Vital Signs Monitoring Using a New Flexible Polymer Integrated PPG Sensor

by

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Abstract

For remote registration of vital signs, non-invasiveness is attractive. The possibility of acute loss of consciousness threatens the lives of employees such as soldiers, fire fighters, police officers, and law enforcement personnel, who perform duties at hazardous or remote conditions. The brain cells die within three minutes after occurrence of hypoxia in cerebrospinal fluid. Consequently, acute occurrence of cardiac or pulmonary system failure reduces an employee’s likelihood of surviving due to the lack of ability for communication and the lack of ability for emergency calls. In the case of severe injury, a medic’s response time becomes a crucial parameter for increasing a person’s likelihood of survival. Continuous monitoring of vital signs therefore assists medics and employees by reducing response time to severe accidents. For detection of vital signs; electrocardiography, capnometry and pulse oximetry are being widely used as the golden standard for extraction of vital signs such as heart rate, respiration rate and blood oxygenation. But, these sensors require motionless attachment to specific areas of the body. The fact that employees are constantly in motion and sometimes covered by protection shields introduces difficulty concerning the continuous obtaining of vital signs. In this dissertation, we studied feasibility of replacing Electrocardiography by Photoplethysmography on mechanically flexible sensors. Three major studies were performed. First, we developed an algorithm for the detection of respiration rate from Photoplethysmography. During this study, a fast respond CO2 sensor was also modulated to detect respiration rate, and both methods were compared to respiration effort transducer. Second, we assessed the feasibility of fabricating PPG sensors on plastic polymers. During this study, we designed and integrated a novel PPG device, using inkjet-printing technology. At last, we developed a computationally inexpensive algorithm for the extraction of heart rate variability (HRV) from the morphology of PPG. Results were compared to HRV from commercial ECG and the performance of the device was evaluated respectively.

Keywords: photoplethysmography, electrocardiography, pulse oximetry, flexible sensors, printed electronics, micro-fabrication
Dedication

To my mother, who encouraged me to continue studying at SFU. Shortly after I started the program, she left this world, and I never had chance to say goodbye to her. I offer my research to her and people who have lost the battle of life, against respiration related problems.

To my father, for his support.

To Kimberly a person who supported me during this study and walked with me through this research.
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I would like to thank my colleagues Farzad Khosravi and Moein Shayegannia for their input and guidance.
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<td>Photoplethysmography</td>
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<tr>
<td>ECG</td>
<td>Electrocardiography</td>
</tr>
<tr>
<td>ABP</td>
<td>Arterial Blood Pressure</td>
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<tr>
<td>PACO2</td>
<td>Partial Arterial Carbon Dioxide</td>
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<tr>
<td>ETCO2</td>
<td>End Tidal Carbon Dioxide</td>
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<tr>
<td>LBNP</td>
<td>Lower Body Negative Pressure</td>
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<tr>
<td>SPO2</td>
<td>Pulse Oxygen Saturation</td>
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<td>HRV</td>
<td>Heart Rate Variability</td>
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<td>PET</td>
<td>Polyethylene terephthalate</td>
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<td>PCB</td>
<td>Printed Circuit Board</td>
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<td>RIIV</td>
<td>Respiration Induced Intensity</td>
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<td>Infrared</td>
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<td>Light Emitting Diode</td>
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<td>Drop On Demand</td>
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<td>DBP</td>
<td>Diastolic Blood Pressure</td>
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<td>SBP</td>
<td>Systolic Blood Pressure</td>
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<tr>
<td>FFT</td>
<td>Fast Fourier Transform</td>
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<td>LCD</td>
<td>Liquid Crystal Display</td>
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<td>SD</td>
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1. Introduction

Over the last decade, the design of wearable physiological measurement systems has become a growing area of interest. As wearable physiological measurement systems hold potential in a variety of fields ranging from medicine and sports to military and safety critical monitoring; advances may be applied to diverse interest groups and populations [1]. These systems may be used to monitor vital signs in high-risk professions, which require one to be relatively active and prone to dangers, and to perform duties under physically and mentally challenging environments and conditions [2]. Advances in wearable medical systems will enable professionals such as soldiers, fire fighters, law enforcement personnel, miners, and deep sea divers to ensure physiological conditions can be monitored both at sporadic snapshots and over extended continuums of time. Not only will healthcare be more accessible, but improvements in wearable physiological measurement systems will detect critical conditions regarding vital organs such as heart and lungs in a proactive and time sensitive fashion.

Wearable systems can be broadly defined as electronic devices, which can be attached directly to one’s body or worn as part of clothing and accessories. Unlike conventional systems, wearable systems can be operational and accessed with very little or no hindrance to user activity [3]. Wearable technologies hold great promise to improve personal safety and security and possible medical services. The main focus of wearable systems is the registration of vital signs such as one’s respiration rate, heart rate, blood oxygenation, temperature and blood pressure [4]. These systems, however, are limited to power consumption and computational resources, and require real-time detection of physiological threats [5].

The main reason for the development of a wearable vital monitoring device is to improve monitoring and diagnosis outside a user’s environment [6], while allowing users to follow their normal routines. There are two methods commonly used for monitoring
vital signs. The first method is a traditional home-care environment, in which clinical equipment is installed in a user’s environment, allowing one to take regular measurements and to transmit data to a medical centre. The second method involves specialized wearable sensors, which are used to record vital signs and transmit them to a medical centre outside of a user’s environment. Today, the trend follows the second alternative with the intention of providing interactive advice appropriate to the changes in the vital signs, and inferred medical condition of the user.

1.1. Motivations

This thesis seeks to address the challenges associated with wearable monitoring device systems, and to enhance one’s comfort regarding the wearable vital sign monitoring of real-time vital sign acquisition and the response time to detection of critical conditions. In particular, emphasis is placed on at risk populations, such as fire fighters, law-enforcement personnel and elderly people who have suffered from severe cardiovascular attacks and are required to use wearable ECG monitoring systems for a prolonged period of time. Through the use of wearable monitoring devices, populations such as those aforementioned would benefit from the detection of critical conditions when working in hazardous environments and/or with significant health concerns. In order to meet wearability requirements, a study of photoplethysmography (PPG) is completed in order to determine if the prerequisites of this intent are valid.

PPG by no means is a new physiological signal. Despite this fact however, there is a lack of research concerning PPG and one’s safety in professional and personal environments. Likewise, there continues to be insufficient research addressing elderly populations that require spontaneous vital sign monitoring outside of clinical settings. For these reasons, we studied PPG for extraction of heart rate and other physiological signals, which will be, discussed in chapter two and three of this thesis.

The heart rate is considered a non-stationary signal, which provides valuable information about cardiovascular disease and warns one of impending cardiac disease. Continuous variation of heart rate (HRV) provides detailed observation of interplay between sympathetic and parasympathetic nervous systems. In addition, HRV analysis
assesses overall cardiovascular health and the state of the autonomic nervous system, which is responsible for regulating cardiac activity [192]. For these reasons, a large portion of literature has been dedicated to developing wearable devices for continuous registration of the heart rate.

Electrocardiography (ECG) acquisition is a common approach used to obtain the estimation of heart rate. ECG acquisition is feasible via two types of electrodes; wet Ag/AgCl electrodes and dry electrodes. The conventional wet adhesive Ag/AgCl ECG electrodes are used almost universally in clinical settings. Yet while Ag/AgCl ECG electrodes provide an excellent signal, they are also cumbersome and irritating for mobile use. Thus while the chief advantage of the standard clinical wet electrodes is the fact that they adhere very well to one’s skin, a deterrent may be the discomfort they cause a patient. From a client centered perspective and a patient’s standpoint, Ag/AgCl ECG electrodes thus become problematic as one considers comfort and long-term use [7].

Adhesive wet electrodes stay fixed to specific, clinical standard locations on the body. Dry and noncontact electrodes address the comfort issues with the adhesive electrode, but are much more difficult to secure against the skin. While these dry electrodes, which operate without gel, do adhere and while skin contact has been known for many decades, dry electrodes have yet to achieve acceptance for medical use [8]. Standard electrodes adhere well to the body, are robust, inexpensive and simple. When properly used, wet electrodes provide an excellent signal. Dry or non-contact electrodes offer few advantages for patients with extremely sensitive skin burn units [9] neonatal care [10], and add cost and complexity for active electrode circuitry.

In order for dry-electrodes to be clinically useful mechanical solutions must be devised to place them in the proper position or an alternative application must be found. It is for these reasons that dry and noncontact electrodes are unlikely to replace the standard ECG electrodes. Several attempts have been made to integrate electrodes in beds [11], chairs [12], and even bathtubs [13] and toilets [14]. Obtaining signs of cardiac activity through air gap (40cm) [15] is also possible. Unfortunately, signal quality in these devices is typically quite poor and riddled with motion artifact, noise and interference problems. At present, nothing has advanced beyond the proof-of-concept.
In order to overcome the challenges previously noted, a wearable device capable of obtaining continuous heart rate is required to satisfy certain strict criteria while operating under significant hardware resource limitations [16] [17]. More specifically, a wearable heart rate sensory design, needs to take into account the following characteristics:

- **User conformability:** Continuous monitoring of cardiac activity requires non-invasive attachment on body of users, without interfering to their daily routine [18].

- **Mechanical flexibility:** A small flexible device greatly improves the comfort of use and further provides a much better and more reliable sensor attachment in the form of wearable accessory, such as that by Kiani [19] and New [20].

- **One-piece node easy to wear:** A multi-sensory platform enables data acquisition, signal processing, and radio transmission simultaneously all in one compact device, such as that by Chou [21]. Such a platform, however, requires substantial power consumption and a number of electronic components. It is important for the platform to be on the chest, as this characteristic limits application of vital monitoring, which requires prolonged physiological signal acquisition.

- **Secure and reliable attachment:** A reliable attachment of device provides excellent physiological data acquisition and clinically interpretable physiological signals, such as that by Shaltis [22]. Reliable ECG acquisition often requires the attachment of two or more electrodes on one’s chest. The attachment of the ECG on one’s chest however poses additional problems regarding user conformability. Poor attachment of electrodes on the chest for instance may arise due to factors such as excessive hair covering the skin of male subjects.

PPG has been studied for monitoring of multiple physiological systems such as cardiovascular and respiratory systems. It has proven to be reflective of multiple physiological indexes [23], and to capture cardiovascular [24], pulmonary [25] and baroreflex [26] responsiveness to the body’s stress, such as progressive haemorrhages [27]. In addition to these indexes, PPG is also considered to be a reliable index of blood oxygenation [28].

The unique characteristics of PPG reduce excessive use of physiological sensors on multisensory platforms. Reduction of electromechanical sensors on vital monitoring devices reduces the demand for power consumption, processing speed, complexity of a
design. In addition, reduction of electromechanically sensors on vital monitoring devices increases user conformability and the possibility of integrating microelectronics and mechanically flexible substrates. While photoplethysmography carries multiple physiological data, significant aspects of research and relevant literature refer to design of wearable sensors for monitoring of cardiovascular and pulmonary systems individually [29]. To overcome challenges of wearable physiological signal acquisition and limited performance of dry electrodes, we will study PPG as an alternative to ECG for continuous monitoring of cardiovascular and pulmonary activity.

1.2. Objectives

Objectives of this thesis have been summarized in figure 1.

Figure 1. This figure demonstrates objectives of the thesis in a flowchart format.
1) Study PPG signal to determine if it is appropriate for easy attachable vital sign monitoring. PPG will be studied to assess detection of critical conditions where a person is unable to continue with their daily routine. Such a condition is considered as acute failure of cardiovascular and respiratory activity.

2) Validate PPG signal for monitoring and medical use.

   I. Extract heart rate and oxygen from PPG sensors for monitoring proposes.

3) Validate PPG implementation with medically relevant information extracted from PPG signal.

   I. Evaluate degree of complexity and accuracy of algorithm for detection of respiration from PPG.

   II. Study hypodynamic response of human body to central hypovolemia during lower body negative pressure test and evaluate feasibility of extracting features form PPG waveform for detection of progressive hemorrhage.

4) Develop an algorithm for identification of PPG features for physiological mentoring and medically relevant information.

5) Develop printable flexible implantation of the sensor.

   I. Upon completion of the aforementioned studies and evaluation of outcomes, integration of PPG on mechanically flexible materials will be pursued using inkjet-printing technology. As inkjet-printing technology does not require special tools to fabricate new sets of elements [38], it is considered perfect for small-scale production and prototyping. In addition, inkjet-printing technology lowers the cost of prototype fabrication by printing from graphic bitmap files straight onto flexible substrates.

1.3. Thesis organization

   As shown in figure 2, this thesis focuses on four related chapters:
I. Detailed review of common vital sign monitoring methodologies and common physiological interpretation of PPG waveform.

II. Develop a mobile platform for PPG acquisition based mobile solution and evaluate feasibility of mobile PPG acquisition in parallel to heart rate, SpO2 and respiration rate. Design a mobile platform for detection of respiration rate using CO2 sensor. Evaluate degree of complexity and accuracy of algorithm for detection of respiration rate from PPG.

III. Study hypodynamic response of human body to central hypovolemia during lower body negative pressure test and evaluate feasibility of extracting features from PPG waveform for detection of progressive hemorrhage. Design and development of an algorithm for detection of anacrotic pulses of PPG and height and raise-fall time of the PPG waveform.


As illustrated above, the work is organized into an introduction and conclusion, with four chapters discussing the main body of information. Beginning with the introduction, chapter one seeks to identify and present the main themes of the thesis, which are further, expanded on throughout subsequent chapters. Chapter two presents background information needed to adequately understand core themes pertinent to the
thesis, such as methods of monitoring vital signs, limitations, typical characteristics and clinical application of PPG waveform. In addition, relevant definitions such as that regarding the man down condition are presented in this section.

In chapter three, two hypotheses are evaluated and discussed. The first hypothesis discusses feasibility of implementing a mobile system on microcontrollers for extraction of Spo2, heart rate and respiration in parallel to PPG acquisition. In addition, the performance of this platform is compared to the same series of hardware implementation for detection of respiration from CO2 sensors. A comparison of these two devices provides a strong understanding of the required model for this application and enables us to evaluate challenges and advantages of micro controller based solutions for vital sign acquisition. The second hypothesis assesses complexity and feasibility concerning algorithm design assisting in the detection of respiration rate form photoplethysmography. Respiration rate obtained from PGG and CO2 are then compared and results presented in the same chapter.

Chapter four discusses morphological variation of PPG signals in relation to hypovolemic stress. In this chapter, synthetic circulatory shock was stimulated using lower body negative pressure tests on four human subjects. This study used PPG signal to observe hypodynamic responses when up to 40% of blood volume was removed from a patient. The chapter discusses both results and proposed features of PPG regarding the detection of progressive haemorrhage.

In Chapter five, background information about inkjet-printing and Diamatix technology are provided. In addition, the electrical and optical design of the PPG sensor are presented, and the process of integrating PPG sensor on transparent polymer is discussed. The present performance of PPG sensors, ECG and commercial PPG devices are also evaluated in this chapter. The results of the study are included within this chapter. Finally, chapter six is the terminating chapter, which seeks to conclude the thesis and summarize results. This chapter consists not only of the author's perspective, but also offers further direction regarding future areas of study.
2. General Background and Literature Review

In this section, background information about vital sign monitoring, challenges and advantages will be presented. Next, PPG waveform, typical clinical application of PPG and the relationship between PPG and respiration rate will be discussed. Finally, a survey regarding the multisensory platform of vital sign monitoring will be presented.

2.1. Vital sign monitoring

Vital sign monitoring is limited by the fact that the data is acquired in mostly unknown environments and on subjects performing various activities. The major challenge for this type of system is the validity and reliability of data. Remote monitoring is based on detection of thresholds or anomalies in the acquired data, which are then used to invoke alarms [30]. The remotely monitored user is mainly in unknown and uncontrolled environments, performing activities that may alter physiological readouts. Physiological data could be measured from various types of devices. The commonly used physiological signals are categorized in the following five groups:

1) Cardiac Activity: Various physiological signals are used for cardiovascular monitoring. For example, electrocardiography (ECG), seismocardiography (ECG), echocardiography (ECG), ballistocardiography (BCG), photoplethysmography (PPG) and blood pressure BP are considered to be a few well-known methodologies. Among these signals, ECG is considered the most commonly used cardiovascular signal. Heart rate (HR) is one of the simplest and most informative cardiovascular parameters. In addition to HR, heart rate variability (HRV) has also gained increasing attention as an indicator of cardiac activity [31].

2) Blood Pressure: Most of the measurements for wearable sensors for Blood Pressure (BP) have been developed based on conventional measurement techniques such as the oscillometric method. The cuffless BP measurement technique however, is based on estimation of BP from the transit time of a pulse travelling along an artery and other related parameters [32].
3) **Blood Oxygen Saturation:** Blood oxygen saturation is a vital indicator of a patient health status. A human being cannot survive for a prolonged time without a constant oxygen supply to the brain. The first prototype of a wearable reflectance pulse oximeter including a radio frequency (RF) data transmission unit was miniaturized in a fingering configuration [33].

4) **Respiration:** Respiration is an important physiologic function that is multidimensional in nature. A detailed quantification of volume, timing and shape of the respiratory waveform can map into different physiological states [34].

5) **Temperature:** Assessment of thermometry provides important information about the state of an individual. People in emergency conditions suffer from a variety of threats including hyperthermia and hypothermia. Consequently, continuous measurements of core body temperature provide valuable information about one’s state of health [35].

Vital monitoring adds a natural extension of state of health, where the victim can call for assistance in the case of an emergency [36]. The key problem is that in the case of major injury, sudden loss of consciousness may occur. In this case, users are unable to transmit emergency alarm signals. For this reason, act of timely rescue can act to complicate the injury through cardiovascular, respiratory failure, or other time related medical problems. In this context, minutes and seconds play a critical role in saving a victim’s life. It is well known that in absence of oxygenation, damage to the brain starts within five minutes with brain death ensuing within another 10–15 minutes [37]. In the case of severe injury, an alarm during early stages provides a medical team with enough time to intervene and respond efficiently. However, there is not a pre-determined method for detection of consciousness. The definition of mysterious phenomena of consciousness is related to the complex structure of the brain.

### 2.1.1. Summary of Challenges for remote vital sign monitoring

Major obstacles to wider use of wearable medical monitoring systems could be summarized as follows:

1) **Motion artifact:** most of wearable design concepts are exposed to intense body movement. These systems must be able to obtain reliable signal without limiting user’s physical activity.

2) **Restricted access to energy resources:** the source of energy in most remote systems is battery. A typical wireless remote monitoring system
consists of data acquisition, processing and transmission units. A suitable system must run efficiently to sustain the power consumption at a sufficient level. Power efficiency is a crucial parameter.

3) Existing sensors are difficult to wear for long periods of time without irritating skin after prolonged periods.

4) Changing contact resistance between electrode and skin over time (For example, gels that are used to improve contact in the case of EEG electrodes dry out over time.)

