 seconds as the step size.

4.3 Alternative Psychological Fatigue Assessment Method

The N-back M-pitch task measures the ability of the short-term memory to restore information changing rapidly (Kirchner, 1958). This task is basically a measure of two parameters: selective and sustained attention, where these parameters are directly affected by fatigue hypothetically. It has been widely used to investigate the working memory processes recently. In the N-Back test it is required that the subjects pay attention to a series of stimuli, either audio or visual stimuli, and determine whether the present stimulus is identical to prior Nth stimulus or not. (Adrian M. Owen, 2005). People with better IQ scores showed higher accuracy baseline during conducting the N-Back task (Raven, 1962) have bigger working memory capacities (Linda Jongman, 1996), for this reason the number of backs was variable depending on the subjects' memory ability whereas the accuracy of the experiment serves as an indicator to mental fatigue. Our MQP team has created an audio based N-Back, M-Pitch, which requires the subjects to determine whether the stimulus presented N backs prior has the same duration as the current stimulus. Four different frequencies were utilized to ensure an appropriate difficulty for the task. These different frequencies serve as additional distracters. The main advantages of using N-Back is that it is easy to implement, requires least amount of effort to perform, limited distracters, parameters could be controlled easily (number of backs, number of frequencies, and inter stimuli interval), does not require any training, and also it has been used over the recent years by many studies to measure the short-term memory capacity.

In recent years, experiments have also been conducted to evaluate different levels of drowsiness while subjects are performing a driving task on a simulator for a period of time. Tasks have been conducted under certain conditions and specified limitations (Wierwille, 1994). This method has several

disadvantages to be used in our experiment, such that, it does have more degrees of parameters, requires much more effort during conducting the procedures of the experiment by the subjects. In addition to that, more attention needed, more physical and mental processes take place, more digital video processing is applied, and an important fact is that evaluations are usually done by trained experimenters. After all it is not as systematic as the N-back M-pitch task.

Chapter 5 Methodologies

5.1 Instrumentation

One goal for this project was to find correlation between heart rate variability (HRV) and the performance on the N-Back experiment. Since HRV can be calculated from continuous heart rates, the objective for this section is to design a hardware that is able to continuously record digitized heart rate information. To meet the requirement, either electrocardiography (ECG) and PPG could be used. We chose PPG over ECG because it only requires one probe, and no electrode gel is needed.

5.1.1 Top Level Module Design

Figure 17 shows the top-level block diagram of the PPG sensor module we designed for data collection during the N-back experiment. It consists of 3 parts: analog filtering, microcontroller, and data recording. There are 4 stages in the analog filtering circuit: sensor input stage, current-to-voltage converter stage, biasing band-pass filter stage, and final noise cancelling stage. The microcontroller part also has 3 stages: analog to digital conversion, serial port communication, and data transmission through USB 2.0 port. When the ez430 serial-to-USB adapter is plugged into a computer, the free software called RS232 data logger is activated. Digitized PPG data are recorded and saved as text files.
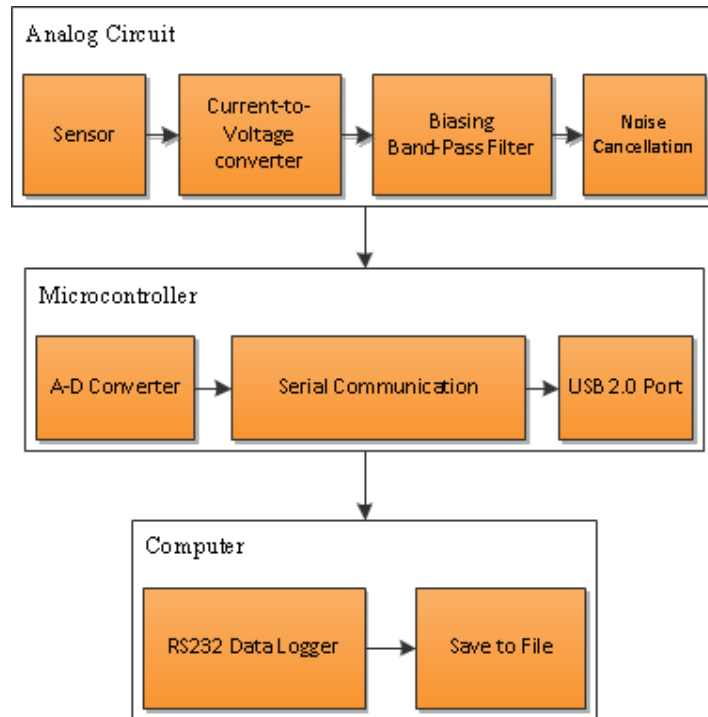
Figure 17 Top Level Block Diagram for Data Collection Using PPG Sensor

5.1.2 Analog Circuit

Figure 18 shows the schematic of the PPG sensor we purchased from a Korea company called APMKorea. It consists of one red LED, one infrared LED, and one photodiode. This sensor is capable of measuring both pulse rate and SpO_2, but in our design we only use the infrared LED and the photodiode because we only needed to measure pulse rate.
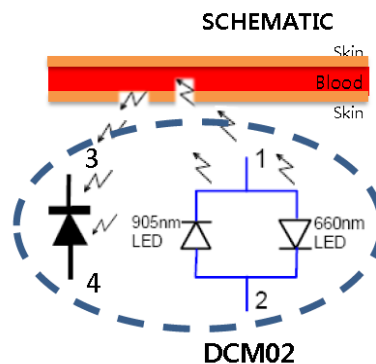
Figure 18 Schematic of DCM02 Reflective Blood Sensor Provided by APMKorea

Figure 19 shows the packaging of the actual PPG sensor we used and Figure 20 shows the connections to all the 4 pins on the sensor. Pin3 is the output of the raw PPG signal (Figure 21) and is the input to the next stage.
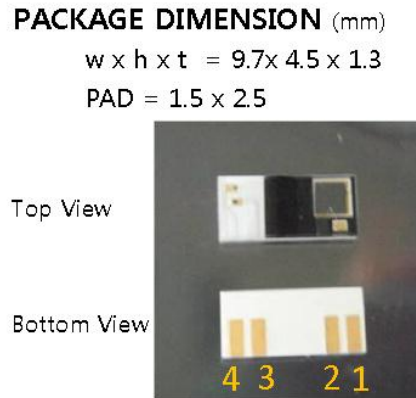
Figure 19 Packaging of the DCM02 Reflective Blood Sensor Provided by APMKorea
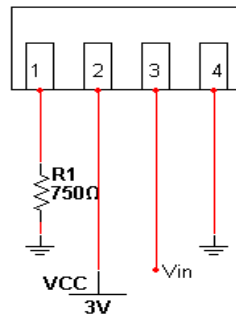
Figure 20 Pin Connection used for DCM02 Reflective Blood Sensor
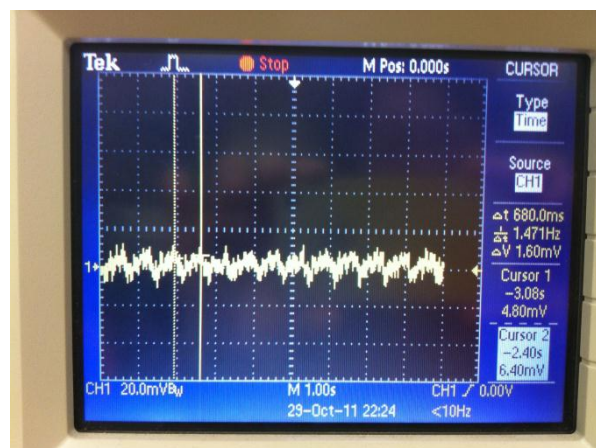
Figure 21 Signal Output Recorded Directly from the DCM02 Sensor

Transimpedance Amplifier
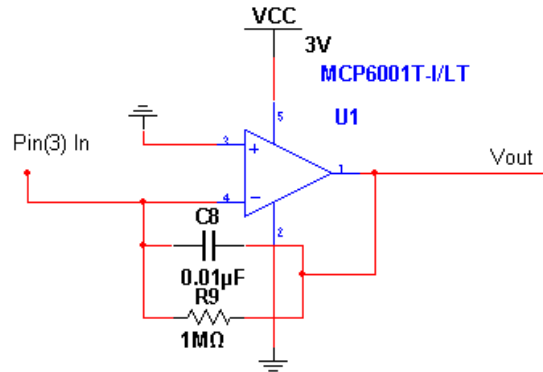
Figure 22 Transimpedance Amplifier Configuration

Figure 22 shows the configuration of the transimpedance amplifier circuit. This stage converts the current from the photodiode into a voltage source. The op-amp is connected using an inverting-configuration and a capacitor is added to reduce the noise. As Professor Bitar from ECE department suggested, we tried 0.001μF, 0.01μF and 0.1μF capacitor, and the one that provided the cleanest waveform among the three was selected. Figure 23 shows the output signal recorded from the tranimpedance amplifier circuit.
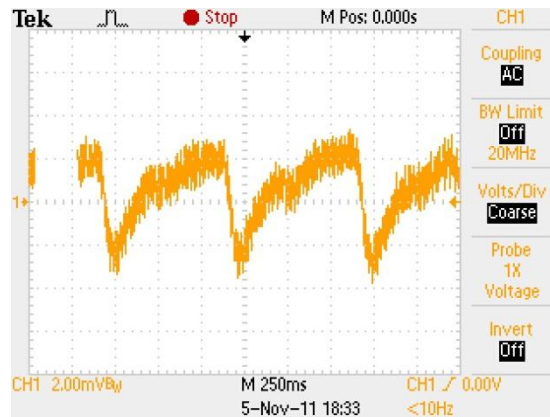
Figure 23 Signal Output After the Transimpedance Stage

Offset Voltage and Biasing
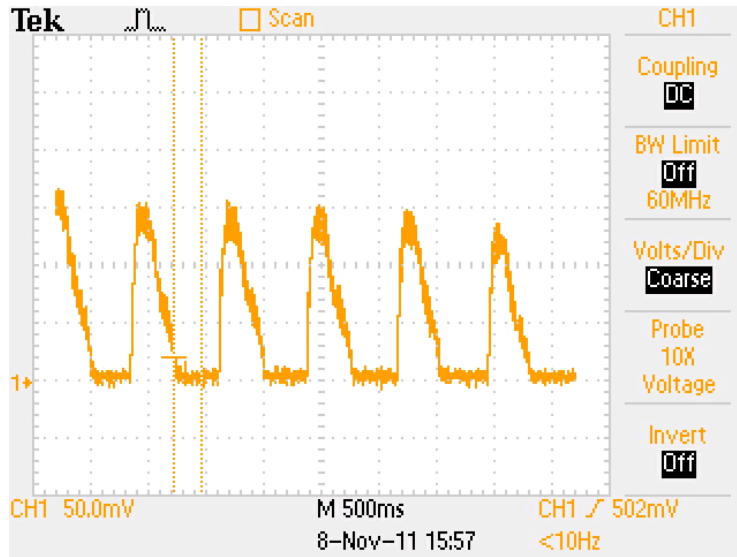
Figure 24 PPG Signal Without Biasing

Biasing an op-amp changes its steady state operating characteristics with no signal being applied. If an op-amp is biased at 1.0V, this means that if there is no incoming signal, the output voltage will rest at 1.0V. Since raw PPG is an AC signal and V- for our op-amp is 0V, any input below 0V will be clipped (Figure 24), thus it was necessary to bias the op-amp. Figure 25 shows the circuit implementation of the biasing stage. Signal came out from the voltage divider circuit was then buffered using an op-amp because it consumed less power. A capacitor was added to reduce the signal noise.
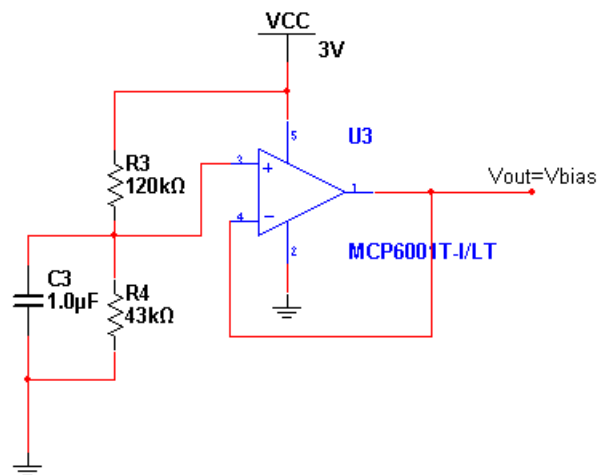
Figure 25 AC Coupled Biasing Circuit

Active Bandpass Filter

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A bandpass filter is needed to extract the information from the raw PPG signal. Since the raw signal is riding on top of a DC signal, a highpass filter is needed to filter the DC signal. A lowpass filter is also needed because the pulse rate is usually under 3Hz. Figure 26 shows the bandpass filter configuration using an op-amp. In the circuit, R2 and C2 form the highpass filter, and R5 and C5 form the lowpass filter. The overall circuit has a passband from 0.53Hz to 7.9Hz, and the gain is 30dB. After this stage, the output PPG signal was already very clean under most of the lab conditions where we tested the circuit. However, when the signal was digitized directly from this stage, some aliasing problems occurred due to 60 Hz power line interference from indoor lightings. Figure 27 shows the bode plot of this bandpass filter and at 60Hz there is still a gain of 15dB, thus further filtering is required to avoid aliasing for digitizing the signal.
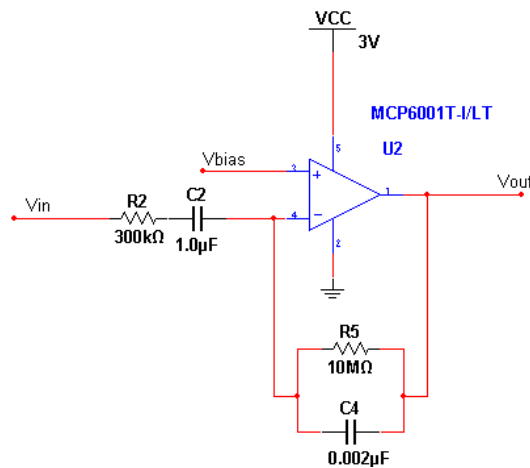
Figure 26 Active Bandpass Configuration for a Passband from 0.53 to 7.9 Hz with a gain of 30dB
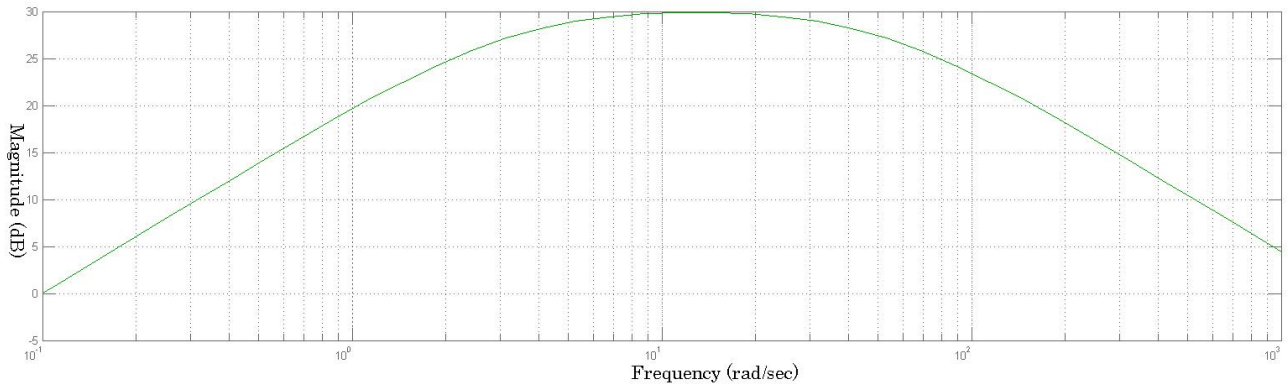
Figure 27 Magnitude Response of the Active Bandpass Filter in Figure 26

41
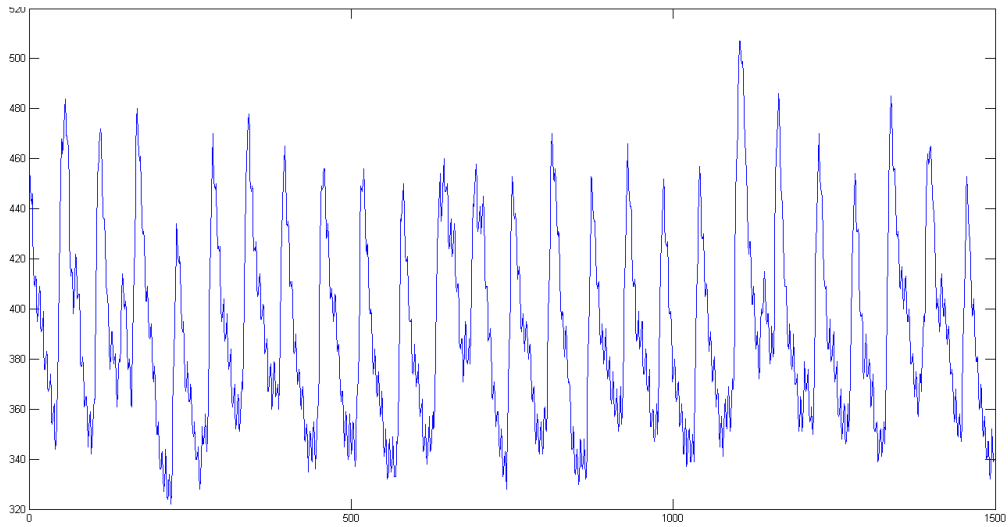
Notch Filter

Figure 28 Digitized PPG Signal with Power Line Interference
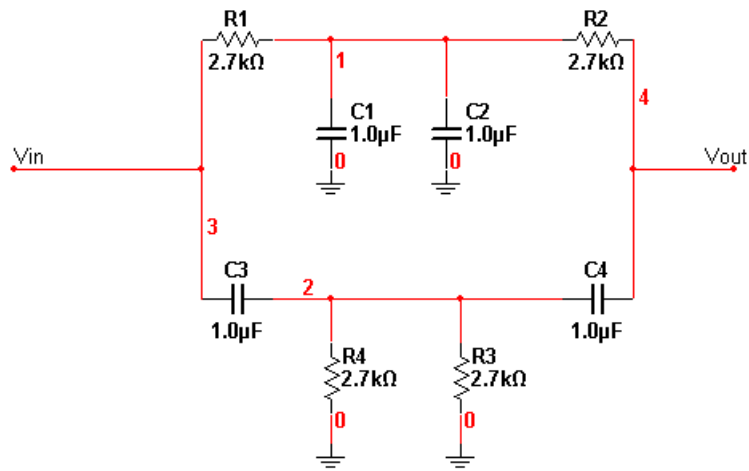
Figure 29 Twin-T Configuration for a Passive 60hz Notch Filter
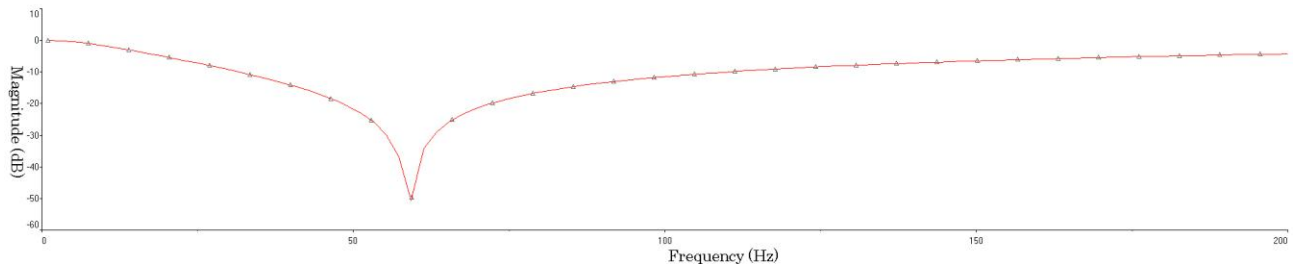
Figure 30 Magnitude Response for the Twin-T Notch Filter in Figure 29

After the bandpass filter stage, the signal still has some noise from the power line (Figure 28). We decided to add a notch filter stage. Figure 29 shows our implementation of this notch filter. Twin-T configuration was used here because it is a very common design in passive notch filters. It gives us about -50dB attenuation at 60Hz as shown in Figure 30.

