# Selected cardiovascular studies based on photoplethysmography technique

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Ph D Thesis submitted to
Cochin University of Science and Technology
In partial fulfillment of the requirements for the
Degree of Doctor of Philosophy

January, 2009

**Selected cardiovascular studies based on photoplethysmography technique**
*Ph D Thesis in the filed of Photonics*

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January 2009

**Front cover** : Recording of PPG signal using the developed hardware setup

*Dedicated to*

*My family*

## CERTIFICATE

Certified that the research work presented in the thesis entitled "***Selected cardiovascular studies based on photoplethysmography technique***" is based on the original work done by Smt. Jayasree V.K under my guidance and supervision at the International School of Photonics, Cochin University of Science and Technology, Cochin–22, India and has not been included in any other thesis submitted previously for award of any degree.

Cochin – 682022
21st January 2009

Dr. P Radhakrishnan
(Supervising Guide)

## DECLARATION

Certified that the work presented in the thesis entitled " ***Selected cardiovascular studies based on photoplethysmography technique***" is based on the original work done by me under the guidance and supervision of Dr. P Radhakrishnan, Professor, International School of Photonics, Cochin University of science and Technology, Cochin – 22, India and has not been included in any other thesis submitted previously for the award of any degree.

Cochin 682022 Jayasree V.K

21st January, 2009

## ACKNOWLEDGEMENTS

With deep sense of gratitude, I express my heartfelt thanks to Prof. P. Radhakrishnan for the guidance, motivation, support and encouragement given throughout my research work.

I am extremely thankful to Prof. V. P. N. Nampoori for his valuable support, inspiration and help without which this work would not have materialized.

I sincerely thank Prof. C.P. Girijavallabhan for his help and support. I am equally thankful to Prof. V.M. Nandakumaran for his encouragement. I also acknowledge Mr. M. Kailasnath.

I owe much to Dr Biju Raju of Ranjini Eye care , Vyttila who provided me the facility for recording the photoplethysmography signals of diabetics. I remember with gratitude the hospitality and help extended to me during my visit to the clinic from the staff there.

I convey my indebtedness and sincere thanks to Ms Shaija P J of Model Engg college, Thrikkakara and Ms Sandhya T V of College of Engg , Munnar who were like two strong pillars supporting me throughout the period of my research. I remember with gratitude Muralichettan of Instrumentation department who helped me in fabricating the sensor head.

I am thankful to all the research scholars of ISP for their constant support and help. They made me feel young at heart and I cherish the wonderful moments I had with Lyjo, Parvathy, Thomas, Nithyaja, Linesh, Litty, Sony, Sudheesh, Murali, Tintu, Sreelekha, Manu, Mathew, Sithara, Saritha, Misha, Vasuja, Sheeba, Jijo, Dann, Rajesh M, Rajesh S and Shanthi. The love and support from my contemporaries Sr. Ritty and Samuel Varghese is hereby acknowledged. I convey my sincere thanks to Prabhathan P of Nanyang Technological University, Singapore for helping me in getting all the reference papers in time.

I am extremely thankful to Dr Geetha K who helped me a lot during the final stages of my thesis writing. At this juncture I would also like

to thank Aneesh of CELOS who helped me in designing the cover page.

I extend my sincere thanks to the non-teaching staff of ISP for all the help and assistance.
The sponsorship from IHRD to pursue the research programme is greatly acknowledged.

In this moment, I would like to remember all the staff of Model Engg college, who in some way or the other helped me and supported me.

I am extremely greatful to my siblings who were a constant source of encouragement. There are no words to express gratitude to my parents who have always guided me, especially when I felt desperate. I am greatly indebted to my mother-in-law who always showed concern for my research and prayed for me.

I don't know how to thank properly my husband Unniettan and my loving daughters Lakshmi & Paru whose encouragement and support helped me in the successful completion of this work. It was a herculean task for me managing both home and research, and it was because of their patience and tolerance that I was able to complete my work.

Last, but most important of all, I thank ***Almighty God***

Jayasree V.K

# Preface

Photoplethysmography (PPG) is a simple and inexpensive optical technique that can be used to detect blood volume changes in the microvascular bed of tissues. With the advancement in optical technology, noninvasive assessment of cardiovascular functions by the peripheral arterial pulse has gained substantial research and clinical interest and PPG is one such technique which has gained popularity during recent decades.

Photoplethymographic signal characteristics have been studied to identify vascular diseases. There has been a resurgence of interest in the technique in recent years, driven by the demand for low cost, simple and portable technology for the primary care and community based clinical settings and the wide availability of low cost and small semiconductor components, and the advancement of computer-based pulse wave analysis techniques. The PPG technology has been used in a wide range of commercially available medical devices for measuring oxygen saturation, blood pressure and cardiac output, assessing autonomic function and also detecting peripheral vascular diseases. PPG being a noninvasive technique has its own attraction when compared to other expensive invasive methodologies used for cardiovascular diagnostics.

The basic PPG waveform comprises of a pulsatile (‘AC’) physiological waveform attributed to cardiac synchronous changes in the blood volume with each heart beat, and is superimposed on a slowly varying (‘DC’) baseline with various lower frequency components attributed to respiration, sympathetic nervous system

activity and thermoregulation. With suitable signal processing techniques the AC and DC components of the PPG signal can be extracted and used for further pulse wave analysis. In the studies reported here the signals were acquired using an indigenously developed hardware setup.

The thesis presented in seven chapters deals with the work involved in the design, development of a sensor probe head and some selected studies on the PPG signals using definite protocols for noninvasive diagnostics.

**Chapter 1** gives an insight into the principle of Photoplethysmography and the different modalities used in this technique. The interaction of light with tissue, early and recent history of PPG, instrumentation, measurement protocol and pulse wave analysis are also discussed. The last part of the chapter focuses on the applications of PPG in clinical physiological measurements, including clinical physiological monitoring , vascular assessment and autonomic function.

**Chapter 2** elaborates on the design, development and characterization of a high sensitivity , low power, low cost sensor for detecting the blood volume pulse using transmission mode PPG from the finger tip for short term monitoring. The mechanical design aspects of the sensor head and material selection for the same are also discussed. A typical application of this sensor head in implementing a heart rate meter using a microcontroller is also explained . A comparison of the performance of the developed sensor with a commercial equipment is

also included. The denoising of the recorded PPG signals using wavelet transform is briefly outlined towards the end of the chapter.

**Chapter 3** deals with age related studies using the PPG signal and its second derivative(SDPPG). Age – related changes in the PPG pulse shape characteristics can yield valuable diagnostic information about the cardiovascular system. This chapter is devoted to the noninvasive studies of the systolic and diastolic characteristics of the resting peripheral volume pulse using a normalized mean pulse as a function of age. The second derivative of the PPG signal has also been used to derive a parameter related to the distensibility of large arteries.

**Chapter 4** is based on the investigations carried out on the PPG signals after local mild cold exposure. The cold exposure test is often used to assess vasoconstrictive responses because it simulates the vasoconstrictive conditions commonly encountered in the clinical setting. Cold exposure is likely to introduce vasoconstriction and increased peripheral resistance as a result of which the PPG waveform will change owing to the alteration in vascular wall properties and pulse wave reflection. This chapter gives an insight into a few new parameters that could be derived from the finger PPG signal during the cold exposure test. The morphological features used in this study allow the detection of changes in the pulse characteristics by monitoring how the shape of individual cardiac pulses change with time. The parameters studied include the normalized pulse width, skin vasomotor reflex, half width amplitude, area index, and the latency between the systolic and the diastolic peaks.

**Chapter 5** describes the variations observed in the Photoplethysmographic waveform due to positional changes of the lower limbs during the recording of the PPG signals. Certain parameters have been derived from spontaneously breathing subjects using Passive leg raising (PLR) which is a reversible maneuver that can mimic rapid fluid loading (FL). Photoplethysmograhic assessment of the haemodynamic variations using the pulsatile tissue blood volume due to the position of the lower limb height seems to follow the theory of basic blood flow dynamics.

**Chapter 6** deals with the studies carried out on the characteristics of PPG signals of non – diabetics and diabetics affected by retinopathy. A measure of the right – left correlation coefficient for the diabetics based on the PPG amplitude was determined and it has been found that this parameter is low compared to that of normal subjects and also less dependent on age. Statistical signal processing approach was also used to confirm this result. The second derivative of the photoplethysmogram (SDPPG) has been used to derive a parameter that is closely related to the distensibility of large arteries. From the studies conducted , we have found that this parameter is lower for age matched diabetic subjects when compared with normals.

Summary and conclusions of the work carried out are given in **chapter 7**

**List of Publications - International journal**

1. **Jayasree V.K**, Shaija P.J, Manu P.John, P. Radhakrishnan, " An optoelectronic sensor configuration for the determination of age related indices using blood volume pulse sensor" , Sensors & Transducers Journal, vol.87, Issue 1, January 2008
2. **Jayasree V.K,** Shaija P.J**,** V.P.N Nampoori, C.P.G Vallabhan**,** P.Radhakrishnan "A simple and novel integrated Opto electronic system for Blood Volume Pulse sensing and Heart rate monitoring" in the International Journal of Optomechatronics, 1; 392- 403, October 2007.
3. **Jayasree V.K,** Sandhya T.V, Radhakrishnan P " Non-invasive Studies on Age related parameters using a blood volume pulse sensor", Measurement Science Review, Vol 8, Section 2, No 4, 2008,82-86.
4. Shaija P J, **Jayasree V K**, Radhakrishnan P " Development of a noninvasive blood volume pulse sensor for determining the arterial pulse wave velocity", communicated to Sensors & Transducers journal.
5. Ritty J. Nedumpara, Thomas K.J, **Jayasree V.K**, C.P Girijavallabhan, V.P.N.Nampoori & P.Radhakrishnan, "Study of solvent effect in laser emission from Coumarin 540 dye solution", *Applied Optics/ vol.46/ No.21/ 20 July 2007.*

**International conference :**

1. **Jayasree V.K,** Sandhya T V, Shaija P J, Radhakrishnan P "Photoplethysmographic assessment of Skin Vasomotor Reflex using the blood volume pulse measured at the finger tip" , *Proceedings of the International Conference Photonics 2008,* IIT Delhi, December 13-17, 2008.
2 Sandhya T V, **Jayasree V .K**, Shaija P J, Radhakrishnan P "Studies on the effects of air pollutants on the peripheral blood volume pulse using an optical plethysmograph", in the *Proceedings of the International Conference Photonics 2008,* IIT Delhi, December 13-17, 2008.
3. Shaija P.J, **Jayasree V.K**, P.Radhakrishnan "Blood Volume Pulse Sensor using peripheral pulse detected in the Finger tips with Photoplethysmograph and Assessment of Bilateral Symmetry" in the International Conference on Sensors and Related Networks, VIT University, 10 to 14 December 2007, Vellore, Tamilnadu, India.
4. **V.K.Jayasree**, M.G.Mini, V.P.N Nampoori , P.Radhakrishnan, "Wavelet based denoising of Photoplethysmographic signals", *Proceedings of the International Conference Photonics 2006,* Hyderabad, India., December 13 – 16, 2006 .
5. **V.K. Jayasree**, V.G. Sreeja, M.Kailasnath, P. Radhakrishnan, " Fiber optic evanescent wave carbohydrate sensor", *Proceedings of the Eigth International conference on*

*Optoelectronics, Fiber optics and Photonics*, **Photonics 2006** held at Hyderabad in December 2006.