5) Size and weight of vital sign monitoring devices; available data acquisition modules are typically large in size, which makes them heavier than desirable. Device intelligence in addition to data storage can increase size and weight. Most medical monitoring applications require a large number of analog input channels. For example, three channels are necessary for ECG monitoring, up to 8 or 16 channels for EEG monitoring, and more than 8 different physiological signals for sleep studies, each with their own particular requirements in terms of signal range, amplification, and filtering.

6) Responsibility for outcome of medical conditions, i.e. a manufacturer will want to minimize the chance of being sued if the device does not correctly predict a medical event. It is difficult to determine if there was a malfunction of device, a lack of knowledge of other conditions of the patient, or whether the lawsuit was justified.

2.2. Typical PPG waveform and its characteristics

Photoplethysmography (PPG) is considered a non-invasive optical signal, which is used for non-invasive estimation of blood oxygenation, which is known as pulse oximetry. Advantages of pulse oximetry have been well studied. By focusing on oxygen saturation, attention was distracted from the pattern of the peripheral pulse wave. Peripheral pulse wave provides a non-invasive window on several dynamics, cardiovascular, and pulmonary parameters. There are two types of displays; pulse oximetry and barograph, however to date, neither is indicative of the PPG waveform. Although the pulse oximetry may indicate changes in perfusion for the tissues being illuminated, its waveform mimics an intra-arterial pressure wave [39]. Figure 3 shows the anatomy of a standard plethysmographic wave. PPG waveform starts with the positive steep volume inflow due to ventricular systole, and follows by the decline from peak light absorption after the maximum volume change has passed.
Figure 3. Typical photoplethysmographic waveform obtained by commercial Nonin 8600 pulse oximeter, sensor was located at finger.

The peripheral pulse wave is generated by blood ejected from the heart during the opening of the aortic valve. This pressure interacting with complex elastic and reflective elements in the vascular tree shapes the PPG waveform (figure 3). Changes in a PPG waveform arise from variation both in path-length between source and detector in optical density of blood [40]. Typical waveform of PGG cycle can be divided into two parts, the anacrotic phase and the catacrotic phase. The anacrotic phase is the rising part of the pulse due to systole. This happens shortly after QRS complex in ECG. The catacrotic phase corresponds to cardiac diastole. Often it contains a secondary peak so called dicrotic north, an effect of diminishing with aging and increasing arterial stiffness [41].

2.2.1. Characteristics of PPG waveform

Peripheral pulse wave provides visualization of local tissue perfusion that results from the interaction of left ventricular stroke volume and peripheral vascular resistance [42]. This resistance will result in a decreasing peripheral flow and a concomitant reduction of the elastic of the arterial tree, which reduces the peripheral pulse amplitude. The peripheral pulse wave generated by blood ejection from the heart has been characterised with eight features, as demonstrated in table 1.
Table 1. Feature of PPG and physiological interpretation

<table>
<thead>
<tr>
<th>PPG Feature</th>
<th>Hypovolemia/Progressive hemorrhage</th>
<th>Respiration rate</th>
<th>Heart rate Hypertension Hypotension</th>
</tr>
</thead>
<tbody>
<tr>
<td>Height amplitude</td>
<td>YES [43]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Raise time</td>
<td>Attended in the current dissertation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fall time</td>
<td>Attended in the current dissertation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Interval between cardiac cycle</td>
<td>Attended in the current dissertation</td>
<td></td>
<td>YES</td>
</tr>
<tr>
<td>Area Under the Curve</td>
<td>YES [43]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respiration component (RIIV)</td>
<td>Very week Correlations coefficient [44]</td>
<td>YES</td>
<td></td>
</tr>
<tr>
<td>Left Ventricular Ejection Time</td>
<td>YES [45]</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

2.2.2. Effects of Left Ventricular Ejection Time (LEVT) on PPG waveform

Left ventricular ejection time (LVET) is one of the first non-invasive measurements used in cardiology for the assessment of ventricular performance of heart (figure 4). An early application of LEVT was identification of heart failure [120] or identification of progressive hypovolemia or blood loss [46]. Common LVET monitoring techniques, including phonocardiograms, carotid tonometry, thoracic bio impedance, echocardiograms and continuous/pulsed wave Doppler flow techniques, are based on measurements at or close to the heart. The main reason given for this is that as the aortic pulse wave travels along the arterial tree, it would be modified by the aggregated influence of vessel compliance and wave reflection [47]. As a result, the pulse waves measured at a peripheral site may have lost the characteristics required for reliable LVET estimation.

Although estimation of LVET with absolute accuracy might not be achievable with peripheral measurements, Geeraerts [48] demonstrated that peripheral LVET measured from a finger blood pressure waveform could reflect variation of central LVET during simulated hypovolaemia. In current medical settings, continuous monitoring of arterial pressure waveform requires insertion of a radial artery catheter, which is an invasive
procedure. Finapress is considered a non-invasive device, which monitors arterial pulse waveform with its use limited to particular patient groups due to demands in terms of expertise and equipment. An alternative method to record a peripheral pulse waveform is photoplethysmography [49]. The application of PPG in LVET monitoring is by no means new. Early work in the 1970s showed that the first derivative of the ear densitogram provided an estimate of LVET that was strongly correlated with the carotid measurement [50]. Limited by the availability of computational resources at that time, the measurement of LVET required manual detection of the characteristic points from the ear waveform, which could be a labour intensive task. However, with the rapid advancement in computer technology and signal processing techniques, automatic detection of arterial pulse waveform features has become more feasible [51].

![Figure 4. Demonstration of LVET from PPG finger comparison to aortic Doppler measurement][52]

### 2.2.3. Respiration Sinus Arrhythmia

Respiration Sinus Arrhythmia was first introduced by Ludwig in mid 19th century [53]. A fundamental function of respiration is to maintain homeostasis as an interface between the interiors and exterior of the human body. The respiration system is open to external factors through ventilation via the alveoli, while the circulatory system consists of two closed loops of pulmonary and systemic circulation. At any given moment,
approximately ten percent of the blood in the pulmonary circulation is distributed in the pulmonary capillary bed [54]. The stroke volume is almost equivalent to the bolus on the blood momentarily circulating in the pulmonary capillary bed. This indicates most of the pulmonary capillary blood volume interfacing with the alveolar gas would be replaced with each heartbeat. Therefore, the distribution of heartbeats within each respiratory cycle could critically affect efficacy of respiratory gas exchange. RSA is influenced by factors such as cardiopulmonary faction, pattern of breathing, sleepiness, anesthesia, body position etc.

2.2.4. Effects of RSA on cardiac output

Respiration Sinus Arrhythmia affects the cardiac cycle by varying the pressure between thoracic walls and the lungs. RSA induces respiratory pumping, which increases venous return and leads to increase cardiac output [55]. Understanding the effect of the RSA on cardiac output is important as respiration and circulation are interrelated. In summary RSA is known as a series of physiological behaviours. This set behaviour could be summarized as follows [56]:

1. By filling blood to the right ventricle, right ventricular stroke volume increases, blood is pumped into the lungs and the left stroke volume is decreased.

2. Next, when systolic pressure decreases to a smaller extent, diastolic blood pressure and heart rate increase.

3. When the blood flow leaves the left side of the heart, left stroke volume also increases in the periphery and the arterial blood pressure. Consequently, the positive ventilation pressure (or RSA) on the circulatory effect occurs.

It is possible to understand the effects of RSA of cardiac output by considering the fact that respiration causes blood volume variation on both the arterial and venous sides. Consequently, this decreases cardiac output during inhalation, while cardiac output returns to initial output volume during exhalation. This variation is strongly correlated to respiration patterns.

Respiratory variations are most pronounced in venous return. This is due to the greater buffering capacity of the right heart chamber and the pulmonary circulation. The
transmural right chamber pressure varies by 32%, whereas the mean arterial blood pressure in the carotid artery varies by only 2% [57].

Also, it is worth mentioning that sympathetic activity in skin is coherent with respiration [58]. It appears more often during the inspiratory phase and is usually not interrupted during periods of apnea. The magnitude of sympathetic contribution to the respiratory is also detectable with PPG signal.

2.2.5. **Respiration Induced Intensity Variation from PPG**

During inspiration, intrapleural pressure decreases by up to four mmHg. This distends the right atrium [59], allows for faster filling from the vena cava and increases ventricular preload and the stroke volume. Conversely, the heart is compressed during exhalation. Consequently, cardiac efficiency and stroke volume are decreased. The overall effect of breathing induces respiratory pumping, which increases venous return, and leads to increased cardiac output. The effect of the RSA on cardiac output is known as respiration induced intensity variation (RIIV) [60]. RIIV is contained in the baseline of PPG signal as demonstrated in figure 5.

![Figure 5](image)

*Figure 5. PPG signal during LBNP experiment acquired from finger (left) and forehead (right), show RIIV in a red line. Upper envelope of PPG corresponds to respiration rate. RIIV is demonstrated in a red line and respiration from Airflow reference sensor in green colour.*

The most common method for estimation of RIIV is the analysis of the PPG signal in frequency domain [61]. Nilsson [62] investigated RIIV as a potential clinical method for monitoring respiratory rate. In this study, PPG was obtained by a non-commercial reflectance PPG sensor. Data was obtained from awaked patients during spontaneous breathing, anaesthetized patients with spontaneous breathing, and anaesthetized patients with positive pressure ventilation mode. Frequency of RIIV was
analyzed by Fast Furrier Transform analysis. It was identified (0.1 - 0.3 Hz). PPG was filtered by Butterworth 3rd order to suppress very low and high frequency variations outside the respiratory range. The mean values of squared coherence between the respiration reference (End-Tidal CO2) and signal under estimate (PPG) was 0.98. This indicated a stable relationship between the signals at the respiratory frequency. To identify variations, an independent analyzer (school student) not familiar with the PPG technique was given unidentified printouts of each signal. He was asked to mark each single breath detected in the signal. The mean of respiration rate from PPG to reference (End-Tidal CO2) was 96, 98 and 98 for awaked spontaneous breathing, anaesthetized spontaneous breathing and anaesthetized positive pressure ventilation respectively.

Nilsson showed that the filling of peripheral veins was a major contributing factor to the RIIV genesis [63]. They found that Peripheral Venous Pressure and RIIV amplitudes were affected similarly when respiration was varied. However, they were not able to demonstrate a clear time relationship between PVP and RIIV during normal breathing. The phase difference between the RIIV was calculated by a digital band pass filter (0.13-0.48Hz, Bessel 16th-order). Respiratory synchronous variations of the PPG were extracted respectively.

Chon presented [64] algorithm for estimation of RIIV. He compared variable frequency complex demodulation (VFCDM) to identify frequency modulation of PPG waveform. He then estimated periodically the respiration cycle and compared performance of this algorithm to continuous wavelet transform (CWT) and auto regression model (AR). It was concluded that VFCMD method provides the best results compared to AV and CWT methods.

2.2.6. Effects of respiration rate on central chemoreceptors

The central chemoreceptors in the respiratory centre and effector organs maintain PaCO2 within a range of 37 to 43 mm Hg in healthy humans. According to Yasuma’s study [65], during progressive hypercapnia lasting approximately 3 minutes, the partial pressure of end tidal CO2 increased from 35 to 55 mm Hg. Concomitantly, the tidal volume increased from 230 to 850 mL, and the respiratory rate from 18 to 22 breathes per minute. Heart rate and blood pressure, however, remained unchanged.
The study also indicated that during progressive hypoxia lasting approximately five minutes, O2 saturation of arterial blood decreased from 95 to 73% and tidal volume increased from 240 to 800 mL and respiration rate from 18 to 24 breaths.

Hypercapnia and Hypoxia refer to an increase of carbon dioxide and decreased oxygen in the cerebrospinal fluid. Cerebrospinal fluid is the fluid found in and around the central nervous system (CNS) [65].

According to the medical counsellor and anaesthesiologist of CiBER, Dr. Savvas notes that after an occurrence of acute hypoxia, a patient loses consciousness due to a lack of oxygen and elevated level of carbon dioxide in cerebrospinal fluid. He recommended monitoring acidity levels of cerebrospinal fluid (CSF) as the main index for state of health. However, non-invasiveness is the prime factor for wearable monitoring devices. According to [66] changes in respiration rate, arterial blood acidity (pH and PCO2) is affected within seconds to minutes. Consequently, acidity of cerebrospinal fluid (pH and PCO2) changes as well. For these reasons, non-invasive detection of blood oxygenation and carbon dioxide is considered a prime factor when monitoring cardiovascular and pulmonary performance.

Figure 6. Cerebrospinal fluid in human skull [192]

2.3. Definition of Man-Down

It is difficult to obtain a perfect vital monitoring device as human's physiology is very complex and the performance of vital monitoring systems is limited to certain boundaries. It is important to consider limitations of wearable vital monitoring systems. For this reason, an optimal goal of this project is to detect acute failure of cardiovascular...
or pulmonary systems. In this thesis, this type of condition is referred to “Man-Down” or critical condition.

2.4. Review of multisensory vital sign platforms

The number of multisensory platforms introduced in literature was quite extensive. Most of them were designed for wearable use. The survey of these devices could undertake a big part of this dissertation, however has been limited to a concise synopsis and outline. Below, a summary of the most cited publications is included.

AMON [29] “Advanced Care and Alert Portable Tele-Medical Monitor” is a wearable medical monitoring and alert system targeting high-risk cardiac/respiratory patients. The system includes continuous vital sign collection. It is capable of measuring blood pressure, SpO2, and ECG using a dry ECG electrode. The biggest challenge reported in this project however, is lack of reliable data acquisition. While measurements of ECG, So2 were poor, measurements of cuff-based systolic blood pressure and heart rate variability were reliable.

Krause [73] presented commercial handheld device for non-invasive monitoring of user’s behaviour. This device measures activity, temperature parameters, and galvanic skin responses. This study stated that a comfortable wearable device could be used to determine level of user’s activity.

Zhang [67] introduced a Health-Shirt capable of estimating blood pressure from electrocardiogram (ECG) and pulse transit time (PTT). The shirt was designed to record ECG and photoplethysmogram (PPG) (figure 7).

Table 2. Summarizes e-textile garments for healthcare.

<table>
<thead>
<tr>
<th>Name of product</th>
<th>Selected measurement parameters</th>
<th>Wireless communication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smart Shirt [68]</td>
<td>Heart rate, ECG, Spo2, Temperature, respiration</td>
<td>Yes</td>
</tr>
<tr>
<td>Life Shirt [192]</td>
<td>B, Spo2, EEG, EOG, Body, temperature, leg movement</td>
<td>NO</td>
</tr>
<tr>
<td>Wealthy [69]</td>
<td>Core temperature, respiration,</td>
<td>YES (GSM)</td>
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Table 3. Summary of Multi sensory platform and based on physiological parameters

<table>
<thead>
<tr>
<th>Reference</th>
<th>ECG</th>
<th>Respiration rate</th>
<th>Blood Pressure</th>
<th>Heart Rate</th>
<th>So2</th>
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<td></td>
<td>Wrist, chest</td>
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<td>Arm</td>
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<td>[79]</td>
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<td>Wrist</td>
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<td></td>
<td>Zigbee</td>
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<tr>
<td>[81]</td>
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<td></td>
<td></td>
<td>YES</td>
<td></td>
<td>Bluetooth</td>
<td></td>
</tr>
</tbody>
</table>

Another bio-sensing integrated health monitoring system was introduced by BIOTEX [71]. The instrumented clothes BIOTEX measures sweat quantity, pH infection and arterial blood oxygenation for detection of metabolic disorder.

VTAMN [70] is a cloth for ambulatory remote monitoring. It delivers physiological information on cardiac frequency, breathing frequency, body temperature, environmental temperature and fall detection. Through the use of a set of sensor networks, it is possible to launch alarms via a cell phone. After setting up an alarm, an automatic system would then send the geographical (GPS) location of a user to the rescue team (figure 7).

In the publication [72], MIT media lab in collaboration with Army Institution of Environmental Medicine (AIEM) introduced core body temperature classification for wearable solider health monitoring systems. They developed a wearable device. This device is capable of measuring shivering accurately. In order to capture dynamic motion
of shivering, a volunteer ranger was instrumented with two accelerometers located on chest and arm, and one esophageal thermometer (figure 7).

**Figure 7. From Left to right MIT hirls [72] and VTAMN [70] are demonstrated.**

In 2005 [70] Dabiri introduced architecture of a medical jacket for monitoring the heart rate. He also investigated methods for detection of falling. He incorporated features extracted from walking behaviour, which were identified by geriatric motion study as precursors to balance abnormality and fall risk.

**Figure 8. Demonstration of wearable pulse oximetry in construction environments [71]**

Forsyth [82] introduced a portable oximetry device. This device is integrated into helmet of workers in residential and commercial construction settings (figure 8). In this application, a photoresistor was located on the forehead of the helmet wearer and noise-cancelling algorithm was designed so that a discrete saturation was applied on the PPG signal. Because of motion artifact, the sensor had difficulty in obtaining a measurement.
Forsyth combined a probabilistic estimation method on the gap distribution to obtain the measurements.

Nagre et al. [83] examined the possibility of integrating pulse oximetry on the forehead, jaw, and chin locations and integration of the system into a military helmet. Furthermore, these studies involved complex motions such as talking, head movement, and riding in a vehicle.

Many of the above technologies have developed comfortable wearable devices for continuous vital sign monitoring. Some devices were capable of gathering multiple vital signals but none of the above has reported reliable devices for clinical settings. Instead, combinations of bio signals incorporated with wireless communication resulted in accurate remote monitoring system for various safety applications. Instances of such systems have been deployed into military applications for detection of mental and physical capability of soldiers performing under extreme hot or extreme cold temperatures [84], and authentication and authorization of users to access nomadic environments [85]. Furthermore, up to date studies for sensing the human body’s activity to ensure safety of people in professional environments are limited to monitoring cardiovascular and respiratory system activity.
3. **Respiration rate From End Tidal CO2 and Photoplethysmography**

This chapter consists of two hypotheses. The first hypothesis discusses feasibility of design and implementation of mobile platform for extraction of Spo2, heart rate and respiration in parallel to PPG acquisition. In this section, we propose a mobile platform microcontroller-based approach for detection of vitals signs. The second hypothesis assesses complexity or feasibility of algorithm design for detection of respiration rate form PPG. Finally, performance of the mobile platform and the algorithm are compared to clinically approved respiratory transducers, and the results of these two hypotheses are analyzed by Bland and Altman analysis.

This chapter is organized as follows:

3.1 Background information about End-tidal CO2 analyzers

3.2 Hypothesis 1:
   i. Proposed mobile platform for detection of respiration from end-tidal CO2.
   ii. Proposed mobile platform for detection of heart rate, Spo2 and PPG in parallel.