Improved: Butterworth Low Pass Filter

Since signal above 15 Hz is not needed for measuring heart rate, a 3 stage, 6th-order Butterworth low pass filter with a cut-off frequency at 15 Hz was designed to replace the notch filter in order to better reduce any aliasing problems that might occur. A Sallen-Key topology was used for filter implementation as shown in Figure 31. Values for all the capacitors were designed to be the same in order to make the overall implementation simpler.
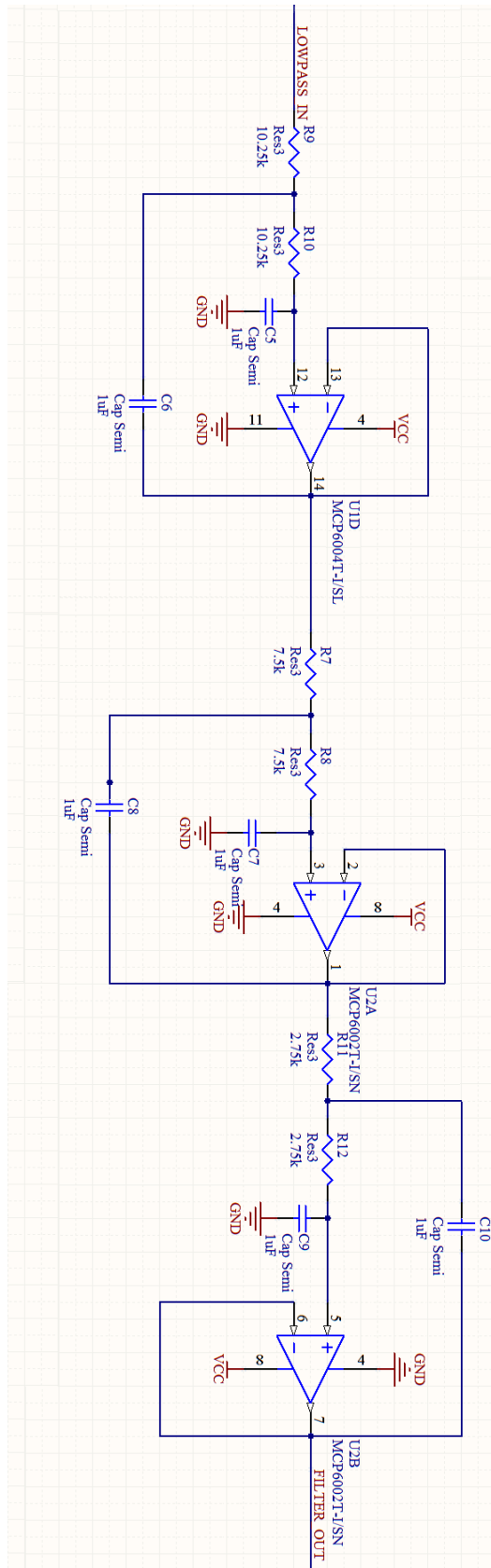
Figure 31 Three Stage, Sixth Order Butterworth Low Pass Filter

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The magnitude response of this low pass filter is shown in Figure 32, where x-axis is the frequency in Hz and the y-axis is the filter gain. As shown on the graph, the filter gives 0.0002441 on the y-axis which approximately equals to -74dB attenuation at 60 Hz. Compare to the notch filter we implemented previously, this active low pass filter only requires one more op-amp, 2 more resistors and 2 more capacitors. Figure 33 shows the final analog output signal coming out from the Butterworth lowpass filter and it is devoid of noise and artifact contamination.
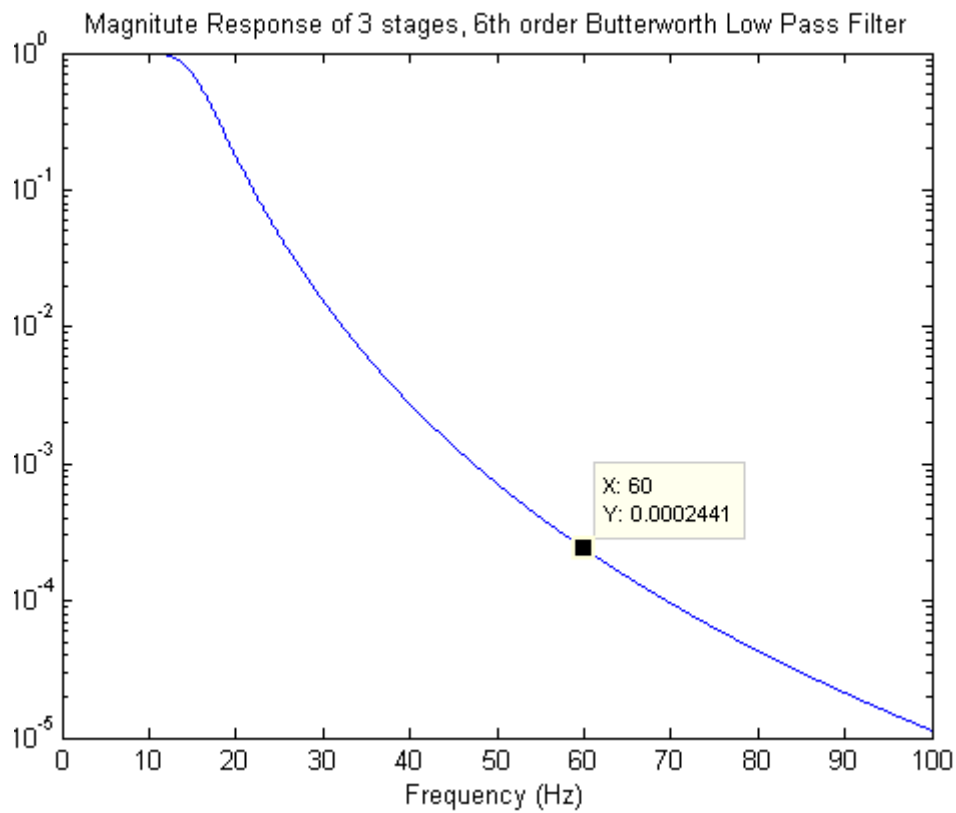
Figure 32 Bode Plot of Butterworth Low Pass Filter
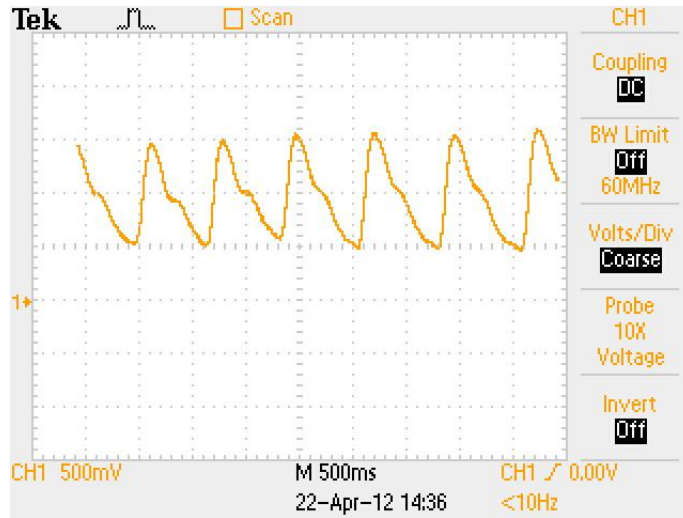
Figure 33 Final Analog Output Signal

Overall Analog Circuit Design
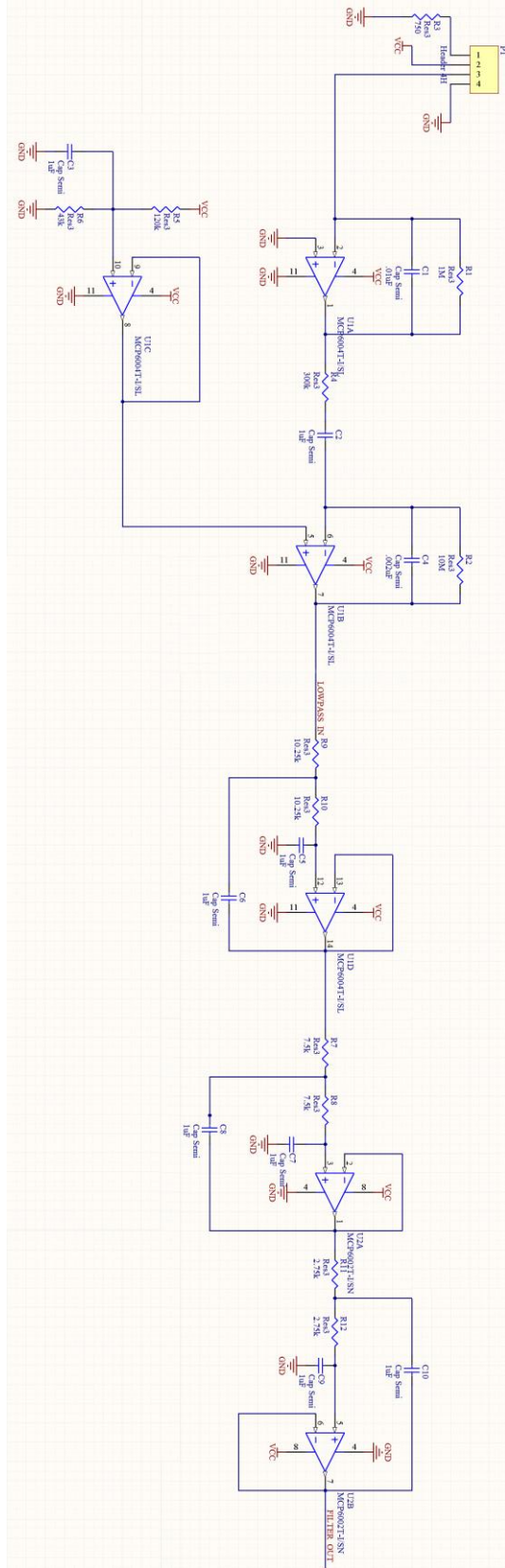
Figure 34 Overall Analog Circuit Design

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Figure 34 shows the overall design of the analog circuit and an output capture from the oscilloscope. It has a total of 5 parts: sensor input, transimpedance amplifer, bandpass filter, biasing circuit, and Butterworth lowpass filter. A 4cm x 2cm printed circuit board was designed based on this analog circuit.

5.1.3 ADC, Serial Port and More
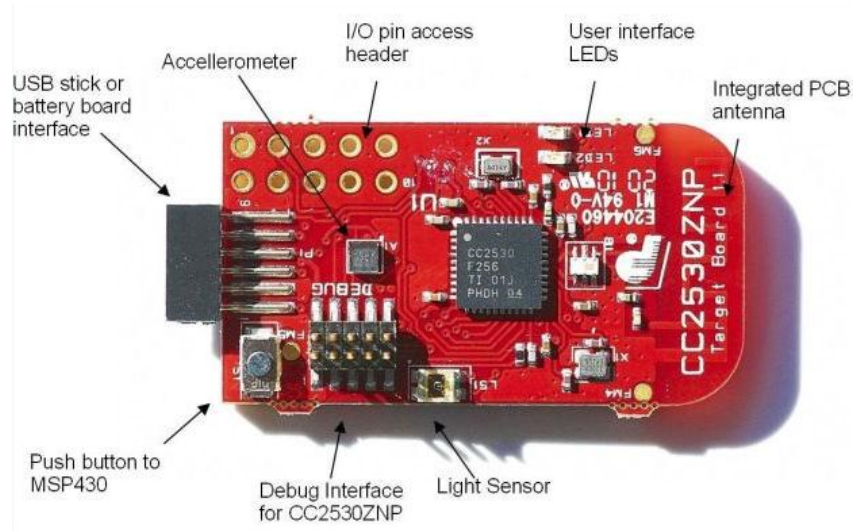
Figure 35 CC2530ZNP Target Board from Taxes Instrument

After the notch filter, PPG signal is ready to be digitized. The CC2530ZNP kit (Figure 36) from Texas Instrument is the microcontroller board we used because it supports ZigBee wireless communication protocol and this whole sensor module was later updated into a wireless one for another project Yichao Joy Xu and Fangjie Ding were involved with. Code implementation for the wireless transmission is attached in Appendix. The development kit contains three CC2530 target boards and one ez430 serial-to-USB adapter for debugging and UART interface. For this project, only one target board (Figure 35) and the ez430 USB adapter were used. The PPG signal was digitized using an on-chip, 10-bit ADC from the MSP430F2274 microcontroller. The ADC was configured as shown in Figure 37. Internal voltage of 1.5V was used as a reference. The sample and hold time was set to 64 ADC clock cycles. Sampling frequency is around 75 Ha when the microcontroller is fully loaded for serial port communication with a baud rate of 9600 bps. A sample of digitized PPG data is shown in Figure 38. Figure 39 shows the product prototype with the designed PCB board stacked together with the

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CC2530ZNP target board. RS232 Data Logger is the software we used for data recording during the N-back experiment.
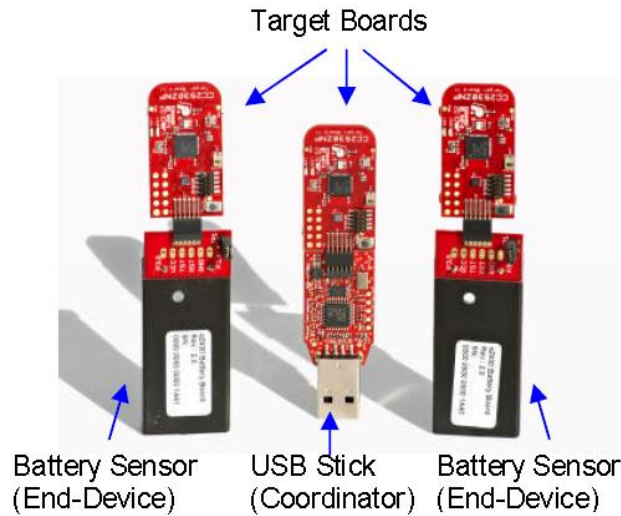
Figure 36 CC2530ZNP Development Kit from Texas Instrument

```
1     unsigned int getPPG()
2   □{
3         ADC10AE0 = 0x08;  //Analog Input A3 enabled
4
5         ADC10CTL0 = SREF_1 + REFON + ADC10ON + ADC10SHT_3;  // use internal ref, turn on 1.5V ref, set samp time = 64 cycles
6         ADC10CTL1 = INCH_3;                          // Analog input A3
7         ADC10CTL0 |= ENC + ADC10SC;                  // Enable conversions
8         while (!(ADC10CTL0 & ADC10IFG));             // Conversion done?
9         long temp;
10        temp = ADC10MEM;
11        return ((unsigned int) temp);
12    └}
```

Figure 37 Code Implementation for ADC
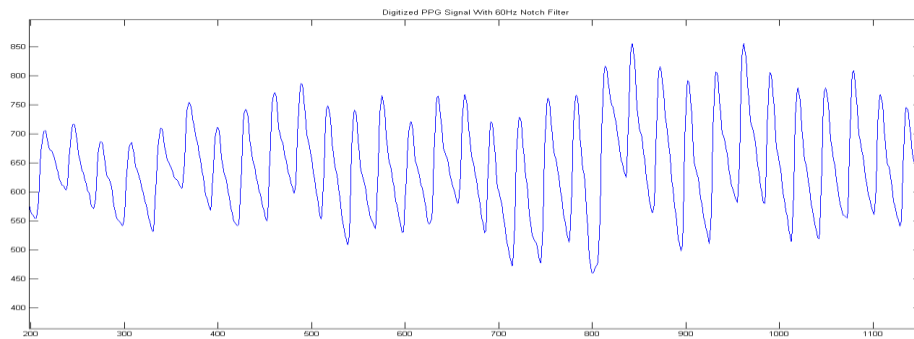
Figure 38 Digitized PPG Data Sample

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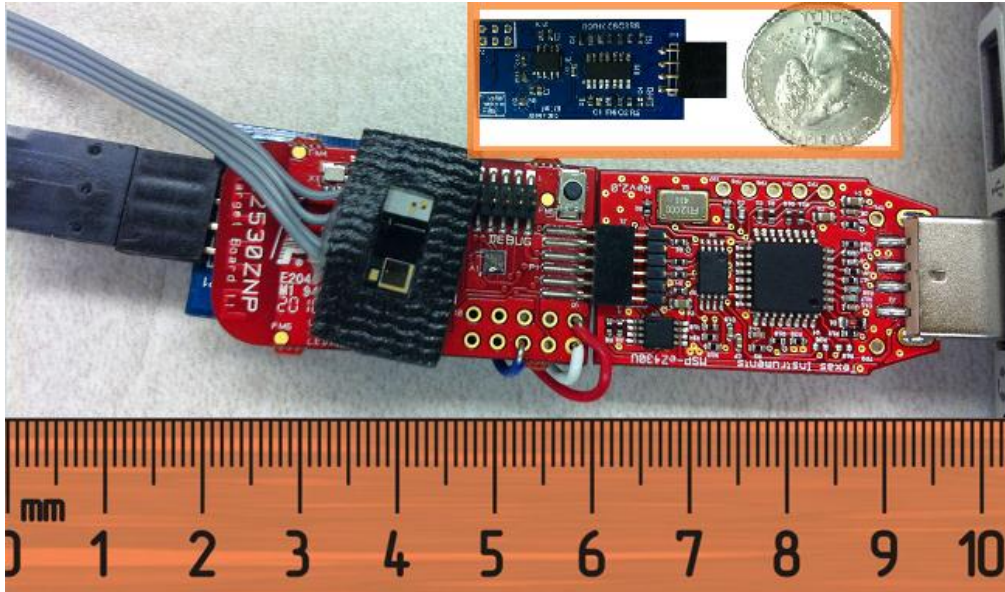
Figure 39 Final Design Prototype for PPG Data Collection

5.2 Signal Processing

The designed instrumentation outputs a string of digitized PPG samplesfrom the sensor at 75 Hz. A processing algorithm has been designed to find heart rate, heart rate variability power spectrum density (HRV-PSD), and areas under the curve of HRV-PSD's high and low frequency region and their ratios. Figure 40shows the block diagram of the processing information from the raw PPG signals, including peak detection, cubic spline interpolation, and power spectrum density processing. Each of these blocks are introduced in detail in the following sections.
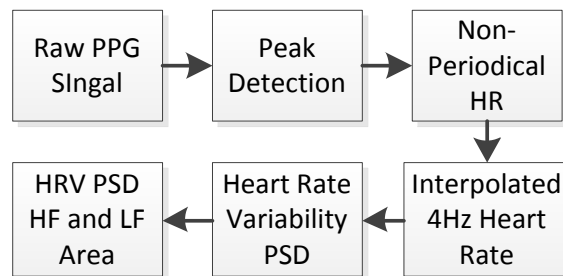
Figure 40 Block diagram of the signal processing procedure

5.2.1 Peak Detection

Peak detection algorithms are dependent on determining the maximum value within a certain region. Unlike ECG, which contains P, QRS and T waves, the PPG waveform from our designed sensor has one clear peak and one clear nadir per heartbeat. Thus, we could implement an algorithm without the use of a filter and threshold. A dynamic peak detection algorithm has been designed, as illustrated in Figure 41.

A MATLAB function has been designed. It takes in two parameters: raw PPG data and sampling frequency. As human resting heart rate is approximately in the range of 60 beats per minute (BPM), we made the assumption that there will be one peak (one heart beat) within the first second. From the peak found, we keep the assumption of 60 bpm to find the next peak from the peak position found at first. Every time the algorithm finds a peak, it remembers the peak position and its value. From the two initial peaks found, we may calculate the peak-to-peak interval and let this value determine the interval assumption in looking for the next peak. This iterative process is terminated by verifying if or not the processed data has exceeded the data length.

In preventing the peak detection algorithm detecting peaks from noises, we limited the peak to peak interval assumption from 0.33 to 1.33 seconds. For example, as the interval assumption is being updated every time a new peak has been found, we implemented a checkpoint to test if the interval found produced a heart rate between 45 BPM to 180 BPM. If the interval corresponds to the set requirement, the interval assumption will be updated. Otherwise, the last assumption of interval is kept from being updated.