6. **V.K. Jayasree**, P. Radhakrishnan, " PIC microcontroller based Heart rate meter using the blood volume pulse sensor", *Proceedings of the Eigth International conference on Optoelectronics, Fiber optics and Photonics*, **Photonics 2006** held at Hyderabad in December 2006.
7. **V .K Jayasree**, C.P.G Vallabhan, V.P.N Nampoori, P.Radhakrishnan, " Design and development of a simple hardware setup for sensing blood volume pulse and a PIC microcontroller based heart rate meter", Proceedings of the International conference on Biomedical & Pharmaceutical Engg, ICBPE 2006 held at Singapore from 11-14$^{th}$ December, 2006.

**National conference/ seminar/symposium:**

1. **Jayasree V.K**, Sandhya T V, Shaija P J, Radhakrishnan P "Assessment of skin microcirculation using Photoplethysmographic signal measured at the finger tip employing cold exposure test", *All India Seminar on emerging trends in information and communication technology"*, August 29 to 30, 2008.
2. Sandhya T V, **Jayasree V K**, Shaija P J, Radhakrishnan P, " Statistical signal processing approach to assess bilateral symmetry of blood volume pulse recorded at the finger tip using an optoelectronic configuration", *All India Seminar on emerging*

*trends in information and communication technology"*, August 29 to 30, 2008

3. Shaija P.J**, Jayasree V.K,** P. Radhakrishnan "Non-Invasive Pulse WaveVelocityMeasurement System Using Optical Plethysmograph" National Seminar on Information, Communication & Intelligent systems at Cochin on 8th & 9th February 2008.
4. Nithyaja B, **Jayasree V.K,** Lyjo k joseph, V.P.N Nampoori, " Studies on the time dependence of Nonlinear optical properties of Deoxyribonucleic acid (DNA) using Z-scan technique", National Laser Symposium, held at M.S. University of Baroda, Vadodara, Gujarat during December 17 to 20, 2007.
5. Linesh J, **Jayasree V.K,** Beena K.S, V.P.N Nampoori, " Optical fiber based sensor to study clay consolidation", National Laser Symposium, held at M.S. University of Baroda, Vadodara, Gujarat during December 17 to 20, 2007.
6. **Jayasree V.K,** Shaija P.J**,** P. Radhakrishnan "Age related Index measurement from Peripheral pulse wave detected using Finger tip Photoplethysmograph" in the National Laser Symposium, held at M.S. University of Baroda, Vadodara, Gujarat during December 17 to 20, 2007.

## Contents

# *Chapter 1*

# *Photoplethysmography and its application in clinical physiological environment - An overview*

**Abstract**

Photoelectric plethysmography, also known as photoplethysmography (PPG) or optical plethysmography, is a non-invasive optical method to detect cardio-vascular pulse wave that propagates through the body . This chapter gives an overview of the basic principle of PPG operation, early and recent history of PPG, instrumentation, measurement protocol and pulse wave analysis. A brief discussion on the current and potential applications of PPG in physiological measurements is also included in this chapter. Towards the end of the chapter, the main objective of the research work carried out is highlighted.

## 1.1 INTRODUCTION

Photoplethysmography (PPG) is an optical measurement technique that can be used to detect blood volume changes in the microvascular bed of a tissue(1). The basic form of PPG technology requires only a few opto-electronic components: a light source to illuminate the tissue (e.g. skin), and a photodetector to measure the small variations in light intensity associated with changes in perfusion in the catchment volume. PPG is most often employed non-invasively and operates in the red region or in the near infrared region. The most recognized waveform feature is the peripheral pulse, and it is synchronized to each heartbeat. Despite its simplicity the origins of the different components of the PPG signal are still not fully understood. It is generally accepted, however, that they can provide valuable information about the cardiovascular system (2). There has been a resurgence of interest in the technique in recent years, driven by the demand for low cost, simple and portable technology for the primary care and community based clinical settings, the wide availability of low cost and small semiconductor components, and the advancement of computer-based pulse wave analysis techniques (3). The PPG technology has been used in a wide range of commercially available medical devices for measuring oxygen saturation, blood pressure and cardiac output, assessing autonomic function and also detecting peripheral vascular diseases.

## 1.2 THE PHOTOPLETHYSMOGRAPHY WAVEFORM

The PPG waveform comprises of a pulsatile ('AC') physiological waveform attributed to cardiac synchronous changes in the blood volume with each heart beat, and is superimposed on a slowly varying ('DC') baseline with various lower frequency components attributed to respiration, sympathetic nervous system activity and thermoregulation (4- 17). These characteristics are also site dependent (18). The AC and DC components of the PPG signal can be extracted with suitable filtering and amplification and subsequently used for pulse wave analysis.

The pulsatile component of the photoplethysmographic signal is supposed to contain clinically valuable information on the blood pumping and transport conditions in the living body. It has been suggested as a measure of skin perfusion, a way to monitor heart rate and respiratory rate as well as respiratory volumes (19). The AC component of the signal has also been used for studying the peripheral vascular compliance as well as the large artery compliance which may be an important indicator of various cardiovascular diseases, such as hypertension (20). A typical PPG waveform showing the AC and DC components is shown in fig 1.1. The PPG waveform is formed due to wave transmission and reflection which is illustrated in fig 1.2. The first part of the volume waveform in the finger is the result of pulse transmission along a direct path from the aortic root to the finger. The

second part is formed by the pulse transmitted from the aortic root to the lower body where it is reflected back along the aorta and subclavian artery to the finger. The time delay between the first and second peak is determined by the transit time of the pressure pulse from the root of the subclavian artery to the apparent sight of reflection and back to the subclavian artery. The height of the second peak relates to the amount of pressure wave reflection. This in turn relates mainly to the tone of small arteries. When the second peak is absent then the point of inflection in the down-slope of the waveform is used.

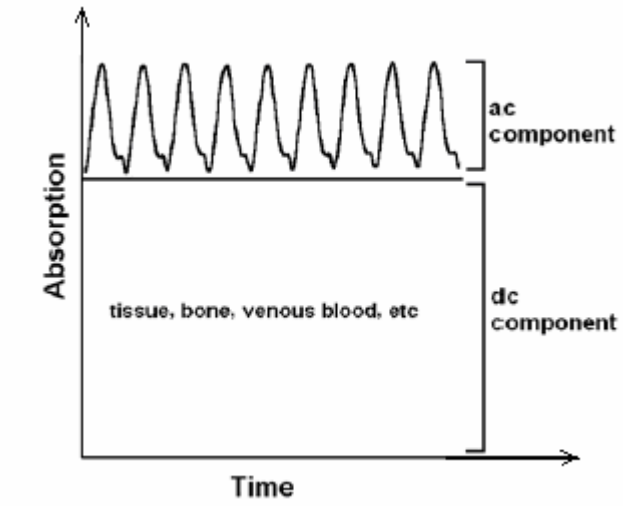


Fig 1.1: Typical PPG waveform showing the 'AC' and 'DC' components

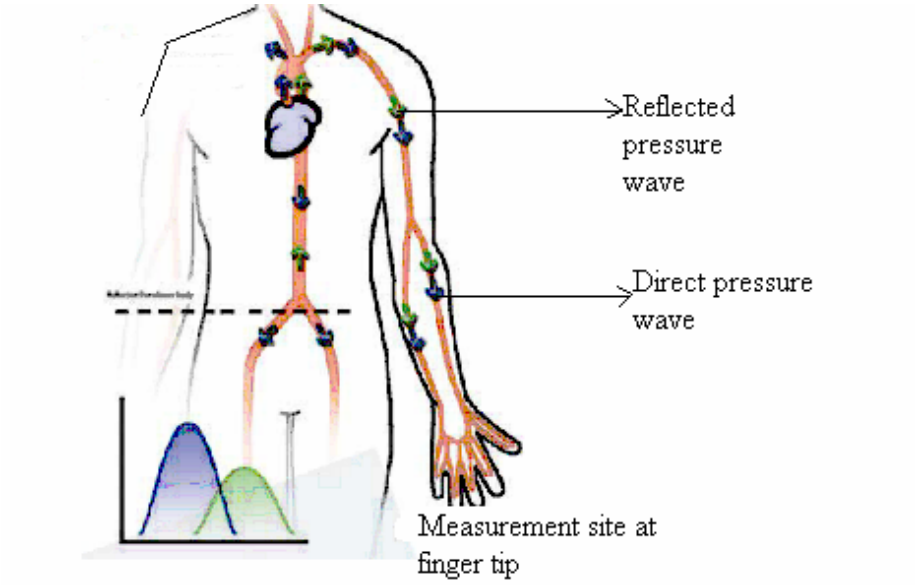


Fig 1.2: Diagram illustrating wave transmission and reflection

## 1.3 OPTICAL CONSIDERATIONS OF THE ORIGINS OF THE PHOTOPLETHYSMOGRAPHY WAVEFORM

The interaction of light with biological tissue is complex and it includes the optical processes of (multiple) scattering, absorption, reflection, transmission and fluorescence (21). Several researchers have investigated the optical processes in relation to PPG measurements (1,2, 22-31) and have highlighted the key factors that can affect the amount of light received by the photodetector: the blood volume, blood vessel wall movement and the orientation of red blood cells (RBC). The orientation effect has been demonstrated by recording pulsatile waveforms from dental pulp and in a glass tube where

volumetric changes should not be possible, and more recently pulsatile waveforms have been detected in bone (32). The recorded pulses do bear a direct relationship with perfusion, and the greater the blood volume the more the light source is attenuated. However, attempts at pulse amplitude quantification (‘calibration’) have been largely unsuccessful (33-36). The wavelength of optical radiation is also important in light–tissue interactions (37), for three main reasons: (1) *The optical water window*: the main constituent of tissue is water that absorbs light very strongly in the ultraviolet and in the longer infrared wavelengths. The shorter wavelengths of light are also strongly absorbed by melanin. There is, however, a window in the absorption spectra of water that allows visible (red) and near infrared light to pass more easily, thereby facilitating the measurement of blood flow or volume at these wavelengths. Thus, the red or near infrared wavelengths are often chosen for the PPG light source (38), (2) *Isobestic wavelength*: significant differences exist in absorption between oxyhaemoglobin (HbO2) and reduced haemoglobin (Hb) except at the isobestic wavelengths (39). For measurements performed at an isobestic wavelength (i.e. close to 805 nm, for near infrared range) the signal should be largely unaffected by changes in blood oxygen saturation, and (3) *Tissue penetration depth*: the depth to which light penetrates the tissue for a given intensity of optical radiation depends on the operating wavelength (40).