3.3 Experiment and evaluation of mobile platforms on 10 healthy subjects

3.4 Hypothesis 2:
   i. Study of PPG for extraction of respiration rate and assessment of degree of complexity of the algorithm

3.5 Evaluation of over all performance of the proposed methodologies by Bland and Altman Analysis.
3.1. Background information about End-tidal CO2 analyzers

Carbon dioxide (CO2) builds up in our blood as a by-product of metabolism, and must be eliminated from our body. While some CO2 is eliminated through the kidneys and a small amount through the skin, most is carried to the lungs and exhaled out. As metabolic needs increase, chemoreceptors of nervous system are trigged to activate a built-in control system. Activation of the nervous system increases difficulty in regards to breathing, and makes it harder to keep the level of blood’s acidity at a safe level. When this control system is not working, as is the case for a patient on a mechanical ventilator, the level of CO2 through exhalation must be monitored continuously.

The expired CO2 or end tidal CO2 is known as a standard non-invasive indicator of deoxygenated hemoglobin in blood [86]. End Tidal (ET) CO2 is the partial pressure or maximal concentration of carbon dioxide (CO2) at the end of an exhaled breath. It is expressed as a percentage of CO2 or mmHg. The normal values are five percent to six percent, which is equivalent to 35-45 mmHg. CO2 reflects cardiac output and pulmonary blood flow as the gas is transported by the venous system to the right side of the heart and then pumped to the lungs by the right ventricles [87]. When CO2 diffuses out of the lungs into the exhaled air, a device called a capnometer measures the partial pressure or maximal concentration of CO2 at the end of exhalation.

There are four stages of normal physiology of CO2 [88]:

a. Production: CO2 is a metabolic by-product of aerobic cell metabolism. As the intracellular CO2 increases, CO2 diffuses out into the tissue capillaries and is carried by the venous circulation to the lungs, where it diffuses from pulmonary capillaries into the alveoli. The partial pressure of CO2 (PaCO2) of venous blood entering pulmonary capillaries is normally 45 mmHg; the partial alveolar pressure of CO2 (PACO2) is normally 40 mmHg. The pressure difference of 5 mmHg will cause all the required CO2 to diffuse out of pulmonary capillaries into the alveoli.

b. Transportation: The second stage is CO2 transport, which is a way of maintaining the CO2 tension of arterial blood at approximately 35-45 mmHg.

c. Buffering: The third stage is where the buffer action of hemoglobin and pulmonary blood flow maintain the normal level of CO2 tension by eliminating the excess CO2. CO2 can either be carried, dissolved or combined with water (H2O) to form carbonic acid (H2CO3), which can
d. Elimination: The fourth stage involves CO2 elimination by alveolar ventilation under the control of the respiratory center. This process allows the diffusion of CO2 from blood to the alveoli where the partial alveolar pressure of CO2 is lower than the tissue pressure. During acutely low cardiac output state as in cardiac arrest; decreased pulmonary blood flow becomes the primary determinant resulting in abrupt decrease of ETCO2. Changes in alveolar ventilation can also influence ETCO2 as PACO2 closely approximates PaCO2 and ETCO2. If ventilation and chest compressions are constant with the assumption that CO2 production is uniform, then the change in ETCO2 reflects the changes in systemic and pulmonary blood flow. Ultimately, ETCO2 can be used as a quantitative index of evaluating adequacy of ventilation and pulmonary blood flow.

![Figure 9](image_url)

**Figure 9.** Production and expiration CO2 are shown in four stages.

### 3.1.1. Capnometer

Capnometers or CO2 analyzers have been used for 50 years to monitor respiration [89]. CO2 analyzers operate by using a tube to continuously sample expired gas. A gas sample is drawn via a capillary tube from the air pump to the analyzer in order to connect the patient. Unfortunately, this capillary tube is prone to clogging from sputum and water vapour and the small passages and traps in such a system could make it difficult to maintain adequate cleanness.
Figure 10. Demonstration of block diagram from conventional HP 47210A capnometer. The output from the CO2 sensor is controlled, amplified and converted to digital data by the analog section in the processor box. This data is optically coupled to the rest of the processor box to be analyzed and displayed [89].

3.1.2. Typical structure of a CO2 sensor

The CO2 analyzer is located on the opposite side of the tube, which transfers end-tidal exhalation for co2 measurement. The CO2 analyzer is equipped with a CO2 sensor. The CO2 sensor contains a rotating filter wheel, a thick film infrared, a band pass filter and a lead selenide phoresentive detector as shown in figure 11 [90][89]. The filter wheel consists of two hermetrical sealed cells with sapphire windows, one open chamber with sapphire windows, and four permanent magnets. Each cell is rotated into the infrared energy beam. The output of the detector is a waveform. The amplitude of this waveform is converted into CO2 value.

The main propose of capnometer or CO2 analyzer is to measure carbon dioxide partial pressure waveform accurately and precisely. The waveform is useful for diagnostic proposes. An airway CO2 waveform looks like a distorted square. The waveform increases to peak value at the end of each breath cycle, which is called end tidal CO2 value. In patients without chronic obstructive lung disease, the ETCO2 value closely approximates the PCO2 level in the arterial blood. In healthy people, a value of ETCO2 is about 40mmHg. People with chronic pulmonary disease however measure at about 90mmGg [89][91].
Some commercial CO2 analyzers attempt to derive an ETCO2 value from a PCO2 waveform by using a simple peak finder detection algorithm. ETCO2 respiration, however, has several requirements. The algorithm requires detection of minimum and maximum ETCO2 the interval between breaths.

![Typical waveform of CO2 Analyzer](image1)
![Typical structure of IR CO2 Sensor](image2)

**Figure 11. Demonstration of typical structure of IR CO2 sensor and corresponding waveform to co2 are shown on Left. Affects of the noise clip and mask on breathing pattern and demonstration of tidal air volume versus time; canopy alone, Mask Mouthpiece and nose clip [90][89].**

After calibration of the sensor, a typical algorithm sets two low pass filtered threshold values. The mean PCO2 value is the low-pass filtered, and is the result of the instantaneous PCO2 waveform. The mean PCO2 value has a time constant of about 60 seconds. The peak-to-peak index is a measure of the deviations of the instantaneous PCO2 waveform from the mean PCO2 value. The peak-to-peak index is scaled down and used to create a hysteresis band, which indicates the mean PCO2 value. Two thresholds levels are derived as [HP-Journal]:

\[
\text{Threshold (High)} = \text{mean} + \frac{(\text{peak to peak index})}{4} \\
\text{Threshold (Medium)} = \text{mean} - \frac{(\text{peak to peak index})}{4}
\]

The waveform is divided into three sections; low, medium and high. By counting the transition from one region to another, the basic breath cycles can be determined. The time interval required to complete a cycle determines the respiration interval as shown in figure 12.
3.1.3. **Accuracy of ETCO2 measurement by commercial CO2 analyzers**

The key characteristic of a CO2 analyzer is its capacity to monitor pulmonary system performance on tissue oxygenation. The accuracy of CO2 analyzers in the detection of high frequency responses to seven commercial Capnometers was assessed in [91]. Data were recorded during pediatric general anesthesia from scope Accucap, Hewlett-Packard 4721OA capnometer, Narkomed 3 Capnomed, Novametrix Capnogard model 1250, Perkin-Elmer Advantage, Puritan-Bennett Datex CO, monitor, and Traverse Medical Monitor model 2200 capnometer. Changes in CO2 concentration were generated by a solenoid valve switching between 100% O2 and 7% CO2. According to this study, differences in ETCO2 ranged from -16.4 to +6.6. Four capnometers over reported and three underreported ETCO2. At frequencies under 31 cycles/min, six capnometers underreported and one over reported ETCO2. Given the results of this [91] study, accurate simultaneous estimation of carbon dioxide proportion requires invasive catheter installation within the peripheral blood vessels of a patient. This study fundamentally questions accuracy of ETCO2 estimation by commercial CO2 analyzers. However, these analyzers were FDA approved and permitted for national wide operation.

In [197] 1986 Phan and Tremper and Lee, evaluated correlation between End tidal carbon dioxide and arterial carbon dioxide on 23 healthy subjects during anesthesia. They concluded a significant correlation between partial arterial carbon dioxide and end tidal carbon dioxide (P<0.001).
In 1994 [69] Barten and Wang studied accuracy of end tidal carbon dioxide level as a measurement of arterial carbon dioxide levels in 76 patients. In all patients, end tidal carbon dioxide was 3.5 mm Hg lower than PACO2 and correlated well with PACo2 ($r^2=0.772$).

### 3.1.4. Interaction between automatic nervous system and PACO2 saturation

Consider holding your breath for 20 seconds. In less than 10 seconds, the acidity (pH) of blood will begin to increase, as will the partial pressure of CO2 in the blood. At this point, the chemoreceptor will be trigged by saturation of CO2 and O2, and the central nervous system will increase the ventilation rhythm automatically [105], in order to keep CO2 concentration at a safe level.

This pattern of automatic physiological response takes place within first 10 seconds from the moment respiration recession occurs. This physiological response leads to a rise in the CO2 concentration and to hypercapnia, while also causing a drop in the arterial O2 concentration and hypoxemia [92]. Now consider breathing at the fastest rate possible for 30 seconds. Arterial pressure of O2 increases, acidity level of blood drops and chemoreceptors are trigged. This is known as hypocapnia or lack of partial pressure of CO2 in arterial blood. In response, the nervous system automatically adjusts ventilation rate and reduces the breathing rhythm.

This simple example demonstrates the sensitivity of our nervous system to CO2 concentration in blood.

### 3.1.5. Interaction between Hemoglobin saturation curve O2 and PACO2 saturation

A hemoglobin molecule can bind up to four oxygen molecules. While it can be difficult to bind the first molecule, having done so, binding the second, third and fourth hemoglobin molecules become much easier.

The speed of hemoglobin binding is affected by PACO2. This affects the binding process in two ways [196]:

a. It influences intracellular pH,

b. Its accumulation causes carbamino compounds to be generated through chemical interactions, which bind to hemoglobin forming carbaminohaemoglobin.

Consequently, low levels of carbamino compounds have the effect of shifting the hemoglobin saturation curve (figure 14) to the left, while higher levels cause a rightward shift. It is the elevated CO2 content that causes a shift in the oxygen–hemoglobin dissociation, and a curve to the right.

When the level of CO2 increases (pH elevation), the first oxygen molecules resist unbinding. However as the level of O2 drops below the line, (80%) of hemoglobin cells begin to lose the rest of the oxygen molecules at a much faster rate. In practice, when the level of Spo2 reaches a critical level, it takes a longer time to return to its initial level.

![Hemoglobin saturation curve](image)

*Figure 14. Hemoglobin saturation curve [196]*

### 3.1.6. Advantages of continuous monitoring of Respiration rate

A normal human adult has a respiratory rate of 12-15 breaths at rest, inhaling and exhaling 6-8 litre of air per minute [93]. A patient with severe inflection however, can instantly decompensate despite appearing to have normal blood pressure and heart rate [109]. Acute respiratory failure can result in hypercapnia, hypoxemia or disturbed blood gas concentration, which eventually can lead to cellular death due to a lack of oxygenation. It is very well known that without adequate respiratory activity, and human life is threatened. A logical conclusion is that the detection of one’s respiratory rate could facilitate a medic’s response time and rescue of a patient. Continuous monitoring of
respiratory activity is therefore an important component in the identification and prediction of high-risk situations. Consequently, this makes appropriate respiratory failure monitoring techniques potentially lifesaving.

### 3.1.7. Survey of respiratory monitoring sensors

The survey of respiratory monitoring sensors is very large, and could require a chapter in and of itself to describe. However, as the purpose of this chapter is to merely introduce the capnometry, a table has been created to summarize the monitoring sensors in regards to this theme.

<table>
<thead>
<tr>
<th>Table 4. Methods/Devices for respiratory monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Category</strong></td>
</tr>
<tr>
<td>Movement, Volume, Tissue compensation detection</td>
</tr>
<tr>
<td>Airflow sensing</td>
</tr>
<tr>
<td>Blood gas measurement</td>
</tr>
<tr>
<td><strong>Measurement quantity</strong></td>
</tr>
<tr>
<td>Electromyography (EMG), Impedance and blood volume</td>
</tr>
<tr>
<td>Respiratory gas flow</td>
</tr>
<tr>
<td>Arterial gas concentration</td>
</tr>
<tr>
<td><strong>Sensor position</strong></td>
</tr>
<tr>
<td>Chest wall</td>
</tr>
<tr>
<td>Oronasal region</td>
</tr>
<tr>
<td>Peripheral organs or oronasal region</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 5. Sensor type for estimation of respiration rate</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Method/Device</strong></td>
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<tr>
<td>Pulse Oximetry</td>
</tr>
<tr>
<td>End tidal O2 measurement</td>
</tr>
<tr>
<td>End tidal CO2 measurement</td>
</tr>
<tr>
<td>Transcutaneous CO2 measurement</td>
</tr>
<tr>
<td><strong>Parameter</strong></td>
</tr>
<tr>
<td>Oxygen saturation in arterial blood</td>
</tr>
<tr>
<td>Oxygen concentration in expired exhale</td>
</tr>
<tr>
<td>Carbon dioxide concentration in expired exhale</td>
</tr>
<tr>
<td>Transcutaneous carbon dioxide concentration</td>
</tr>
<tr>
<td><strong>Sensor Type</strong></td>
</tr>
<tr>
<td>Photoresistor, peripheral organs</td>
</tr>
<tr>
<td>Measurement from oronasal region, spectrometry, electric analyzer or paramagnetic O2 sensor</td>
</tr>
<tr>
<td>Infrared absorption CO2 sensor, spectrometry, acoustic measurement of has from oronasal region</td>
</tr>
<tr>
<td>Chemical skin sensor</td>
</tr>
<tr>
<td><strong>Reference</strong></td>
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<tr>
<td>[94]</td>
</tr>
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<td>[95]</td>
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<tr>
<td>[96][97][98]</td>
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<tr>
<td>[99]</td>
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</table>
3.2. Hypothesis 1:

3.2.1. Proposed mobile platform for detection of respiration, heart rate, Spo2, from CO2 and PPG sensors

As we discussed in previous subsections of chapter 3, respiration rate is a valid indicator of acute pulmonary failure. In addition, the hypothesis was made that continuous registration of respiration rate from End-Tidal CO2 on a mobile platform could be a reliable method for application of vital sign monitoring systems. However, as demonstrated by Askanazi [100] (figure 11), the use of a mask, mouth and nose clip affects breathing patterns and add limitations on a user’s mobility and comfort. Consequently, an evaluation regarding the feasibility of respiratory rate extraction from End-Tidal sensor without the use of a mask ensued. Moreover, as mentioned in chapter 2, PPG is a rich reflection of multiple physiological signals. An evaluation of the feasibility of Spo2, heart rate and PPG acquisition from single sensor was therefore completed. Finally, the following components were evaluated:

1) Assessment of co2 sensor implementation on microcontrollers-based platform.

2) Assessment of respiration rate detection without use of cannula mouth or nose clip.

3) Assessment of Spo2, heart rate and PPG acquisition on microcontroller-based platform.

3.2.2. Detection of Respiration from End Tidal CO2 on mobile platform

In order to detect respiration, a mobile platform from off-the-shelf components was developed. A fast respond IR CO2 sensor in parallel to two fast respond temperature sensors were modulated on a microcontroller. This device was capable of reading CO2 concentration and temperature. It was designed to process data in real time. Data was stored in two different locations, on SD card and on a desktop computer. As demonstrated in figure 15, the microcontroller was programmed to operate at two different modes.
• Mode 1: An algorithm was designed to communicate to a CO2 sensor, request data in hex format, read data from the buffer, extract CO2 concentration, convert data into string, save data on SD card, present data on LED, and transfer a copy of CO2 concentration to a computer.

• Mode 2: An algorithm was designed to send a request to two temperature sensors at the same time, establish communication channel for each sensor, read temperature in hex format from each sensor, convert data to actual temperature, demonstrate data on LED, save actual temperature on SD card, and send copy of acquired temperature to a computer.

Figure 15. Data processing on the AVR microprocessor for detection of End Tidal CO2 concentration and Temperature

3.2.3. Hardware implementation of CO2 and temperature sensors on mobile platform

As demonstrated in figure 16, an Arduino Uno was used as the main microprocessor. This module included an IR CO2 sensor, two temperature sensors, LCD for visual feedback, and a SD card for saving data on board.
As demonstrated in figure Sprint IR, carbon dioxide sensor is based on NDIR technology and uses advanced solid state Indium Antimonide LEDs. The sensor is equipped with standard UART Serial port.

Figure 17. a. Sprint IR, Laser CO2 gas sensor, sampling frequency at 20Hz, b. TMP-102 sensor is a relatively tiny, fast and accurate thermometer. It operates at 8 Hz sampling frequency, and its response time is less than 0.6. c. Digital thermometer [DS18B20-one wire] (One wire is commercial brand name of the sensor)

In addition to Sprint IR, two thermometers were also added on the same board; Dallas DSB1820 and TMP 102 IC. Both thermometers belong to the same family of thermometer ICs. An Advantage of this IC is that every sensor has its own unique address, which allows a developer to request value from a specific sensor.

The algorithm was implemented entirely in C. Detail of the algorithm is attached in the appendix 1. The goal of this project was to use the sensory platform to detect respiration, however the thermometers were unfortunately not able to detect this rate. Although the thermometers respond very quickly to the temperature variation in exhalation, the exhale’s temperature varies very little. In contrast, CO2 was capable of detecting respiration rate without use of mask.

The performance of the CO2 sensor was compared to Biopac Respiratory Rate Belt (figure 18). Biopac Transthoracic Transducer Belt (TTB) is considered to be a commonly used device for the measurement of respiratory rate. Performance of the End Tidal CO2 sensor was tested in parallel with Biopac respiratory on ten healthy subjects,
the results of which are presented in section 3.5 of this thesis. A Labview sketch was developed to obtain data from the CO2 sensor and Biopac in parallel.

Since data was processed on an Arduino Board, a Virtual Digital Port was required to acquire data in Labview sketch. Each set of data was transferred in bytes to a computer through the use of a VISA port. On the other hand, output signal from Biopac was a DC voltage. Amplitude of this signal varied from 0 to 10 VDC. In order to acquire data from Biopac, NI 9205 DAQ was added to the Labview sketch.

![Image](image_url)

**Figure 18.** End Tidal CO2 sensor and temperature sensors on Arduino and RSP100C Transthoracic Transducer Belt are demonstrated the right and left side of figure.

In order to synchronize signals from Arduino and Biopac, a control loop was designed on Labview as demonstrated in figure 19.
3.2.4. **Hardware implementation of pulse oximeter on mobile platform**

Xpod is a portable pulse oximetry microcontroller, which is being manufactured by Nonin (figure 20.a). It extracts three parameters; beat-to-beat blood oxygenation, heart rate, and PPG. Xpod is capable of obtaining measurement from finger and forehead PPG probes (figure 20b&c) and is able to provide a continuous data transmission at a 125Hz resolution. A set of 5-byte long packets are being transferred via UART Serial port every 0.41 seconds (figure 20.c).