Figure 42 shows the raw PPG waveform with peaks marked. This dynamic peak detection algorithm is free from filtering and static amplitude threshold. Thus, detected peaks are free from start-up transients. A visual inspection has been performed on peaks detected from a set of sample data. The designed algorithm achieved 100% accuracy.
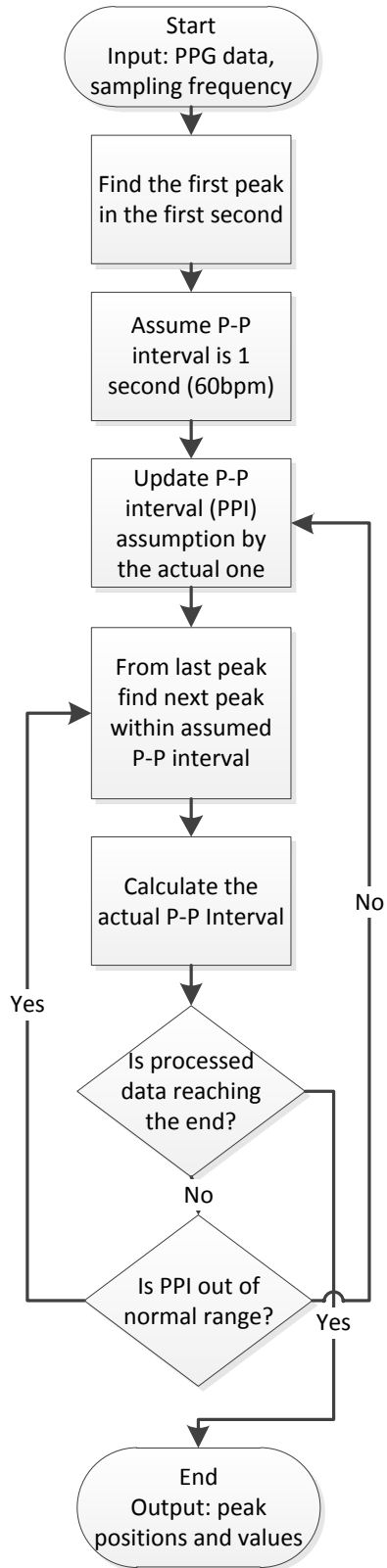
Figure 41 Dynamic range peak detection algorithm design
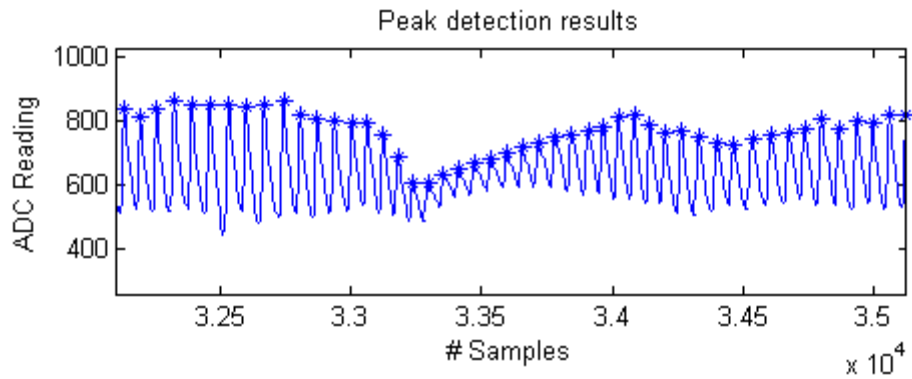
Figure 42 Peak detection results

5.2.2 Heart Rate and Interpolation

Once the RR-interval time series of a set of PPG data are found, the heart rate within the interval could be determined by the inverse of the interval, multiplied by 60 seconds/minute to make the heart rate into Beats per Minute (BPM). However, this array of heart rate information was not useful or accurate for heart rate variability calculation, as it does not have a constant sampling frequency. Thus its power spectrum density under the assumption of 1 Hz was highly unreliable. Finding the heart rate with uniform intervals became critical to the algorithm design. In order to obtain uniformly sampled data, we interpolated and re-sampled the RR-interval time series using cubic spline. This process was completed simply by a MATLAB function (spline). During the process, the re-sampling frequency was selected to be 4Hz, which suffices the Nyquist sampling theory, since the highest frequency of interest when estimating the PSD of HRV is 0.4Hz.

The MATLAB function spline uses a cubic spline interpolation to calculate the output. The syntax of the spline function is yy = spline(x, Y, xx), where x defines the window of the output; Y is the signal to be interpolated; and xx defines the values of the interpolant (The MathWorks). For instance, let a be a sequence of +1's and -1's: [1 -1 1 -1 1 -1 1], Figure 43 below shows the up-sampled versions of a using spline. The top figure shows the original sequence a; the second figure shows the result after up-sampling a by a factor of 4; the third figure shows the result after up-sampling a by a factor of 10; and the

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bottom figure shows the result after up-sampling a by a factor of 100. If the original sequence was a down-sampled version of a cosine wave at time instant $t = n\pi$, where n is an integer. After up-sampling a by a factor that is at least 2, theoretically, we are able to reconstruct the original continuous-time cosine signal.
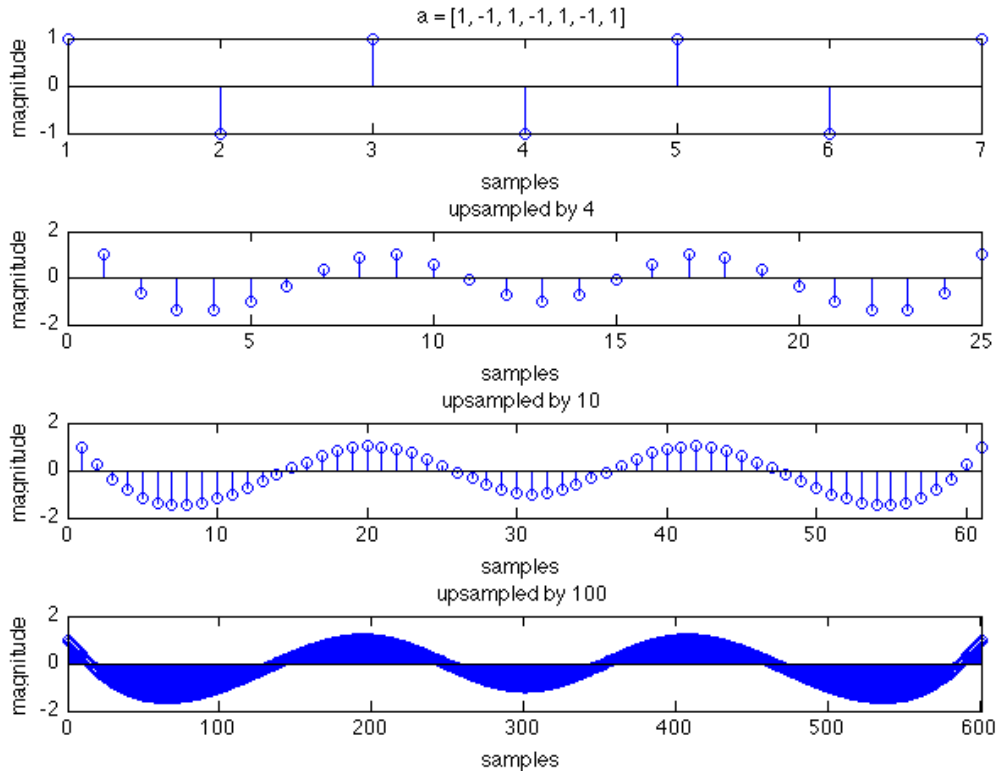
Figure 43 Example of Cubic Spline Data Interpolation

A customized heart rate interpolation method has been designed to include heart rate calculation, easier function syntax and an artifacts cancelation process.

The signal processing function takes in the peak positions generated from the previous cascading function, the original sampling frequency and user defined desired heart rate sampling frequency. Usually it is set to 4Hz. This function produces an array of periodical heart rate at the desired frequency which is ready for power spectrum density estimation for heart rate variability.

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As the biomedical experiment in testing mental fatigue places our subjects mainly at seats without any extraneous exercises, the normal heart rate range would be surely within 45 to 90 BPM. Motion artifacts may cause PPG signal to swing, causing inaccurate heart rates. These heart rates information needs to be removed prior to interpolation. This motion artifacts removal process was included with a check point in the beginning of the function. Any heart rates out of the range will not be used in cubic interpolation. Therefore, periodical heart rate estimation accuracy was significantly improved by the customized the algorithm. Figure 44 shows the interpolation results.
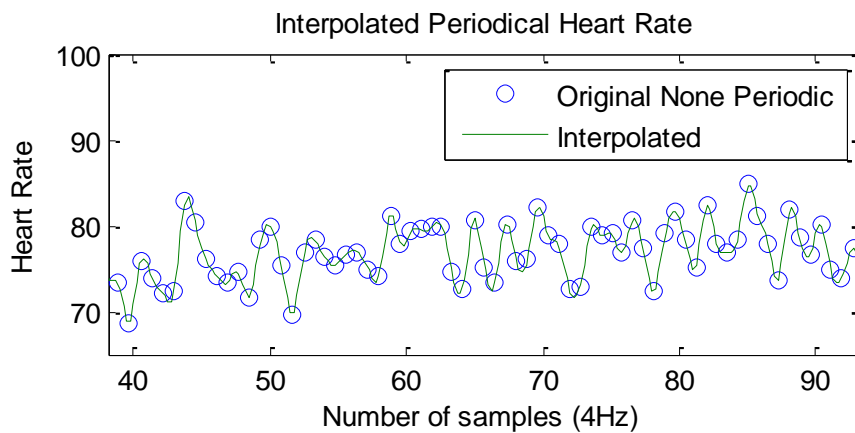
Figure 44 Interpolated Periodical Heart Rate

5.2.3 Windowed Power Spectral Density Estimation

Based on the resampled RR-interval time series, we used MATLAB functions *pwelch* to obtain the corresponding PSD estimations. The theories behind these two functions are described in Chapter 2, Section 5.

The syntax for periodogram is [Pxx,f] = periodogram(x, window, nfft, fs), where x is the upsampled RR-interval time series; the vector window specifies the coefficients of the window used to compute a modified periodogram of the input signal x, when it is not specified, the default window used by periodogram is a rectangular window (rectwin); nfft specifies the length of FFT; and fs is the sampling

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frequency, the default value for fs without specification is 1Hz. The output Pxx returns the PSD estimate, and f is the corresponding vector of frequencies (The MathWorks).

The syntax for pwelch is [Pww, f] = pwelch(x, window, noverlap, nfft, fs), where similar to periodogram, x is the upsampled RR-interval time series, which is segmented into certain number of segments with equal length; the vector window specifies the coefficients of the window, if not specified, the default window is a Hamming window; noverlap is the number of the signal samples that are common to two adjacent segments, if not specified, pwelch segments the signal x with 50% overlap; NFFT is the length of FFT; and FS is the sampling frequency (The MathWorks).

Initially, the power spectrum density was performed on the entire 10 minutes data set from each trial. There were little or no correlations between the 10 minutes data HRV-PSD with mental fatigue. We then lowered the data size for PSD estimation, from 10 minutes to 2 minutes. If truncating the PPD data into pieces of 2 minutes, we can only get 5 of them, which is still not enough to observe or find correlation between mental fatigue and HRV-PSD. We decided to make the 2 minutes as a "moving window". Starting from the very beginning of available PPG data, the first section of 2 minutes PPG has been performed the analysis of power spectrum density estimation, the next estimation starts from the beginning of the 5th seconds, the third one from the beginning of the 9th. This enables the moving window to "walk" through the entire dataset, with a 4 seconds "step size", as illustrated in Figure 45.

As the output from this PSD estimation stage, we obtained a more continuous HRV-PSD estimation, updated every four seconds, while the 2 minutes window kept the estimation accuracy.
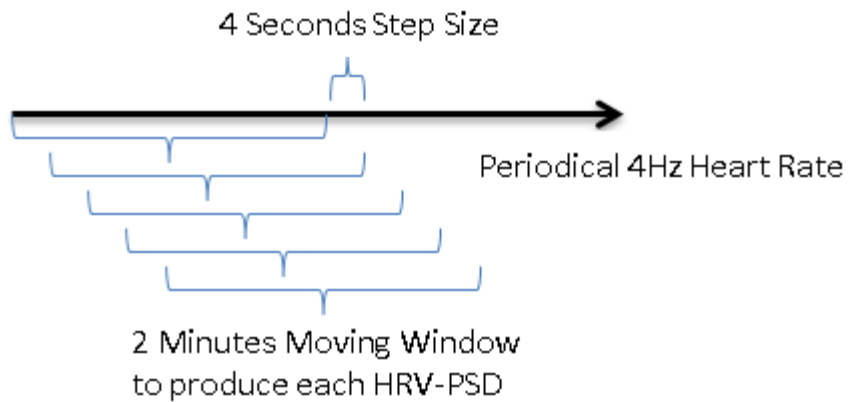
Figure 45 Moving window HRV PSD estimation

5.2.4 Area under the Curve Integration

Once the PSD estimation of each testing session is obtained, different frequency components were then examined and compared over time. Table 2 Definitions of Frequency Domain HRV Parameters shows the frequency parameters that are considered in this report. The energy in each of the frequency band was computed and compared (plotted) over time. The trend of each frequency parameter against time suggests how each parameter is affected as the level of fatigue increases. Note that the level of fatigue is directly measured by the accuracy of the N-back M-pitch test.

Table 2 Definitions of Frequency Domain HRV Parameters

Parameter	Definition
VLF	Very-low-frequency range (≤ 0.04Hz)
LF	Low-frequency range (0.04-0.15Hz)
HF	High-frequency range (0.15-0.4Hz)

A Matlab function has been designed to output the interested parameters for this project – LF, HF and the ratio of LF/HF. Three methods of interpolation have been tested – trapezoidal, rectangular and Simpson's Rule. Detailed methodology analysis has been shown in Chapter 7, and trapezoidal rule has been chosen because of its accuracy and stability in accuracy. A MATLAB function has been written using trapezoidal rule in calculating LF and HF area under the curve, taking in the PSD, desired LF and HF range, outputting the areas of LF, HF and their ratios.

A top level processing program has been written to massively process the datasets. This program reads in the available data folders, opens each folder and produces the desired parameters, including LF and HF area under the curve, LF/HF ratios, and heart rate, each come with averages within a session and high-resolution results with moving windows. This program outputs and saves a set of processed data under each of processed data, automatically, which saved tremendous amount of data-processing labor hours.

5.3 Experimental Design

5.3.1 N-back M-pitch Memory Task

The N-Back M-Pitch task is a working memory paradigm that yields reliable measures of cognitive performance. During the task, subjects will be instructed to report whether the auditory stimulus presented N steps prior has the same or different stimulus duration as the current.

In this experiment, the N-back M-pitch task will be carried out in MATLAB on a computer, a user interface consisting of two keys on a keyboard: "S" for SAME and 'D" for DIFFERENT" which allow subjects to report their decisions. At the same time, pressing "S" on the keyboard is programmed to have same effect as clicking "SAME" on the screen, so does "D" for "DIFFERENT". The variable N will be a positive integer (i.e. N = 1, 2, 3…). The auditory stimuli will have four different pitches (500, 600, 700, and 800 Hz), so the variable M will be set to 4. There will be two possible stimuli durations: 50 and

100 msec. Subjects will be instructed to neglect the difference in frequency, and focus solely on determining whether there is a change in duration.

Once a stimulus goes off, subjects will have 2 seconds to respond by choosing either "SAME" or "DIFFERENT". If subjects choose correctly, they will receive a score of 1 for the current trial. If not, they will receive a score of 0. If subjects fail to respond within the time limit, the current trial will be considered a miss and a score of 0 will be recorded. The accuracy will be calculated according to the following formulas:

Number of correct responses/Total number of trials $\times 100\% =$ Accuracy $\qquad$ (3)

Total number of trials=Total number of stimuli-N $\qquad$ (4)

The top level functional modules of N-Back M-Pitch testing software are shown in Figure 46. A Matlab program has been written according to the function outlines. There are couple of parameters could be set and adjusted prior to the start of the program, and the major ones are listed below:

N - number of backs for subjects to compare

M - number of different pitch frequencies involved in the experiment

Inter-Stimulus Interval (ISI) - interval length in seconds between two pitches

PL - longer duration pitch stimulus

PS - shorter duration pitch stimulus

N represents number of backs for subjects to compare. For example, if N is one, only one back of pitch duration information needs to be remembered in order to be compared with the most recent one. If N equals to two, then the subject is obligated to remember two backs of pitches for comparison.

M represents number of different pitch frequencies involved in the experiment. In the current experimental setting, M is set to 4, and the different with pitch frequencies are 500 Hz, 600 Hz, 700 Hz, and 800 Hz. Besides, there are two different pitch durations -- PL and PS, which could be adjusted. In order to exclude the factor of auditory perception diversity, PL was set as 200 ms and PS, 20 ms initially. After the preliminary testing, PL and PS are set to the standard durations 100 ms and 50 ms, of which differences may be easily neglected if subject is not paying attention. Similarly, the inter-stimulus interval

(ISI) has been initially set to 3 seconds to help the learning process for the program. During the initial experiments, it has been found that the response times distributed across the 1-1.5 seconds. Furthermore, as the auditory short-term memory fades out rapidly, the ISI has then been moved down to 2 seconds.

During the process of experiment, the subject needs to remember the durations of the N stimuli prior to the most recent one, while neglecting the pitch differences. In our latest preliminary testing for program design validation, N is set to 1. The subjects thus need to memorize the duration of the last stimulus, compare the length of the duration with that of the current one, and respond to the program within the ISI - 2 seconds. Upon the subject's response, the response time is recorded along with its accuracy. There are typically four situations -- correct, wrong, omitted and multiple responses. In the case of omission, the accuracy of that trial is marked same as wrong at 0% accuracy. In the case of multiple responses-- when the subject responds to the program more than one time, the accuracy only depends on the last response prior to the next stimulus, and yet the instances of multiple responses within a trial will also be positioned and recorded.
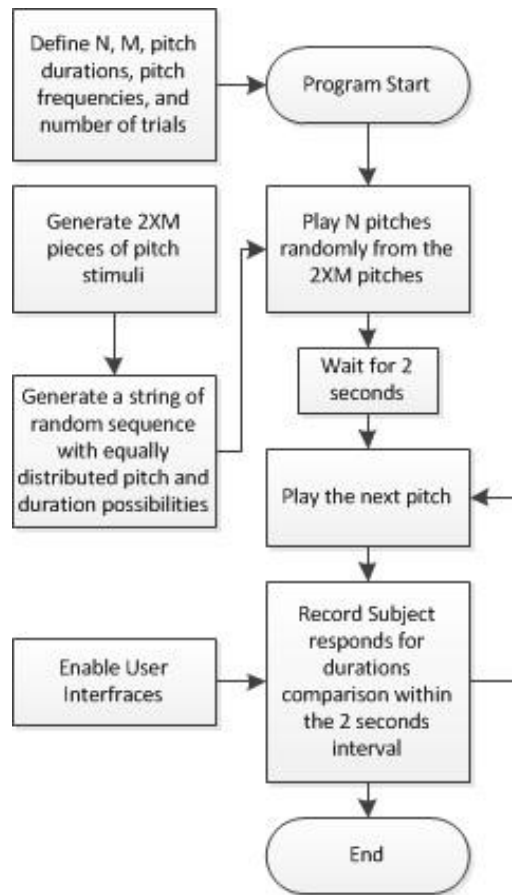
Figure 46 Top level N-back M-pitch experiment program design

5.3.2 Training Sessions and Expectation

A week prior to the experiment, subjects will be instructed to complete a total of 6 or more training sessions on their own. The schedule for the training sessions is shown in Table 3. During each session, subjects will need to complete a 10-minute N-back M-Pitch test. It is mandatory for the subjects to submit their accuracy results/plots generated by the MATLAB program to navalmqp@wpi.edu immediately after the completion of each session. We reviewed the accuracy results for all subjects. If a subject's accuracy exceeds 90% for two consecutive sessions with N=x (x=1, 2, 3…), the subject will then be asked to increase N to x+1. For example, if a subject scores over 90% for two consecutive sessions with N=1, he/she will be instructed to increase N to 2. Once the subject's percent accuracy plateaus at around upper 80%, he/she is ready for the experiment.

Table 3 Training Sessions Schedule

	Day 1	Day 2	Day 3	…
Anytime between 8 – 12 AM	Session 1	Session 3	Session 5	…
Anytime between 3 – 8 PM	Session 2	Session 4	Session 6	…

The purpose of the training sessions is to avoid a saturation effect, where a subject's performance stabilizes at the maximal score for a given task. In the case of a saturation effect, a sleep deprivation might not cause an obvious drop in the subject's performance.

Figure 47 illustrates an example of the learning curves of a subject. The subject is instructed to begin the N-back M-pitch task with N=1. After three sessions, the subject's percent accuracy stays above 90%, which is not desirable according to the experimental design as previously described. The subject will be notified to increase N by 1, and continue onto the next training session with N=2. By increasing N, the difficulty of the N-back M-pitch task increases and the subject's performance is expected to drop. As the subject completes more sessions with N=2, the performance may rise but at a slower rate. We keep increasing the number of backs as long as the accuracy exceeds the 90% limit consecutively.