## 1.4. EARLY AND RECENT HISTORY OF PHOTOPLETHYSMOGRAPHY

.In 1936 Molitor and Kniazuk were the first to describe the recordings made with a reflection mode PPG system from human fingers. A pioneer who helped establish the PPG technique was Alrick Hertzman from the Department of Physiology at St. Louis University School of Medicine, St. Louis, MO. In 1937, Hertzman and his colleagues published their first paper on PPG describing the use of a reflection mode system to measure blood volume changes in the fingers induced by the Valsalva manoeuvre, exercise and with exposure to cold. This excellent contribution to the field demonstrated the potential clinical utility of the technique. In 1938, Hertzman undertook a validation of the PPG technique by comparing blood volume changes with those measured simultaneously by mechanical plethysmography. Preliminary observations on the PPG technique were also reported in the same year by Matthes and Hauss. Hertzman and Dillon (41) split theAC and DC components with separate electronic amplifiers and monitored vasomotor activity. Potential sources of error with the technique have been identified by Hertzman (33), who emphasized that good contact with skin was needed, but without excessive pressure that would result in blanching. He advised that movement of the measurement probe against the skin should be avoided. These observations led to the development of elaborate positioning devices. Illumination was identified as another important design consideration. Hertzman also used a battery powered torch bulb which was less than ideal because of its relatively wide spectrum, particularly in the infrared because of

local tissue heating, errors due to the effects of oxygen saturation, and the widespread illumination which can mix skin microvascular blood flow with larger vessel signals. Furthermore, constant light intensity could not be guaranteed. In more recent decades the desire for small, reliable, low-cost and simple-to-use noninvasive (cardiovascular) assessment techniques were the key factors that have helped re-establish photoplethysmography. Advances in opto-electronics and clinical instrumentation have also significantly contributed to its advancement. The developments in semiconductor technology, i.e. light emitting diodes (LED), photodiodes and phototransistors, have made considerable improvements in the size, sensitivity, reliability and reproducibility of PPG probe design. A major advance in the clinical use of a PPG-based technology came with the introduction of the pulse oximeter as a non-invasive method for monitoring patients' arterial oxygen saturation (42,43). There have also been considerable developments in computer-based digital signal processing and pulse wave analysis..

## 1.5. PHOTOPLETHYSMOGRAPHY INSTRUMENTATION

Modern PPG sensors often utilize low cost semiconductor technology with LED and matched photodetector devices working at the red and/or near infrared wavelengths (44,45) . The choice of light source is important (46,47,48). LEDs convert electrical energy into light energy and have a narrow single bandwidth (typically 50 nm). They are compact, have a very long operating life ($>10^5$ hours), operate over a

wide temperature range with small shifts in the peak-emitted wavelength, with small shifts in the peak-emitted wavelength, and are mechanically robust and reliable. The averaged intensity of the LED should be constant and preferably be sufficiently low to minimize excessive local tissue heating and also to reduce the risk of a non-ionizing radiation hazard. The choice of photodetector is also important and its spectral characteristics are chosen to match with that of the light source (49,50). A photodetector converts light energy into an electrical current. They are compact, low-cost, sensitive, and have fast response times. Near infrared devices can be encased with daylight filters. The photodetector connects to a low noise electronic circuitry that includes a transimpedance amplifier and filtering circuitry. A high pass filter reduces the dominant DC component and enables the pulsatile AC component to be boosted to a nominal 1 V peak-to-peak level. Carefully chosen filtering circuitry is also needed to remove the unwanted higher frequency noise such as electrical pick up from (50 Hz) mains . Figure 1.3(a) shows a transimpedance amplifier design and figure 1.3(b) shows the signal conditioning stages surrounding this, including low pass filtering, high pass filtering and further amplification, signal inversion and signal interface. The choice of high pass filter cut-off frequency is particularly important and is often a design compromise; excessive filtering can distort the pulse shape but too little filtering can result in the quasi-DC component dominating over the AC pulse (51,52).

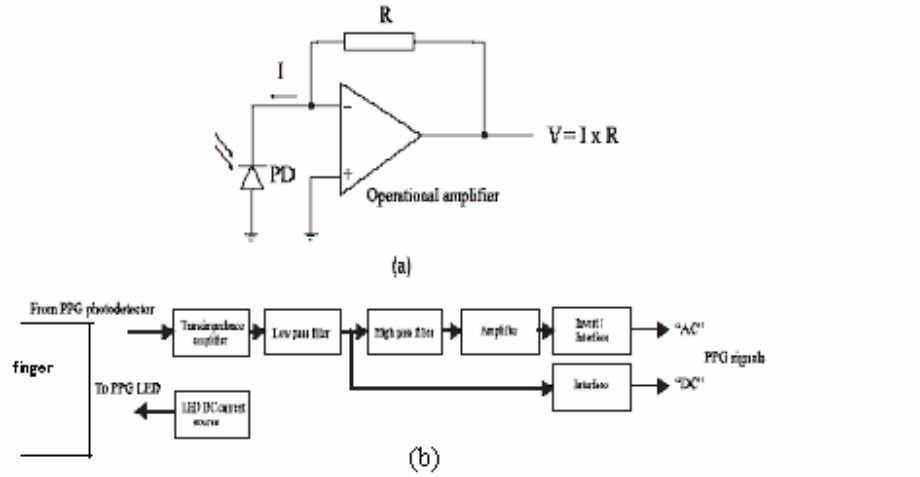


Fig 1.3: Electronic building blocks used in a typical PPG measurement system (a) A transimpedance (current-to-voltage) amplifier stage that converts light intensity at the photodiode (PD) to an amplifier output voltage ($V = I \times R$, transimpedance gain proportional to feedback resistor value $R$). (b) The signal conditioning stages surrounding the transimpedance amplifier

There are two main PPG operational configurations: transmission ('trans-illumination') mode operation where the tissue sample (e.g. fingertip) is placed between the source and the detector, and reflection ('adjacent') mode operation where the LED and the detector are placed side-by-side. Figure 1.4 shows the arrangement of photodiode and the LED in the two configurations. Clearly, transmission mode PPG imposes more restrictions than the reflection mode PPG on the body locations available for study. The PPG probe should be held securely in place to minimize probe-tissue movement artefact. There are other

sources of artefacts that need to be considered in the measurement technology. For example, artefact can arise from ambient light interference which can be reduced in several ways: by suitable probe attachment to the skin (e.g. using a dark Velcro wrap-around cuff), by further shading of the study site area and performing measurements in subdued lighting, and by electronic filtering (45,53).

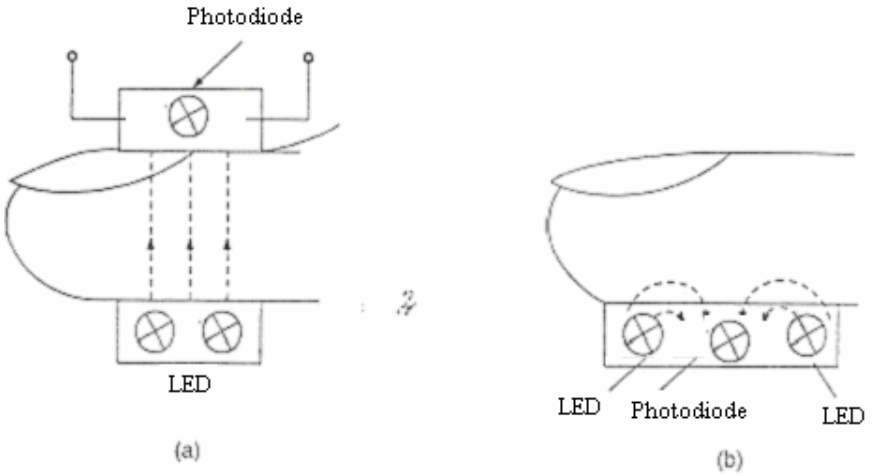


Fig 1.4: Arrangement of photodiode and LED in a PPG probe (a) Transmission method (b ) Reflection method.

Many of the studies reported in the PPG literature are for a single site, often the ear, finger or toe, where pulses can easily be detected (54-63). .Other sites of measurement have also been mentioned ( 64,65). There have also been studies published which investigated PPG pulses at two sites simultaneously (17,66-73). Multichannel PPG acquisition systems have also been reported either for individual PPG data measurements or for simultaneous multi-bilateral site PPG data measurements (i.e.

the right and left ear lobes, index fingers or thumbs, and great toes) (74-81). The importance of the electrical and optical matching of pulse amplifier chanels to allow the right-left side physiological differences to be detected with confidence has also been emphasized (79).

Other emerging technologies include PPG imaging technology, telemedicine and remote monitoring (82-84). PPG has considerable potential for telemedicine including the remote/home health monitoring of the patients. Miniaturization, ease of use and robustness are key design requirements for such systems and this has been illustrated in the design of finger-ring based sensors ( 85-87).