The first byte of the packet is always set to 1 (hex format). The second byte of the packet provides status information such as presence of motion artifact or status of...
the PPG sensor. The third byte represents magnitude of PPG waveform, and the fourth byte contains heart rate and Spo2. Finally, the last byte is the checksum of the packet.

Figure 20. Demonstration of: a. Xpod Nonin, b. finger probe PPG sensor, c. forehead probe PPG sensor, d. structure of data transition by Xpod.

Two Xpods were used in this study; one for data acquisition from the forehead, and the other for data acquisition from the finger. Each unit was connected to the VISA port on the Labview. Data from the Xpod was recorded on Labview synchronous to End-tidal CO2 and Biopac (respiration rate). On the Labview sketch, data was processed in real-time. As shown in figure 21, structure of the algorithm is as following:

i. Read first byte in buffer

ii. Make sure it is the equal to 1

iii. If yes, read the next four bytes

iv. Save the packet

v. Extract PPG from third packet

vi. If it is packet number 1, then fourth byte is heart rate, extract and save it

vii. If else packet is number 2, then fourth byte is Spo2, extract and save it

viii. Else ignore fifth packet

ix. Check the sum

x. Save the packet read the next byte from buffer
Figure 21. Demonstration of Labview sketch for obtaining Spo2, heart rate and PPG from Xpod.

As demonstrated in figure 22, data from two Xpods and Arduino is being saved synchronously on the computer.
Figure 22. Structure of the Labview algorithm for extraction of data from Xpod, CO2 sensor Biopac

As shown in figures 23 to 26, vital signs from CO2 sensors, Xpods and Biopac were recorded in “csv” format and saved on personal computers. These figures demonstrate that the mobile platform was capable of obtaining vital signs. Based on these waveforms, we can conclude that the detection of respiration without the use of cannula or a mouth/nose clip from an End-Tidal CO2 sensor is feasible. We can also conclude that acquisition of Spo2, heart rate and PPG is feasible in parallel to respiration rate from a CO2 sensor.
Figure 23 Demonstration of oxygen saturation by Xpod from finger sensor and forehead sensor are shown in left and right side of this figure.

Figure 24 Demonstration of PPG waveform by Xpod from finger sensor and forehead sensor are shown in left and right side of this figure.

Figure 25 Demonstration of heart rate by Xpod from finger sensor and forehead sensor are shown in left and right side of this figure.
In conclusion, the PPG was extracted from two pulse oximeter sensors, in parallel to heart rate and SPO2. The Labview sketch processes data in real-time and extracts vital signs synchronously from pulse oximeter sensor in parallel to respiration rate from the wearable CO2 sensor.

At this part of the thesis, we achieved a proof of concept for acquisition of respiration rate, heart rate and Spo2 from two wearable devices. In conclusion, performance of pulmonary system is feasible by extracting respiration rate from portable AVR microcontroller. In order to evaluate the accuracy of AVR capnometer, respiration rate will be compared to Biopac respiratory effort transducer. This will be presented at chapter 3.5 of the thesis. In addition performance of cardiovascular activity could also be monitored by continuous monitoring of heart rate and SPO2 from forehead as well as finger, and PPG signal could be extract in parallel to the HR and SPO2. In chapter 3.3 this PPG device will be used for evaluating feasibility of extracting respiration rate from PPG and the accuracy of the algorithm and the device will be also compared to Biopac respiration effort transducer in chapter 3.5.

3.3. Experiment setup for evaluation of CO2 analyzer and pulse oximeter wearable platform on 10 healthy subjects

In this chapter, the mobile system for the acquisition of respiration rate, Spo2, heart rate and PPG was evaluated on ten healthy subjects. These two devices were tested for sensitivity and specificity. A total of ten participants took place in this study,
including three healthy female (age: 25.5±4.3 years) and seven healthy male subjects (age: 28.4±4.8 years).

Subjects participated in three measurement sets; breathing at a normal pace, breathing at a controlled respiration rate by following a visual sinusoidal signal at 0.2Hz, and breathing at a controlled respiration rate by following a visual sinusoidal signal at 0.3Hz. All measurement sets were completed in a sitting position. The subjects breathed for five minutes at normal pace, and one minute respectively for both a controlled respiration rate of 0.2Hz, and a controlled respiration rate of 0.3 Hz. A total of four signals were captured on Labview at 75 Hz sampling rate; PPG from forehead (Nonin, Xpod), PPG from Finger (Nonin, Xpod), End-Tidal gas CO2 (SprintIR 20Hz, 20%) and respiration rate (Biopac RSP100C, US, CA).

The first objective of this study was to demonstrate capability of mobile CO2 and pulse oximeter devices. The second objective was to assess feasibility in the detection of respiration rate from PPG.

3.4. Hypothesis 2:

3.4.1. Assessment of respiration measurement from PPG

As was discussed in chapter two, the Respiration Sinus Arrhythmia (RSA) phenomena reduced cardiac output during inhales, and recovers during exhale. RSA affects morphological variation of PPG waveform, a variation known as Respiration Induced Intensity Variation (RIIV). RIIV waveform is a low frequency sinusoidal signal, which is contained in the baseline of PPG. PPG can be obtained from pulse oximetry devices, however most of commercial pulse oximetry devices remove the AC components of PPG [101].

We have proposed an algorithm for detection of respiration rate (figure 23), which consists of the following four steps.

1. PPG acquisition: PPG was acquired using two pulse oximeter sensors. One PPG was obtained from finger and forehead.
2. Low pass filtering: A 5th order of Butterworth filter was used to extract the lower and upper envelope of the PPG signal. The algorithm required a learning cycle to determine the corresponding cut-off frequency. In this learning cycle, Fast Fourier Transform (FFT) was used to analyze the frequency spectrum of the unprocessed PPG signal in a range of 0.69 Hz to 0.70 Hz for each subject.

3. Hilbert transformation: Each set of PPG was Hilbert transformed. Hilbert transformation read the upper envelop of the low pass filtered signal.

4. Peak detection: A peak detection algorithm was used to identify the peaks in envelope of PPG. The number of peaks identified as RIIV.

As demonstrated in figure 27, respiration rate from CO2 analyzer and Biopac were detected using a peak detector algorithm. This sketch then read PPG from the finger and forehead for RIIV identification.

![Labview sketch demonstrates algorithm for detection of RIIV.](image.png)

**Figure 27. Labview sketch demonstrates algorithm for detection of RIIV.**

In figure 28, respiration was extracted from a forehead PPG sensor. Window “a” shows respiration from the End-Tidal CO2 analyzer, “b” shows respiration rate from the Biopac respiratory transducer, “c” shows PPG obtained from the forehead, “d” shows PPG obtained from the finger, and “e” represents the upper envelope of the PPG.
Figure 28. Front panel, results of the respiratory detection algorithm from PPG. PPG was obtained from finger. The cut-off frequency in Butterworth filter was set to 0.64 in this particular example.

3.5. Evaluation of mobile data acquisition platform and RIIV detection algorithm

Bland and Altman’s analysis was used to evaluate efficiency and accuracy of the proposed mobile platform and RIIV detection algorithm.

The Bland-Altman analysis is mainly a tool for clinical interpretation. The bias and the agreement limits provide the variation of the values of one technique compared to the other. The difference between the two methods of measurement is plotted against the average obtained with each of the two techniques. Bland and Altman’s analysis stresses the need to assess two aspects of agreement: how well the methods agree on average of the two signals, and how well the measurements agree for individuals. If one method reads lower than the other for half of the subjects but higher than the other for the other subjects, then the overall the average discrepancy (the difference between measures on the same subject) may be close to 0 [102].

Examination of the Bland–Altman plot should be looked at to see whether there seems to be any relationship between discrepancy and the level of measurement (figure 29).
Figure 29. The Bland–Altman plot shows the difference against the average of a test and standard measurements of simulated data. This plot shows evidence of increasing variability of differences between two signals [139].

Three sets of data were analysed by the Bland and Altman technique; respiration rates from Biopac, End-Tidal CO2 analyzer and PPG. Each set of data were recorded at normal, 0.3Hz and 0.2Hz breathing rates. The respiration rate from the end tidal CO2 analyzer was compared to a respiration reference (Biopac RRB), as was the respiration rate form PPG.

To create a Bland-Altman analysis, the average difference of respiration rate from CO2 and PPG to reference signal (Biopac) was calculated. A dot representing each subject was then placed on the plot, with dots close to 0 representing no difference between the two methods [103].

According to figure 29, the mean difference between respiration rates obtained from CO2 and Biopac respiratory transducer was 0 at normal pace. This implies that the end tidal CO2 sensor is as accurate as the Biopac respiratory belt.

According to figures 30.a, 30.b and 30.c, the mean difference between respiration rates from pulse oximeter and Biopac standard at normal pace was estimated -0.1 and -0.2 from finger probe and forehead probe respectively.
Figure 30.a. Bland and Altman assessment for showing agreement between respiration rates from Biopac and end tidal CO2 analyzer. Data points show the average bias. Most of the dots are close to the mean.

Figure 30.b and 30.c imply that respiration rate from pulse oximeter could be used for detection of acute pulmonary failure. As shown in table 6 and 7, the mean difference of upper and lower limits and the relative error of each assessment were estimated in regards to normal breathing and controlled breathing at 0.2Hz and 0.3Hz.

Figure 30.b. Bland and Altman assessment for showing agreement between respiration rates from Biopac and finger pulse oximeter. Data points show the average bias. Most of the dots are close to the mean.
Figure 30.c Bland and Altman assessment for showing agreement between respiration rates from Biopac and forehead pulse oximeter. Data points show the average bias. Most of the dots are close to mean.

Table 6. Demonstration of agreement between respiration rates form reference Biopac, end tidal CO2 and pulse oximeters.

<table>
<thead>
<tr>
<th>Breathing speed</th>
<th>CO2</th>
<th>Forehead, PPG</th>
<th>Finger PPG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Difference</td>
<td>0</td>
<td>-0.2</td>
<td>-0.1</td>
</tr>
<tr>
<td>Upper Limit of agreement +1.95</td>
<td>0</td>
<td>2.094</td>
<td>1.8491</td>
</tr>
<tr>
<td>Lower Limit of agreement -1.95</td>
<td>0</td>
<td>-2.6094</td>
<td>-2.0491</td>
</tr>
<tr>
<td>Breathing speed</td>
<td>Controlled 0.2Hz</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean Difference</td>
<td>0</td>
<td>-0.5</td>
<td>-0.7</td>
</tr>
<tr>
<td>Upper Limit of agreement +1.95</td>
<td>0.924</td>
<td>1.8099</td>
<td>1.373</td>
</tr>
<tr>
<td>Lower Limit of agreement -1.95</td>
<td>-0.924</td>
<td>-2.8099</td>
<td>2.7763</td>
</tr>
<tr>
<td>Breathing speed</td>
<td>Controlled 0.3Hz</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean Difference</td>
<td>0.1</td>
<td>-0.3</td>
<td>-0.2</td>
</tr>
<tr>
<td>Upper Limit of agreement +1.95</td>
<td>0.7198</td>
<td>0.6468</td>
<td>1.6011</td>
</tr>
<tr>
<td>Lower Limit of agreement -1.95</td>
<td>-0.5198</td>
<td>-1.2468</td>
<td>-2.0011</td>
</tr>
</tbody>
</table>
Table 7. Demonstrated error between respiration rates from Biopac compared to end tidal CO2, and two pulse oximeters.

<table>
<thead>
<tr>
<th></th>
<th>CO2</th>
<th>Forehead, PPG</th>
<th>Finger PPG</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Uncontrolled Breathing</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MARE_Mean Absolute Relative Error</td>
<td>0</td>
<td>0.0395</td>
<td>0.0428</td>
</tr>
<tr>
<td>MSRE_Mean Squared Relative Error</td>
<td>0</td>
<td>0.0054</td>
<td>0.0033</td>
</tr>
<tr>
<td><strong>Controlled 0.2Hz</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MARE_Mean Absolute Relative Error</td>
<td>0.0309</td>
<td>0.0833</td>
<td>0.0476</td>
</tr>
<tr>
<td>MSRE_Mean Squared Relative Error</td>
<td>0.0048</td>
<td>0.0194</td>
<td>0.0075</td>
</tr>
<tr>
<td><strong>Controlled 0.3Hz</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MARE_Mean Absolute Relative Error</td>
<td>0.0111</td>
<td>0.0555</td>
<td>0.0444</td>
</tr>
<tr>
<td>MSRE_Mean Squared Relative Error</td>
<td>0.0012</td>
<td>0.0086</td>
<td>0.0049</td>
</tr>
</tbody>
</table>

3.6. Discussion

We can conclude that the proposed wearable AVR comptometer and Nonin Xpod were capable of obtaining vital signs. In particular, we developed two sensory platforms for detection of respiration rate from end-tidal CO2, Spo2, heart rate and PPG.

The CO2 mobile analyzer was shown to be capable of obtaining respiration rate without the use of cannula. The fact that the CO2 sensor must be located close to oronasal areas however interferes with user comfort. Operation of this platform is therefore limited to applications where the use of a helmet or mask is mandatory. Instances of this type of occupations are deep divers, fire fighters, bikers and workers in a construction field.

On the other hand, technological advances enable the detection of respiration by employing a cluster of carbon nanotubes on two plane electrodes. These electrodes use dielectrophoresis techniques such as those demonstrated by Lan [104], in this document the author did not mention about the lifetime of the samples. Employment of this sensor on the mobile platform instead of the Sprint IR CO2 sensor potentially increases distance between a user and the sensor. However, despite contacting Lan to acquire a sample of the sensor, we were unable to obtain a response or reply. As this sensor is not commercially available, the reliability of the sensor is not well known to public.
The mobile platform used for the acquisition of PPG, heart rate and Spo2 proves to be reliable and provide accurate results. The sampling frequency of the Xpod however was limited to 75Hz for PPG and 25 Hz for Spo2 and heart rate. This consequently limits the deployment of the mobile platform in applications where, high quality of data acquisition is required.

As demonstrated in figure 31, comparison of respiration rate derived from End-Tidal CO2 and PPG to reference respiration rate (Biopac) shows that PPG signal is a rich reflection of human’s physiology. It was confirmed that PPG could be used as a prime signal to extract not only Spo2 and heart rate but also respiration rate. It was also shown that this sensor could be implemented on a mobile platform.

Figure 31. This figure demonstrates RRIV on upper envelope of PPG and respiration waveform from CO2 sensor and Biopac.

In conclusion, accuracy of wearable CO2 meter was compared to Biopac respiration effort transducer. During this process, 10 healthy subjects were tested at three different paces normal, 0.2 and 0.3 Hz. Mean difference between CO2 meter and Biopac were estimated using Bland and Altman analysis, as 0, 0 and 0.1 at normal, 0.2 and 0.3 Hz respectively. This demonstrates that detection of respiration without use of mask is feasible with high accuracy.

In addition, PPG was acquired from two sites of human body, forehead and finger. An algorithm on Labview was designed and developed entirety by myself. This
algorithm extracted upper envelope of PPG signal corresponding to respiration rate. In order to evaluate the accuracy of the algorithm, PPG from forehead and finger of 10 healthy subjects were collected at three different paces normal, 0.2 and 0.3 Hz. By applying FFT on data and respiration frequency was identified between 0.69 and 0.7 Hz. Using Hilbert transform upper envelope of signal was extracted. Hence the peaks on top of this envelope corresponded to respiration rate. Hence in order to evaluate accuracy of this algorithm PPG from forehead and finger of 10 healthy subjects were recorded simultaneously for one minute at three different paces, normal 0.2 and 0.3 Hz. Then using Bland and Altman mean difference between respiration rates from PPG forehead was estimated as -0.2, -0.5 and -0.3 at normal, 0.2 and 0.3 Hz. According to this result, respiration could be extracted with high accuracy from forehead at normal pace. Also, mean absolute error between these two methods was also estimated as 0.039, 0.083 and 0.055 at normal, 0.2 and 0.3 Hz respectively. According to these results, respiration rate from PPG forehead could be obtained with high accuracy at normal breathing as well. Hence, proposed algorithm is capable of acquiring respiration rate from forehead with high accuracy at normal breathing. In addition, mean difference between respiration rates obtained from PPG finger at three paces were estimated using Bland and Altman analysis as -0.1, -0.7 and -0.2 at normal, 0.2 and 0.3 Hz respectively. According to this data, feasibility of obtaining respiration rate from finger is also confirmed with higher accuracy at normal breathing.

According to the results in tables 6 and 7, it is shown that respiration rate could be obtained from forehead and finger and the algorithm was shown to be reliable method of obtaining respiration rate with slightly better performance from PPG finger in comparison to PPG forehead.
4. **Assessment of Hypovolemia by LBNP**

In this chapter background information about progressive hypovolemia will be introduced along with discussion about effects of acute blood volume reduction on PPG waveform. Morphological variation of PPG during the Lower Body Negative Pressure experiment was studied during LBNP test. The experiment took place in Aerospace laboratory at department of kinesiology under supervision of Dr. Blender and Dr. Tavakolian. Dr. Tavakolian designed the experimental protocol. I contributed in setting up the instruments with Dr. Tavakolian. Each subject was paid $20 and they signed concern form. Ethics was obtained and approved by SFU under the name of Dr. Blender and Dr. Tavakolian. The protocol required presence of a registered nurse or medical doctor during the experiment. A licenced cardiac surgeon was present during data acquisition.

In this chapter, I was offered the help of Dr. Tavakolian and we both performed LBNP.

I contacted Dr. Paul Linder (Dartmouth college), and my colleague Moein Shayegannia and I implemented (The code is available for review) an algorithm on matlab. This algorithm follows the recommendation of Dr. Paul Linder, adjusted and implemented for identification of successful peaks of cardiac cycle from PPG.

The purpose of this study was to evaluate feasibility of extracting features from PPG waveform, for detection of progressive hemorrhage. This section consists of the following:

4.1 Hemorrhage and hypodynamic response, and experiment of Lower Body Negative Pressure

4.2 Hemorrhage Lower Body Negative Pressure, experimental setup and protocol

4.3 Results from LBNP and discussion on variation of PPG
4.1. Hemorrhage and hypodynamic response, an experiment of Lower Body Negative Pressure

Hemorrhage is the loss of blood from the circulatory system and a major cause of death, particularly in car accident trauma and on the battlefields [105]. The early application of life saving interventions, particularly before the development of circulatory shock, is a priority when dealing with hemorrhage. Mortality can be significantly reduced when patient’s immediate care can be identified early. Traditionally, hemorrhage is diagnosed based on mental status, pulse and systolic blood pressure (dropping below 90 mmHg). However, it may be impossible to rescue when significant hypotension has developed. Pulse pressure (difference between systolic and diastolic blood pressure) has therefore been proposed for early non-invasive identification of hemorrhage, when the systolic blood pressure is greater than 90 mmHg [105]. The association of pulse pressure (PP) to stroke volume has been recently challenged and the equivalent sensitivity of PP to blood loss has not been validated [106].