After seeing stabilization in the N-Back task performance around an accuracy of 80%, we could take this N number of backs and start to implement the sleep deprivation-fatigue experiment.
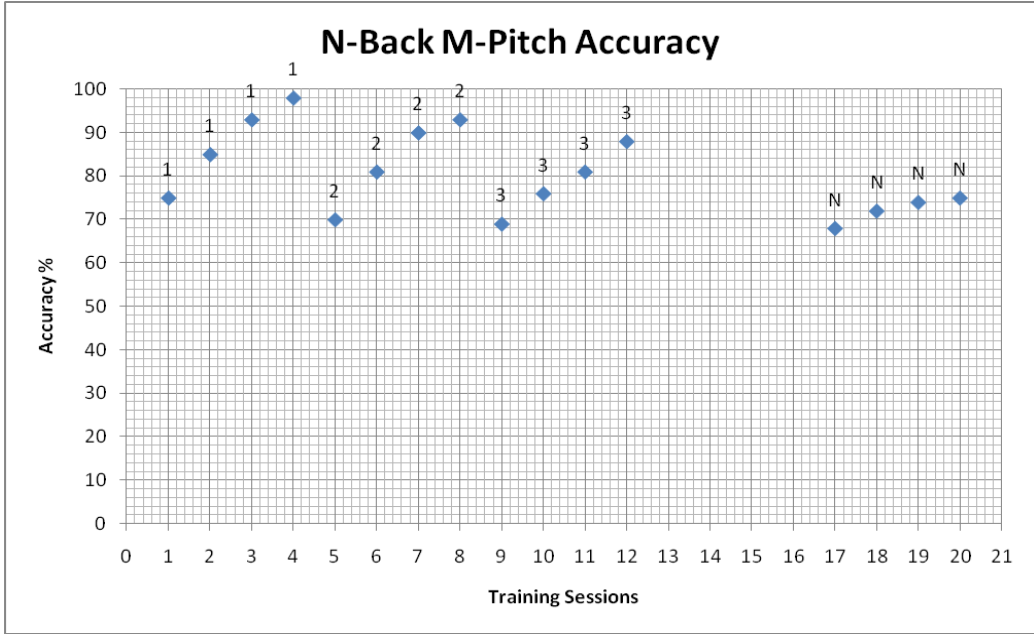
Figure 47 An Example of Performance vs. Training Sessions

5.3.3 Data Collection During N-Back Experiment

During each N-back experiment session, PPG data were recorded for the entire duration. Figure 48 shows the actual circuit we used during N-back experiment for one of the subjects. We used a breadboard at that time because the PCB layout was not yet available. Power supply for the analog circuit is provided by the USB port from the computer. The PPG sensor is placed either on forehead or fingertip of the subject. When USB adapter is plugged in, a COM port is generated and digitized PPG data are ready to be transmitted through serial port using any RS232 port communication software. Figure 49 shows a screen shot of the software used during N-back experiment. On the left part, it shows a list of available COM ports and on the right part it shows the configuration of the COM port and the file location for data recording. When a user starts the N-back experiment on MATLAB, "start logging" button on the software needs to be pressed. When one session is finished, "stop logging" button needs to be pressed. The saved text files can be used as direct inputs into MATLAB for signal processing.

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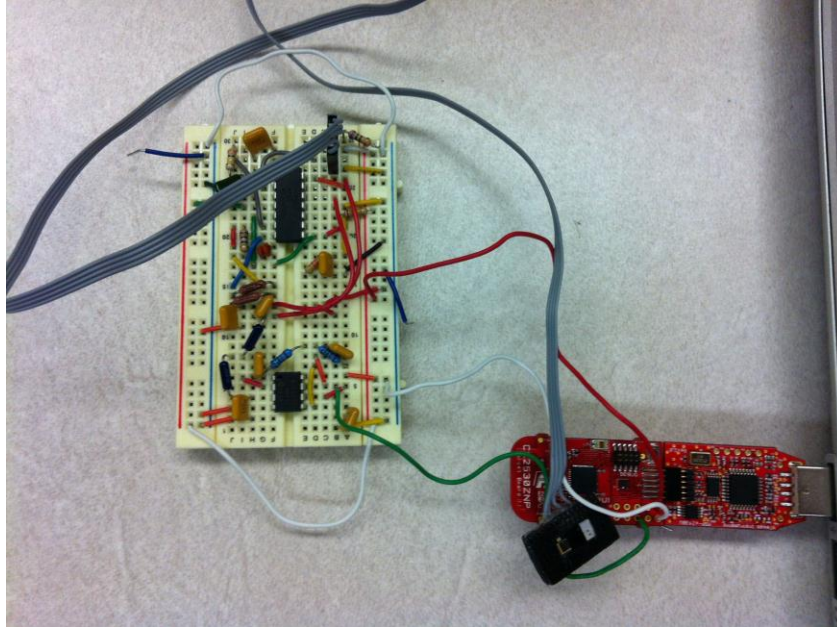
Figure 48 Actual Circuit Used During N-Back Experiment
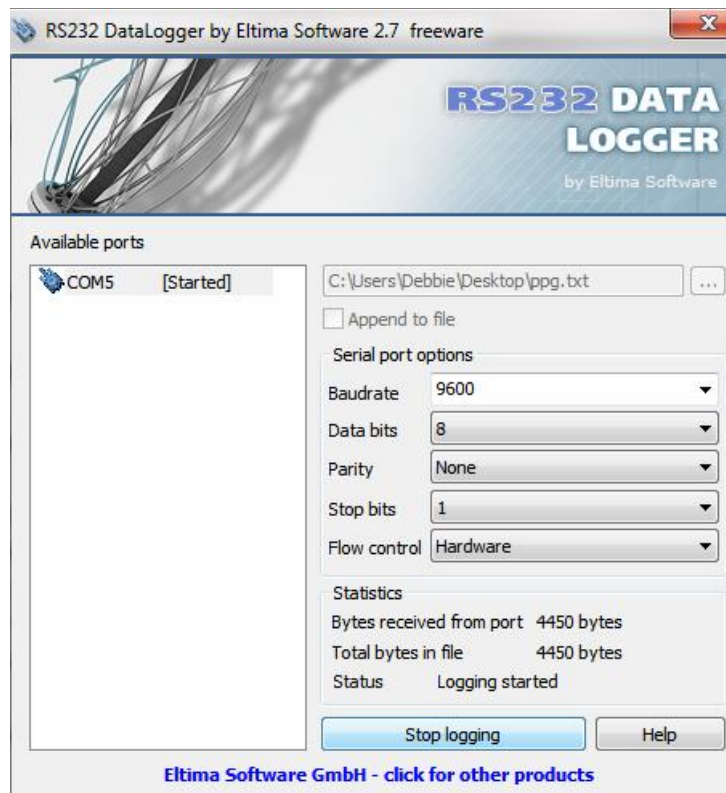
Figure 49 Software Screen Shot During PPG Data Collection

5.3.4 Study Procedures

The experiment was conducted for two consecutive days, noted as Day 1 and Day 2. The day before the experiment will be noted as Day 0.

Day 0 –

- Subjects were asked to sleep for a total of 8 hours the night before Day 1.

Day 1 & 2 –

- Subjects were asked to wake up at approximately 8AM, and report to Room 219/218 in Atwater Kent Laboratories at 9:30AM.

- The N-Back M-Pitch test were conducted every hour starting from 10AM Day 1 to 9AM Day 2. A total of 24 sessions were conducted.

- During each test session, subjects were asked to wear a pulse oximeter on their finger; data were collected for the duration of the session.

- In between sessions, subjects were asked to remain in a room, but they were free to use the restrooms, do homework, play video games and so on. Subjects were cautioned to avoid napping and caffeine consumption throughout the experiment.

- A total of 4 meals were provided at the following times: 12:30 PM (Day 1), 6:30 PM (Day 1), 12:30 AM (Day 2) and 6:30 AM (Day 2). Snacks and water were provided at all times.

- End of the experiment: after completing the last session at 9AM on Day 2, subjects were dismissed, transportation was provided from Atwater Kent Laboratories to the residences of the subjects.

5.3.5 Preliminary Testing Results and Confidence Assessment

The MATLAB script developed by our team has been tested and we were successful in creating test session consisting of 200 different acoustic stimuli and collection of reaction data. The reaction data include both response answer (Same or Different) and the time of the reaction. This program was then able to calculate percentage of accuracy and plot the data on a graph, as well as plotting the reaction time as a function of trials.

The team examined different situations in order to reach a conclusion of how the test should be done. The inter stimuli interval (ISI) and the actual length of the stimuli were varied throughout the sessions. It was found that the test became more difficult when the duration of the ISI was decreased. Consequently, decreasing the ISI duration also decreased the accuracy of the N-Back performance. It was also noticed that when the lengths of the actual stimuli got closer to each other, the N-Back performance also decreased as well, which means the task became more difficult.

The initial written script used a mouse cursor to click on two buttons (Same and Different) on the screen. This feature was changed to be controlled by two keyboard buttons. This change caused a significant decrease in the reaction time by a subject. The following figure (Figure 50) shows the output of a 10 minutes session (200 stimuli, 3 sec ISI). The top figure describes the performance of the subject. For example, when the subject makes the right decision, a score of 1 is recorded, and when the subject gives an incorrect answer, a score of 0 is recorded instead. The bottom figure shows a record of the response time.
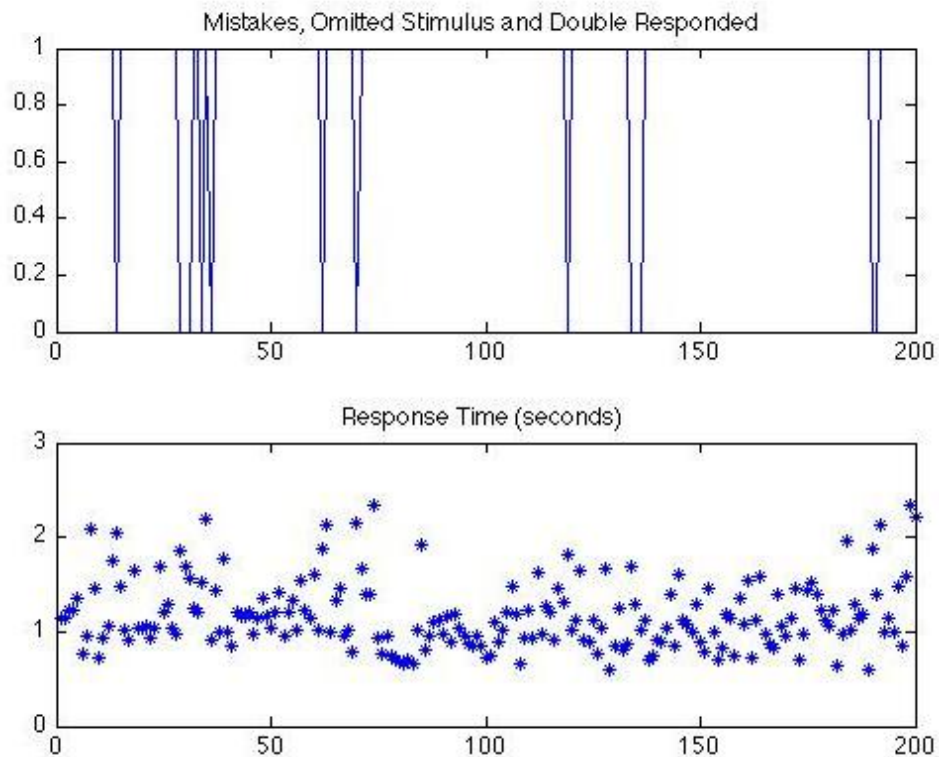
Figure 50 Performance and Response Time Record

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Number of trials and confidence assessment:

It is very important to have enough accurate number of trials in each N-Back session to indicate results with a statistical confidence interval. The following equation is usually used in determining the sample size (for example: a number of subjects to recruit in a statistical research):

$$n \geq \left(\frac{z}{m}\right)^2 \times \widehat{p}(1 - \widehat{p})$$

Where

n: number of samples, trials, subjects ... etc.

z: normal distribution for a specific confidence interval.

m: margins of error.

p: expected, or already known, statistical results percentage.

This experiment is an indicator of mental fatigue. It is measuring the capacity of the working memory through accomplishing memory tasks, which is the N-Back test. This task includes either one of the options: Same or Different. Thus, the probability of getting the correct answer is 50 percent. For such a task, the trend of a required sample size can show a maximum peak at 50 percentage of the maximum. This can be easily examined by plugging 0.50 in p in the equation above. This can be illustrated by Figure 51.

$\widehat{p}$	0	.1	.2	.3	.4	.5
$\widehat{p}$	1	.9	.8	.7	.6	.5
$\widehat{p}(1 - \widehat{p})$	0	.09	.16	.21	.24	.25
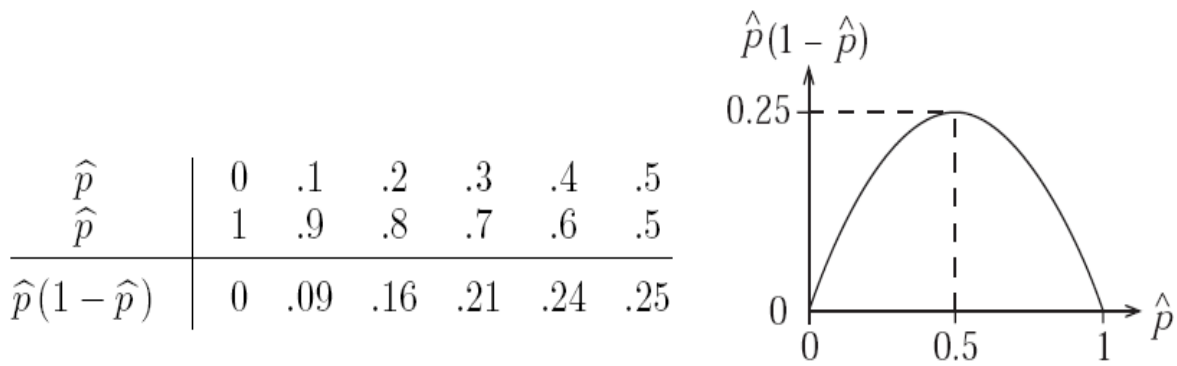
Figure 51 Plot of p(1-p) as a function of p. p(1-p) is also proportional to the sample size

In our experiment, the subjects will be doing several training sessions in order to set a baseline of their N-Back performances. This performance will be a measure of the accuracy of the N-Back task. The baseline is decided to be within an accuracy range (correct responses) of 75% to 85%. Nevertheless, the performance is expected to decrease, by 10 percent of the accuracy, during the actual experiment due to sleep deprivation. A sample number (trials) based on a 65% accuracy should be calculated to best represent actual capability of the working memory. This number of trials will be also a good representation for higher accuracies as noted from the Figure above, where 0.65 is closer to the half, where the sample size peak located, compared to any higher accuracies. This sample number will be used in all the sessions during the experiment. Solving for the equation shows that we need 360 stimuli every session:

$p = 0.65$

Confidence 95%, gives a normal distribution z value of 1.96

m = expected variance in the accuracy ($\pm 5\%$)

$p = 65\%$

Thus, $n = (1.96/0.025)^2 * 0.65 * 0.35 = 360$.

5.4 Correlation Determination

We made three hypothesis on the correlations between psychological performance, which in this case is mental fatigue assessed by N-back M-pitch program, and physiological performances, which in this case is features from Heart Rate Variability (HRV). First, we hypothesized that there is observable correlations between one or more features from HRV with mental fatigue. To prove or disprove this hypothesis, we made plots with all of the investigated features on one plot over time along with the N-back M-pitch accuracy and response time over time to visually inspect the correlations.

Secondly, we hypothesized that there is mathematical correlations between mental fatigue, measured by N-back M-pitch test with one or the other features from HRV. For example, we hypothesized that we can linearly fit the correlation between HRV-LF and N-back accuracy. To prove or

disprove this hypothesis, we plot the correlation 1.1 to 3.4, as shown in **Error! Reference source not found.**, with physiological data as Y-axis and psychological data as X-axis, as shown in Figure 52 .Appendix A will include all the 12 graphs, while 2 of them will be explained in the results section.

Table 4 One-to-one correlations between psychological performances and physiological parameters

	N-back Accuracy	N-back Response time	N-back Throughput
Heart Rate	1.1	1.2	1.3
HRV-LF	2.1	2.2	2.3
HRV-HF	3.1	3.2	3.3
HRV-LF/HF	4.1	4.2	4.4
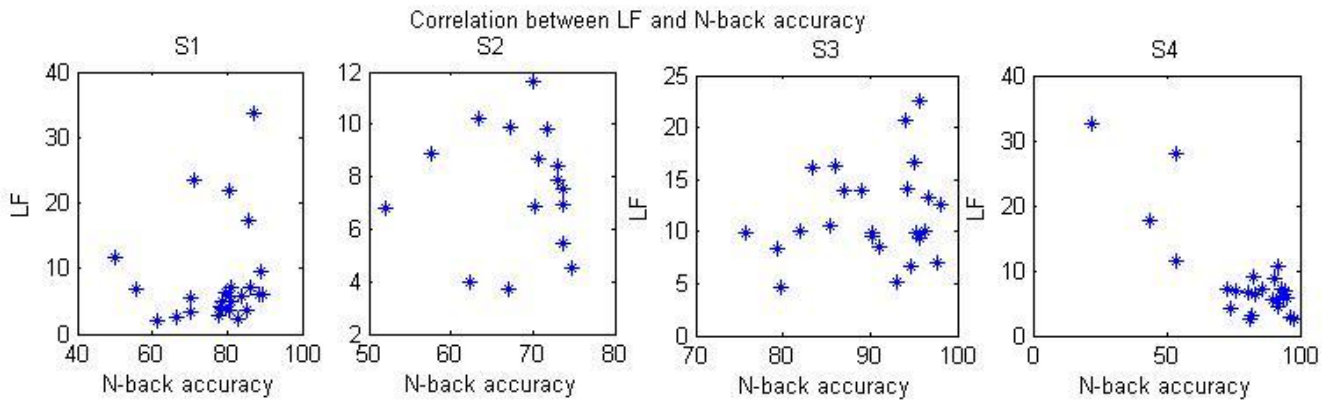
Figure 52 One-to-one correlation example

Third, we hypothesized that there are distinct statistical features of HRV from fatigued stage and active stage. We calculated average HF and LF feature values and its variations from the first 6 sessions and last 6 sessions across each subjects to investigate the correlations, as well as outstanding statistic values.

For fatigue index production for real-time drowsiness-control use, an abstract description of fatigue index production from multiple physiological features is included in Appendix B. It is part of

Cornel Cup Intel Embedded System Design Competition, participated by author Yichao Joy Xu and

Fangjie Ding, teamed up with three other teammates discrete from this MQP.

Chapter 6 Experiment Results

6.1 Correlation Observation

The PPG data and results of the N-back M-pitch test were processed and analyzed across all sessions of the experiment. Four physiological parameters were examined: the HF component of HRV (0.15-0.4Hz), the LF component of HRV (0.04-0.15Hz), the ratio between LF and HF components, and heart rate. The psychological parameters include the percent accuracy of the N-back M-pitch test, and the average response time of each test.

Upon completion of the experiment, subjects were asked to give a self-report of their stress level throughout the experiment. Specifically, subjects were asked to give an approximate answer for the following two questions. The answers to these questions were used later as a reference for results interpretation.

> *- Which sessions did you find to be the most stressful (i.e. you were very fatigued but were trying hard to achieve a high percent accuracy)?*
>
> *- When did you find yourself stop trying to achieve a high percent accuracy because you were too fatigued?*

Figure 53 shows the results from Subject #1. Please note that, for the five figures included below, the x-axis indicates the time of the day in military time format (i.e. a "10" indicates 10AM; a "18" indicates 6PM). It can be clearly seen that 1) HF shows a significant increase near the end of the experiment, after 6:00; 2) LF shows a significant increase near the end of the experiment, after 6:00; 3) The LF/HF ratio does not exhibit a clear trend over time; 4) The heart rate fluctuates, does not exhibit a clear trend over time; 5) The percent accuracy is decreasing over time; 6) The response time is increasing over time. According to Subject #1, he/she experienced the most stress near the end of the experiment, when he/she was struggling not falling asleep. Subject #1 also reported that he/she only stopped trying to achieve a high accuracy in the last two sessions of the experiment.

Figure 54 shows the results from Subject #2. It can be clearly seen that 1) HF shows an increase from 14:00 to 15:00, and from 16:00 to 17:00; 2) LF shows a significant increase between 23:00 and 00:00; 3) The LF/HF ratio does not exhibit a clear trend over time; 4) The heart rate shows small fluctuations, but does not exhibit a clear trend over time; 5) The percent accuracy is decreasing over time; 6) The response time does not show a clear trend over time. According to Subject #2, he/she experienced the most stress from midnight to 03:00. He/she stopped trying to achieve a high accuracy after approximately 01:00.

Figure 55 shows the results from Subject #3. It can be clearly seen that 1) HF shows a noticeable increase in the middle of the experiment, from 15:00 to 23:00; 2) LF shows a significant increase between 21:00 and 23:00; 3) The LF/HF ratio appears to be higher at the beginning of the experiment, between 10:00 to 14:00; 4) The heart rate shows a clear decreasing trend over time; 5) The percent accuracy is first decreasing till 06:00, and has a small increase afterwards; 6) The response time shows an increasing trend over time. According to Subject #3, he/she experienced the most stress from 19:00 to 21:00, when he/she felt very fatigued but still tried to achieve a high accuracy. Subject #3 also reported that he/she stopped trying hard at the test from 02:00 to 07:00.