## 1.6. PHOTOPLETHYSMOGRAPHY PULSE WAVE CHARACTERIZATION AND ANALYSIS

### 1.6.1 Pulse wave characterization

Two important characteristics of the PPG AC pulse waveform were described by Hertzman and Spealman (88). The appearance of the pulse was defined as two phases: the anacrotic phase being the rising edge of the pulse, and the catacrotic phase being the falling edge of the pulse. The first phase is primarily concerned with systole, and the second phase with diastole and wave reflections from the periphery. A dicrotic notch is usually seen in catacrotic phase of subjects with healthy compliant arteries. It is also useful to consider the blood pressure pulse and its propagation along individual arteries. The pressure wave pulse is known to change in shape as it moves toward

the periphery and undergoes amplification and alterations in its shape and temporal characteristics. These changes are thought to be largely due to reflection of the pulse wave and the tapering down of the arteries towards the periphery. Pulse propagation in arteries is further complicated by frequency dependent phase distortion (89) phenomena. The blood pressure pulse has similarities with the PPG blood volume pulse, with similar changes occurring in vascular disease, such as damping and a loss of pulsatility. The damping has been associated with a reduction in vessel compliance and increased peripheral resistance.

### 1.6.2 Pulse wave analysis

Manual measurement and feature extraction techniques were often used in the very early days of pulse wave analysis, using various media including chart recorder paper and ruler or photographic recording/magnetic tape (57,66,88). Recent developments in computing technology and software data analysis tools have enabled the sophisticated pre- and post-processing of physiological waveforms. MATLAB (MathWorks Inc.) is a digital signal processing environment that is well suited to pulse wave analysis algorithm prototyping, and often appears in the PPG literature. It is well established that PPG measurements are quite sensitive to patient and/or probe–tissue movement artefact (3). The automatic detection of such motion artefact, and its separation from good quality although highly variable

pulse recordings, is a non-trivial exercise in computer signal processing.

Computer-based filtering, feature extraction and waveform averaging have also been employed in PPG pulse wave analysis, including the analysis of frequency (31,57,70,90-93), joint-time frequency (94), artificial neural network (95-96), systems identification and transfer function modelling (97-99), principal component analysis (100), nonlinear and chaos theory (101-102), cross correlation (79,103) and double differentiation ((acceleration plethysmogram), (61,104-105) ).

## 1.7 CLINICAL APPLICATIONS

PPG has been applied in many different clinical settings, including clinical physiological monitoring (blood oxygen saturation, heart rate, blood pressure, cardiac output and respiration), vascular assessment (arterial disease, arterial compliance and ageing, endothelial function, venous assessment, vasospastic conditions, e.g. Raynaud's phenomenon, microvascular blood flow and tissue viability) and autonomic function (vasomotor function and thermoregulation, blood pressure and heart rate variability, orthostatic intolerance, neurology and other cardiovascular variability assessments).

PPG measurements can be used to determine arterial blood oxygen saturation by shining red and then near infrared light through the vascular tissue with rapid switching between the wavelengths (42,45,106). The AC component of the PPG signal is synchronous with the beating heart and therefore it will be a source of

heart rate information (94,107-108). Arterial blood pressure is a very important clinical parameter to measure. Several approaches to noninvasive PPG based blood pressure measurements have been described (109-110). Physiological monitoring of breathing interval (respiratory rate) is important in many clinical settings, including critical and neonatal care, sleep study assessment and anaesthetics. Respiration causes variation in the peripheral circulation, making it possible to monitor breathing using a PPG sensor attached to the skin (111-112). PPG signals have also been widely used in vascular assessment, studies related to arterial compliance, age and endo thelial dysfunction (63,113).

## 1.8 SCOPE OF THE THESIS

The main objective of the present research work is the design of a PPG sensor for recording the blood volume pulse signals and carry out selected cardiovascular studies based on these signals.This thesis focuses on the fabrication of a sensor head and studies based on the changes in the pulsatile component of the PPG signal observed under specific conditions. The effect of aging, mild cold exposure, and variation in the body posture on the PPG signal have been experimentally studied. A comparative study between normal subjects and diabetics using certain parameters deduced from the PPG signals has also been discussed.

**References**


1. Challoner A V J, *Noninvasive Physiological measurements,* vol 1ed, P Rolfe ( London Academic), 125-151 (1979)
2. Kamal A A, Harness J B, Irving G and Mearns A J, *Comp. Method.Prog. Biomed,* **28,** 257–69 ( 1989)
3. John Allen, *Physiol Meas,* **28,** R1-R39 ( 2007)
4. Burton A C, *Am. J. Physiol,* **127,** 437-453 (1939)
5. Burton A C and Taylor R A, *Am. J. Physiol,* **129,** 565-577 (1940)
6. Hertzman A B and Dillon J B, *Am. Heart. J.,***20,** 750-761 (1940b)
7. Hertzman A B and Roth L W, *Am. J. Physiol,* **136,** 669-679 (1942a)
8. Hertzman A B and Roth L W, *Am. J. Physiol,* **136,** 680-691 (1942b)
9. Hertzman A B and Roth L W, *Am. J. Physiol,* **136,** 692-697 (1942c)
10. Hertzman A B and Flath F, *Aerospace Med.,* **34,** 710-713 (1963)
11. Hyndman B W, Kitney R I and Sayers B M, *Nature,* **233,** 339-341 (1971)
12. Penaz J, *Automedica*, **2,** 135-141 ( 1978 )
13. Ahmed A K, Harness J B and Mearns A J, *Eur. J. Appl. Physiol.,* **50,** 95-104 (1982)
14. Harness J B and Marjanovic D Z, *Clin. Phy. Phy. Meas,* **10,** 365-368 (1989)
15. Nitzan M, Babchenko A, Milston A, Turivnenko S, Khanokh B and Mahler Y, *Appl. Surf. Sci.,* **106,** 478-482 ( 1996a)
16. Nitzan M, Turivnenko S , Milston A, Babchenko A S and Mahler, *J. Biomed. Opt.,* **1,** 223-229 ( 1996b)
17. Nitzan M, Babchenko A, Shemesh D and Alberton J, *Med. Biol. Eng.comput.,* **39,** 579-583 (2001)
18. Allen J and Murray A, *IEEE. Proc. Sci. Meas. Technol.,* **147,** 403-407 (2000b)
19. Johansson A and Oberg P A, *Med.Biol.Engg.Comput,* **37,** 42-47 (1999a)
20. Millasseau S C, Guigui F G, Kelly R P, Prasad K, Cockcroft J R, Ritter J M and Chowienzyk P J, *Hypertension,* **36,** 952-956

(2000)
21. Anderson R R and Parrish J A, *J. Invest. Dermatol,* **77,** 13-19 (1981)
22. Hertzman A B and Randall W C, *J. Appl. Physiol,* **1,** 234-241 (1948)
23. Brown C C, Giddon D B and Dean E D, *Psychophysiol,* **1,** 253-266 (1965)
24. D' Agrosa L S and Hertzman A B, *Appl.Physiol: Resp. Environ. Exercise Physiol,* **23,** 613-620 (1967)
25. Weinman J, *Photoplethysmography manual of psycho-physiological methods* ed P H Venables and I Martin ( Amsterdam : North Holland) (1967)
26. Zweifler A J, Cushing G and Conway J, *Angiology,* **18,** 591-598 (1967)
27. Ochoa W and Ohara I, *Tohoku J. Exp. Med.,* **132,** 413-419 (1980)
28. Nijboer J A, Dorlas J C and Mahien H F, *Clin.Phy.Physiol.Meas,* **2,** 205-215 (1981)
29. Roberts V C, *Trans.Inst.Meas.Control,* **4,** 101-106 (1982)
30. Lindberg G and Oberg PA, *Opt Engg,* **32,** 253-257 (1993)
31. de Trafford and Lafferty K, *Med.Biol.Engg.Comput,* **22,** 479-480 (1984)
32. Naslund J, Pettersson J, Lindeberg T, Linnersson D and Lindberg LG, *Med Biol.Engg.Comput,* **44,** 501-509 (2006)
33. Hertzman A B, *Am.J.Physiollogy,* **124,** 328-340 (1938)
34. Challoner A V and Ramsay C A, *Phy.Med.Biol,* **19,** 317-328 (1974)
35. Jesperson L T and Pederson O L, *Heart vessels,* **2,** 186-190 (1986)
36. Cejnar M, Kobler H, Hunyor S N, *J.Biomed.Engg,* **15,** 151-154 (1993)
37. Cui W J, Ostrander L E and Lee B Y, *IEEE Trans.Biomed.Engg,* **37,** 632-639 (1990)
38. Jones D P, *Phys.Technol,* **18,** 79-85 (1987)
39. Gordy E and Drabkin D L, *J,Biol.Chem,* **227,** 285-299 (1957)
40. Murray A and Marjanovic D , *Med.Biol.Engg.Comput,* **35,** 425-427 (1997)
41. Hertzman A B and Dillon J B, *Am.J.Physiol,* **130,** 177-185 (1940a)
42. Aoyagi T, Kiahi M, Yamaguchi K and Watanabe S, *Abstracts*

*of the 13th Annual meeting of the japanese society of Medical Electronics & Biological Engg,* 90-91 (1974)
43. Yoshiya I, Shimada Y and Tanaka K, *Med.Biol.Engg.Comput,* **18,** 27-32 (1980)
44. Duck F A, *Physical properties of tissue* (London: Academic) (1990)
45. Webster J G, *Design of pulse oximeters* (Bristol: Institute of physics publishing) (1997)
46. Burke M J and Whelan M V, *Med.Biol.Engg&Comput,* **24,** 647-650 (1986)
47. Lindberg L G and Oberg P A, *Med.Biol.Engg&Comput,* **29,** 48-54 (1991)
48. Ugnell H and Oberg P A, *Med.Engg.Phy,* **17,** 571-578 (1995
49. Weinman J and Fine S, *J.Life.Sci,* **2,** 121-127 (1972)
50. Fine S and Weinman J, *Med.Biol.Eng,* **11,** 455-463 (1973)
51. Allen J and Murray A, *Physiol.Meas,* **24,** 297-307 (2003)
52. Allen J and Murray A, *IEEE Comput.Cardiol,* **31,** 485-488 (2004)
53. Hanowell L, Eisele J H and Downs D, *Anesthesiology,* **67,** 864-865 (1987)
54. Stern R M, *Psychophysiology,* **11,** 73-75 (1974)
55. Barnes R W, Clayton J M, Bone G E, Slaymaker E E and Reinertson J, *J.Surg.Res,* **22,** 319-327 (1977a)
56. Barnes R W, Garrett W V, Slaymaker E E and Reinertson J E, *Am.J.Surg,* **134,** 183-186 (1977b)
57. Sherebrin M H and Sherebrin R Z, *IEEE Trans.BME,* **37,** 313-317 (1990)
58. Allen J and Murray A, *Physiol.Meas,* **14,** 13-22 (1993)
59. Chowienzyk P J, Kelly R P, MacCallum H, Millasseau S C, Andersson T L G, Gosling R G, Ritter J M and Anggard E, *J.Am.Coll.Cardiol,* **34,** 2007-2014 (1999)
60. Hahn M, Hahn C, Junger M, Steins A, Zuder D, Klyscz T, Buchtemann A, Ranner G and Blazek V, *Microvas.Res,* **57,** 187-198 (1999)
61. Bortolotto L A, Blacher J, Kondo T, Takazawa K and Safar M E, *Am.J.Hypertens,* **13,** 165-171 (2000)
62. Foo J Y, Lim C S, Wang P, *Physiol.Meas,* **27,** 685-694 (2006)
63. Millasseau S C, Ritter J M, Takazawa K and Chowienczyk P J, *J.Hypertens,* **24,** 1449-1456 (2006)
64. Lee B Y, Trainor F S, Thoden W R and Kavner D, *Handbook*