Application of negative pressure to the lower body redistributes fluid from the upper body to the lower extremities, allowing for the study of hemodynamic response to central hypovolemia [107]. The description of lower body negative pressure (LBNP) has been used by aerospace investigators to study such physiological phenomena as post spaceflight orthostatic intolerance and exposure to vertical acceleration in high performance aircrafts.

Convertino [107] investigated the utility and reproducibility of LBNP as a technique to study cardiovascular adjustments to such stressors. Based on his research, Covertino suggested that LBNP might also be a useful surrogate to study hemodynamic effects associated with severe hemorrhage in humans for military applications, specifically combat casualty care research.

It should be emphasized that there is renewed interest studying hemorrhage in a human model, as hemorrhage is the primary cause of death on the battlefield [145] and a leading cause of death in civilian trauma [108]. During all relevant laboratory studies, hemorrhage is simulated by creating graded lower body negative pressure (LBNP) to compensate for the loss.
Reduction of central venous pressure is directly related to the magnitude of LBNP and reflects reduced venous return. Application of LBNP between -10 and -60 mmHg reduces central venous pressure by 3–7 mmHg [109]. This is in good agreement with equations derived from animal studies predicting reductions of central venous pressure as a function of reductions of blood volumes [110]. Norsk [111] demonstrated that central venous pressure decreases by 2 mmHg for every 10-mmHg-chamber pressure, up to 30 mmHg.

The response to hemorrhage is divided into three phases [112], mild, moderate, and severe. The first phase is the mild phase, and occurs when less than 10% of total blood has been lost. This results in sympathetic activity increasing, and either maintenance or slight increase of blood pressure. In the second phase, there is a blood loss of up to 20% and the sympathetic nervous system fails to compensate for the loss. Finally, the last phase starts when more than 20% of blood has been lost (approximately one liter). In the last phase, severe haemorrhage and tachycardia are presented with a failure to maintain blood flow to the vital organs. This is fatal and results in death.

For an effective diagnosis and treatment, it would be ideal to detect the progression of hemorrhage to phase two before phase three occurs. LBNP, during which the blood is trans-located to the lower portions of the body, provides a safe tool to reproduce conditions similar to hemorrhage, while maintaining total blood volume.
4.1.1. Amplitude modulation of PPG (Time Domain Analysis)

Using the PPG signal enables us to see the effect of the LBNP on stroke volume. The height of PPG is proportional to the pulse pressure, the difference between the systolic and diastolic pressure in the arteries [113]. A reduction of pulsatile amplitude can be directly attributed to either a loss of central blood pressure or a constriction of the arterioles perfusing the dermis. A limitation worth noting when using pulse height as a feature is that it cannot be calibrated. In addition, the absolute pulse height will vary depending on how and where the sensor was applied to the skin.

Since volume sequestration of blood in the lower extremities mimics the effect of blood loss from traumatic detection of haemorrhage, we performed lower body negative pressure experiments to study the variation of PPG signal. This test was performed in Aerospace Physiology Laboratory in Simon Fraser University. Prior to the testing, four participants (1 female and 3 males) were provided with an orientation to the protocol and instrumentation, and also provided written informed consent. This research was approved by the Simon Fraser University Ethics Review Board and adheres to the guideline established by declaration of 2012S0078.
4.2. Hemorrhage Lower Body Negative Pressure, Experimental setup and protocol

The experimental protocol involved one day of testing beginning with measurements of stature and body mass in order to fit instrumentation, followed by a 72 minute progressive lower body negative pressure (LBNP) protocol. This technique has been used to simulate orthostasis in a variety of situations and populations as a means to study cardiovascular response to central hypovolemia and haemorrhage [150]. After 12 minutes of baseline data collection at ambient barometric pressure, four 12-minute stages of progressive LBNP at -15, -30, -40 and -50 mmHg were applied. The negative pressure was terminated if any of the following symptoms were observed: 1) a sudden drop in heart rate or blood pressure, or a sustained drop in systolic blood pressure (SBP) below 90 mmHg along with qualitative symptoms, and/or 2) at the participant’s request. Close monitoring of qualitative symptoms of nausea, excessive sweating, tunnel vision, light-headedness, and/or dizziness were also used to identify presyncope. A final recovery stage took place where ambient pressure was reapplied for the final 12 minutes of data collection after the last negative pressure stage.

Hypodynamic measurements

All hemodynamic measurements were collected continuously throughout all stages of the LBNP protocol using a NI-DAQ (National Instrument 9205), interfaced with a Labview on a computer. Continuous Electrocardiograph was measured using electrocardiography (Biopac, CA) Beat-by-beat SBP and diastolic (DBP) blood pressure was measured noninvasively using a Finapres finger cuff blood pressure device (Ohmeda, Englewood, CO). Blood pressure was also measured every three minutes using automated cuff occlusion (BMP-100 VSM Medtech, Coquitlam, BC) and used to verify readings obtained from the Finapres. Stroke volume was estimated using impedance cardiography (HIC-3000, Bio-Impedance Technology, Inc., Chapel Hill, NC), which has been validated for its use during LBNP, and strongly correlated with echocardiography [156]. Photoplethysmography was measured from the forehead and finger (Nonin 8600, MN). Pulse arrival was measured (Nonin 8600, MN), which evaluated the arrival time of the pulse. Respiration (BD785 airflow sensor, Braebon, NY) and Seismocardiography (Odin Metrology, CA) where also recorded in parallel.
4.3. Results from LBNP and discussion about variation of PPG during the LBNP

In human studies in which mild blood loss is induced by voluntary blood donation, the cardiovascular system easily compensates for the removal of only small percentages of the total blood volume. As such, this experimental model fails to provide a point of hemodynamic decompensating, as would occur in cases of non-compressible hemorrhage [114]. Hypodynamic decompensation is defined as a precipitous fall in systolic BP greater than 15mm concurrent with the onset of symptoms such as tachycardia, gray out, tunnel vision, sweating, nausea or dizziness [115].

To accomplish the objective of investigating the dynamics of severe hemorrhage in humans and providing early detection of imminent cardiovascular collapse, LBNP study was designed to safely and noninvasively induce decompensation in 4 human subjects in Aerospace Laboratory at Simon Fraser University. In the presence of compensatory hemodynamic, autonomic and metabolic responses during LBNP, the dynamics of standard vital signs have been monitored. A registered cardiac surgeon was present during the LBNP experiment. He verified that during the early compensatory phase of hemorrhage, no clinical alterations occurred in mental status, pulse character, systolic and mean BPs, arterial oxygen saturation or respiration rate.

Results from LBNP suggest [117] that humans can lose as much as “40%” or more of their central blood volume before clinically significant changes may occur in standard vital signs and mental status. The LBNP verified that such changes in current standard vital signs fail to provide early prediction of clinical outcomes but that they correlate well with mortality. It is therefore clear that there is a requirement for a device that quickly and reliably detects and estimates the level of blood loss based on real time integration of physiologic signals that represent the response of dynamic and complex mechanisms during the compensatory phase of haemorrhage. This is the true gap (figure 33) that exists with current medical monitoring capabilities.
As stated by V. Convertino [115][116], the heart rate or pulse pressure alone is not sensitive enough to make changes in stroke volume induced by LBNP. Current medical monitoring capabilities, i.e. failure of BP and HR regulation can be defined by standard vital signs. Physiologic dynamics that lead to failure, however, cannot be defined by current medical monitoring technologies.

This study confirmed PPG waveform changes analogous to changes of stroke volume induced by LBNP. In particular, PPG waveform was shown to be affected at changes of negative pressure of at -15, -30, -40 and -50 mmHg. As can be seen in figure 34, the height of PPG shows a gradual drop in stroke volume form the resting LBNP stage to the peak negative pressure of LBNP.
Figure 34. 72 minutes of LBNP data. One could observe that prior to the presyncope period, the height of pulse oximeter (PPG) from the finger and forehead becomes shorter due to the limited degree of stroke volume. Upon termination of the experiment, the stroke volume returns to the normal level and the height of the PPG signal returns to initial value.

As can be seen in figure 35, the PPG waveform from the finger illustrates a significant drop in pulse magnitude. The signal was compared to BP from finapress. The blue line shows an end of LBNP at -50 Hg mm. After termination of LBNP, the blood volume contained in the lower body of a subject due to negative pressure returns to its initial level. This was proven in height of the PPG signal.
Figure 35. PPG waveform obtained from finger in green and BP from finapress in black shows the hypodynamic response of the body on PPG waveform during -50 Hg mm negative pressure.

Figure 36. PPG waveform obtained from forehead in red and BP from finapress in black show the hypodynamic response of body on PPG waveform during -50 Hg mm negative pressure.

PPG waveform form the finger (figure 35) returned to standard morphology right after termination of the LBNP. However PPG waveform form the forehead (figure 36) introduced a few peak high points before returning to standard height. These peaks were not observed with the PPG of the finger. In addition, the waveform of PPG from the forehead followed a standard morphology during negative pressure. PPG waveform from the finger disappeared however, and no pulses were observed for a short period of time from finger pulse oximeter. These two segments are pointed out in figure 35 and 36.
Figure 37. PPG waveform obtained from forehead. By setting initial values for peak detector algorithm peaks of PPG waveform was detected automatically. A significant pulse magnitude was detected at 1.811e5 second.

The height of PPG waveform from the forehead was reduced analogous to stroke volume. After the termination of LBNP, the first significantly large peak was detected at 1.811e-05 second (figure 37). This was observed after termination of LBNP. This suggests that reduction of stroke volume is correlated to the height of the PPG. This feature of the waveform may be used in future studies for estimation of LBNP levels.

This study was designed to identify features of the PPG waveform, which may be potentially reliable for detection of hypovolemia. It was demonstrated that hypovolemic subjects experience a reduction of stroke volume in parallel to reduction of PPG height. Also, it is shown that the algorithm designed for this study is reliable and capable of automatically collecting peaks of the PPG waveform during the LBNP. Consequently, this study proves the initial values used in this algorithm to be reliable for detection of peaks of PPG waveform.
Figure 38. PPG waveform obtained from finger. By setting initial values for peak detector algorithm peaks of PPG was detected automatically.

Figure 39. ECG waveform. By setting initial values for peak detector algorithm peaks of complex QRS were detected automatically. Height of ECG does not change during or after LBNP test.
A comparison of PPG waveform to ECG (figure 39 and 39) shows that the PPG waveform during LBNP and after LBNP differs morphologically in height for each cardiac cycle. The height of ECG does not reduce during or after the LBNP test however. Figure 39 shows standard morphological waveform before and after the presyncopal period of the LBNP test.

![Height of PPG Forehead and Finger Presyncopy](image)

**Figure 40. Height of PPG waveform from finger in red and PPG from forehead in blue increases after termination of LBNP.**

Using automated peak detector algorithm, the distance between the peaks and valleys of each cardiac cycle pair was estimated (figure 40 and 41). The height of PPG from the finger and forehead showed a significant increase after termination of LBNP test.

According to figure 41, it was proven that the height of PPG waveform returns to initial level (Base line of LBNP) earlier than BP. This figure shows a reverse relation of PPG and BP to stroke volume. It confirms that at the end of LBNP, PPG responds to the return of blood to the upper body before BP does. However, this also demonstrates sensitivity of the PPG compared to the BP. The next stage of this process will evaluate the PPG waveform for prediction of stages of LBNP.
This study confirmed that the height of PPG waveform varies analogous to levels of LBNP. The influence of arterial wall stiffness affects the degree of changes in the height of PPG, and was not constant from subject to subject. To evaluate the effects of LBNP stages on PPG, it was important to know the exact behaviour of PPG waveforms at different stages of LBNP. Amplitude components of PPG were the dominant feature during all levels of LBNP. Overall results showed gradual decline in PPG, with amplitude declining with LBNP in all four subjects. Based on these results, the amplitude of PPG could be used as an index for the estimation of reduction in blood volume.

In addition, it was observed that PPG obtained from forehead and PPG obtained from finger contained a shorter height in comparison to PPG obtained from finger. This is due t
5. Mechanically Flexible PPG sensor

The conventional hospital-centered healthcare system, which focuses on diagnosis and treatment, is beginning to shift its focus. In its place, a more individualized healthcare system with emphasis on early detection of risk factors, early diagnosis, and early treatment [118] [119] is beginning to emerge. This new paradigm aims to encourage participation of the whole nation in the prevention of illness and in the early prediction of diseases in order to achieve a pervasive and personalized healthcare system [120].

In this paradigm shift, wearable vital sign systems have been recognized as an enabling technology for monitoring an individual’s health condition on a continuous basis, feeding relevant information back to the users and/or medical professionals, and firing an alarm signal when an adverse condition occurs [121] [122][123]. Consequently, the prospect of efficient remote health and activity monitoring using wireless sensors has recently gained a lot of interest and stimulate research in the area of wearable electronics. Technological advances in sensors, wireless communication and integrated circuits have brought about small, inexpensive wearable physiological monitors. These devices are usually capable of sensing one or more vital signs, e.g. heart rate, respiration rate, body temperature and/or blood pressure, and in then communicating the acquired data to a local or remote processing and interpretation centre.

Previously, in this dissertation, an application of photoplethysmographic waveform was introduced. In addition, morphological characteristics of PPG waveform were also studied for extraction of respiration and heart rate. The hypodynamic response of human body to progressive hemorrhage was also studied by the LBNP model. According to these studies, a PPG device could be employed on human subjects for continuous monitoring of cardiovascular and pulmonary systems as well as to assist in the prediction of hemorrhage. Results from the previous chapters of this dissertation confirmed that, PPG contains multiple physiological data such as heart and respiration
rate, heart rate variability, and index of progressive hemorrhage. Since PPG was shown to be a strong signal and current pulse oximeter sensors are unsuitable for wearable vital sign systems, we proposed a mechanically flexible PPG sensor, integrated on plastic polymer using ink-jet technology.

The main propose of his chapter is assessment of biomedical measurements from the cardiovascular system. In particular, identification of heart rate (HR) and heart rate variability (HRV) by flexible PPG sensor are emphasized.

5.1. Conventional structure of PPG sensors

There are two models for obtaining PPG (figure 42). In the first model, a light emitter is located on the opposite side of the photoreceptor. In this case, the emitted light passes through skin tissue and a photoreceptor on the other side of the tissue detects a portion of the light passed through the finger. In the second model, LED and photodetectors are placed side by side on top of the tissue. In this case, the photodetector observes the reflected light in the same planar surface as the LED.

Figure 42. Models of pulse oximetry probes [124]

The PPG probe could be located on the body surface where transmitted light can be detected. Locations meeting this criterion are fingertips, ear and forehead [124]. The placement of PPG on the fingertips or earlobe could result in problems during low blood perfusion, when arterial pulsation in the limbs is diminished [125]. Common instances of low perfusion are hyperthermia and hypovolemia. In these cases, sympathetic reflection reduces the blood perfusion to the peripheral tissues and keeps continuous circulation to the vital organs of the body, such as the brain heart and lungs [126]. The placement of
PPG sensors on earlobes involves the integration of a mechanical clip to stabilize the sensor on the skin. Prolonged attachment of the sensor by a clip depresses blood perfusion in the earlobe however, and in some cases may cause pain to users.

Compared to other peripheral body locations [127], allocation of the PPG sensor on the forehead has shown greater sensitivity to PPG changes during low perfusion situations. This attribute makes the forehead more effective for PPG acquisition during hyperthermia and hypovolemia. The forehead has also been proven to detect hypoxemia 90 seconds before a fingertip or ear sensor during peripheral vasoconstriction [128]. Moreover, the thin layer of skin on the forehead in addition to its prominent bone structure helps to direct the light back to the photo detectors, which potentially results in the collection of a more accurate PPG signal [129]. The PPG sensor on the forehead therefore affiliates appropriate placement for application of wearable vital sign monitoring.

5.2. Possible source of noise on PPG waveform

Motion artefact is considered to be the major challenge of PPG measurement [39]. Any form of physical activity may lead to motion artifact, which corrupts the PPG signal and makes accurate measurements of physiological parameters difficult, if not impossible. One common method to improve physiological measurements during motion is through signal processing, as reviewed by Hayes [130]. There have been numerous algorithms developed, with varying effects on measurement accuracy [131] [132]. Of the most notable, Masimo (Irvin, CA), a leading pulse oximeter manufacturer, has developed advanced digital signal processing algorithms that have shown to significantly improve measurement accuracy [133] [134]. Celka [135] investigated use of an accelerometer device to capture motion rhythms, Gibbs [136], Renevey [137] and Wood [138] investigated the use of post-processing methods such as spatio temporal PCA, Laguerre expansion. For artifact removal from PPG, discrete wavelet analysis and filter banks were investigated [139][140], Wigner–Ville distribution in [141] and nonlinear methods in [142]. Despite these improvements however, measurement accuracy does not meet clinical standards [143].
Although signal processing has shown improvement in measurement and accuracy during motion, sophisticated algorithms require more powerful microprocessors. This results in increased weight, size, and power consumption of the PPG measurement. When an individual is required to wear the unit over extended periods of time for a simultaneous monitoring of vital signs, the PPG device must be small and lightweight. These demands limit performance and signal processing, and decrease user comfort.

Past studies investigated whether a particular measurement site improved measurement accuracy. Dassel [144] and Mendelson [145] have shown that a reflective mode sensor located on the forehead provides more consistent PPG readings while a subject remains motionless. In addition, a reflective mode sensor located on the forehead may provide more consistent readings in the presence of moderate amounts of motion artifact in comparison to other facial regions. Although these studies make the placement of the sensor on the forehead attractive, one must however still be aware of the underlying issue with this measurement site. Mannheimer [146] has demonstrated that placement of the sensor directly over larger cardio-synchronously pulsating or moving vasculature can result in PPG inaccuracies. In this study, it was observed that placement of the sensor directly over the eyebrow slightly lateral to the iris avoids these inaccuracies. Although selection of an appropriate measurement site can improve measurement accuracy, motion artifact will be present no matter where the sensor is located. Therefore, other methods must be investigated to further reduce the effect of motion artifact on pulse oximetry.

It was also stated that source of motion artifact can be attributed to the formation of air gaps created between the skin and the PPG sensor during physical activity [147], which may cause measurement errors. Another source of motion artifact can be attributed to low venous pressure blood “slosh” with back and fourth movement [148]. This is seen when an individual is physically active. This local perturbation of venous blood adds to the AC component of the PPG signal, and can result in inaccurate PPG waveform.

Since the development of pulse oximeters, there have been numerous studies conducted in an attempt to overcome the effects of movement artifact. These studies
have investigated a variety of methods that improved measurement accuracy. Measurement inaccuracy due to motion artefact is however still prevalent, and limits quality of PPG acquisition. It is important to note that motion artifact due to rigorous physical activity such as running will most likely not be eliminated completely. It can however be assumed that if a subject is involved in rigorous activity, he or she will be relatively healthy. The most important situations where motion artifact must be reduced are during times of moderate levels of activity such as walking. This is due to the fact that individuals with health problems are still able to walk and engage in moderate levels of activity.