Figures 47 and 48 are the results from preliminary testing, where the experiment was shorter than 24 hours.
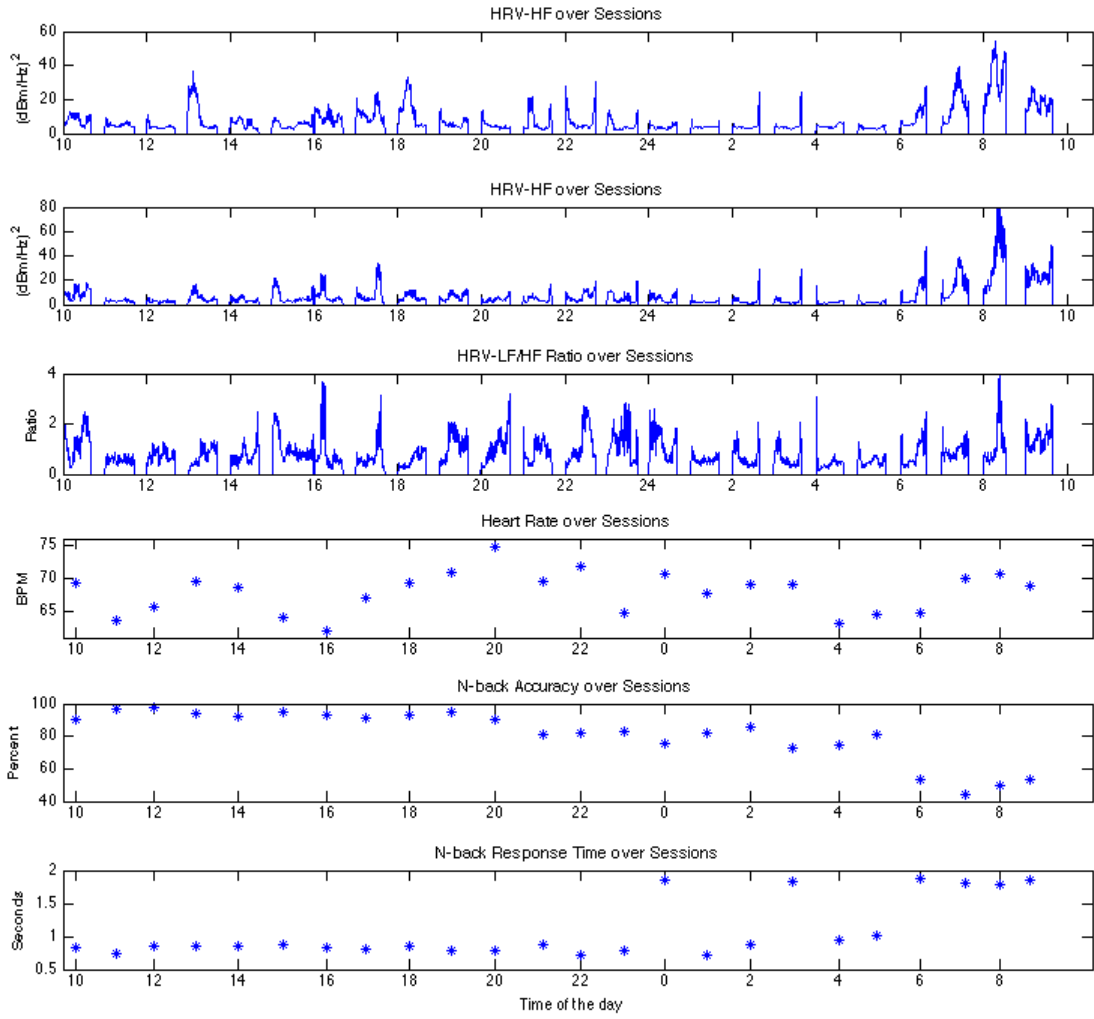
Figure 53 Experiment results of Subject #1
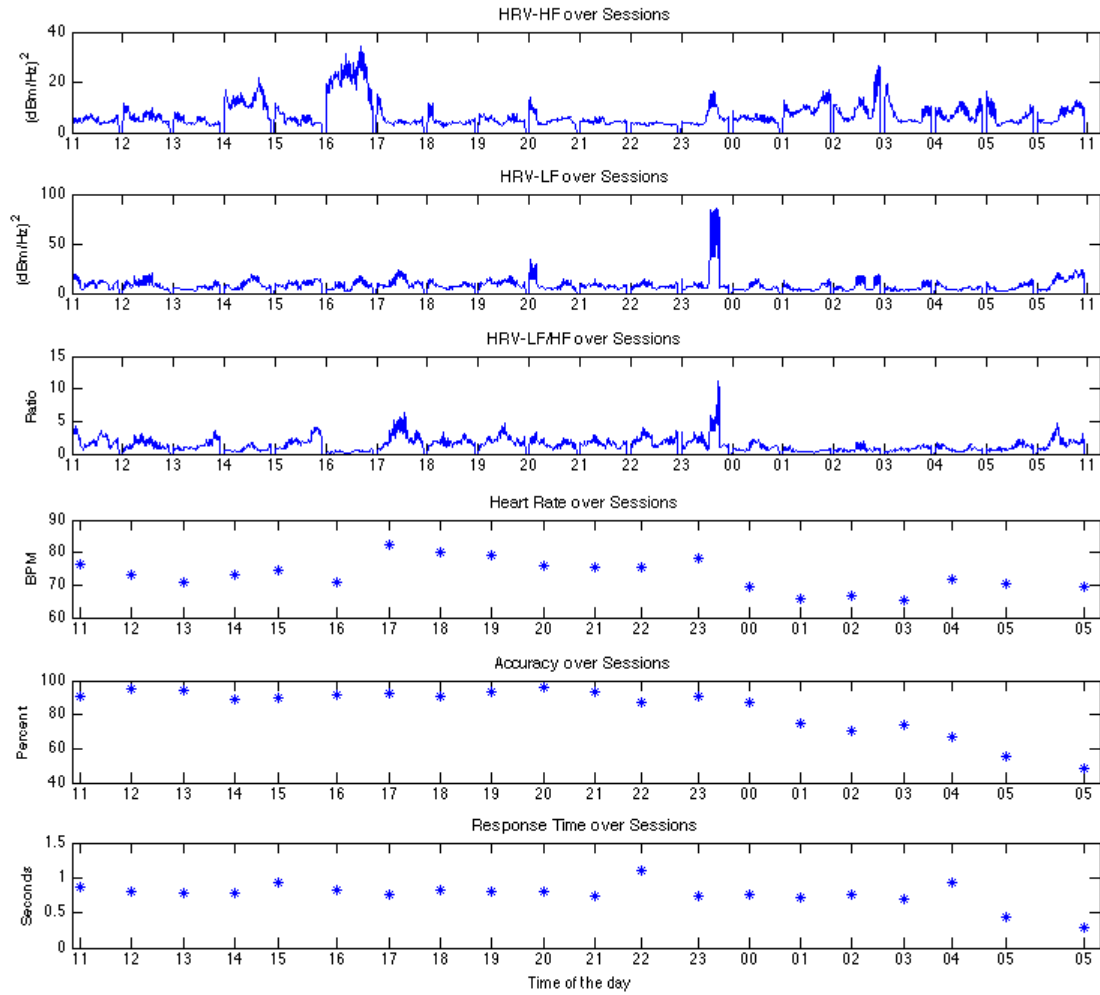
Figure 54 Experiment results of Subject #2
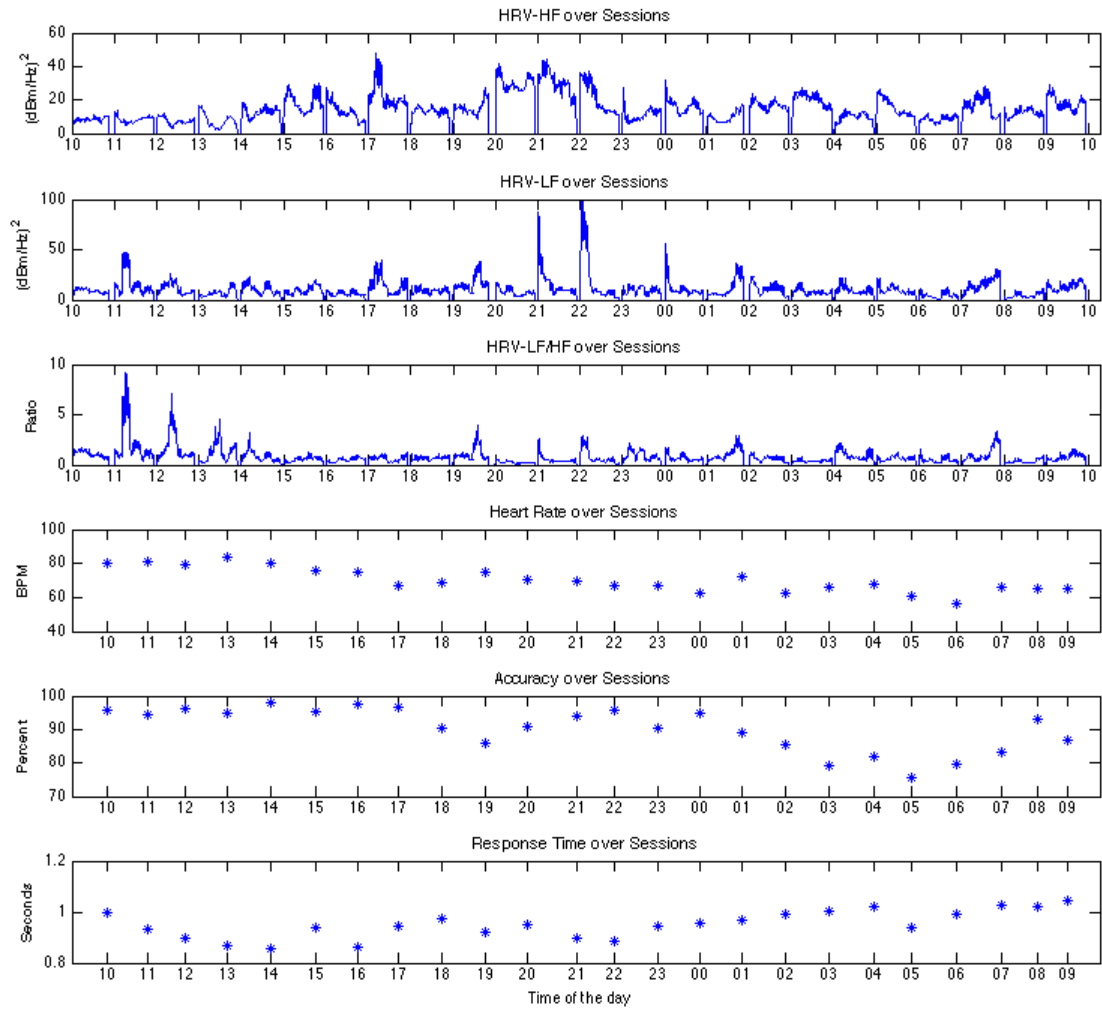
Figure 55 Experiment results of Subject #3
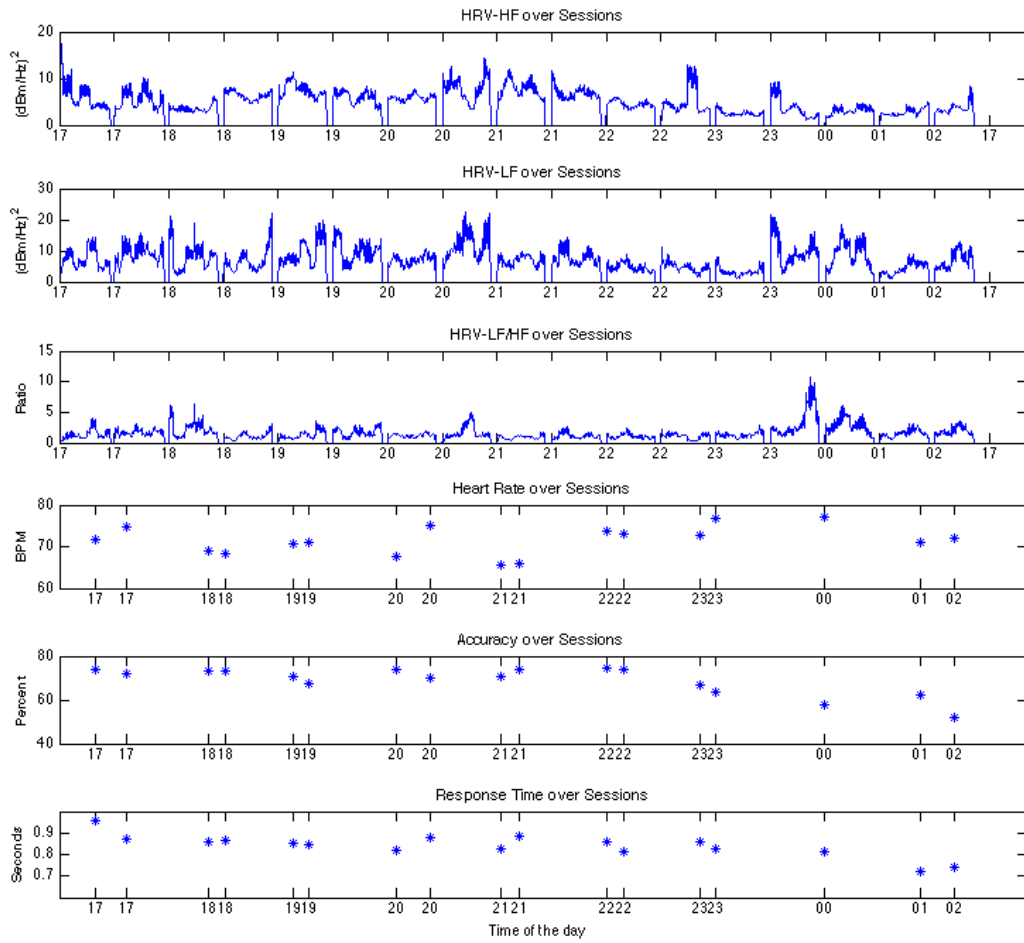
Figure 56 Experiment results of Subject #4

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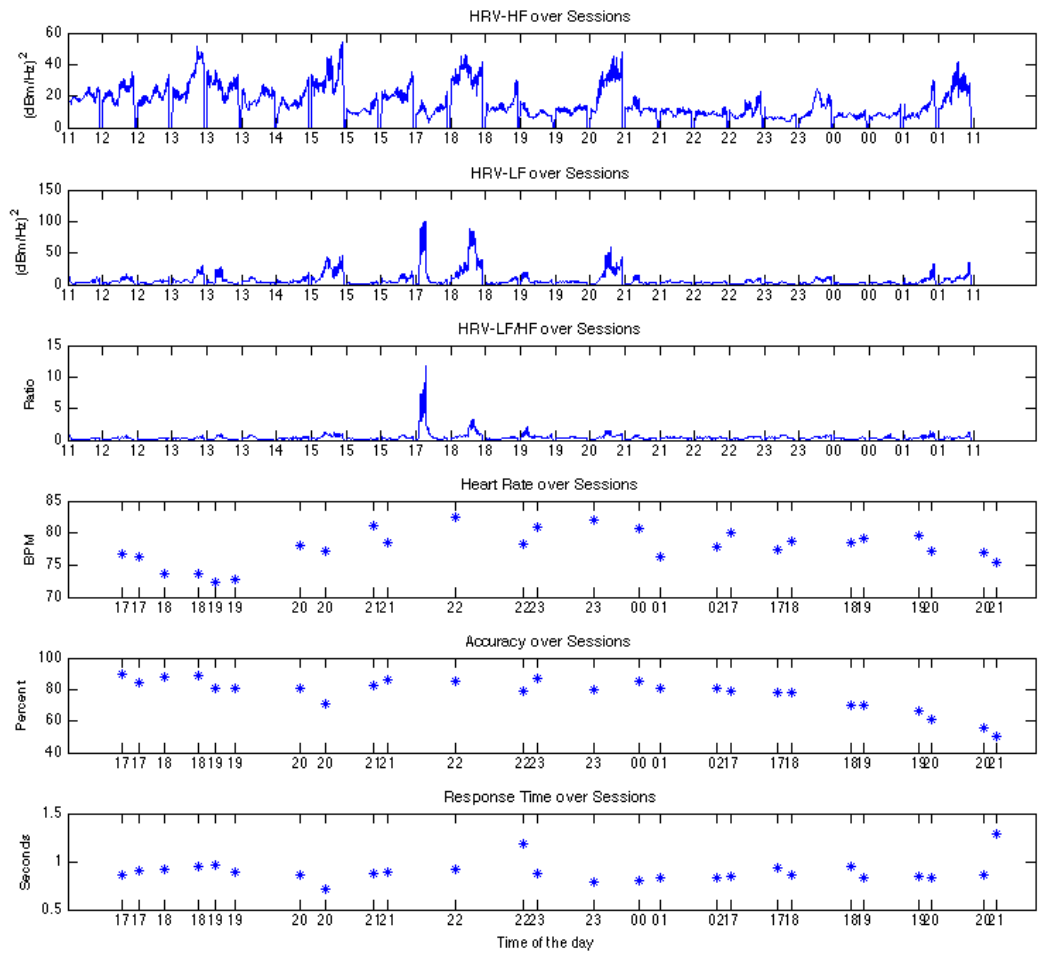
Figure 57 Experiment results of Subject #5

6.2 HRV-LF and HF Statics of Awake and Fatigue

It has been hypothesized that HRV HF and LF will show statistical distinctions during awake and fatigue status. We calculated averages of HF and LF as well as their variations. According to literature review, HF corresponds to parasympathetic nervous system activity, while LF corresponds to both parasympathetic system and sympathetic system activity. Thus, the assumption of HF and LF distinctions was made that HF is higher during fatigue and LF is relatively higher during wake status.

In order to prove or disprove this assumption, the average and standard deviation have been calculated for LF and HF. The data from the first six sessions of the N-back M-pitch have been computed for wake status, and the last six sessions of the test have been computed for fatigue status. Table 5 shows the statistics of HRV during awake and fatigue status according to the description. The analysis results correspond to our expectations. Subject 1 to 4 shows higher high frequency region area under the curve and higher variations, while subject 5 only shows higher variation of HF. The average HF across five subjects corresponds to our hypothesis that fatigue corresponds to higher HF area.

Subject 1,2,3, and 5 shows lower low frequency level during fatigue which also corresponds to our assumption. Meanwhile, low frequency variation was also lower in subject 1,2,3, and 5. We observe one outstanding figure in Subject 4, which has significantly higher LF level than others. This may be explained by the stressed condition of Subject 4, who was reaching the end of the test, highly fatigued but been pushed to finish because of the experimental compliment. Overall, the statistical results agree with our literature review that HF increases with fatigue while LF dominates while awake.