*of Non-invasive Diagnostic Techniques in VascularSurgery* (New York: Appleton-century-crofts) (1981)
65. Loukogeorgakis S, Dawson R, Philips N, Martyn C N and Greenwald S E, *Physiol.Meas,* **23,** 581-596 (2002)
66. Dillon J B and Hertzman A B, *Am.Heart.J,* **21,** 172-190 (1941)
67. NijboerJ A and Dorlas J C, *Br.J.Anaesth,* **57,** 531-534 (1985)
68. Cooke E D, Bowcock S A and Smith A T, *Angiology,* **36,** 33-40 (1985)
69. Grossmann K, Rolka H, Reinhardt H and Reissmann H C, *VASA,* **16,** 324-329 (1987)
70. Okada M, Kimura S and Okada M, *Med.Biol.Engg.Comput,* **24,** 255-260 (1986)
71. Porret C A, Stergiopulos N, Hayoz D, brunner H R and Meister J J, *Am.J.Physiol,* **269,** H1852-1858 (1995)
72. Nitzan M, Babchenko A, Khanokh B and Landau D, *Physiol.Meas,* **19,** 93-102 (1998a)
73. Nitzan M, Vatine J J, Babchenko A, Khanokh B, Tsenter J and Stessman J, *Laser.Med.Sci,* **13,** 189-195 (1998b)
74. Evans M L and Geddes L A, *Med.Instru,* **22,** 29-32 (1988)
75. Buchs A, Slovik Y, Rapoport M, Rosenfield C, Khanokh B and Nitzan M, *Med.Biol.Engg.Comput,* **43,** 252-257 (2005)
76. Erts R, Spigulis J, Kukulis I and Ozols M, *Physiol.Meas,* **26,** 865-874 (2005)
77. Dyszkiewicz A and Tendura M, *Physiol.Meas,* **27,** 353-369 (2006)
78. Allen J, Frame J R and Murray A, *Physiol.Meas,* **23,** 365-373 (2002)
79. Allen J and Murray A, *Physiol.Meas,* **21,** 369-377 (2000a)
80. Allen J, Oates C P, Lees T A and Murray A, *Physiol.Meas,* **26,** 811-821 (2005)
81. Allen J, Overbeck K, Stamby G and Murray A, *Meas.Control,* **39,** 80-83 (2006)
82. Schultz-Ehrenburg U and Blazek V, *Skin.Pharmacol.Appl.Skin.Physiol,* **14,** 316-323 (2001)
83. Huelsbusch M and Blazek V, *Proc.SPIE: Medical Imaging : Physiol &Function from multidimensional images* ed A V Clough and C-T Chen, **4683,** 110-117 (2002)
84. Wieringa F P, Mastik F and Van der steen A, *Ann.Biomed. Engg,* **33,** 1034-1041 (2005)

85. Rhee S, Yang B Hand Asada H H, *IEEE.Trans. Biomed.Engg,* **48,** 795-805 (2001)
86. Zheng D C and Zhang Y T, *Proc. 25th Annual Conf. Of the IEEE EMBC,* **4,** 3184-3187 (2003)
87. Yoon G, Lee J Y, Jeon K J, Park K K and Kim S H, *Telemed.J.E.Health,* **11,** 660-667
88. Hertzman and Spealman C R, *Am.J.Physiol,* **119,** 334-335 (1937)
89. O' Rourke M F and Gallagher D E, *J.Hypertens.Suppl,* **14,** S147-157 (1996)
90. Nitzan M, de Boer H, Turivnenko S, Babchenko A and Sapoznikov D, *J.Basic. Clin. Physiol.Pharmacol,* **5,** 269-276 (1994)
91. Grohmann G, Krauss M, Lindloh C, Pohlmann G and Eidner G, *Perfusion,* **9,** 268-277 (1996a)
92. Grohmann G, Krauss M, Lindloh C, Pohlmann G and Eidner G, *Perfusion,* **9,** 300-310 (1996b)
93. Larsen P D, Harty M, Thiruchelvam M and Galletly D C, *Int.J.Clin.Monit.Comput,* **14,** 89-95 (1997)
94. Yan Y S, Poon C C and Zhang Y T, *J.Neuroeng.Rehabi.,* **23** ( 2005)
95. Allen J and Murray A, *Physiol.Meas,* **16,** 29-38 (1995)
96. Weng J, Knoop P, Hornberger C and Konecny E, *Biomed Tech,***43** (suppl) 92-93 (1998)
97. Cohn J N, Finkelstein S, Mcveigh G, Morgan D, LeMay L, Robinson J and Mock J, *Hypertension,* **26,** 503-508 (1995)
98. Mcveigh G E, Bratteli C W, Morgan D J, Alinder C M, Glasser S P, Finkelstein S M and Cohn J N, *Hypertension*, **33,** 1392-1398 (1999)
99. Millasseau S C, Guigui F G, Kelly R P, Prasad K, Cockcroft J R, Ritter J M and Chowienczyk P J, *Hypertension,* **36,** 952-956 (2000)
100. Enr'iquez R H, Castellanos M S, Rodr'iguez J F and C'aceres J L H, *Physiol.Meas,* **23,** N17-29 (2002)
101. Christ F, Abicht J M, Atheloogou M, Baschnegger H, Niklas M, Peter K and Messmer K, *Int.J.Microcirc.Clin.Exp,* **17,** 374-384 (1997)
102. Bhattacharya J, Kanjilal P P and Muralidhar V, *IEEE Trans.BME,* **48,** 5-11 (2001)
103. Drinnan M J, Allen J and Murray A, *Physiol.Meas,* **22,** 425-

432 (2001)
104. Takada H, Washino K, Harrell J S and Iwata H, *Med.Prog.Technol,* **21,** 205-210 (1996-7)
105. Takazawa K, tanaka N, Fujita M, Matsuoka O, Seiki T, Aikawa M, Tamura S and Ibukiyama C, *Hypertension,* **32,** 365-370 (1998)
106. Kyriacou P A, *Physiol.Meas,* **27,** R1-35 (2006)
107. Nakajima K, Tamura T and Mike H, *Med.Engg.Phy,* **18,** 965-972 (1996)
108. Bland M, *An Introduction to Med.Statistics 2nd edition( Oxford:Oxford university press)* (1995)
109. Laurent C, Jonsson B, Vegfors M and Lindberg L G, *Med.Biol.Engg.Comput,* **43,** 131-135 (2005)
110. Jonsson B, Laurent C, Eneling M, Skau T and Lindberg L G, *Eur.J.Vasc. Endovasc. Surg,* **30,** 395-401 (2005a)
111. Nilsson K, Johansson A and kalman S, *Med.Biol.Engg.Comput,* **41,** 249-254 (2003a)
112. Nilsson K, Johansson A and kalman S, *Physiol.Meas,* **24,** 925-937 (2003b)
113. Tsai W C, Chen J Y, Way M C, Wu H T, Chi C K, chen Y K, Chen J H and Lin L J, *Am.J.Hypertens,* **18,** 118-122 (2005)

# *Chapter 2*

# *Design and development of blood volume pulse sensor and heart rate meter*

**Abstract**

A low power, low cost sensor has been developed for sensing the blood volume pulse using transmission mode photoplethysmography (PPG) from the finger tip. A PIC microcontroller is used for the implementation of the measurement protocol. The wavelet denoising algorithm is used to suppress the noise component in the PPG signal. The main advantages of the proposed approach are the reduction in cost, dimensions and power consumption. The probe is well suited for the proposed measurements and is self-contained and portable.

## 2.1 INTRODUCTION

Photoplethysmography (PPG) is a non-invasive method for the detection of cardiovascular pulse waves propagating around the human body (1). It is based on the determination of optical properties of vascular tissue using a light source and a photodetector. The emitted light is reflected, absorbed or scattered by the blood and tissues, and the resultant transmitted light is measured using a suitable photodetector. There are two different modes of detection: transmission mode and reflection mode. In the transmission mode, the light source is placed on one side of the tissue and the detector on the other, and is limited to areas such as the finger, earlobe, or toe. In the reflection mode, where the light source and the photodetector are placed in parallel, the measurement of backscattered light from any skin surface is allowed. The intensity of light reaching the photodetector is measured and the variations are amplified, filtered and recorded as a voltage signal – PPG. Variations in the photodetector signal are related to changes in blood flow and blood volume in the underlying tissue
(2-5).