5.3. Advantages of mechanically flexible design of PPG sensor

In recent years, various signal-processing methods have been investigated for minimizing motion artifact in wearable PPG signals. Advances in inkjet printing technology, enable the fabrication of various electrical components on flexible materials. Inkjet patterning is considered to be one of the key technologies in the field of defined polymer deposition, particularly in relation to plastic electronics. The purpose of this dissertation was to explore a reflective PPG sensor design that can be integrated into a wearable platform such as a plastic polymer. The device had to be small, mechanically flexible to wear, and thus suitable for long-term pervasive monitoring.

Mechanical flexibility is one of the main advantages of organic materials. Despite this fact however, organic semiconductor’s strain properties have yet to be fully developed in a way that enables the device to detect physical parameters such as pressure and bending [149]. The effect of strain on the mechanical and electronic properties of organic semiconductors is an emerging research topic in fundamental physics and applications. In flexible printed electronics based on organic semiconductors, devices such as organic field effect transistors [150], organic light emitting diodes [151], organic solar cells [152], organic resistors [153] and capacitors [154] are fabricated building up multilayered structures formed by thin films on different flexible materials.
Organic printed electronic devices have attracted much attention due to their low cost, non-vacuum, and environment friendly processability. Two of the main advantages when comparing organic printed electronics to traditional inorganic electronic manufacturing techniques are low production costs and low temperature. In regards to the temperature, the low temperature of the process allows the employment of flexible substrates such as plastics foils or paper, which enable a simpler fabrication technique and the possibility of easily covering large area surfaces [155].

While organic printed electronics still require the development of optimal ink and require investments on relevant research, production cost nonetheless remains low. The reduction in manufacturing costs in organic printed electronic technologies is due to a reduction in material waste. Organic printed electronic technologies are based on an additive process i.e. the inks are selectively deposited only on the areas of interest. On the contrary, more conventional fabrication techniques such as photolithography continue to use subtracting processes. In subtracting processes, a homogeneous layer of material is typically deposited over the whole substrate and the final pattern is achieved by subtracting excess material.

Compared to traditional techniques, printing not only limits material waste, but also significantly reduces the manufacturing steps. Due to the controlled direct printing of a desired pattern on the substrate, this technique does not require the employment of high-resolution masks, which are generally very expensive. Moreover, printing does not require special processing conditions such as a cleanroom or a darkroom. A greater range of materials can be deposited by this technology, such as bioactive fluids, which cannot tolerate exposure to photolithography and the etching chemicals present in conventional techniques [156].

Organic printing electronic technologies consist of contact printing technologies such as Flexography, Gravure printing and Soft lithography, as well as non-contact printing technologies such as Laser, Direct Wiring, Aerosol printing and Inkjet-printing technology. The non-contact patterning method permits one to obtain accurate alignment with patterns already on the substrate, which is an indispensable function when seeking to pattern multilayered devices. Conversely, contact techniques could encounter difficulties in completing multilayered devices [157].
In other words, even if some noncontact methods like inkjet printing are 2D deposition techniques, it is possible to easily build 3D structures. This can be done additively by printing multiple layers of the same or different materials, provided one takes into consideration post processing and drying requirements of the deposited films and the compatibility between different solvents contained in the inks used [158]. In terms of the amount of organic printed electronic techniques; the inkjet printing technique is one of the most powerful processes for direct patterning of inks on the substrates of organic plastic films. The production process and the room requirements of the apparatus are simple and modest, the consumption of chemicals, energy, materials and manpower is extensively diminished and low-cost manufacturing strategy can be achieved by this technique [159].

5.4. Inkjet printing

Inkjet printing technology involves ejection of a fixed quantity of liquid material called ink in the form of droplets from a chamber through nozzles [160]. This method is considered an ejected drops fall onto a substrate under the gravity force and air resistance to form a pattern. The solidification of the liquid may occur through the evaporation of a solvent, chemical changes (for example the cross-linking of polymers) or crystallization. Often some post-processing treatments are required, such as thermal annealing or sintering, i.e. the melting of metallic nanoparticles in metallic inks, achieved by heating to elevated temperatures [161]. Inkjet printers work in two different most commonly used operation modes: Continuous or Drop-on-Demand (DOD). The major difference between continuous and DOD inkjet printing is that the material throughput, which a single nozzle can sustain, is very different. In a continuous inkjet printing system, a higher printing speed is achievable. In a DOD technology however, higher placement and accuracy of drop size are the main focus. In this type of technology higher resolution of printed patterns are achievable.

5.4.1. Continuous inkjet printing

Continuous mode inkjet printing system is pumped through a nozzle forming a continuous jet (figure 43). This uniform drop formation technique which forms a stream
of liquid issuing from an orifice, was first reported in 1833 by Savart [162] and described mathematically by Lord Rayleigh [163] [164]. Based on observations, Savart and Rayleigh noted how fluid under pressure issues from a nozzle, typically 50-80 um in diameter, and breaks up into uniform drops by the amplification of capillary waves induced onto the jet. This process usually takes place by an electromechanical device that causes pressure oscillations to propagate through the fluid. The drops break off from the jet in the presence of an electrostatic field, referred to as the charging field, and thus acquire an electrostatic charge. The charged drops are then directed to their desired location, either the catcher or one of several locations on the substrate by another electrostatic field, the deflection field.

This type of system is generally referred to as ‘continuous’ because drops are continuously produced and their trajectories are varied by the amount of charge applied. Continuous mode inkjet printing systems produce droplets that are approximately twice the nozzle diameter of the droplet generator [165]. Droplet generation rates for commercially available continuous mode inkjet systems are usually in the 80-100 kHz range, but systems with operating frequencies up to 1MHz are in use. Droplet sizes can be as small as 20 um in a continuous system, but 150 um are typical.

![Figure 43. Schematics of a continuous type ink jet printing system [165] and a 50um wide jet of water breaking up due to Rayleigh instability into 100 um droplets at 20kHz](image)

Figure 43. Schematics of a continuous type ink jet printing system [165] and a 50um wide jet of water breaking up due to Rayleigh instability into 100 um droplets at 20kHz
5.4.2. **Drop-on-demand inkjet printing**

In the 1950s, the production of drops by electromechanically induced pressure waves was observed by Hansell [166]. In this type of system, a volumetric change in the fluid is induced by the application of a voltage pulse to a piezoelectric material that is coupled, directly or indirectly, to the fluid figure (4.2). This volumetric change causes pressure and velocity transients to occur in the fluid, which are directed in a way that enables them to produce a drop that issues from an orifice [167]. Since the voltage is applied only when a drop is desired, these types of systems are referred to as drop-on-demand, or ‘demand mode’. A recent demand mode droplet generation technology uses focused acoustic energy to cause a droplet to be emitted from a free surface. This type of technology has been employed in industrial processes for adhesive coating, and in NASA’s liquid metal droplet free form fabrication efforts [168].

![Figure 42. Schematic of drop on demand type of inkjet printing and droplet of 60um diameter ejected at 4kHz [170].](image)

Demand mode ink-jet printing systems produce droplets that are approximately equal to the orifice diameter of the droplet generator [169]. Demand mode systems are conceptually far less complex than continuous mode systems. On the other hand, demand mode droplet generation requires the transducer to deliver three or more orders of magnitude greater energy to produce a droplet. Compared with continuous mode, demand mode presents many complex arrays in regards to demand mode print head designs [170]
5.4.3. Drop formation and impact phenomena

The physical properties of ink, viscosity, and surface tension constitute a very crucial property of inkjet printing technologies. The surface tension of ink is strictly related to the shape of the drop as it is jetted from the nozzles. Common values of surface tension according to [171] are from 28mNm\(^{-1}\) to 350 mNm\(^{-1}\). In parallel, viscosity values lower than 20 mPas are suitable for droplet ejection from nozzles. The relation between various forces to inertial and surface tension forces is expressed by dimensionless Ohnesorge number (oh) [172].

\[
Oh = \frac{\sqrt{We}}{Re} = \frac{\eta}{\sqrt{\rho D \sigma}}
\]

Where \(\eta\), \(\rho\) and \(\sigma\) are viscosity, density and surface tension of the ink and \(D\) is a length parameter, \(Re\) is the Reynolds number and \(We\) is the Weber number, defined respectively as:

\[
Re = \frac{\rho V D}{\eta}
\]

\[
We = \frac{\rho V^2 D}{\sigma}
\]

Where \(V\) indicates the velocity, \(\eta\), \(\rho\) and \(\sigma\) refer to the viscosity, density and surface tension of the ink, and \(D\) to the length of the parameter. \(Re\) is the Reynolds number and \(We\) is the Weber number. The Reynolds number is the ratio of the inertial force and the viscous force, while the Weber number is the ratio of inertial force to surface tension. Thus, the Ohnesorge number defines the ratio between viscous force and the square root of the product of inertial force and surface tension. Literature refers to the inverse of Ohnesorge number: \(Z = Oh^{-1}\). In the earliest studies of drop formation in a drop on demand printing technology, it was [173] predicted that the drop formation would have been guaranteed only for \(Z > 2\). Reis and Derby [174] indicated the range \(1 < Z < 10\), where the lower limit is controlled by ink viscosity i.e. for \(Z < 1\) viscous dissipation in the fluid prevents drop ejection, and the upper limit is related to unwanted satellite drops formation rather than a single drop in ejection process [175]. The \(Z\) range founded by Reis and Derby was later confirmed by subsequent studies [176].
It should be noted that the drop formation dynamics for polymer-based inks differ from that of ordinary Newtonian fluid described above. Because of the increase of viscoelastic forces, when adding even a small amount of polymer to ink, the ejection of a droplet involves the formation of a filament connecting the ejected droplet to the nozzle of a printer (figure 44). As the concentration or molecular weight of the polymer increases, only a few satellite drops occur. With a further increase, droplets without satellites are formed and finally, if the concentration/molecular weight of polymer is higher than a certain value, the capillary force is unable to break the filament, which forced the drop to retract to the nozzle.

*Figure 44. Stroboscopic images of the formation of a Newtonian drop on tope. Effect of adding a small mount of polymer in bottom [171]*

De Gans [177] stated that the micro-rheological explanation for the filament formation is the sudden transition of the polymer chain from a coiled to a stretched structure. This transition can be controlled by another dimensionless parameter, the Weissemberg number, defined as:

\[ Wi = \dot{\xi} t \]

Where \( \dot{\xi} \) is the elongation rate, \( t \) is the elongation time of the filament. At \( Wi = 0.5 \), the transition occurs.
5.5. Drop splashing and rebound impact on a dry surface

A wide range of behaviour is possible when a liquid drop strikes a solid surface. As reviewed by Yarin [178], outcomes can be numerous. The variables involved in process of drop formation on solid surface are drop velocity, direction with respect to the substrate, drop size, ink properties, wettability and roughness of the substrate.

According to Yarin’s [178][179] study, the formation of drops on a film follow two characteristics; low and high impact of velocity. At low impact, the drops spread over the surface of the substrate and take the shape of lamellae, which looks like an outer rim. By contrast, at higher impact, when the drops spread over the surface of the substrate, they take the shape of lamellae, which looks like a crowns consisting (figure 45)

![Figure 45](image)

_Figure 45._a Spreading ethanol drops stroboscopically illuminated. Spreading lamellae at two different stages can be recognized. Drop diameter D = 279 um, impact velocity $V_0 = 7.8$ m/s, $We = 588$, $Re = 1409$, $Oh = 1.72$. 45.b. Splashing ethanol drops illuminated by a single flash. Drop diameter D = 276 um, impact velocity $V_0 = 12.7$ m/s, $We = 1542$, $Re = 2270$, $Oh = 1.73$. From Yarin & Weiss (1995). Courtesy of Cambridge University Press [178][179].

Drop spreading occurs at the impact velocities $V_0 < V_0S$, whereas splashing and the formation of a crown and multiple secondary droplets occur at $V_0 > V_0S$, as in Figure 45 (b). The real pattern of drop splashing on substrate appears to be too complicated for any theoretical tools.

Due to the influence of surface texture such as wettability and roughness, drop impacts on dry surfaces exhibit more complicated flow patterns than those on the wetted surfaces. Rioboo [180] introduced six possible outcomes of drop impact on a dry surface. The outcomes of drop impact on a dry surface can be seen in figure 46 [181].
5.6. Challenges and benefits of Inkjet printing technology

Due to the high speed of printing and jetting frequency, values higher than 50kHz and an increased number of nozzles on a printing head, the Inkjet printing technology is a popular technology compared to its counterparts. The highest number of nozzles in a cartridge was reported at almost 200 nozzles per inch [157][182]. Inkjet printing also presents a number of challenges however, including a limited resolution of inkjet printing [183]. Implementation of high quality printed transistors, for instance, requires high resolution jetting. The minimum distance between drops is limited by the diameter of the jetting nozzles and by the surface tension of the ink. In addition, another limitation of inkjet printing technology is the interaction between the ink and the substrate. In particular, the spreading-splashing phenomena, which was introduced in previous section continues to be a concern.

The process of preparing ink is crucial. As physical properties such as density, viscosity, surface tension, volatility and shelf time all affect the quality of the printed ink [184][185], preparation becomes essential. In addition, feasibility of clot formation in nozzles are directly affected by these physical characteristics. Each type of ink requires
a specific post healing process, such as sintering, annealing or heating. These strongly affect morphology and the uniformity of the printed pattern and thereby extend manufacturing processing time [186].

In addition, the inkjet printing technology is considered a slow fabrication process in comparison to screen-printing technology. The inkjet printing technology is a suitable fabrication method for prototyping proposes. For that reason in this application, it was proposed to use Dimatix material printer as the main tool for printing conductive lines on tope of flexible materials. The process of printing the conductive pattern using silver ink will be discussed in 4.11 in more detail.

5.7. Inkjet printing Diamatix Materials Printer technology

The Diamatix Materials Printer 2800 (DMP2800) is a piezoelectric Drop-on-Demand inkjet printer manufactured by FUJIFILM. Diamatix was used in this dissertation for fabrication of PPG devices (figure 47).

![Figure 47. Diamatix Materials Printer 2800. This printer consists of three major parts, print carriage, and platen and drop watcher. The detail information about the printer could be found in the manual of the hardware. However, in this dissertation we focus on the parts, which involves in printing process of PPG devices. Courtesy of Diamatix.](image)

It is worth mentioning that in this particular section of the thesis, most of the information and resources are based on experience of working with the Diamatix. The fabrication techniques were developed based on documentation provided by FUJIFILM.
These documentations are not available to the public. Consequently, parts of this section have not been cited to public journals or documentations. However, this data is available per request to the examiner committee.

The Diamatix printer includes three major parts, which are involved in the fabrication process; printer carriage, and platen control and drop watcher.

- **Cartridge:** The printer carriage is the core of the hardware. It controls the cartridge’s location precisely. This module is being controlled by the predesigned software provided by the manufacturer. This application is being used for coordination of a printing sketch on two dimensions. A high quality digital camera is added to the cartridge. This camera provides an accurate observation of fabricating process. The cartridge has the capability of heating the ink up to 70 degrees Celsius. However, according to our experience, heating ink within the cartridge increases the possibility of clot formation. Formation of clot in nozzles strongly affects the quality of the drop jetting or disables nozzles from jetting. The physical characteristics of the fluid required by Diamatix to reach the optimum jetting performances are outlined in table 8:

<table>
<thead>
<tr>
<th>Fluid Requirement</th>
<th>Specification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Viscosity</td>
<td>10 - 12 cps at jetting temperature</td>
</tr>
<tr>
<td>Surface Tension</td>
<td>28 - 33 dyne/cm at jetting temperature</td>
</tr>
<tr>
<td>Low Volatility</td>
<td>Boiling points higher than 100 C</td>
</tr>
<tr>
<td>Degassing</td>
<td>Degassing can be done with a vacuum system, by ultrasonic baths</td>
</tr>
<tr>
<td>Filtering</td>
<td>It is recommended to filter the fluids with a 0.2 µm nylon filter</td>
</tr>
<tr>
<td>Acidity</td>
<td>pH between 4 and 9 is suggested</td>
</tr>
</tbody>
</table>

- **Platen:** The main objective of platen is to hold the substrate during the fabrication process. The metallic surface of the platen could be heated up to 60 degree. This is a very crucial process, especially concerning the fabrication of conductive nanoparticles. Due to small size of the nozzle’s diameter, the nanoparticles used in the ink are required to meet the specification defined by FUJIFILM. Heating surface of the platen results in transferring the heat from the surface to the substrate prior ejecting process. A preheated substrate contributes to evaporation of solvent from the ink and decreases viscosity of the ink as soon as the ink reaches the substrate’s surface. This process has been shown to be very effective for printing silver nanoparticles in our study. Various experiments were performed to identify the appropriate degree of surface temperature according to particular type of the ink. This pre-heating process considered prime quality factor. In addition, the vacuum holds the
substrate on the metallic surface, preventing dislocation of the substrate during fabrication process.

- Drop watcher considered drop control centre: This module is equipped with a high quality digital magnifier. The magnifier is manufactured to control quality of the drops and jetting process. Drop watcher provides accurate measurements of drop formation. Drops are being formed according to jetting waveform. The physical quality and characteristics of the drop such could be measured in a drop watcher. Depending on the application and physical characteristics of ink, appropriate distance between cartridge and substrate may be studied using the drop watcher menu as well. Figure 48 demonstrates an instance of drop watcher application. In this particular example, the distance between the substrate and the cartridge was set to 700 um.

![Figure 48](image.png)

Figure 48. Demonstrates a view of drop watcher. Silver ink Novacentrix was used in this particular instance, nine nozzles jet silver ink in parallel. The appropriate distance between the drops to surface could be studied according to quality of drop formations.

### 5.8. Drop formation, jet control

To achieve appropriate printing quality, controlling the quality of jetted drops is essential. For these purposes, a jetting waveform is being designed analogous to physical properties of the ink. The jetting waveform consists of four segments, with each having the properties of duration, level and slew rate. The first segment of the waveform is not connected to any other segment. The level value, which resembles a percentage
of the voltage in segments one and two, has the most impact on the jetting process. The duration of segment one and the slew rate or duration of segment two has a strong influence on drop formation two. The applied voltage relates directly to the volume of the pumping chamber. Rapid alternation of voltage therefore results in bigger changes in drop volume.

In this thesis, one particular type of conductive silver ink was used. A jetting waveform was designed analogous to particular physical characteristics of the ink. Figure 49 demonstrates start and standby position of waveform in four stages; the start, stage one, stage two and stage three.