Table 5 HRV statistical distinctions between fatigue and awake

	Condition	S1	S2	S3	S4	S5	Average
HF	Awake	11.3±3.3	3.5±1.4	10.3±2.9	7.0±3.4	9.7±2.1	8.4±2.6
	Fatigue	22.1±4.8	6.0±1.5	14.2±3.3	13.8±5.4	7.4±2.8	12.7±3.5
LF	Awake	5.9±3.9	8.3±3.2	11.1±5.9	5.3±2.8	8.5±3.3	7.8±3.7
	Fatigue	4.1±2.4	6.4±2.8	9.2±3.5	**14.2±7.8**	6.2±3.4	6.5±3.0

Chapter 7 Methodology Validation Analysis

7.1 Analog Design Validation

To verify our sensor design, electrocardiogram (ECG) is used. Digitized PPG signal is verified with the signal acquisition equipment called BIOPAC system available in biomedical engineering labs. Digitized signals were recorded and plotted in MATLAB. Since the sampling frequency for the ECG is 200 and 75 for the PPG, upsampling method is applied to the PPG signals in order to better compare the two signals. As we can see in Figure 58, a nadir on the PPG occurred a little late after a corresponding peak on the ECG. This is because it always takes time for blood to propagate from the heart to various parts on the body. The R-R interval on both ECG and PPG are observed visually first and then the verified by the calculating the actual durations from the data arrays. For a random selected data segment, both ECG and PPG signals show the same durations for consecutive four pulses. Thus we have successfully verified that our designed PPG circuit measures the correct heart rates.
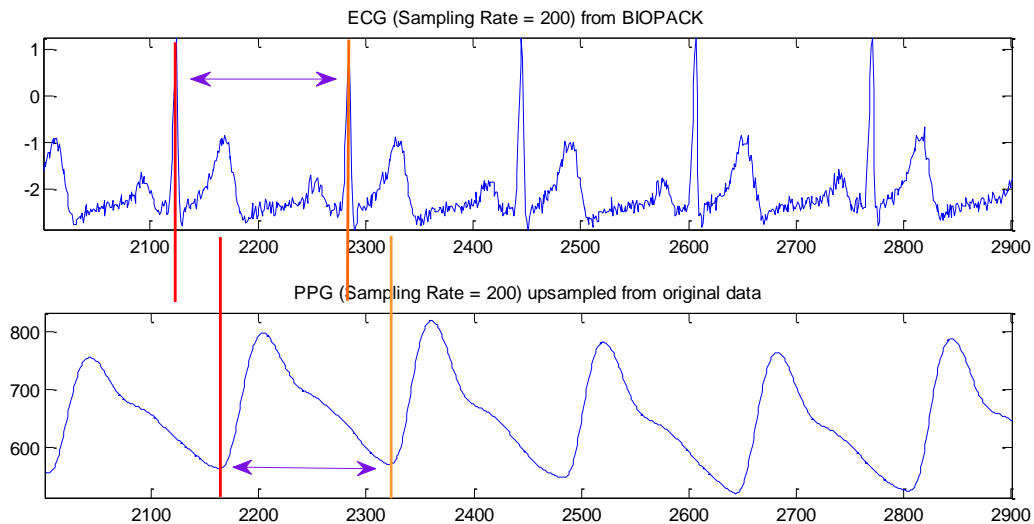
Figure 58 Verification of Digitized PPG Signal with ECG

7.2 Signal Processing Design Validation

7.2.1 Comparison of Integral Methods

While developing algorithms, we need simulations in getting known value to compare with algorithm estimated values As calculating the integral of Power Spectrum Density (PSD) across certain frequencies is needed in many cases in this project, analysis by simulated functions in selecting algorithms have been done. Equations 1, 2, and 3 have been selected due to their similar shape as Heart Rate Variability PSD.

$$Y = \text{sinc}(x) \quad (1)$$

$$Y = 1/x \quad (2)$$

$$Y = e^x \quad (3)$$

The estimated area calculated by Rectangular rule, trapezoidal rule and Simpson's rule were compared to the true value of integral of equation (1), (2) and (3). Error rate converge to zero with the decrease of step sizes. Figure 59 shows, Integral by rectangular methods has the biggest error, while trapezoidal and Simpson's rule methods have similar trend line. As Simpson's Rule fluctuates, trapezoidal rule is thus preferred.
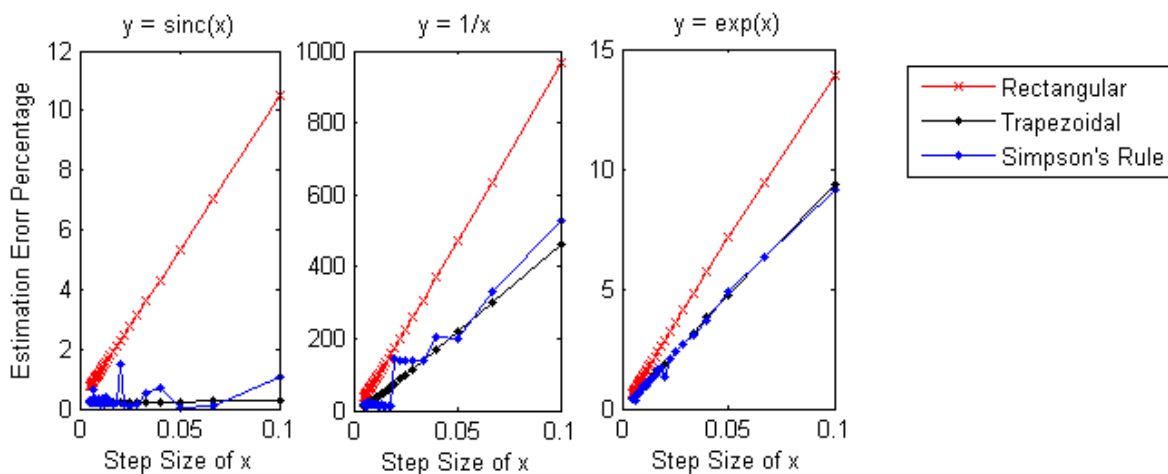
Figure 59 Integral interpolation analysis

Figure 59 shows the analysis of integral interpolation by the three rules using a section of real PPG signal. All of the results from the three methods converge into 29.4 approximately in the end.

Simpson's Rule fluctuates significantly compared to trapezoidal rule, while rectangular rule is far off from the other two's estimation trend line. Therefore, it has been concluded that trapezoidal rule is the selected method for interpolated integral.
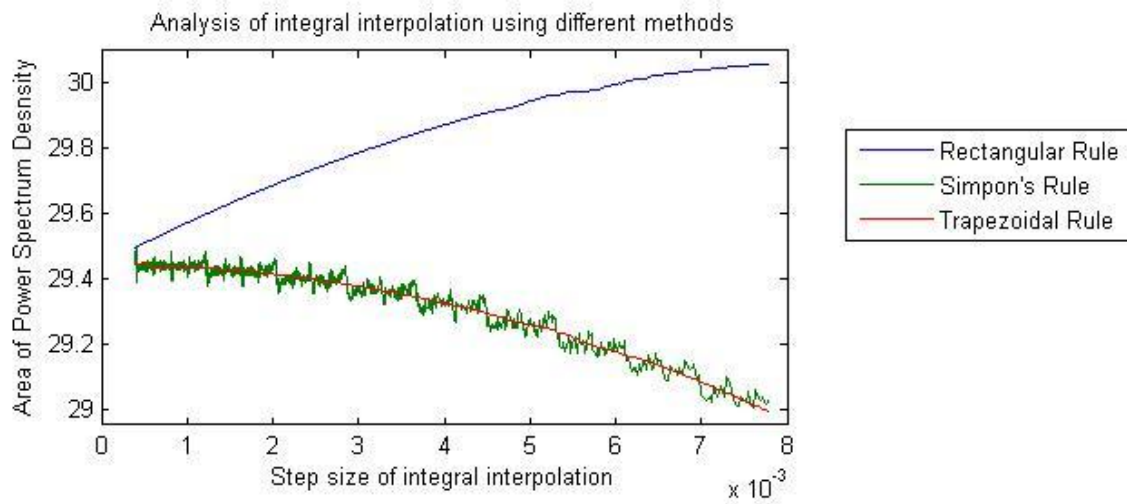
Figure 60 Analysis of interpolation with real PSD data

Chapter 8 Discussion and Conclusion

8.1 N-back M-pitch

In order to correlate mental fatigue with heart rate variability (HRV), we needed an accurate method to assess the mental fatigue caused by sleep deprivation. The N-back task has been used in a recent research as a method to investigate the short memory, and has been considered an efficient way to assess a number of major processes within working memory. In our experiment, it was hypothesized that N-back M-pitch performance is a direct indicator of the level of mental fatigue. The issue was in determining what number of N-back stimuli would best represent mental fatigue, taking into consideration the fact that N-back test is a binomial probability: "same" or "different", where either right or wrong answers have an equal probability of 50%. Using the following statistical equation, assuming that the accuracy (represented by p) will drop in state of fatigue to 65%:

$$n \geq \left(\frac{z}{m}\right)^2 \times \widehat{p}\left(1 - \widehat{p}\right)$$

It was determined that the number of stimuli should be in a range of 300 to 400 stimuli per session with a statistical confidence interval. It was decided to test the subjects with an N-Back M-Pitch procedure presented the stimuli as tones with four distinct frequencies (M = 4) and two different durations: 50 and 100 ms, of which differences may be easily neglected if subject is not paying attention. The performance of the subjects was reflected by the percent of correct responses, and the missed responses were considered incorrect (Michael Qin, 2011). The inter-stimulus interval (ISI) was initially set to 3 seconds to help the learning process for the program. During the initial experiments, it has been found that the response times distributed across the 1-1.5 seconds. Therefore, the ISI has been changed to 2 seconds.

As expected, the accuracy of the N-back M-pitch task was going down especially during the last few hours of the experiment, where the subjects' alertness decreased significantly. In other words, when

the mental fatigue level increased, the accuracy of the N-Back task decreased. At the same time, the reaction time was also increasing through the experiment sessions, especially during the last couple of hours. According to the data we have collected, it is obvious that all the subjects suffered from a steep drop in their performances during the last couple of sessions, whereas the experimenters have recorded that the subject was having multiple micro-sleeps, which sometimes exceeded a few seconds. It was also recorded that at sometimes the subjects were not responding to the task at all.

8.2 PPG Sensor

A wearable sensor was designed and implemented to successfully acquire PPG signal from a finger of subjects while performing the N-back M-pitch test. Using the PPG signals collected, we found the peaks of the signal and calculate the instantaneous heart rate, average heart rate, as well as the variability of the heart rate. To verify the sensor accuracy, we recorded an ECG signal at the same time while recording a PPG signal for two minutes. Then, we compared them by the number of peaks detected, and the average heart rate. The results showed same number of peaks and heart rate. It was also observed that the placement of the PPG sensor and the amount of pressure applied on the sensor could affect signal quality, and its amplitude. Nevertheless, the signal was clean enough, under different pressures and placements, and the peak detection algorithm was working perfectly as well.

8.3 HRV Spectral Analysis

HRV data have been calculated for all the sessions while conducting the N-back M-pitch task, in order to correlate it with the accuracy and the response time of the task. The data were obtained from PPG physiological signal by the sensor, our team designed, to derive the HRV calculation from. A correlation was found between calculated heart rate, the low frequency component of the HRV (from 0.15 to 0.4Hz), the high frequency component of the HRV (from 0.04 to 0.15Hz), the LF/HF ratio, and the N-back M-pitch performance, which includes the percent accuracy and response time. The MQP group implemented software algorithms to determine and calculate all these parameters through signal dynamic peak

detection algorithm, HRV algorithm, LF and HF area integration algorithm. The peak detection algorithm was examined and compared to another peak detection algorithm that was developed previously by Professor Ki Chon, head of Biomedical Engineering Department at WPI, and it was also examined visually. It was shown that the peaks were detected successfully and corresponded to same number of peaks from the other algorithm.

According to the results, the accuracy of the memory task was decreasing (while reaction time increased) over time; the HF component of the PSD (representing the parasympathetic system) fluctuated a lot when the subjects recorded stress. Although LF/HF did not show an obvious relation to the mental fatigue, it was shown from the results that the sympathetic system (which is measured by the area of the LF component) was going up while the subjects were performing poorly on the memory task. This result is consistent with the hypothesis introduced, and the conclusions from prior research studies (Verwey, 1999).

Having long breaks between every two sessions give enough time for the subject to rest and be alert again at the beginning of the following session, which might be one of the reasons that led to the high fluctuation in the HRV of the subjects over time.

Another methodology, where the memory task has to be performed continuously for 6 hours with short breaks every half an hour at night instead of 10-minute sessions every hour, is suggested. This might allow seeing a clearer linear relation between the LF and HF with fatigue level.

8.4 Conclusion

The major purpose of this project was to determine whether healthy participants experienced changes in spectral HRV as their level of mental fatigue increased. The participants in this study were found to experience increased level of fatigue as the experiment progressed. This result was supported by the steady decrease in the N-back M-pitch accuracy for every subject. Based on this result as well as the self-reported experiences, the participants have provided, N-back M-pitch task is found to be an efficient method in assessing the level of mental fatigue. As described in previous chapters, the negative impact

and potential danger related to fatigue have been growing concerns in society. Research studies are being conducted every year to seek ways of preventing serious risks associated with monotonous tasks, such as watchstanding and driving. Nevertheless, studies have also suggested that, fatigue is not well understood and thus needs further investigation and clarification to effectively control its complications (U. Bultmann, 2002). In the present project, we were unable to separate mental fatigue from physical fatigue, since both of them increased evidently as the 24-hour experiment progressed.

The PPG sensor designed and utilized for this project has been verified to work accurately, and has provided the functionalities needed. The algorithms (including peak detection, interpolation, and calculation of HF and LF components) developed to extract spectral HRV information from raw PPG signals have been proved to perform adequately with moderate motion artifacts.

The findings of this project also suggest that sympathetic activity is associated with increased fatigue, meaning there is a positive correlation between increased fatigue and increased LF component of HRV. The results of the 24-hour experiment and the self-reports from subjects suggest that, when the subjects were trying hard to keep themselves awake as well as achieve a high accuracy on the N-back M-pitch test, the LF component of HRV increased considerably. However, no clear one-to-one associations have been found between fatigue, heart rate, HF and LF/HF ratio of HRV in the present study. Clearly, the correlation of mental fatigue and HRV needs further investigation. The results provided by this project only suggests the association of mental fatigue and LF of HRV of a very small population, since it was not feasible to utilize a large sample size for the experiment within the given time frame.

Chapter 9 Recommendations

9.1 Study Procedures

The experiment for this project was designed to have a time span of 24 hours. The purpose of the 24-hour duration was to help us understand the effects of circadian rhythm. Another purpose was to understand how sleep deprivation plays a role in HRV as well as cognitive functioning. However, the study procedure utilized for this project was not the best simulation of naval watchstanding. Watchstanding in the Navy typically has a duration of 4 hours. Sentries are expected to devote full attention continuously during this period of time. The experiment in this project consisted of a total of 24 sessions, with each session being 10-minute long, and a break of 50-minute between consecutive sessions. The subjects were not assigned to any tasks from the end of one session to the beginning of the next session. Therefore, the experiment did not simulate a continuous task that requires constant attention for at least 4 hours.

Subjects of the experiment have reported that although they felt tired and distracted near the end of one session, they were able to focus again when the next session began, since they were not assigned to any specific tasks during the 50-minute break. The fluctuations observed in the HF (indicating parasympathetic activity) and LF (indicating sympathetic activity) components of HRV could possibly be related to the discontinuity of the study procedure. If recordings were done continuously for 4 hours (instead of 10 minutes every hour), the spectral analysis of HRV may show a clearer trend of increased sympathetic activity as well as decreased parasympathetic activity.

For future investigations, it is recommended that the duration of the experiment corresponds to the actual duration of watchstanding. Subjects will not be taking break during the experiment. Instead, they will be instructed to take the N-back M-pitch test from beginning to end continuously. The recording of PPG should also be continuous for the entire duration. Since watchstanding is necessary at any time of the day, the same experiment could be conducted around different times (e.g. in the morning,

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afternoon, evening, and after midnight) on **different** groups of subjects. Please note that it is not meant for one subject to complete more than one experiment within one day. The reduced span of duration evidently provides more flexibility for investigators as well as participants. One difficulty of this project directly had to do with the long duration of 24 hours. To ensure enough time for subjects to recover from sleep deprivation, the experiments were conducted only on Saturdays. So that the subjects had Sunday to catch up on lost sleep before a new week began.

9.2 Sample Size

Due to the time constraint of the project, it was not feasible to include a large sample size for the experiment. Although studies have been conducted in the past to investigate the correlation between HRV and fatigue, the majority of them utilized low numbers of subjects, which led to lower confidence they could have in their conclusions. Unfortunately, we experienced the same situation. As suggested in Section 9.1, if the experiment were not 24 hours long, subject recruitment could be presumably easier. For future investigations, it is recommended to include a large number of participants if feasible.

9.3 Sensor Design

One thing we recommend to improve our current PPG sensor design is to add an electrostatic discharge (ESD) protection circuit. ESD is a transient discharge of static charge caused from either human handling or a machine contact. It could be a serious issue in integrated circuits when the electrostatic energy level is really high. When energy is dissipated through solid state devices such as the integrated circuits, it often causes damages. Common ESD protection circuits include connecting either a Zener diode or a ceramic capacitor between power rail and ground. We did not encounter any ESD problems when collecting data during the N-back experiment, but we do recommend adding ESD protection to the PPG filtering circuit for safe purpose.

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Bibliography

Adrian M. Owen, K. M. (2005). N-Back Working Memory Paradigm: A Meta-Analysis of Normative Functional Neuroimaging Studies. *Human Brain Mapping* , 46-59.

Artaud, P. P. (1994). An on-board system for detecting lapses of alertness in car driving. *14th E. S. V. Conference Session 2—Intelligent Vehicle Highway system and Human Factors.* Munich.

Ayumi Tsuchida, M. S. (2009). *Estimation of Drowsiness Level Based on Eyelid Closure and Heart Rate Variability* . Minneapolis, Minnesota, USA: 31st Annual International Conference of the IEEE EMBS.

Brown M, M. M. (2006). ISCEV Standard for Clinical Electro-oculography. *Doc Ophthalmol* , 205-212.

Bruce Pomeranz, R. J. (1985). Assessment of autonomic function in humans by hear rate spectral analysis. *Heart , 248*, 51-53.

Coren, S. (1996). *Sleep Thieves: an Eye-Opening Exploration into the Science and Mysteries of Sleep.* New York: Free Press.

D. Norman, T. S. (1980). Attention to action: Willed and automatic control of behaviour. In M. S. Gazzaniga, *Cognitive neuroscience: a reader* (pp. 376-377). Oxford: Blackwell.

D. Williams, J. S. (1998). *Fatigue in Naval Tactical Aviators.* San Diego: Naval Health Research Center.

Gary G. Berntson, J. T. (1997). Heart rate variability: Origins, methods, and interpretive caveats. *Psychophysiology* , 623-648.

Häck, M. R. (2007). *The Navy.* AuthorHouse.

Horne, J. A. (1993). Human sleep, sleep loss and behaviour. Implications for the prefrontal cortex and psychiatric disorder. *Br J Psychiatry* .

Ivan Barofsky, M. W. (1991). Definition and Measurement of Fatigue. *Review of Infectious Diseases , 13*, 94-97.

K. Jones, Y. H. (2001). Frontal lobe function, sleep loss and fragmented sleep. *Sleep Medicine Reviews* , 463-475.

Kanav Kahol, M. J. (2008). Effect of fatigue on psychomotor and cognitive skills. *The American Journal of Surgery* , 195-204.

Khushaba, R. K. (2011, January). Driver Drowsiness Classification Using Fuzzy Wavelet-Packet-Based Feature-Extraction Algorithm. *IEEE Transactions on Biomedical Engineering* , 121-131.

Kirchner, W. K. (1958). Age Differences in Short-Term Retention of Rapidly Changing Information. *Journal of Experimental Psychology* , 352-358.

Linda Jongman, T. M. (1996). *The working memory hypothesis of mental fatigue.* University of Groningen, Department of Experimental and Work Psychology. Groningen: ppsw.rug.nl.

Loomis, J. M. (1971). *The Photopigment Bleaching Hypothesis of Complementary After-Images: A Psychophysical Test.* Ann Arbor: Vision Res. Pergamon Press.

Malik, M. (1996). *Heart Rate Variability Standards of Measurement, Physiological Interpretation, and Clinical Use* (Vol. 93). Cranmer Terrace, London, UK: Circulation.

Mark F. Bear, B. W. (2007). *Neruoscience Exploring the Brain.* Philadelphia, PA, USA: Lippincott Williams and Wilkins.

Michael Qin, D. F. (2011). MA, USA: Naval Submarine Medical Research Laboratory.

Michael W. Wukitsch, M. T. (1988). Pulse Oximetry: Analysis of Theory. *Monitoring Equipment* , 290-301.

Millikan, G. A. (1942). The Oximeter, an Instrument for Measuring Continuously the Oxygen Saturation of Arterial Blood in Man. *Review of Scientific Instruments* , 434.

Myers, D. G. (2010). *Psychology* (9th Edition ed.). Worth Publishers.

NAVEDTRA. (1996, 1 1). *Military SIGNALMAN 1 & C.* Retrieved 10 17, 2011, from Global Security: http://www.globalsecurity.org/military/library/policy/navy/nrtc/14243.htm

NHSTA. (2009). *Traffic Safety Facts.* NHSTA. Washington, DC: NHTSA's National Center for Statistics and Analysis .

Oximetry. (2006). *Pulse Oximetry*. Retrieved 10 16, 2011, from Oximetry.org: http://www.oximetry.org/pulseox/principles.htm

Paula Alhola, P. P.-K. (2007). Sleep deprivation: Impact on cognitive performance. *Neuropsychiatric Disease and Treatment* , 553-567.

Peter Manu, T. J. (1992). Chronic Fatigue Syndromes in Clinical Practice. *Psychotherapy and Psychosomatics* , 60-68.

R. Schleicher, N. G. (2008). Blinks and saccades as indicators of fatigue in sleepiness warnings: looking tired? *Ergonomics* .

Raven, J. (1962). *Advanced Progressive Matrices, Set II.* London.

Saroj K.L. LAL, A. C. (2002). Driver fatigue: Electroencephalography and psychological assessment. *Psychophysiology* , 313-321.

Sheng Lu, H. Z. (2008). Can Photoplethysmography Variability Serve as an Alternative Approach to Obtain Heart Rate Variability Information? *JOURNAL OF CLINICAL MONITORING AND COMPUTING* , 23-29.

Sherwood, L. (2005). *Human Physiology From Cells to Systems* (Fifth ed.). Belmont, CA, USA: Thomson Learning.

SPO Medical's Pulse Oximeter Technology at A G & R Distributors. (n.d.). Retrieved October 16, 2011, from A G & R Distributors Inc.: http://www.agrdistributors.com/technology.php

Stanford University. (1999, January). *Disorders of the Sleep/Wake Cycle*. Retrieved October 15, 2011, from Stanford University: http://www.stanford.edu/~dement/circadian.html

Susan Torres-Harding, L. A. (2005). What is Fatigue? History and Epidemiology. In L. A. Susan Torres-Harding, *Fatigue as a Window to the Brain.* Cambridge, MA: The MIT Press.

T.L. Morris, J. M. (1996). Electrooculograhic and Performance Indices of Fatigue During Simulated Flight. *Biological Psychology* , 343-360.