The PPG signal has an ac component and and a dc component. The ac component is synchronous with the heart rate and depends both on the pulsatile pressure and pulsatile blood volume changes. The dc component of the signal varies slowly and reflects variations in the total blood volume of the examined tissue. The ac pulse shapes are indicative of vessel compliance and cardiac performance and the amplitude is usually 1 to 2% of the dc value. The pulsatile component of the PPG signal (blood volume pulse) has a

contour which includes a content descriptive of vascular health. Two such parameters are the minimum rise time (MRT) and the stiffness index (SI) which can be derived from the contour analysis of the peripheral pulse wave (6-9). Also, PPG has considerable potential for tele-medicine including the remote home monitoring of patients. Miniaturization, ease-of use and robustness are key design requirements for such systems (9). So, the design of a high fidelity photoplethysmograph transducer with signal conditioning circuit is indispensable to obtain an extremely accurate and noise-free signal of the blood volume pulse (BVP). There are quite a few developments in this field and researchers around the world have been attempting to design PPG sensors for long term, short term and ambulatory recording. An artifact resistant power efficient finger-ring PPG sensor which could be used for long term recording with much emphasis on mechanical design is available in the literature (10). A pulse oximeter that could be fully powered by human heat was designed with considerable power saving (11). This design demands for fairly expensive thermocouples. A reflective photoplethysmograph earpiece sensor for long-term pervasive monitoring was developed for long term pervasive monitoring (12). During recent times a LED-LED based photoplethysmographic sensor which is low in cost and power consumption was proposed (13). The proposed sensor in the present studies has good spectral sensitivity, increased and adjustable resolution, and avoids the need for expensive and precise operational amplifiers although its performance was not compared with that of a commercial equipment.. In this chapter the design and development of a simple blood volume pulse sensor and a heart rate meter using a PIC

microcontroller is described using the acquired blood volume pulse signals. The use of a microcontroller makes the system compact, cost effective and easily programmable. The use of wavelet transform helps in removing the high frequency noise from the acquired blood volume pulse.

## 2.2 PRINCIPLE OF MEASUREMENT

Photoelectric plethysmography, also known as photoplethysmography (PPG) or optical plethysmography is a non-invasive method to detect cardio-vascular pulse wave that propagates through the body using a light source and a detector. Hertzman and Spielman (2) were the first to use the term ‘‘photoplethysmography’’ and suggested that the resultant ‘‘plethysmogram’’ represented volumetric changes in the blood vessels. Light traveling through biological tissue (e.g., the fingertip or earlobe) undergoes scattering and absorption by different absorbing substances such as skin pigmentation, bones and arterial and venous blood. The arteries contain more blood during systole than during diastole and their diameter increases due to the increased pressure. This blood volume change occurs mainly in the arteries and arterioles but not in the veins. The pulse shape and amplitude can vary with the relative position between the detector and the vessel under study. The amplitude of the volume pulsations with each heartbeat is correlated with the flow. In PPG, the volume under study, depending

on the probe design, can be of the order of 1 $cm^3$ for transmission mode systems.

The principle of operation of PPG is based on the fact that light is attenuated when it is shown onto the skin and the attenuation shows variation depending on the volume of blood entering the tissue under observation. The optical system arrangement for acquiring the PPG signals in the transmission mode is shown in figure 2.1.

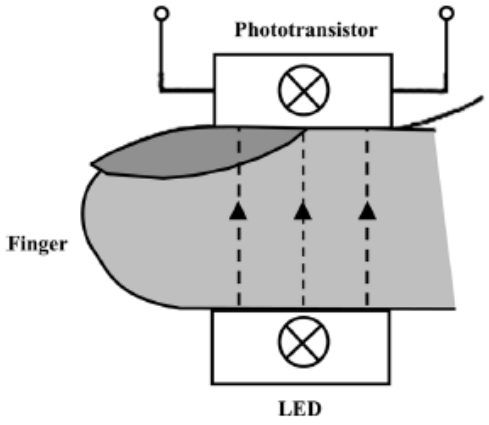


Fig 2.1: Optical system arrangement for transmission mode photoplethysmography

The Beer-Lambert law for light transmission in an absorbing medium, as shown in equation 2.1, is the primary basis for the functioning of the photoplethysmograph.

$$I = I_o e^{-\mu_a d} \quad \text{----------(2.1)}$$

where I is the transmitted intensity, $I_o$ is the input light intensity, $\mu_a$ is the absorption coefficient, and d is the distance between source and detector.

Since blood is a highly scattering medium, the Beer Lamberts law must be modified to include an additive term 'G' due to scattering losses and a multiplier 'B' to account for the increased optical path length due to scattering and absorption. Now, the modified Beer Lambert's law which incorporates these two additions is shown in equation 2.2 and this equation has been used as the basic theory for our measurement (14,15). This approach helps to develop an understanding of the absorbance of light as it passes through living tissues and explains why and how PPG works.

$$I = I_0 e^{-(\mu_a dB+G)} \quad \text{----------(2.2)}$$

Here G is a factor dependent on the measurement geometry and the scattering coefficient of the tissue interrogated. The wavelength of the source used is of significant importance in PPG. Light sources that operate in the near red (600–700 nm) and near infrared (880–940 nm) of the spectrum are most effective because whole blood has a relatively small absorption at wavelengths greater than 620nm (9).

## 2.3 DESIGN OF THE HARDWARE SETUP AND THE HEART RATE METER

PPG has been used in oxygen saturation measurement, heart rate monitoring, and the assessment of peripheral circulation and large artery compliance. However, the waveform of the PPG signal may be affected by the contacting force between the sensor and the measurement site (16). The sensor head was designed by taking this factor into consideration. The PPG signals were recorded by using this self-designed transmission mode PPG sensor. The GaAs infrared light emitting diode (LED55c) with a peak wavelength of 940nm and a matching silicon phototransistor LF141 were used for the present studies. The intensity of the LED is sufficiently low to minimize excessive local tissue heating. The LED is driven by a continuous current between 10mA and 15 mA, the value of which can be varied by signals from the microcontroller depending on the tissue perfusion characteristics (17). We have not used any modulation and the power level used is around 5mW. The sensor probe is fabricated using a commercial material called delrin and is enclosed within a compartment so that the effect of ambient light is minimized. Delrin is a crystalline plastic which offers an excellent balance of properties that bridge the gap between metals and plastics. It has good machinability, high fatigue endurance, and low moisture absorption. The acquired blood volume pulse waveform is fed to a microcontroller (16F873) which is programmed to calculate the heart rate in beats per minute (bpm), as each heart beat gives rise to a blood volume pulse. The details involved in the mechanical design of the probe and the block diagram of the hardware setup are as shown in fig 2.2.

### 2.3.1. Mechanical design

The material that we had used for making the springs in the probe head is SS302 grade steel. Using the standard data available for the material we were able to calculate the shear stress (18). We have used a spring of diameter 4mm and the wire diameter was 0.5 mm. Using these values and by assuming the deflection of the spring to be 10 mm, we arrived at the value of the applied force. In the probe head we have used six springs which were arranged in parallel. Assuming the value of the modulus of rigidity as $0.79\times10^5$ Pa for the material used and correlating the same to the applied force, one can calculate the number of turns to be used for the spring. Using standard relations (18), the length of the spring was evaluated as 39 mm. As shown in figure 2.2, the portion of the sensor head above the dotted line can be lifted so as to accommodate the finger of the subject. The contacting force was determined using a flexiforce sensor which was attached to the inner side of the probe. The contacting forces were determined by using a force to voltage circuit and the PPG signals were recorded for different contacting forces. The contacting forces could be varied from 0.2 to 1.8 N, but however it has been observed that the contacting force is within the range of 0.2 to 0.5N for satisfactory acquisition of PPG signals from various subjects.

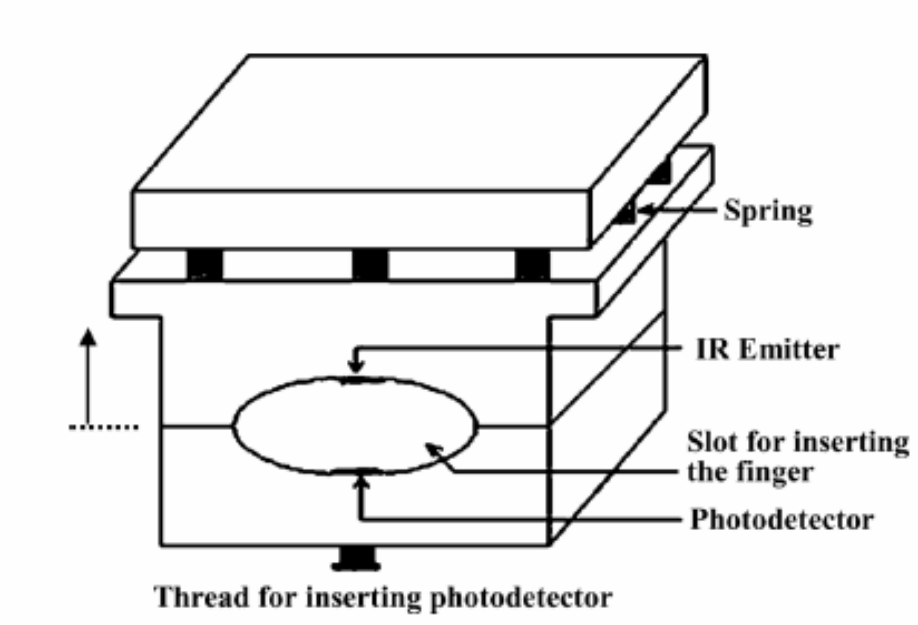


Fig 2.2: Schematic diagram of sensor head

The sensor head was designed such that it was small in size, light in weight and rigid in construction. It was designed in such a way that it does not either occlude the flow of blood, or allow the finger to move freely so that motion artifact can be greatly reduced and a nominal contacting pressure can be applied to the finger to get a satisfactory PPG signal. Ambient light is prevented from reaching the detector so that the effect of artifact on signal acquisition is minimized. The LED and the detector inside the probe were mounted on a reflection free

surrounding. To prevent the signal from being affected by electromagnetic interference a shielded cable was used to pick up the signal from the probe end.

### 2.3.2. Hardware design

The block diagram of the designed hardware setup is shown in figure 2.3. The sensor probe houses the LED and the photodetector. The slot for introducing the finger is elliptical in shape with major axis and minor axis of 2.1 cm and 1 cm, respectively. The design of our hardware is for short term recording of PPG signals. The output from the photodetector is fed to a voltage follower so that there is no loading of the original signal. The circuit is implemented using operational amplifiers (OP 07 and LF 356) which are ultra low offset and FET input amplifiers, respectively. The baseline restoration circuit helps in eliminating the low frequency baseline fluctuations, which if present will corrupt the acquired signal. A switched capacitor filter (low pass, 8th order) helps in eliminating signals above 10 Hz, within which limit the BVP signals are expected to occur. The special feature of switched capacitor filter is that it has a cut off frequency which has a typical accuracy of ± 0.3% and is less sensitive to temperature changes. The band-limited signal is then amplified, clamped so that only the pulsatile component of the PPG waveform is recorded. The final output is fed to a microcontroller for calculating the heart rate and displayed using an LCD module. The program has been developed using assembly language.