![Figure 49](image)

**Figure 49. Conductive silver ink, jetting and pulse single wave setting.**

During the first phase or start, the voltage is reduced to zero volts and neutral position, with the chamber at its maximum volume. During this phase, the ink is pushed to the chamber via the inlet and pulls on the meniscus at the nozzle. During phase one, the drop is ejected and the chamber is repressed to eject the drop. The following phase is considered the recovery phase, where the voltage returns to its biased level. The chamber is decompressed at first partially and then refills for the next pulse cycle. The rest of setting such as pulse duration, maximum jetting frequency were set as shown in figure 49. The optimum setting for this ink was studied by communicating to Dimatix and performing number experiments on the various substrates.
Figure 50. Conductive silver ink, jetting and pulse double wave setting.

To gain larger droplets as demonstrated in figure 51, an additional pulse wave was also added prior to the single pulse wave following the setting as shown in figure 50. By increasing the size of the drops, speed of fabrication is also being increased. According to experiments performed in CiBER, this method extends the thickness of printed silver ink. The double wave settings require at least 25um distance between. The mathematical relation that links drop spacing and resolution is report is: Drop Space= Drop Diameter/2.

Figure 51. Drop test using the single and double waveform.
According to figures 52 and 53 and in accordance with the physical characteristics of ink, there are three parameters required to be set prior to the printing process. These refer to firing voltage, jetting frequency and numbers of nozzles.

1- Firing Voltage: This is associated with bias applied on the piezoelectric head of nozzles for drop ejection. This parameter is correlated to the physical characteristics of the ink and in particular, to the ink’s velocity. To maintain a given drop velocity, higher jetting voltages are required. In contrast, higher viscosity fluids have lower velocity and they require lower jetting frequency. A high firing voltage results in compact drops with longer tails, whereas a low firing frequency produces shorter tail length. Also, an inappropriate low firing voltage may misdirect jetting process and increase the possibility of clot occurrence in nozzles.

2- Jetting Frequency: Jetting Frequency is the frequency with which nozzles eject droplets. It affects the print velocity and the print precision.

3- Number of Jetting Nozzles: The choice of the number of nozzles used is strictly dependent on the specific pattern and precision required. If high precision and definition of the printed pattern are required, using a few jets is suitable. On the contrary, when rough layers of material have to be printed, the use of many nozzles leads to a faster print process together with a good uniformity of the material deposited.

Figure 52, Velocity verses voltage on left. Drop verses voltage on right. The Higher voltages lead to faster and bigger drops.
Figure 53. Drop velocity versus firing frequency. Higher viscosity fluids have lower velocity and better high frequency performance due to their damping effect.

5.9. Material Conductive Ink

In this dissertation, silver was used as a conductive material for the fabrication of PPG devices. The silver ink used in this dissertation was manufactured by Novacentrix with the trade name Metanon JS-B25HV. This ink was specially designed for Diamatix material printers. JS-B25HV was specially formulated for compatibility and stability with Diamatix on substrates such as PET, polymide and glass. Chemical formulation of JS-B25HV was kept confidential by the manufacturer. It contains 60 nm of silver nanoparticles, and ink that is water-based with 8 cp and 30 to 32 dyne/cm viscosity and surface tension respectively. Consequently, printed patterns by JS-B25HV require curing process at low heat temperature. Tables 8 and 9 show the physical properties of silver ink.

Table 8 physical characteristics of JS-B25HV, courtesy of Novacentrix.

<table>
<thead>
<tr>
<th>Sample Conductivity</th>
<th>Units</th>
<th>JS-B25HV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Think Film Sensitivity</td>
<td>Micro ohm-cm</td>
<td>2.8</td>
</tr>
<tr>
<td>Think Film Sheet Resistance</td>
<td>Milliohm/square</td>
<td>50</td>
</tr>
<tr>
<td>Bulk Resistivity Comparison</td>
<td>$\rho_{\text{film}}/\rho_{\text{bulk Ag}}$</td>
<td>1.8</td>
</tr>
<tr>
<td>Ag content</td>
<td>wt%</td>
<td>25</td>
</tr>
<tr>
<td>Viscosity</td>
<td>cP</td>
<td>8</td>
</tr>
<tr>
<td>Surface Tension</td>
<td>Dyne/cm</td>
<td>30-32</td>
</tr>
<tr>
<td>Specific gravity</td>
<td>-</td>
<td>1.3</td>
</tr>
</tbody>
</table>
Table 9 resistivity performance of JS-B25HV on traditional over thermal processing. Courtesy of Novacentrix.

<table>
<thead>
<tr>
<th>Time-minutes</th>
<th>25C</th>
<th>60C</th>
<th>100C</th>
<th>125C</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>31</td>
<td>35</td>
<td>38</td>
<td>35</td>
</tr>
<tr>
<td>5</td>
<td>25</td>
<td>9.8</td>
<td>6.9</td>
<td>5.8</td>
</tr>
<tr>
<td>480</td>
<td>8</td>
<td>7.4</td>
<td>6.5</td>
<td>5.7</td>
</tr>
<tr>
<td>(Eight hours)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

5.10. Material Substrate

In this dissertation, it was discovered that Novele introduced the best performance among various types of substrates. Novele is manufactured by Mitsubishi Imaging for Novacentrix. This film commercially known as IJ-220 was designed to specially promote uniform deposition and strong adhesion when processed with JS-B25HV. IJ-220 is highly transparent and flexible. This substrate was heated for one hour at 100 C in a traditional oven. It was discovered that IJ-220 maintains the same physical characteristics after curing process as demonstrated in figure 54 and table 10.

Table 10 physical characteristics of IJ-220 according to manufacturer's manual

<table>
<thead>
<tr>
<th></th>
<th>Results</th>
<th>Units</th>
<th>Standard</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basic weight</td>
<td>175±10</td>
<td>g/m²</td>
<td>ISO 536</td>
</tr>
<tr>
<td>Caliper</td>
<td>140±12</td>
<td>Mm</td>
<td>JIS P-8118</td>
</tr>
<tr>
<td>Bulk conductivity</td>
<td>&lt;22</td>
<td>%</td>
<td>ISO 2471</td>
</tr>
<tr>
<td>Smoothness Bekk</td>
<td>&gt;1000</td>
<td>Seconds</td>
<td>ISO 5627</td>
</tr>
<tr>
<td>Stiffness (MD)</td>
<td>0.5±0.3</td>
<td>MN*m</td>
<td>ISO 2493</td>
</tr>
</tbody>
</table>

IJ-220 is 36 um thick. Obviously there is thinner and more flexible substrate than the IJ-220 available for use, however thickness of the substrate affects the quality of printing. In particular, more flexible substrate than IJ-220 was exposed to the possibility of cracking.

IJ-220 also contains undisclosed chemical layers on top of the film. This thin layer observes the water and the solvent of the ink, and accelerates the evaporation.
process. An experiment was performed on platen of Diamatix in which 42 C was observed to be sufficient temperature for this substrate (figure 54.b). At this temperature, homogeneous surface was observed on the top layer of each printed sample.

![Comparison of the IJ-220 with commercial PET](image1)

**Figure 54.** Demonstrates the homogeneous surface of IJ-220 after curing in over for an hour at 100 C. In contrast commercial PET was deformed due to heating and lost its initial physical characteristics.

As demonstrated in figures 54.c and 55, a pattern of JS-B25HV was printed and cured on IJ-220 and commercial PET. Both substrates were cured at 100 C for an hour. Comparison of commercial PET to IJ-220 showed that IJ-220 maintained the initial homogeneous surface after the curing process, whereas, commercial PET did not maintain its initial physical characteristics.
Figure 55. Demonstration of printed JS-B25HV on IJ-220. This sample was cured on 100 C for two hours in an oven.

5.11. Inkjet printing optimization of JS-B25HV based inks

Inkjet printing of JS-B25HV introduced a series of issues during the jetting process. Misdirected jets, clogging of nozzles and unmatched velocities of jets occurred very frequently. Several attempts were made to change jetting settings, such as firing voltage, frequency, drop size (resolution), numbers of nozzles and numbers of printed layers. After performing a number of experiments however, the best results were achieved as indicated in table 11. The rest of the printing process in this thesis was performed according to the setting in table 11.

Table 11. Main printing setting used in printing JS-B25HV

<table>
<thead>
<tr>
<th>Main settings</th>
<th>Unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Firing voltage</td>
<td>22 to 24 Volt</td>
</tr>
<tr>
<td>Platen Temperature</td>
<td>40 to 42 Celsius</td>
</tr>
<tr>
<td>Number of nozzles</td>
<td>5 to 10</td>
</tr>
<tr>
<td>Printing layer</td>
<td>4</td>
</tr>
<tr>
<td>Dropping space</td>
<td>20 Mm</td>
</tr>
<tr>
<td>Cartridge temperature</td>
<td>22 Celsius</td>
</tr>
<tr>
<td>Jetting frequency</td>
<td>10 Hz</td>
</tr>
<tr>
<td>Cartridge print height</td>
<td>0.9 Mm</td>
</tr>
<tr>
<td>Cleaning cycle</td>
<td>Purge 0.3</td>
</tr>
<tr>
<td>Rest between printing layer</td>
<td>30 Seconds</td>
</tr>
<tr>
<td></td>
<td>360 seconds or 100 bands</td>
</tr>
</tbody>
</table>

In order to demonstrate the importance of optimized inkjet settings, a few samples of misprinted JS-B25HV images were shown in figure 56. In figure 56.ab, the temperature of platen was set at 38C and35C instead of 42C. Consequently, the surface of this pattern was not dried homogeneously. In case of figure 56.b, a portion of the silver had not dried completely.
Figure 56. a. Demonstration of layers printed JS-B25HV on low heated platen. The temperature of the platen was set at 32°C. 56.b. This figure demonstrates affects of wrong heating settings on the printed JS-25BHV. In this experiment the platen was heated at 40°C and the printed pattern was cured on printer’s surface. c. In this picture a conductive silver based pattern was printed using 16 nozzles of cartridge. In these settings, the height of the cartridge and jetting frequency were not set according to table 11. So, as results, there are so many splashes around the printed pattern. 56.d. Demonstrates, affects of wrong resolution. In this experiment, the resolution of the layout was not at 1020 dpi. So, consequently, the patterns were not conductive.

As demonstrated in figure 56.c, the surface of the platen was set at 42°C. The height of the carriage however was not set as recommended in table 11. The height of the cartridge needs to be calculated and adjusted according to thickness of substrate and quality formation of drops. Inappropriate settings of these parameters result in splashes around the printing pattern, which consequently may shorten the printed layout. In addition, figure 56.d illustrates the effects of poor printing resolution. The distance between drops requires calculation according to viscosity and jetting voltage. Inappropriate settings affect conductivity of printed silver ink.
Figure 57. a. Footprint of surface mounted resistor with (0603) metric foot printed was printed 585 um wide. 57b. 410um wide horizontal line, connects passive component, c. demonstration of diagonal patterns, d. demonstrates quality of jetting droplets. Drops were produced in parallel and jetted vertically captured and studied using drop watcher. The tail of the drop was 200um long. Drops reached the surface at 900 um. According to drop watcher, at this height all drops reach the surface at the same time. The blue line at 800um shows 6 drops being formed that reached this height synchronously.

Figure 57 demonstrates three different silver printed patterns, which were printed according to the setting in table 11. The silver printed patterns were formed homogeneously with a flat surface. Figure 57.d demonstrates quality of drop formation. Following the setting in table 11, drops were jetted in parallel and reached 800 um distance form the cartridge simultaneously.
5.12. Application: Inkjet-integrated PPG sensor on flexible substrate

Upon successful jet printing of JS-B25HV on IJ-220 using Diamatix technology, we proposed to study feasibility of integrating a PPG sensor on IJ-220. As we have discussed in chapter two of this thesis, PPG could be obtained by pulse oximeters. A typical structure of pulse oximeter consists of two LEDs (660nm and 940nm). These two wavelengths are used to estimate the proportion of oxygenated to deoxygenated hemoglobin cells [187]. As the PPG does not require the same electronic structure as pulse oximeters, we proposed to replace the excessive use of LEDs, with a single LED at a lower spectrum of light.

Advantages of the proposed PPG design on IJ-220, could be outlined as follows:

- Possibility of reducing power consumption: By decreasing numbers of LDEs and relative electrical components, the demand for energy consumption is reduced.

- Possibility of replacing LED with Organic LEDs: It is known that performance of organic LEDs is limited within a certain light spectrum as demonstrated in figure 58.b. Consequently, the feasibility of obtaining PPG at wavelength of 550 nm (figure 58.c) was investigated.

- Possibility of replacing photodiode with organic photovoltaic cells: It is known that the performance of flexible photovoltaic cells is limited by two parameters, wavelength of light and life time of photovoltaic cells (as shown in figure 58.a). We therefore investigated whether PPG could be obtained reliably at a lower light spectrum, particularly between 520nm to 540 nm (figure 58.d).

- Possibility of increasing user comfort and decreasing motion artifact: Commercial pulse oximeter sensors such as Nonin 8000AA have been used in a variety of studies for the detection of PPG [187] [188] [145]. The sensor was attached by conventional adhesive tape, and PPG waveform was degraded due to the presence of motion artifact. Consequently, this sensor was proven to be unsuitable for experiments where subjects were involved in physical activity. We therefore investigated the possibility of integrating a PPG sensor on flexible, light, and inexpensive substrates.
Figure 58. a. Demonstrates spectrum of organic photovoltaic cells and also illustrates reduction of cell’s performance over period of time as stated by Lou [189]. 58.b. Sensitivity and limited spectrum of OLEDs within was demonstrated by Han [190]. 58.c Demonstration of light spectrum of LED, which was used in this study [194], 58.d Demonstration of light spectrum of photovoltaic sensor used in this study [195].

5.12.1. Circuit design of PPG Device

The electrical design of the PPG sensor was optimized for integration on IJ-220 Novacentrix. Thanks to transparency and thinness of IJ-220 and according to bench-based experiments, it was discovered that PPG acquisition was feasible by allocation of IJ-220 between the commercial PPG sensor and human tissue.

The PPG signal is comprised of a non-pulsatile part referred to as the DC component, and a pulsatile part referred to as the AC component. The DC component is caused by light absorption through skin, tissue, venous blood, and non-pulsatile arterial blood. The AC component is caused by light absorption associated with pulsatile arterial blood flow [191].

It was proposed to use an active pulse amplification circuit in combination with use of AVAGO ADPS 9008 photodiode for the extraction of the AC component of PPG. AVAGO is considered a photodiode, and has been designed especially to observe variation of light intensity. As shown in table 13, the rest of the circuit consisted of King-
bright LED, passive components with small metric 0603 footprints, and Opamp MCP6001.

Figure 56 demonstrates a sketch of the PPG sensor. The circuit was optimized for 3.3 volts DC, however is operational for up to 5 volts. The Opamp was designed to amplify the output of photodiode 330 times. This was implemented according to the formula below:

\[
\text{Amplification magnitude} = \frac{R_6}{R_5} \approx \frac{3.3\text{Mohm}}{10\text{Kohm}} = 330
\]

<table>
<thead>
<tr>
<th>Name</th>
<th>Part number</th>
<th>Manufacturer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Opamp</td>
<td>IC OPAMP 1.8V 1MHZ SNGL SOT23-5</td>
<td>Microchip Technology</td>
</tr>
<tr>
<td>LED</td>
<td>IC PHOTOSENSOR AMBIENT 6CHIPLED</td>
<td>AVAGO</td>
</tr>
<tr>
<td>Surface mounted cap</td>
<td>CAP CER 4.7UF/2.2UF 6.3V 10% X7S 0603</td>
<td>TDK</td>
</tr>
<tr>
<td>Surface mounted resistor</td>
<td>RES 100K-10K-3.3M-47.0 OHM 1/10W 1% 0603</td>
<td>Panasonic Electronics</td>
</tr>
</tbody>
</table>

Table 13. Detail components of the device are demonstrated.

Figure 56. Demonstration of PPG circuit consists of five sections. LED, photodiode, active high pass filter, amplification and input-output put of circuit have been designed on Eagle, the electronic
5.12.2. **PCB design for PPG sensor**

Commercial pulse oximeter circuits are normally fabricated on PCB. Traditionally, simple electronic circuits could be printed on single layers of PCB, however it is very common to use multilayer printing techniques in order to connect all components of a complex circuit design. In some instances, this technique is being used to reduce the size of a circuit. In this chapter of thesis, a PPG circuit was designed on simulated on eagle engineering application. A PCB sketch was also designed for the PPG sensor entirely by the author of the thesis. Next, the pattern of the PCB was transferred to Dimatix material printer to be printed on top of flexible PET (IJ-220) using conductive silver ink JS-B25HV.

![Diagram of PCB layout](image)

**Figure 57.a.** Single side PCB layout of PPG sensor was transferred to Diamatix in bitmap format. This layout was designed in Eagles and exported 1060 dpi. 57.b. Demonstration of the sensor’s layout and the footprint of electrical components illustrate where component were attached on the layout. 57.c In order to reduce the size of the layout, conductive lines, were printed as close as 0.6 mm to each other.

Consequently, we proposed a single layer (Figure 57) PCB layout of the PPG sensor. This layout was designed on Eagle software. The sketch (figure 57.a) was transferred to the Diamatix printer in bitmap format. Thanks to the precision and accuracy of Diamatix jetting technology, the PCB layout was printed 2.05 * 2.2 cm wide in epiphany. Allocation of the component’s footprint on the sketch was manually set on eagle, and lines were printed as close as 0.65 mm to one another (figure 57.c).
According to the setting in table 11, the PCB’s layout was printed on each sheet of IJ-220. These sheets were cured at 100C in the oven for an hour. Individual sketches were tested for conductivity by bench-based voltage generator and oscilloscope.

5.12.3. **Micro integrated of PPG circuit on plastic substrate**

After testing and ensuring conductivity of each printed circuit, PCB layouts were passed for fabrication process. During this process, passive, optical and electrical components of the PPG device were attached and mapped to the PCB layout. This process took place under a microscope. Silver Epoxy 8830 is being manufactured by MG chemicals. As shown in figure 58, this epoxy was used for the attachment of the components on the printed layout of a PPG device. First, a type of adhesive epoxy was used to bind the passive components, Opamp, Photodiode and LED on the surface of the IJ-220. Afterwards, each sample was cured in room temperature for ten minutes. Small drops of silver 8830 were then used to add connectivity between the circuit’s components and the inkjet printed PCB layout of the PPG sensor. Upon completion of this stage, samples were cured at room temperature for two days. The particular model of Silver epoxy (8830) added high frequency noise on the PPG signal. This noise disappeared after a week post fabrication. It is also worth mentioning that despite the manufacturer’s recommendation that the 8830 requires five hours curing period at 25C, it was discovered that this particular silver epoxy requires up to a week curing period at 25C.
The surface layer of LED is hemispheric, whereas the surface of photodiode is flat. In addition, the height of LED was 0.6 mm, which is 0.24 mm higher than photodiode. To compensate the difference of the height between these two components, photodiode and LED were located side by side and attached upside down on IJ-220. Consequently the surface layer of the PPG sensor was homogenous and even.