The Franklin Institute. (2004). *The Human Brain - Sleep and Stress*. Retrieved 10 9, 2011, from The Franklin Institute: Resources for Science Learning: http://www.fi.edu/learn/brain/sleep.html

United States Navy. (1999). *Basic Military Requirements.* Retrieved 10 8, 2011, from Global Security: http://www.globalsecurity.org/military/library/policy/navy/nrtc/12018_ch3.pdf

Vöhringer-Kuhnt T., T. B. (2004). *Wierwille's method of driver drowsiness evaluation revisited.* Nottingham.

Yvonne Tran, N. W. (2009). The Relationship Between Spectral Changes in Heart Rate Variability and Fatigue. *Journal of Psychophysiology , 23* (3), 143-151.

Appendix A: Fatigue Index

$$a11 \times LF + a12 \times LF(N-1) + a21 \times HF + a22 \times HF(N-1) + a31 \times \frac{LF}{HF} + a32 \times \frac{LF}{HF}(N-1) +$$

$$a41 \times HR + a42 \times HR(N-1) = Accuracy\ of\ N\text{-}\ back\ M\ pitch\ \ (b1)$$

We made an assumption that there are linear correlations between four features – HRV-LF, HF, LF/HF and HR with one dynamic. We can thus fit eight coefficients onto this equation – from a11 to a42. Each of the sessions produces one set of coefficients. These coefficients could then be used to apply onto extracted features from testing data. Figure 61 shows the estimated fatigue index along with the actual N-back M-pitch accuracy using this method. The coefficients were calculated from the averages of one subject, across all experimental data. The average accuracy within the data from this subject is 79.8%. Higher dynamics and orders have been investigated for the Intel Competition in outputting fatigue index.
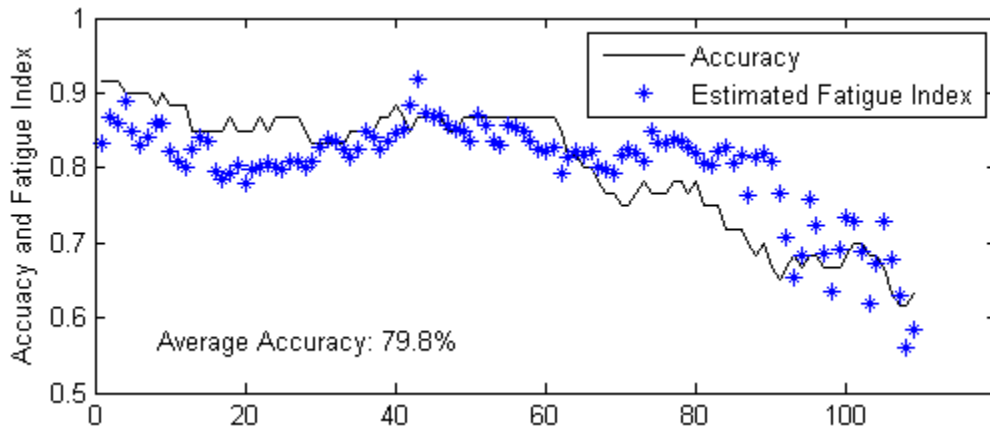
Figure 61 Fatigue index estimation

Appendix B: Consent Form

Informed Consent Agreement for Participation in a Research Study

Investigators: Sinan Asaad, Fangjie Ding, Ningxin Fu, Yichao Xu

Contact Information: navalmqp@wpi.edu

Title of Research Study: Psychophysiological Stress Monitor

1. Background

Watch standing in the Navy concerns those on watch operating a ship continuously and being responsive to emergencies. During the watch, the watch stander must devote full attention to events, such as the crew, operation, and safety of the ship. It is ultimately important for the watch stander to be alert and responsive at all times, as failing to do so may lead to severe consequences. However, due to the repetitive nature of watch standing, the alertness of the watch stander tends to decrease when their fatigue level increases over time. The problems caused by fatigue and the extent to which fatigue can compromise both physiological and psychological performance have been growing concerns.

2. Rationale

In order to detect when the watch stander is too exhausted to perform efficiently and accurately during the watch, we can examine the change in the physiological parameters that are greatly impacted by the level of fatigue.

The goal of this project is to detect and analyze the correlation between fatigue and these physiological parameters, which are extracted from the data that we acquire using a wearable pulse oximeter. The specific physiological parameter we will be analyzing is the Heart Rate Variability (HRV), which is a measure of the variation in the time interval between heartbeats.

3. Inclusion criteria

- Must be a current WPI student
- Must be between 18-30 years of age

4. Exclusion criteria

- Hearing impairment
- Involving as a subject in another research study

5. Study procedures

Sound-based Memory Test

A sound-based memory test, known as N-Back M-Pitch is a working memory paradigm that yields reliable measures of cognitive performance. During the task, subjects will be instructed to report whether the auditory stimulus, which can have a number of M possible pitches, presented N steps prior has the same or different stimulus duration as the current.

Subjects will be asked to complete the N-Back M-Pitch task multiple times during the experiment. Their performance (i.e. percent accuracy) will be recorded accordingly.

<u>Non-invasive monitoring</u>

A pulse oximeter will be utilized to record Photoplethysmogram (PPG) signal from subjects. It is a noninvasive battery-operated device that is worn on the forehead.

<u>Schedule and procedures to follow</u>

The experiment will be conducted for two consecutive days, noted as Day 1 and Day 2. The day before the experiment will be noted as Day 0.

Day 0 –

- Subjects will be asked to sleep for a total of 8 hours the night before Day 1

Day 1 & 2 –

- Subjects will be asked to wake up at approximately 8AM, and report to Room 219/218 in Atwater Kent Laboratories at 9:30AM
- The N-Back M-Pitch test will be conducted every hour starting from 10AM Day 1 to 9AM Day 2. A total of 24 sessions will be conducted
- During each test session, subjects will be asked to wear the pulse oximeter on their forehead/fingertip, the described recordings will be collected for the duration of the session
- In between sessions, subjects will be asked to remain in the room, but they are free to use the restrooms in Atwater Kent Laboratories, they are also free to do homework, play video games and so on. Subjects will be cautioned to avoid napping and caffeine consumption throughout the experiment
- A total of 4 meals will be provided at the following times: 12:30 PM (Day 1), 6:30 PM (Day 1), 12:30 AM (Day 2) and 6:30 AM (Day 2). Snacks and water will be provided at all times
- End of the experiment: after completing the last session at 9AM on Day 2, subjects will be dismissed, transportation will be provided from Atwater Kent Laboratories to the residences of the subjects

6. Risks

No potential risk exists for this experiment.

7. Benefits to research participants

Each participant will be rewarded with $100 at the completion of the study.

8. Confidentiality

All of the recordings from the experiment will be kept strictly confidential. Names of the participants will not appear anywhere with the recordings. We will use a random "subject number" for different recordings. Names of the subjects will not be used in any talks or publications related to this research.

9. Compensation or treatment in the event of injury

There will be no compensation to the participants in this study.

10. Cost/Payment

There will be no cost for the participants in this study.

For more information about this research or about the rights of research participants, or in case of research-related injury, contact: (Fill in your contact information or make reference to information provided at top of page. In addition, include the contact information for the IRB Chair (Professor Kent Rissmiller, Tel. 508-831-5019, Email: kjr@wpi.edu) and the University Compliance Officer (Michael J. Curley, Tel. 508-831-6919, Email: mjcurley@wpi.edu).

Your participation in this research is voluntary. Your refusal to participate will not result in any penalty to you or any loss of benefits to which you may otherwise be entitled. You may decide to stop participating in the research at any time without penalty or loss of other benefits. The project investigators retain the right to cancel or postpone the experimental procedures at any time they see fit.

By signing below, you acknowledge that you have been informed about and consent to be a participant in the study described above. Make sure that your questions are answered to your satisfaction before signing. You are entitled to retain a copy of this consent agreement.

_____   _____

Study Participant Signature   Date

Appendix C: Code Implementation for MSP430F2274 Microcontroller

```
#include "../HAL/hal.h"
#include "../ZNP/znp_interface.h"
#include "../ZNP/application_configuration.h"
#include "../ZNP/af_zdo.h"
#include "ppg.h"
#include "znp_simple_app_utils.h"
#include "fv_packet.h"
#include "fv_packet_queue.h"
#include <string.h>

extern signed int znpResult;        //from znp_interface

/** function pointer (in hal file) for the function that gets called
when the timer generates an int*/
extern void (*timerIsr)(void);

/** This is the current state of the application.
* Gets changed by other states, or based on messages that arrive. */
unsigned int state = STATE_ZNP_STARTUP;

/** The main application state machine */
void stateMachine();

/** Various flags between states */
unsigned int stateFlags = 0;
#define STATE_FLAG_SEND_INFO_MESSAGE 0x01

/** Handles timer interrupt */
void handleTimer();
unsigned int timerSeq;
struct FVPacketQueue PacketQueue;

int main( void )
{
    halInit();
    HAL_DISABLE_INTERRUPTS();

printf("\r\n**************************************************\r\n")
;
    printf("Fivolts V1.0 - END DEVICE - using AFZDO\r\n");
    timerIsr = &handleTimer;
      HAL_ENABLE_INTERRUPTS();

      timerSeq = 0;

    //run the state machine
    stateMachine();
}
```

```c
void stateMachine()
{
    while (1)
    {
        switch (state)
        {
        case STATE_IDLE:
            {
                if (stateFlags & STATE_FLAG_SEND_INFO_MESSAGE)  //if
there is a pending info message to be sent
                {
                    state = STATE_SEND_INFO_MESSAGE;            //then
send the message and clear the flag
                    stateFlags &= ~STATE_FLAG_SEND_INFO_MESSAGE;
                }
                //note: other flags (for different messages or events)
can be added here
                break;
            }

        case STATE_ZNP_STARTUP:
            {
#define ZNP_START_DELAY_IF_FAIL_MS 1000
                /* Start the network; if fails then wait a second and
try again. */
                signed int startResult = startZnp(END_DEVICE);
                while (startResult != ZNP_SUCCESS)
                {
                    printf("FAILED. Error Code %i, ZNP Result %i.
Retrying...\r\n", startResult, znpResult);
                    delayMs(ZNP_START_DELAY_IF_FAIL_MS);
                    startResult = startZnp(END_DEVICE);
                }
                printf("Success\r\n");

                signed int timerResult = initTimer(0.01, NO_WAKEUP);
// start timer
                if (timerResult != 0)
                {
                    printf("timerResult Error %i, STOPPING\r\n",
timerResult);
                    while (1);
                }
                    FVPQ_init(&PacketQueue);

                    state = STATE_SEND_INFO_MESSAGE;
                break;
            }
        case STATE_SEND_INFO_MESSAGE:
            {
#define ZNP_RESTART_DELAY_IF_MESSAGE_FAIL_MS 5000
#define MSG_LIMIT 64
```

```c
#define BUFFER_TRIGGER 16   /* limited by 84 bytes payload per packet*/
                    if(PacketQueue.count > BUFFER_TRIGGER){
                            unsigned char msgBuf[MSG_LIMIT];
                            int msgSize = 0;
                            struct FVPacket p;

                            for(int j = 0; j < BUFFER_TRIGGER; j++) {
                                    FVPQ_dequeue(&PacketQueue, &p);
                                    memcpy(msgBuf+msgSize, &p,
sizeof(struct FVPacket));

                                    msgSize += sizeof(struct FVPacket);

                            } // copy BUFFER_TRIGGER size of packets
into the buffer
                            setLed(1);

    afSendData(DEFAULT_ENDPOINT,DEFAULT_ENDPOINT,0, 0, msgBuf,
msgSize);   // send buffer
                            if (znpResult != ZNP_SUCCESS)
                            {
                                    printf("afSendData error %i;
restarting...\r\n", znpResult);

    delayMs(ZNP_RESTART_DELAY_IF_MESSAGE_FAIL_MS);  //allow enough
time for coordinator to fully restart, if that caused our problem
                                    state = STATE_ZNP_STARTUP;

                            } else {
                                    clearLeds();
                            }
                        }
                break;
            }
        default:     //should never happen
            {
                printf("UNKNOWN STATE\r\n");
                state = STATE_ZNP_STARTUP;
            }
            break;
        }
    }
}


/** Handles timer interrupt */
void handleTimer()
{
    struct FVPacket p;
    FVP_init(&p);
    timerSeq++;
    if(state == STATE_SEND_INFO_MESSAGE) {
```

```
            startPPG();                  // start ADC conversion
            while(!isPPGReady());  // wait for conversion
            FVP_setAdcA(&p, getPPGAsync());   // get ADC result
            FVP_setTimerSeq(&p, timerSeq);    // create packet
            FVPQ_enqueue(&PacketQueue, &p);   // push packet into queue
        }
    }
    /* @} */
```