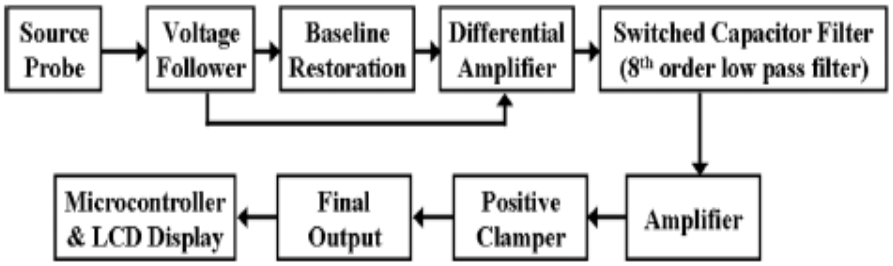


Fig 2.3: Block diagram of the hardware setup

The heart rate acquisition circuit is shown in figure 2.4. Depending on the amplitude of the signal that is acquired from the subject, a proper thresholding is also incorporated so that erroneous beats are eliminated. The PPG signal that is acquired from different subjects depends on their tissue perfusion characteristics. So the peak to peak value (Vp-p) of the acquired signal is calculated from which the value of 0.5Vp-p is evaluated. The middle values of 0.5Vp-p to Vmax and 0.5Vp-p to Vmin are then calculated. Only if the incoming signal has amplitudes above and below these two values respectively it will be considered for incrementing the counter which counts the number of beats. The above procedure is adopted to eliminate erroneous beats from being counted. The resolution of the ADC used is 10 bits. The PPG signal was sampled at a rate of 500 Hz. There is a beep circuit which is included along with the heart rate meter so that once the heart

rate goes below 60 bpm or above100bpm an alarm will be produced. A dual EIA driver/receiver (MAX232) chip can be used for further interfacing with a computer. The use of a PIC microcontroller makes the system very cost effective, with a very low requirement for additional external components. Programs can be modified with much ease and the whole system can be made compact by using microcontrollers.

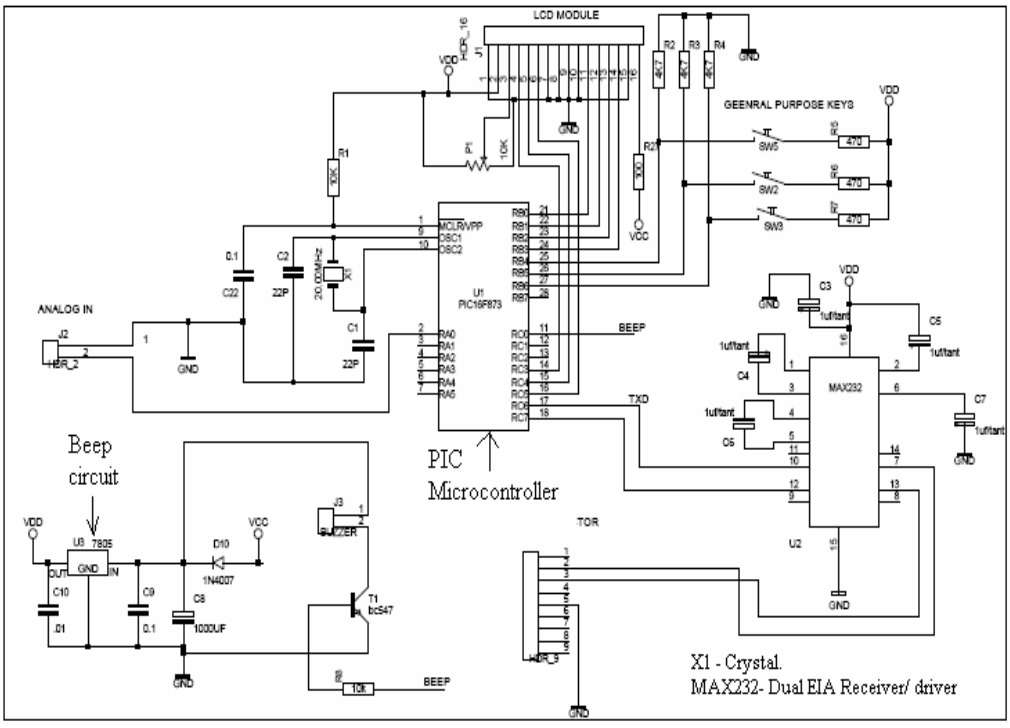


Fig 2.4: Heart rate acquisition circuit

### 2.3.3. Denoising of PPG using wavelet transform

In order to avoid the high frequency noise superimposed on the PPG signal denoising technique was employed.Wavelet analysis is a time scale analysis rather than a time frequency analysis. This also helps in extracting the relevant time-amplitude information from a signal (19). It can also be used to improve the signal to noise ratio based on our prior knowledge of the signal characteristics. The wavelet transform decomposes the signal into different scales with different levels of resolution by dilating a single prototype function, the mother wavelet. The differences between different mother wavelet functions (e.g., Haar, Daubechies, Coiflets, Symlet etc) consist in how the scaling of signals and the wavelets are defined. To have a unique reconstructed signal from wavelet transform, we need to select the orthogonal wavelets to perform the transforms. The wavelet decomposition results in levels of approximated and detailed coefficients and the high frequency noise is normally seen in the detailed coefficients. By proper low pass filtering we were able to remove noise to a satisfactory level. The acquired signal was subjected to denoising using wavelet transform (19,20). The Daubechies2 (db2) wavelet was used and it was found that with five levels of decomposition, the high frequency noise could be satisfactorily eliminated. The denoised version of the acquired PPG signal is shown in figure 2.5. The denoised PPG signals were employed for analysis.

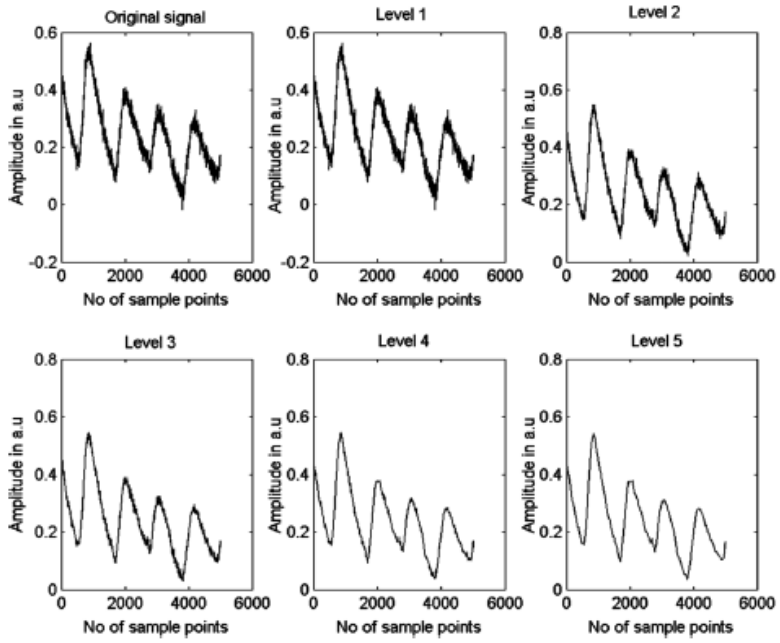


Fig 2.5: Recorded PPG and its denoised version

## 2.4. RESULTS AND DISCUSSION

The blood volume pulse sensor developed here has been tested in its heart rate configuration. The BVP was recorded from 5 individuals using the proposed setup. The amplitude of the signals obtained from the designed setup, which were in the range of 100 to 200 mV, were boosted in the last stage (as shown in figure 2.2) to 5V before being fed to the analog input channel of the PIC microcontroller. The heart rate displayed using the designed HR meter seemed to correlate well with

the beat-beat estimates calculated using the R-R interval of an electrocardiogram. The ECG and PPG signals recorded using a clinical instrument (L&T Micromon 7142 L) and the PPG signal recorded using the developed setup and their respective FFT's in respect of a subject are shown in figures 2.6–2.8, respectively.

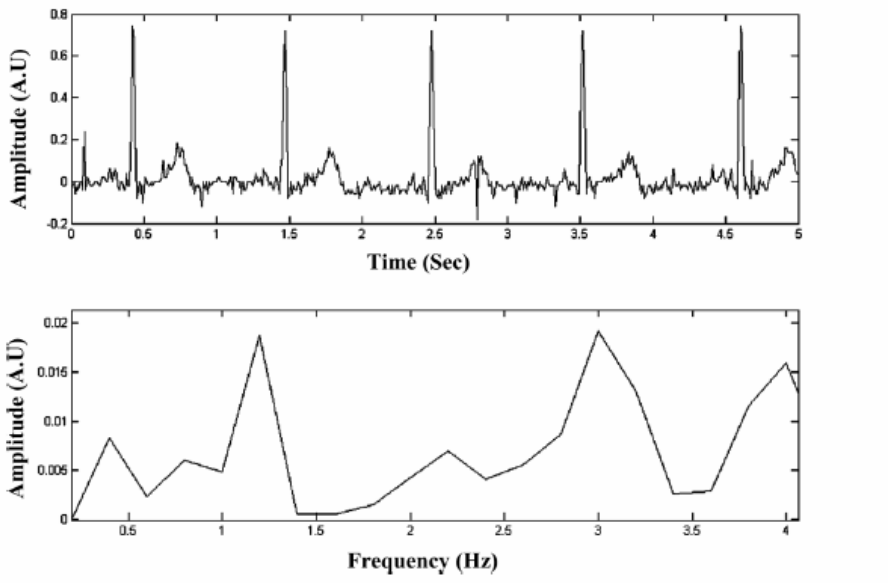


Fig 2.6: ECG recording and its FFT (using L&T Micromon)