5.12.4. **Flexibility of PPG sensor**

The flexibility of the printed PBC sketch on the IJ-220 was proven to meet requirements of the project. As demonstrated in figure 59a.b, using proposed settings for inkjet printing JS-B25HV allowed the silver ink to bind strongly on the surface of the plastic substrate (figure 59 b). Electrical components used in the PPG sensor were small, but still bulky and non-flexible. Thanks to the small footprint of these components however, the final version of the sensor as shown in figure 59.c.c was bendable and flexible.
Opamp and LED were the largest parts of the PPG device (Figure 59.d). By bending the substrate 180 degrees, passive components were still able to remain attached and bound to the surface of the substrate. While connections of the Opamp were cracked and disconnected from the surface, the body of the Opamp was still attached and adhered on top of the substrate. This demonstrates the importance of using adhesive epoxy.

5.12.5. Encapsulation of PPG sensor

The PPG sensor was required to be protected from an uncontrolled amount of pressure applied on this sensor. Sylgard 184 is a Polydimethylsiloxane (PDMS), which is manufactured by Dow Corning. This ultra transparent silicon was used to encapsulate the PPG sensor. The PPG sensor was required to be protected from humidity and user contact as well. The thin layer of PDMS was therefore first vacuumed and then applied on top of each sensor. The sensor was then cured for two day in room temperature.

5.13. Application of PPG flexible sensor, detection of HRV

In order to evaluate the performance of the flexible sensor, PPG sensor was compared to a commercial pulse oximeter and an ECG. Two-minute data was recorded from five healthy subjects, with flexible PPG sensors and Nonin pulse oximeters located on the forehead side by side. PPG waveform was obtained from the flexible PPG sensor and commercial pulse oximeter in parallel to ECG.

A PPG anacrotic notch was used to evaluate the cardiac cycle. Complex QRS was identified with the same algorithm used for identification of the cardiac cycle form PPGs. An interval between peaks of PPG (P-P) and R-R of ECG was identified as full cardiac cycle. The time difference between a pair of cardiac cycles was measured as instantaneous heart rate. An automated algorithm was designed on matlab to detect instantaneous heart rate from PPGs and ECG automatically. The initial PPG waveform
from both sensors was fragmented into different frames. Initial constants such as maximum and minimum expected peak to valley values, maximum window size, and maximum or minimum window change were set.

5.13.1. **Detection of HRV from flexible PPG sensor**

The algorithm actively allocated a variable sized window to each frame. A peak detector was used to measure the peaks, valleys and the associated time index values, within each window frame. The size of the window was then varied based on initial window size, interval between the peaks and pulse width to frame ratio. The peaks, valleys and their time index of each window were padded in to a vector. The spontaneous heartbeat was then obtained by differentiating consecutive time index values. The initial ECG waveform was also fragmented into different frames. Since QRS height is larger than anacrotic pitch in PPG waveform, initial constants were adjusted differently than PPG. The rest of the algorithm remained the same as in the case of PPG. Pitches of R wave in ECG were automatically obtained.

5.13.2. **Results**

Heart rate variability was (HRV) obtained from flexible PPG, commercial PPG and ECG devices. In particular, two parameters were used for comparison; mean and standard deviation (SD).

This table demonstrates mean and standard deviation of instantaneous HR for ECG, PPG from commercial pulse oximeter and PPG obtained by flexible sensor.

In addition, bit-to-bit mean of heart rate from ECG was compared to bit-to-bit mean of heart rate from flexible PPG sensor. Absolute error was also estimated between ECG and PPG flexible and demonstrated in table 14.

These results confirm that HRV obtained from PPG flexible devices are similar to HRV of PPG obtained by commercial pulse oximeter. Absolute error obtained from comparison of PPG commercial to ECG and PPG flexible to ECG illustrate that flexible PPG sensors could be used as a main source of PPG signal for estimation of HRV, instead of commercial pulse oximeter.
Table 14. This table demonstrates mean square error and standard deviation of PPG obtained from flexible sensor to ECG and PPG from pulse oximeter.

<table>
<thead>
<tr>
<th>Test Subject</th>
<th>Mean ECG</th>
<th>SD ECG</th>
<th>Mean Nonin</th>
<th>SD Nonin</th>
<th>MSE PPG commercial and ECG</th>
<th>Mean Flexible</th>
<th>SD Flexible</th>
<th>MSE PPF flexible and ECG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test1x</td>
<td>0.09259</td>
<td>0.006559</td>
<td>0.09254</td>
<td>0.009981</td>
<td>0.0000000013</td>
<td>0.092684</td>
<td>0.008266</td>
<td>0.0000000044</td>
</tr>
<tr>
<td>Test2x</td>
<td>0.086563</td>
<td>0.007565</td>
<td>0.086849</td>
<td>0.0144</td>
<td>0.0000000409</td>
<td>0.088816</td>
<td>0.014906</td>
<td>0.0000025380</td>
</tr>
<tr>
<td>Test3x</td>
<td>0.087635</td>
<td>0.007656</td>
<td>0.087754</td>
<td>0.008067</td>
<td>0.0000000071</td>
<td>0.087949</td>
<td>0.010544</td>
<td>0.0000000493</td>
</tr>
<tr>
<td>Test4x</td>
<td>0.086584</td>
<td>0.005351</td>
<td>0.086373</td>
<td>0.006545</td>
<td>0.0000000223</td>
<td>0.092445</td>
<td>0.024378</td>
<td>0.0000171757</td>
</tr>
<tr>
<td>Test5x</td>
<td>0.09318</td>
<td>0.007777</td>
<td>0.093912</td>
<td>0.006901</td>
<td>0.0000002679</td>
<td>0.105995</td>
<td>0.036625</td>
<td>0.0000821121</td>
</tr>
</tbody>
</table>

The mean and standard deviation of beat-to-beat heart rate from ECG and beat-to-beat heart rate from PPG intervals were also analyzed by the Bland and Altman analysis. The corresponding 95% limits of agreement was estimated 0.034 to -0.01 for PPG flexible compared to ECG and 0.0081 to 0.0037 for PPG flexible to PPG commercial device.
According to figure 60, all data points were within upper and lower limits of Bland and Altman analysis. In conclusion, heart rate variability could also be obtained from flexible PPG sensors with high accuracy.

As demonstrated in figure 61, the morphological variations of the PPG from flexible sensors match the morphological variation of PPG from commercial pulse oximeter. Red dots in this figure represent the occurrence of anacrotic peaks in PPG waveform, which are synchronized in both PPG waveforms.

According to figure 61, the anacrotic pulse occurs at the same time in both PPGs, right after the QRS complex, and a little later than the R wave. Also, the catacrotic pulse occurs after the anacrotic pulse however this second pulse is missing in PPG obtained from commercial pulse oximeter.
In conclusion, a PPG circuit was designed and implemented using off the shelf components on the surface of a flexible PET. Diamatix was used as a tool for fabricating conductive lines on top of the PET. This technology was used to print schematics of PPG circuit and connect the passive components, photodiode and LED on the PET.

Consequently, I assessed feasibility of integrating a PPG circuit on flexible materials and used Diamatix technology for integration of components on the PET. The PPG device was used to obtain PPG signal from five healthy subjects. The similarity of PPG signal obtained from the prototyped PPG device was compared to commercial PPG and ECG device. For these propose, the algorithm presented in chapter three of this thesis was used to extract bit-to-bit heart rate. As presented in figures 62 and 63 the heart rates obtained from prototyped PPG device were compared to the ECG as well as ECG. The figure 62 demonstrates similarity of the heart rates obtained from flexible PPG device to ECG. Hence, most of the heart rates are within upper and lower levels of the analysis, which implies strong correlation between the heart rate obtained from the ECG and flexible PPG.

![Bland-Altman Plot Comparison of Beat to Beat HR from PPG Flex to ECG](image)

**Figure 62, demonstration of bit-to-bit heart rate obtained from prototype PPG device and ECG. The data belongs to the subject number four, and the duration of the test was one minute.**

In addition, as demonstrated in figure 63, bit-to-bit heart rates obtained from flexible PPG device were compared to the heat rates obtained from commercial PPG device. This analysis demonstrates strong similarity between two PPG signals. Hence, most of the heat bits are within upper and lower boundaries of the Bland and Altman analysis.
Figure 63, demonstration of bit-to-bit heart rate obtained from prototype PPG device and commercial PPG device. The data belongs to the subject number four, and the duration of the test was one minute.
6. Conclusion and future work

6.1. Contribution of author and collaborators

The contribution of the author was particularly focused on engineering aspects of the project rather physiological studies of the PPG signal. The AVR capnometer and Nonin Xpod were entirely developed and coded by the author alone. Next Moein Shayeggania and the author performed data acquisition via Biopac, AVR capnometer and Nonin Xpod. The algorithm proposed for extraction of respiration from the PPG signals on Labview was entirely developed and proposed by the author alone. In chapter three of the thesis PPG signal was studied during LBNP test and an algorithm was proposed to extract bit-to-bit heart rate and height of PPG signal. The author had collaborated with Dr. Tavakolian and Dr. Blaber for data acquisition. The protocol of the LBNP was designed by Dr. Tavakolian. Ethics were approved for Dr. Tavakolian, the author collaborated and collected PPG during LBNP and used this data for the study, which will be presented in this chapter. In addition, the algorithm used for extraction of PPG feature, was developed in collaboration with Dr. Paul Linder. The author and Moein Shayegannia were in communication with Dr. Linder. He recommended the methodology for implementing the algorithm. Hence the author and Moein Shayegannia implemented and coded Dr. Linder’s recommendation on matlab. During chapter four of the thesis, the PPG circuit was entirely developed and designed by the author. The author also printed schematic of the PCB circuit on PET using Diamatix inkjet printing technology, entirely by himself. Also off the shield passive and active components were entirely implemented by the author on surface of flexible materials. At last, the process of testing and extracting heart rate from the flexible PPG sensor, and comparison of performance of this device to commercial PPG and ECG devices were entirely performed by the author.

Finally, the author thanks Dr. Tavakolian, Dr. Blaber, Dr. Linder and Moein Shayegannia for their contribution into this research.
6.2. Conclusion

During this research the PPG signal was evaluated as an alternative method for heart and respiration rates monitoring.

PPG signal was studied to assess detection of critical condition. A critical condition was defined as a medical condition in which a person is unable to continue daily routine. In particular, PPG was examined for detection of acute failure of cardiovascular and pulmonary activity. It was proven that respiration and heart rate could be obtained from a single PPG node (Objective #1).

Feasibility of PPG implantation on a mobile platform was then examined. An appropriate hardware modulation of PPG sensors for continuous vital sign monitoring was developed. It was shown that heart rate, Spo2 and PPG could be reliably acquired from the forehead and the finger synchronously. (Objective #2)

The complexity and accuracy of an algorithm for respiration monitoring from PPG were hereafter evaluated. In particular, PPG was assessed for respiration rate monitoring at controlled and uncontrolled (0.2Hz, 0.3Hz and normal) breathing paces on healthy subjects. It was concluded that respiration rate could be detected with high accuracy. (Objective #3.1)

PPG was also investigated for detection of progressive hemorrhage on four human subjects. In particular, morphological variation of PPG waveform was studied during Lower Body Negative Pressure tests. It was proven that the hypodynamic response of the human body to reduction of stroke volume (<40%) causes significant reduction in the height of PPG. (Objective #3.2)

In addition, an algorithm was designed and tested for identification of hypovolemic response of PPG waveform. In particular, the presyncopal state of four healthy subjects was identified by PPG. Using this algorithm, the variation in height of
PPG, ECG and Arterial Blood Pressure (ABP), was identified. It was validated that presycope occurs in PPG before ECG or ABP. (Objective #4)

Furthermore, a new proof-of-concept device was designed for the acquisition of PPG. In particular, this new design was integrated with mechanically flexible materials. Using Diamatix inkjet printing technology, a PPG sensor was implemented on flexible materials. It was demonstrated that this sensor is capable of obtaining PPG waveform. (Objective #5)

In the end, performance of the flexible polymer integrated PPG sensor was studied. In particular, the PPG device was tested for heart rate acquisition. HRV was obtained from the flexible PPG device in addition to commercial PPG sensor and ECG. It was demonstrated that the PPG waveform obtained by the flexible device matches commercial PPG sensors. It was also shown that HRV could be detected from flexible sensors with high accuracy. (Objective #5.1)

6.3. Future work

Performance of the PPG for wearable vital mentoring is mostly limited to three factors; motion artifact, mechanical flexibility and complex physiology of human body.

Motion artifact: Findings of this thesis were in parallel to the statement of Russel [198]. PPG reliability is diminished in the presence of physical activity. To increase the quality of PPG acquisition, a mechanical design must be investigated to adhere the flexible sensor on skin. In addition, an ideal solution must consider user comfort. Studies that focus on mechanical solutions that secure the PPG sensor on easy accessible sites such as the forehead are therefore recommended.

Complex Physiology of human body: The human body is a complex system. During progressive hypovolemia, the hypodynamic response of the body to the reduction of stroke volume was studied during LBNP. During actual haemorrhage, however, additional physiological parameters also affect the hypodynamic response, such as pain and stress. The effects of pain and stress therefore also need to be investigated in further detail.
Finally, a proof-of-concept device was designed in this thesis to assess feasibility of integrating a PPG sensor using Inkjet printing technology on flexible materials. However, prior to prototyping the device, the desirable degree of flexibility must be investigated and a threshold must be defined between user comfort and practicality of the sensor.

6.4. Limitation of flexible PPG device

At last, the technology introduced in this thesis contains certain limitations. The device was implemented using inkjet-printing technology, this method is slow in comparison to screen-printing technology, and one could observe that fabrication of a PCB sketch on conductive layer of polymer using alternative technology improves the speed of integrating.

The prototype PPG device was tested on forehead of 5 subjects during LBNP. It was concluded that termination of LBNP was detectable by continuous monitoring of PPG height. However, one could consider locating the PPG sensor in areas of body with more arterial blood vessels. This increases the quality of the PPG acquisition due to significant amount of the oxygenated hemoglobin under the tissue.

The wavelength used for this application was particularly chosen to evaluate possibility of using photovoltaic cells instead of photodiode. As mentioned in this thesis, the performance of the photovoltaic cells is limited to the lifetime of the cells. Hence it was proposed to evaluate the 530 nm because the photovoltaic cells are most stable in this range of wavelength. One could consider replacing this wavelength with red LED (640 nm) or IR (940 nm). These wavelengths are considered a reliable light for acquisition of pulse oximetry so the secure better quality of PPG in comparison to green light.

Furthermore, the LBNP was applied on three male subjects and one female. One could consider the limited number of the subjects and unbalanced gender of participates. Response of women to LBNP differs from men. During our experiment, the female subject lasted more than males in the LBNP test. She completed the experiment but male subjects experienced nausea and dizziness before termination of the experiment,
which resulted to termination of the test. Also, the PPG signal was also observed from forehead and finger, one could consider other sites of the human body in addition to these two sites, such as ear and elbow.
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Appendix A.

“C” Code for extraction of CO2 from CO2 sensor via Atmel’s microchip

```c
#include <SoftwareSerial.h>
SoftwareSerial mySerial(3, 2); // RX, TX
#include <LiquidCrystal.h>
LiquidCrystal lcd(12, 11, 8, 7, 6, 5);
int i=0;
int k=0;
byte CO2;
char array[10];
int j=0;
uint8_t buffer[25];
uint8_t ind =0;
String val= ""; //holds the string of the value
double co2 =0; // holds the actual value
int co2ForLabview =0;
double multiplier = 10; //each range of sensor has a different value. //upto2%--1

void setup ()
{
    Serial.begin(9600);
    mySerial.begin(9600);
}

void loop() {

    while(buffer[ind-1] != 0x0A)
    {
        if(mySerial.available()) {
            buffer[ind] = mySerial.read();
            ind++; }
    }
```
report(); //Once we get the '0x0A' we will report what is in the buffer

void report() {
    double multiplier = 10; //each range of sensor has a different value. //upto2%=1
    int kian=0;
    for(int i=0; i < ind+1; i++)
    {
        if(buffer[i] == 'z') //once we hit the 'z' we can stop
            break;

        if((buffer[i] != 0x5A)&&(buffer[i] != 0x20)) //ignore 'Z' and white space
        {
            //Serial.println(kian);
            val += buffer[i]-48;
        
            kian++;
        
        } //END OF FOR LOOP
    co2 = (multiplier * val.toInt());
    Serial.println(val);
    // Serial.println(buffer[i], HEX);
    // Serial.println(kian);

    lcd.clear();
    lcd.setCursor(0, 0);
    lcd.print("co2");
    lcd.setCursor(6, 0);
    lcd.print(co2);
    ind=0; //Reset the buffer index to overwrite the previous packet
    val=""; //Reset the value string
}


Appendix B.

“Processing” Code for acquisition of CO2 from Arduino and demonstration of respiration curve graphical format.

```java
import processing.serial.*;
Serial port;
int Sensor;
int sample=0;
int xPos=0;
PrintWriter output;

int time;
void setup()
{
  size(1000, 1500);
  // GO FIND THE ARDUINO
  println(Serial.list());    // print a list of available serial ports
  // choose the number between the [] that is connected to the Arduino
  port = new Serial(this, Serial.list()[1], 9600);  // make sure Arduino is talking serial at this baud rate
  port.clear();            // flush buffer
  port.bufferUntil('
'); // set buffer full flag on receipt of carriage return
  output = createWriter("test2.csv");
/* beginShape();
  vertex(30, 40);
  vertex(250, 40);
  vertex(250, 100);
  vertex(30, 100);
endShape(CLOSE);*/
}
void draw()
{
  time  = millis();
  //output.println("CO2="+","+Sensor+","+"Time="+time+","+"samples#="+sample+"n");
```
print("CO2=",Sensor,"\n"+"Time=",time,"\n"+"Sample=",sample); output.println(Sensor);
{
    /*beginShape();
        vertex(30, 40);
        vertex(250, 40);
        vertex(250, 100);
        vertex(30, 100);
        endShape(CLOSE);
    */
}

void serialEvent(Serial port){
    String inData = port.readStringUntil("\n");
inData = trim(inData); // cut off white space (carriage return)
Sensor = int(inData); // convert the string to usable int
println(Sensor);
sample++;

//DRAW GRAPH
float inByte = float(Sensor);
inByte = map(inByte, 0, 3000, 0, height);
// draw the line:
stroke(127,34,255);
line(xPos, height, xPos, height

if (xPos >= width) {
    xPos = 0;
    background(255);
}
else {
    xPos++;
}
}

void keyPressed(){
    switch(key){
        case 's': // pressing 's' or 'S' will take a jpg of the processing window
case 'S':
  output.flush(); // Writes the remaining data to the file
  output.close(); // Finishes the file
  exit(); // Stops the program
}