Appendix D: MATLAB Code Implementation for Signal Processing

```matlab
function [peak_positions, peak_values]=ppg_peak_m1(data, fs, duration)
%--------------FUNCTION PPG PEAK DETECTION METHOD 1 V1.0 -------------
%PUERPOSE: find the positions and values for photoplethysmogram.
%INPUT:
%OUTPUT:
%FEATURES: Filter-free, threshold-free, dynamic and real time.
%CASCADED FUNCTIONS: no preceding, hr_justification_m1 forward.
        %method options for periodical_heat_rate: berger, interpolate,
lpfilter or
        %instantanous.
%AUTHORS: Yichao Joy Xu Feb 21 2012
%REVISIONS: Feb 21 2012 v 1.0 constructed function framework with clean
        %names for each variables.
%TEAKABLE PARAMETERS: regions for locating the peak
        %limit for dynamic interval settings
%-----------------------------------------------------------------
% ppg_name = 'data_ppg.txt';
% data = load(ppg_name);
% duration = length(data);
[first_peak_v, first_peak_p] = max(data(1:fs));
peak_values = zeros(1,round(duration/fs*1.5)); peak_positions = peak_values;%
initialize peak strings
peak_values(1)= first_peak_v; peak_positions(1) = first_peak_p;
rrinterval = fs; % initial guess for rr interval to find the second peak.
n = 1; % initialize peak number counts
i = 0;
while i < duration - first_peak_p-fs %% BUG
    [next_peak_v, next_peak_p] = max((data(round(peak_positions(n)+
rrinterval - fs*0.4)...
        :round(peak_positions(n)+ rrinterval + fs*0.2))));
    % limit the region for peak detection 0.4 seconds arcoss the guessed
    % position, 0.2 to the left, 0.2 to the right. %%% Parameter for
performance analysis.
    peak_values(n+1)= next_peak_v;
    peak_positions(n+1) = next_peak_p + peak_positions(n)+ rrinterval -
fs*0.4;
    rrinterval_real = peak_positions(n+1)-peak_positions(n);
    % calculate everytime a peak has been found, will be used by a limited
    % conditions.
    if rrinterval_real<=1.3*fs && rrinterval_real >=0.4*fs
        % update rrinterval for detecting next peak only if the bmp was
        % found between 45 to 150. %%% Parameters for performance analysis.
        rrinterval = abs(rrinterval_real);
    end
n = n + 1;
i = i + rrinterval_real; %walk to next peak detection region.
end
peak_positions = peak_positions(1:n); peak_values = peak_values(1:n);
%figure;
%plot(data); hold on; plot(peak_positions, peak_values, '*'); hold off;
end
```

```matlab
function [heart_rate] = hr_m1(peak_positions, fso, fshr, duration)
%--------------HEART RATE JUSTIFICATION METHOD 1 V1.0 --------------
```

```matlab
%PUERPOSE: make heart rate in higher frequency and periodical.
%INPUT: detected peak positions, original sampling frequency (fso),
        %heart rate smapling frequency(fshr)
%OUTPUT: justified heart rate as fso Hz.
%FEATURES: Using interpolation method.
%CASCADED FUNCTIONS: ppg_peak_detection_m1 preceding, hr_psd forward.
%AUTHORS: Yichao Joy Xu Feb 21 2012
%REVISIONS: Feb 21 2012 v 1.0 constructed function framework with clean
        %names for each variables.
%TEAKABLE PARAMETERS: regions for locating the peak
        %limit for dynamic interval settings
%-----------------------------------------------------------
%
% ppg_name = 'data_ppg.txt';
% data = load(ppg_name);
% duration = length(data); fso = 50; fshr = 4;
% %
peak_numbers = length(peak_positions);
rr_interval = peak_positions(2:peak_numbers)- peak_positions(1:peak_numbers-
1);
heart_rate_np = 60./(rr_interval./fso); % non-periodical heart rate (y-axis)
before interpolation

pe = find(heart_rate_np>90); pn = find(heart_rate_np<50); pe = [pe pn];
heart_rate_np(pe)=[];peak_positions(pe)=[];
peak_numbers = length(heart_rate_np);
peak_np = peak_positions(1:peak_numbers)./fso; % time (x-axis) for each of
the peak positions.
heart_rate_psp = 0:1/fshr:(duration-2*fso)/fso; % periodical heart rate
sampling positions

%heart_rate = heart_rate_np;
%------------------
heart_rate = spline(peak_np,heart_rate_np,heart_rate_psp);%plot(heart_rate);
heart_rate = heart_rate(11:end-11);
%dump abnormal ones
%     hrm = mean(heart_rate);hrstd = std(heart_rate);
%     hrabnp = find(heart_rate>(hrm+hrm));
%     heart_rate(hrabnp) = [];
%     hrabnn = find(heart_rate<(hrm-0.2*hrm));
%     heart_rate(hrabnn) = [];
%------------------------
%figure;
%plot(peak_np,heart_rate_np,'o',heart_rate_psp,heart_rate);
%plot(heart_rate);
function [area_ratio area1 area2] = psdratio(Pxx, f, a1l,a1h,a2l,a2h)
area1 = trapz(f(round(a1l/f(end)*length(f)):round(a1h/f(end)*length(f))),...
    Pxx(round(a1l/f(end)*length(f)):round(a1h/f(end)*length(f))));
area2 = trapz(f(round(a2l/f(end)*length(f)):round(a2h/f(end)*length(f))),...
    Pxx(round(a2l/f(end)*length(f)):round(a2h/f(end)*length(f))));
area_ratio = area1/area2;
end


%M:\000FIVOLTS\Signal Processing\data\subject_1
```

```matlab
%[Pxxt,arrt,arr,area_ratiom, lff, hff, lfm, hfm, llfm, hhfm, f2,
hrm]=unidatacheck('M:\000FIVOLTS\Signal Processing\universal
pack\data\ppg\fd');
function [Pxxt,arrt,area_ratiom, lff, hff, lfm, hfm, f2,
hrmm,hrm]=unidatacheck(location)
%[Pxxt,arrt,arr,area_ratiom, lff, hff, lfm, hfm, llfm, hhfm, f2,
hrm]=unidatacheck(location)
%----------- visual inspection of the collected data ----------- %
%fucntion: visual inspection and port corrupted data removal
fs = 75;
cd(location);
names = ls;
for n = 1:length(names)-2
ppg = load(names(n+2,:));
kn = find(ppg>1000);
ppg(kn)=[];
kn = find(ppg<200);
ppg(kn)=[];
duration = length(ppg);
[peak_positions, peak_values1] = ppg_peak_m1(ppg, fs, duration);
%plot(ppg);hold on; plot(peak_positions, peak_values1,'*'); hold off;
%title('Peak Detection Results')
%pause;
[heart_rate_1] = hr_m1(peak_positions, fs, 4, duration);
hrm(n) = mean(heart_rate_1);
%plot(heart_rate_1);
%title('4 Hz Periodical Heart Rate')
%pause;
fshr = 4;
for k = 0: round((length(heart_rate_1)- 500)/(fshr*4))
    [Pxxm(k+1,:),f2] = pwelch(heart_rate_1(k*fshr*4+1:k*fshr*4+480)...
        -mean(heart_rate_1(k*fshr*2+1:k*fshr*2+480)), 128, 50, [], 4);
    %pause;
    %plot(f2, Pxxm(k+1,:)); title('HRV PSD over 2 minutes window with 1
minute step size');
    [area_ratiom(n,k+1) lfm(n,k+1) hfm(n,k+1)] = psdratio(Pxxm(k+1,:), f2,
0.04,0.15,0.15,0.5);
    hrmm(n,k+1) = mean(heart_rate_1(k*fshr*4+1:k*fshr*4+480));
end

[Pxxt(n,:), f2] = pwelch(heart_rate_1-mean(heart_rate_1),128,50, [], 4);
%plot(f2, Pxxt); title('HRV PSD over the entire session');
[arrt(n) lff(n) hff(n)] = psdratio(Pxxt(n,:), f2, 0.04, 0.15, 0.15, 0.4);
%pause;
end


% straight out matrix
% arr = []; arrra = area_ratiom(:,1:119);
% for n = 1:length(names)-2
% arr = [arr arrra(n,:)];
% end
%
% llfm = []; lfmr = lfm(:,1:119);
% for n = 1:length(names)-2
% llfm = [llfm lfmr(n,:)];
```

```matlab
% end
%
% hhfm = []; hfmr = hfm(:,1:119);
% for n = 1:length(names)-2
% hhfm = [hhfm hfmr(n,:)];
% end

%plot(arr); title('LF/HF ratio over each 2 minutes window across all the
data'); xlabel('No. of 2-min window');
%figure; plot(arrt); title('LF/HF ratio over entire session across all the
data');
end
% location11 = 'M:\000FIVOLTS\Signal Processing\data\nback\fd';
% location12 = 'M:\000FIVOLTS\Signal Processing\data\ppg\FD_3_26';


location11 = 'M:\000FIVOLTS\Signal Processing\data\nback\fd';
location12 = 'M:\000FIVOLTS\Signal Processing\data\ppg\FD_3_26';
[acrt, acrp, respt, respp, scoret, score] = getnbackdata(location11);
% copy paste in the above first
% mount back to universal pack run the rest of the code.. %% add path.
[Pxxt,arrt,arr,area_ratiom,lff, hff, lfm, hfm, llfm, hhfm,
f2,hrm]=unidatacheck(location12);
%% correlation across each session
subplot(3,1,1); plot(acrt,arrt, '*'); title('Correlation bewteen accuracy and
LF/HF over the entire 10 min session');
xlabel('Accuracy'); ylabel('LF/HF Ratio');
subplot(3,1,2); plot(respt,arrt, '*'); title('Correlation bewteen response
time and total LF/HF over the entire 10 min session');
xlabel('Response Time'); ylabel('LF/HF Ratio');
subplot(3,1,3); plot(scoret,arrt, '*'); title('Correlation bewteen throughput
and total LF/HF over the entire 10 min session');
xlabel('Throughput'); ylabel('LF/HF Ratio');

%% correlation aross each 2 min interval;
acrpa = acrp(:,2:end-1); %acurracy to be used;
resppa = respp(:, 2:end-1); % response to be used;
scorea = score(:, 2:end-1); % throughput tp be used;
acrpaa = []; resppaa = []; scoreaa = [];
for n = 1:length(acrpa);
    acrpaa = [acrpaa acrpa(n,:)];
    resppaa = [resppaa resppa(n,:)];
    scoreaa = [scoreaa scorea(n,:)];
end
figure;
subplot(3,1,1); plot(acrpaa,arr, '*'); title('Correlation bewteen accuracy
and LF/HF over each 2min interval');
xlabel('Accuracy'); ylabel('LF/HF Ratio');
subplot(3,1,2); plot(resppaa,arr, '*'); title('Correlation bewteen response
time and total LF/HF over each 2min interval');
xlabel('Response Time'); ylabel('LF/HF Ratio');
subplot(3,1,3); plot(scoreaa,arr, '*'); title('Correlation bewteen throughput
and total LF/HF over each 2min interval');
xlabel('Throughput'); ylabel('LF/HF Ratio');

%% LF;
```

```matlab
subplot(3,1,1); plot(acrpaa,llfm, '*'); title('Correlation bewteen accuracy
and LF Area over each 2min interval');
xlabel('Accuracy'); ylabel('LF Area');
subplot(3,1,2); plot(resppaa,llfm, '*'); title('Correlation bewteen response
time and total LF Area over each 2min interval');
xlabel('Response Time'); ylabel('LF Area');
subplot(3,1,3); plot(scoreaa,llfm, '*'); title('Correlation bewteen
throughput and total LF Area over each 2min interval');
xlabel('Throughput'); ylabel('LF Area');

%% HF
figure;
xx = 1/192:1/192:1;
p = polyfit(xx,hhfm,1);
y1 = p(1)*xx+p(2);

xx2 = (2-0.6175)/192+0.6175:(2-0.6175)/192:2;
p2 = polyfit(xx2,hhfm,1);
y2 = p2(1)*xx2+p2(2);

xx3 = 1.6195/192:1.6195/192:1.6195;
p3 = polyfit(xx3,hhfm,1);
y3 = p3(1)*xx2+p3(2);

subplot(3,1,1); plot(acrpaa,hhfm, '*'); title('Correlation bewteen accuracy
and HF Area over each 2min interval');
hold on; plot(xx, y1); hold off; xlabel('Accuracy'); ylabel('HF Area');
subplot(3,1,2); plot(resppaa,hhfm, '*'); title('Correlation bewteen response
time and total HF Area over each 2min interval');
hold on; plot(xx2, y2); hold off; xlabel('Response Time'); ylabel('HF Area');
subplot(3,1,3); plot(scoreaa,hhfm, '*'); title('Correlation bewteen
throughput and total HF Area over each 2min interval');
hold on; plot(xx3, y3); hold off; xlabel('Throughput'); ylabel('HF Area');

%% Over time plot
figure;subplot(2,1,1);
plot(acrpaa); title('Accuracy Over Each Minute'); xlabel('minutes of
experiment'); ylabel('average accuracy');
subplot(2,1,2);
plot(acrt); title('Accuracy Over Each session'); xlabel('session no. of
experiment'); ylabel('average accuracy');

figure;subplot(2,1,1);
plot(resppaa); title('Response Time Over Each Minute'); xlabel('minutes of
experiment'); ylabel('average response time');
subplot(2,1,2);
plot(respt); title('Response Time Over Each session'); xlabel('session no. of
experiment'); ylabel('average response time');

namess = ['fd'; 'yx'; 'tf'; 's1'];
names2 = ['S1'; 'S2'; 'S3'; 'S4'];
%% Acc
acrtt  = zeros(4, 208); % get data
for n = 1:4
    load([namess(n,:),'.mat']);
```

```matlab
    acrp = acrp(:,1:8);
    acrt1 = [];
    for m = 1:length(acrt)
    acrt1 = [acrt1 acrp(m,:)];
    end
    acrtt(n,1:length(acrt1)) = acrt1;
end
%%resp
resptt  = zeros(4, 208); % get data
for n = 1:4
    load([namess(n,:),'.mat']);
    respp = respp(:,1:8);
    resp1 = [];
    for m = 1:length(acrt)
    resp1 = [resp1 respp(m,:)];
    end
    resptt(n,1:length(resp1)) = resp1;
end
% RESPONSE TIME ADJUSTED FOR SUBJECT1 (4) DUE TO DEVICE CHANGE.
resptt(4,89:192) =
resptt(4,89:192)./mean(resptt(4,89:192)).*mean(resptt(4,1:88));

%% Throughput
throughput = acrtt./resptt;

%% LF
lf = zeros(4, 208); % get data
for n = 1:4
    load([namess(n,:),'.mat']);
    lf(n,1:length(llfm)) = llfm;
end

%% HF
hhfa = zeros(4, 208); % get data
for n = 1:4
    load([namess(n,:),'.mat']);
    hhfa(n,1:length(hhfm)) = hhfm;
end

%% LF/HF
arrta = zeros(4, 208); % get data
for n = 1:4
    load([namess(n,:),'.mat']);
    arrta(n,1:length(arr)) = arr;
end

% %% Plot
% %%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
% %Template
% lgth = [26 17 24 24]; % length of each subjects session numbers
% f7 = figure;
% for n = 1:4
% subplot(4,1,n);
% plot(acrtt(n,1:lgth(n)), hffa(n,1:lgth(n)),'*--');
% fign7(n,:) = [names2(n,:) , ' ' 'Correlation between N-back accuracy and
HRV-LF'];
```

```matlab
% title(fign7(n,:));
% xlabel('N-back accuracy'); ylabel('HRV-LF');
% end
% saveas(fN, ['5_3_1_1 ' fignN(n,:),'.fig']);
% %%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%

lgth = [208 136 192 192]; % length of each subjects session numbers

f4 = figure;
for n = 1:4
subplot(1,4,n);
plot(acrtt(n,1:lgth(n)), lf(n,1:lgth(n)),'*');
fign4(n,:) = [names2(n,:) , ' ' 'Correlation between LF and N-back accuracy
across each minute'];
title(fign4(n,:));
xlabel('N-back accuracy'); ylabel('LF');
end
saveas(f4, ['5_2_1_2 ' fign4(n,:),'.fig']);

f5 = figure;
for n = 1:4
subplot(1,4,n);
plot(resptt(n,1:lgth(n)), lf(n,1:lgth(n)),'*');
fign5(n,:) = [names2(n,:) , ' ' 'Correlation between LF and N-back response
time across each minute'];
title(fign5(n,:));
xlabel('N-back response time'); ylabel('LF');
end
saveas(f5, ['5_2_2_2 ' fign5(n,:),'.fig']);

f6 = figure;
for n = 1:4
subplot(1,4,n);
plot(throughput(n,1:lgth(n)), lf(n,1:lgth(n)),'*');
fign6(n,:) = [names2(n,:) , ' ' 'Correlation between LF and N-back throughput
across each minute'];
title(fign6(n,:));
xlabel('Throughput'); ylabel('LF');
end
saveas(f6, ['5_2_3_2 ' fign6(n,:),'.fig']);

f7 = figure;
for n = 1:4
subplot(1,4,n);
plot(acrtt(n,1:lgth(n)), hhfa(n,1:lgth(n)),'*');
fign7(n,:) = [names2(n,:) , ' ' 'Correlation between N-back accuracy and HRV-
HF across each minute'];
xlabel('N-back accuracy'); ylabel('HRV-HF');
if n == 2
    title(fign7(n,:));
end
end
saveas(f7, ['5_3_1_2 ' fign7(n,:),'.fig']);

f8 = figure;
for n = 1:4
```

```matlab
subplot(1,4,n);
plot(resptt(n,1:lgth(n)), hhfa(n,1:lgth(n)),'*');
fign8(n,:) = [names2(n,:) , ' ' 'Correlation between N-back response time and
HRV-HF across each minute'];
xlabel('N-back response time'); ylabel('HRV-HF');
if n == 2
    title(fign8(n,:));
end
end
saveas(f8, ['5_3_2_2 ' fign8(n,:),'.fig']);

f9 = figure;
for n = 1:4
subplot(1,4,n);
plot(throughput(n,1:lgth(n)), hhfa(n,1:lgth(n)),'*');
fign9(n,:) = [names2(n,:) , ' ' 'Correlation between N-back throughput and
HRV-HF across each minute'];
xlabel('N-back throughput'); ylabel('HRV-HF');
if n == 2
    title(fign9(n,:));
end
end
title(fign9(n,:));
saveas(f9, ['5_3_3_2 ' fign9(n,:),'.fig']);

f10 = figure;
for n = 1:4
subplot(1,4,n);
plot(acrtt(n,1:lgth(n)), arrta(n,1:lgth(n)),'*');
fign10(n,:) = [names2(n,:) , ' ' 'Correlation between N-back accuracy and HRV
LF over HF across each minute'];
xlabel('N-back accuracy'); ylabel('HRV LF/HF');
if n == 2
    title(fign10(n,:));
end
end
saveas(f10, ['5_4_1_2 ' fign10(n,:),'.fig']);

f11 = figure;
for n = 1:4
subplot(1,4,n);
plot(resptt(n,1:lgth(n)), arrta(n,1:lgth(n)),'*');
fign11(n,:) = [names2(n,:) , ' ' 'Correlation between N-back response time
and HRV LF over HF across each minute'];
xlabel('N-back response time'); ylabel('HRV LF/HF');
if n == 2
    title(fign11(n,:));
end
end
saveas(f11, ['5_4_2_2 ' fign11(n,:),'.fig']);

f12 = figure;
for n = 1:4
subplot(1,4,n);
plot(throughput(n,1:lgth(n)), arrta(n,1:lgth(n)),'*');
```

```matlab
fign12(n,:) = [names2(n,:) , ' ' 'Correlation between N-back throughput and
HRV LF over HF across each minute'];
xlabel('N-back throughput'); ylabel('HRV LF/HF');
if n == 2
    title(fign12(n,:));
end
end
title(fign12(n,:));
saveas(f12, ['5_4_3_2 ' fign12(n,:),'.fig']);
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
f16 = figure;
for n = 1:4
subplot(1,4,n);
plot(lf(n,1:lgth(n)), hhfa(n,1:lgth(n)),'*');
fign16(n,:) = [names2(n,:) , ' ' 'Correlation between HRV-LF and HRV-HF
across each minute'];
xlabel('HRV-LF'); ylabel('HRV LF/HF');
if n == 2
    title(fign16(n,:));
end
end
saveas(f16, ['3_4_2 ' fign16(n,:),'.fig']);

f17 = figure;
for n = 1:4
subplot(1,4,n);
plot(resptt(n,1:lgth(n)), acrtt(n,1:lgth(n)),'*');
fign17(n,:) = [names2(n,:) , ' ' 'Correlation between N-back response time
and accuracy across each minute'];
xlabel('N-back response time'); ylabel('N-back accuracy');
if n == 2
    title(fign17(n,:));
end
end
saveas(f17, ['4_1_2 ' fign17(n,:),'.fig']);
```

```matlab
function [acrt, acrp, respt, respp, scoret, score] = getnbackdata(location)
cd(location);
names = ls;
rn = length(names);
for n = 1:rn-2
load(names(n+2,:));
acrt(n) = acr;
respt(n) = mean(response_time);
scoret = acrt/respt;
for k = 0:(length(err)-59)/2
acrp(n,k+1) = 1-mean(err(2*k+1:2*k+60));
respp(n,k+1) = mean(response_time(2*k+1:2*k+60));
end
% acrp(n,:) = results.mean_acr_perminute;
% respp(n,:) = results.response_time_mean_perminute;
score = acrp./respp;
end
```

```
clear all
% BETA 11/28 version 1.0
% 12/6 v 1.1
% fixed key board response
% fixed standard deviation of reaction time over a session and average
% error per minute
% fixed standard deviation of average error per minute
% fixed the output to results_date.dat
% changed option of number of trials to minute of test (mot)


%function [acr, r, nocr]= NbackMpitch(notr, nofr, drl, drs, isi, fra, nob)
% i.e. [acr, notr, nocr]= NbackMpitch(10, 4, 0.1, 0.05, 1, [500 600 700 800],
1);
%% Define Parameters
fs = 44100; csel = 3; fra = [700 800,900,1000]; nob = 1; sclock = clock;
%******% try this first train your self for a couple times until acr = 100 %
only 10 trials******%
%mot = 5; nofr = 4; drl = 0.2; drs = 0.02; isi = 2;
%******% Then try this, by uncommenting the following line, it is 10 minutes
session, 3 sec isi 200 msec vs 20 msec%******%
%mot = 10; nofr = 4; drl = 0.2; drs = 0.02; isi = 3;
%******% Then try this, it is 10 minutes session, 3 sec isi, 100 msec vs 50
msec%******%
%mot = 10; nofr = 4; drl = 0.1; drs = 0.05; isi = 3;
%******% Then try this, it is 10 minutes session, 1 sec isi, 100 msec vs 50
msec%******%
%Standard%%Standard%%Standard%%Standard%%Standard%
mot = 10; nofr = 4; drl = 0.1; drs = 0.05; isi = 2;
%******% Then try this, it is 10 minutes session, 1 sec isi, 100 msec vs 50
msec% with 8 frequency variation******%
%mot = 10;  fra = [400,500 600 700 800,900,1000,1100]; nofr = 8; drl = 0.1;
drs = 0.05; isi = 1;
%******% Then try this, it is 10 minutes session, 1 sec isi, 75 msec vs 50
msec% with 4 frequency variation******%
%mot = 10;  nofr = 4; drl = 0.075; drs = 0.05; isi = 1;



% acr -- accuracy
% notr -- number of trials
% nocr -- number of corret
% nost -- number of stimuli
% nofr -- number of frequencies
% drl  -- the longer stimulus duration
% drs  -- the shorter stimulus duration
% isi  -- stimulus interval
% nob  -- number of backs
% r -- position of the ommitted error

%% Create beep stimulation waveform
notr = mot*60/isi;
drlstr = 0:1/fs:drl; % build string of samples at a rate of fs Hz.
drsstr = 0:1/fs:drs;
shortws = zeros(nofr, length(drsstr)); longws =
zeros(nofr,length(drlstr)); %predefine stimulus waveforms
for i1 = 1:nofr
```

```matlab
shortws(i1,:) = sin(fra(i1)*2*pi*drsstr);
longws(i1,:) = sin(fra(i1)*2*pi*drlstr);
end
%% Create orders for trials
orders = zeros(notr+nob,2); % predefine
for i3 = 1: notr+nob
orders(i3,1) =  ceil(rand*2);
end
for i4 = 1: notr+nob
orders(i4,2) =  ceil(rand*nofr);
end
%orders
%% GUI
screen_size = get(0, 'ScreenSize');
set(figure(1), 'Position', [0 0 screen_size(3) screen_size(4) ] );
handle.sameu = uicontrol('Style', 'pushbutton',...
            'String', 'Same',...
            'Position', [200 340 400 200], ...
            'Fontsize', 28,...
            'Value', 0) ;
h1 = handle.sameu;
%set(handle.sameu,'Callback','h=gcbo');
set(handle.sameu,'Callback','[csel,sclock]=fetcher(h1,h2,sclock);');

%h2 = 0;
handle.diffu = uicontrol('Style', 'pushbutton',...
            'String', 'Different',...
            'Position', [700 340 400 200], ...
             'Fontsize', 28,...
             'Value', 0);
h2 = handle.diffu;
%set(handle.diffu,'Callback','h=gcbo');
set(handle.diffu,'Callback','[csel,sclock]=fetcher(h1,h2,sclock);');
%% Comparison by system
compc = abs(orders((1:1:notr+nob-1),1)-orders((2:1:notr+nob),1));
%% play the sound and get user input
i2 = 1;
while i2 <= notr+nob
    if orders(i2,1) == 1
sound(shortws(orders(i2,2),:),fs);
starc = clock; % record the clock time
pause(isi-drs);
    else
sound(longws(orders(i2,2),:),fs);
starc = clock;
pause(isi-drl);
    end
    %compu = ones(1,i2-nob)*3;
    %response_time = zeros(i2-nob,1); rtsstr = response_time;
    if i2>nob
        compu(i2-nob)= csel;
        rts = size(sclock,1); % the times subject has responded
        rtsstr(i2-nob) = rts-1; % the array of the times subject has
responded
        response_time(i2-nob) = sclock(rts,6)-starc(6)+(sclock(rts,5)-
starc(5))*60;
    end
```

```matlab
i2 = i2+nob;
    handle.text = uicontrol('Style', 'Text',...
            'Str', 'Please now enter your result',...
            'Position', [250 80 800 80],...
            'Fontsize', 20);
end
err = abs(compc-compu');
dres= rtsstr(1:length(rtsstr))- [0 rtsstr(1:length(rtsstr)-1)]; % double
responded
dr = find(dres>1);
r = find(response_time<0); %ommitted positions
err(r) = 1;
acr = (1-sum(err)/notr)*100 %printed results
nocr = notr - sum(err);


%% Output
finish_time = clock;
file_name = [num2str(finish_time(2)) '_' num2str(finish_time(3)) '_' ...
    num2str(finish_time(4)) '_' num2str(finish_time(5)) '.mat'];
response_timeforcal= response_time;
results.mean_acr_perminute = acr;
pr = find(response_timeforcal<0); response_timeforcal(pr)= isi;
if notr > 60/isi % per minute
    for i5 = 1:(notr/(60/isi))
    results.mean_acr_perminute(i5)  = mean(1-(err(60/isi*(i5-1)+1:i5*60/isi)));
    results.std_acr_perminute(i5) = std(1-(err(60/isi*(i5-1)+1:i5*60/isi)));
    results.response_time_mean_perminute(i5) =
mean(response_timeforcal(60/isi*(i5-1)+1:i5*60/isi));
    results.response_time_std_perminute(i5) =
std(response_timeforcal(60/isi*(i5-1)+1:i5*60/isi));
    end
end
results.std_acr = std(results.mean_acr_perminute);
results.response_time = response_timeforcal;
results.response_time_std = std(response_timeforcal);
save(file_name);
figure;
subplot(2,1,1);
plot(1:length(err), 1-err); hold on; plot(r, 1-err(r), 'o'); plot(dr, 1-
err(dr), '*');hold off
title('Mistakes, Omitted Stimulus and Double Responded')
fig_name_1 = [num2str(finish_time(2)) '_' num2str(finish_time(3)) '_' ...
    num2str(finish_time(4)) '_' num2str(finish_time(5)) '_accuracy_response
time' '.fig'];
saveas(gcf,fig_name_1);
subplot(2,1,2);
plot(response_time,'*');
title('Response Time (seconds)'); ylim([0 isi]);
fig_name_2 = [num2str(finish_time(2)) '_' num2str(finish_time(3)) '_' ...
    num2str(finish_time(4)) '_' num2str(finish_time(5)) '_windowed_results'
'.fig'];
saveas(gcf,fig_name_2);
% figure;
% subplot(2,1,1);
% errorbar(results.mean_acr_perminute,results.std_acr_perminute);
% subplot(2,1,2);
```

```
%
errorbar(results.response_time_mean_perminute,results.response_time_std_permi
nute);
```

```
function [csel,sclock]= fetcher(h1,h2,sclock)
h = gcbo;
if h == h1
   csel = 0;
else if h == h2
   csel = 1;
    end
end
sclock = [sclock; clock];
end
```