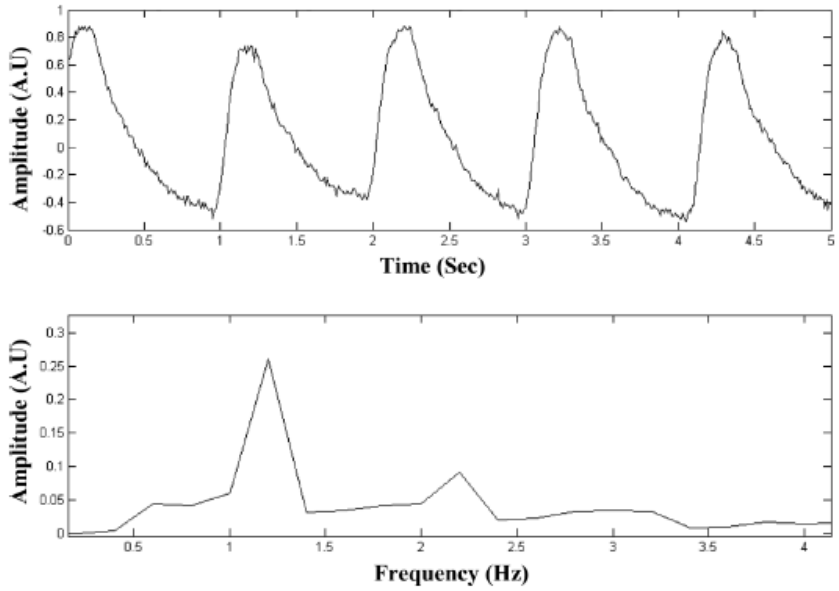


Fig 2.7: PPG recording and its FFT ( using L&T Micromon )

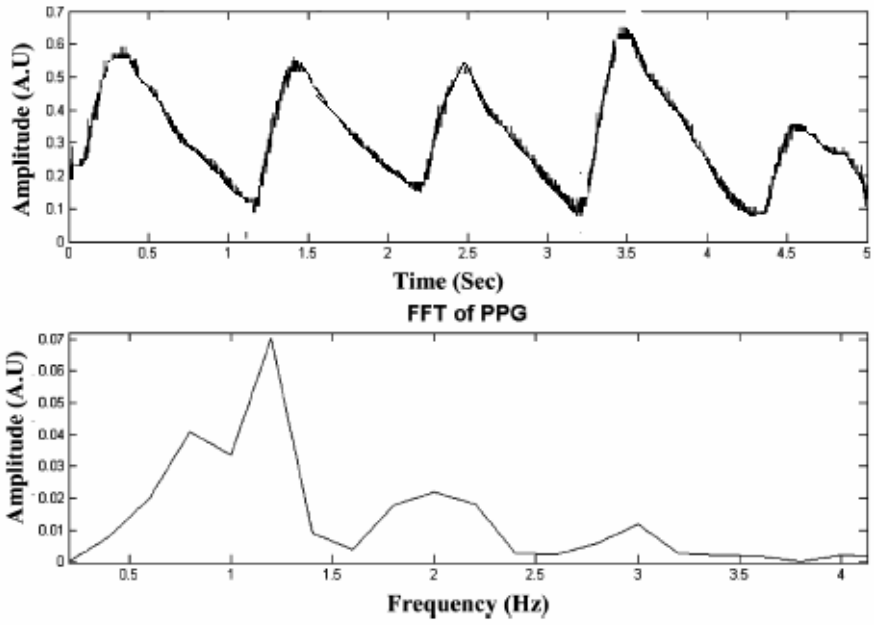


Fig 2.8: PPG recording and its FFT ( using developed sensor)

There seems to be a close correlation among all of them with respect to the heart rate parameter. From the plots of the heart rate variation over a period of one minute derived from both the developed sensor and the clinical instrument, as shown in figure 2.9, we were able to see that the sensor developed by us is quite comparable with that of a clinical instrument. The accuracy of our present sensor was found to be within ±3 bpm for the subjects we had studied. The use of wavelet transforms for denoising the acquired signals makes the developed method more versatile. The heart rate determined using the present method and those calculated using the R-R interval of the electrocardiogram for five subjects are shown in Table 2.1 and they show good agrrement. The calculation of the parameters can be made simple by making use of a microcontroller. The signal when recorded with the forearm of the subject placed at a comfortable position, and approximately at the heart level is found to be of good quality. The acquired signals may be analysed offline using Matlab.

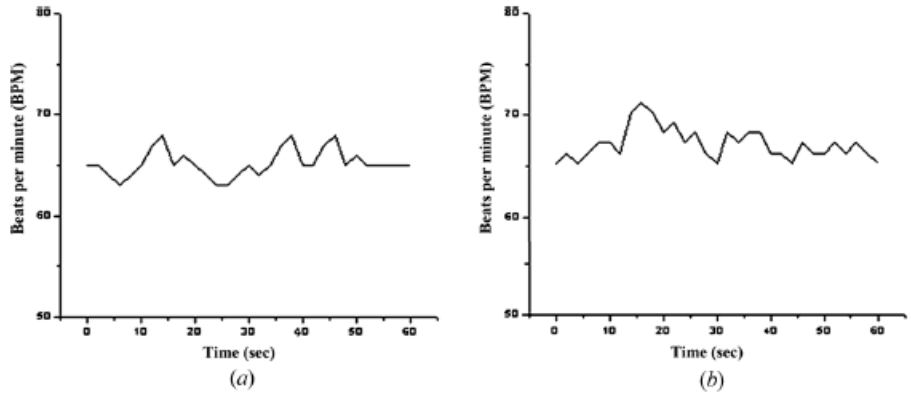


Fig 2.9: Heart rate variation with respect to time for recordings from the developed sensor and ECG.
a) heart rate (bpm) from proposed sensor and b) heart rate (bpm) from ECG.

| Sl. no. subject | Heart rate (bpm) using the proposed method | Heart rate (bpm) using ECG |
|---|---|---|
| 1. | $73 \pm 2$ | $72 \pm 1$ |
| 2. | $65 \pm 3$ | $67 \pm 4$ |
| 3. | $82 \pm 1$ | $83 \pm 3$ |
| 4. | $78 \pm 3$ | $80 \pm 2$ |
| 5. | $69 \pm 1$ | $68 \pm 2$ |

Table 2.1: Heart rate determined using the proposed method and ECG

## 2.5. CONCLUSIONS

The optoelectronic setup designed and developed here is simple, easy to use, and can be used in home health care monitoring because of its small size and portability. The use of microcontroller for heart rate monitoring makes the system miniaturized and also modular in nature. The complex interfacing of external peripherals like ADC/DACs can be eliminated. The material that has been used for making the sensor head has excellent machinability and hence can be used for mass production of cost effective, self contained portable probe heads. The probe head can be operated in wet environments or at elevated temperatures with little effect on the performance or dimensions.. Simple and cost effective stand-alone systems could be developed for

deducing indices related to cardiovascular system non-invasively using the present setup.

**References**


1**.** Mendelson Y, *clinical chemistry,* **38,** 1601-1607 (1992)
2. Hertman A B and Spielman C R, *Am. Journal of Physiology,* **119,** 334-335 (1937)
3. Challoner A V J, *Non-Invasive physiological measurements,* vol1 ed P Rolfe (1979) London: Academic press
4. Nijboer J A, Dorlas J and Mahien H F**,** *Clinical Phys. Physiological Measurements***, 2,** 205-215 (1981)
5. De Trafford and Lafferty K, *Med.biol. Engg&Computing,* **22,** 479-480 (1984)
6. ChowienczykP J, Kelly R P, MaCallum H, Millasseau S C, Anderson T L G, Gosling R G, Ritter J M, and Anggard A A, *J. Am. Coll. Cardiol,* **34(7**), 2007–2014 ( 1999)
7. Millaseau S C, Guigui F G, Kelly R P, Prasad K, Cockcroft J R, Ritter J M and Chowiencyk P J, *Hypertension*, **36,** 952-956 ( 2000)
8. Millasseau S C, Kelly R P, Ritter J M and Chowienczyk P J, *Clin.Sci,* **103,** 371-377 (2002)
9. Allen J, *Physiol.Meas,* **28,** R1-R39 (2007)
10. Rhee Sokwoo, Boo-Ho Yang and Haruhiko Harry Asada, *IEEE Transactions on Biomedical Engineering,* **48(7),** 795–805 (2001)
11. Trofs Tom, Vladimir Leonov and Vullers J M, *Sensors and Transducers Journal,* **80(6**),1230–1238 (2007 )
12. Wang L., Lo B, and Yang G, *4th International Workshop on Wearable and IimplantableBody Sensor Networks***, 13**, 179–183 (2004)
13. Stojanovic R and Karadaglic D, *Physiol. Meas***, 28,** N19–N27 (2007)
14. Delphy D T, Cope M, Vander ee, Arridge S, Susan Wray, Wyatt J, *Phys.Med.Biol,* **33(12),** 1433-1442 (1988)
15. Sassaroli, Angelo and Sergio Fantini, *Phys.Med.Biol,* **49,** N255-N257 (2004)
16. Teng X F and Zhang Y T, *Physiol.Meas*, **25,** 1323-1335 (2007)
17. Clayton D G, Webb R K, Ralston A C, Kara.Duthie D and Runciman W B, *Anaesthesia,* **46(4),** 260-265 (1991)

18. Ashby, Michael and kara Johnson, *Materials and design: The art and science of material selection in product design,* Oxford: Butterworth- Heinemann (2002)
19. Daubechies, *IEEE Transactions on Information theory,* **36(9),** 961-1005 (1990)
20. Donoho L, *IEEE Transactions on Information theory,* **41(3),** 613-627 (1995)

# *Chapter 3*

# *Assessment of age-related changes using the photoplethysmographic signal*

**Abstract**

Cardiac induced changes related to age can be explored by investigating the photoplethysmographic pulse timing and shape characteristics. Objective assessment of vascular aging is very important since arterial stiffness is associated with hypertension, a risk factor for stroke and heart disease. Noninvasive determination the age related parameters from a normalised mean pulse function of the resting peripheral volume pulse and its second derivative has been discussed in this chapter.

## 3.1 INTRODUCTION

Photoplethysmography (PPG) provides an estimation of cutaneous blood flow by measuring the dynamic attenuation of infrared light by the blood volume present in tissue. The contour of the pulsatile component of the PPG signal has been found to include content descriptive of vascular health (1). PPG pulse signals can be easily obtained from the tissue pads of the ears, fingers and toes where there is a high degree of superficial vasculature (2). The non-invasive assessment of cardiovascular function by means of the peripheral arterial pulse has gained substantial interest in recent years due to the integration of sensor technology and the ubiquitous application of microprocessors (2). An influence of vascular aging on the contour of the peripheral volume pulse in the upper limb is well recognized (3). Aging is accompanied by increased stiffness of large elastic arteries leading to an increase in pulse wave velocity (PWV) (4-5). The process of hardening of arteries has been shown to start from around the first or second decades of life in healthy subjects and it can be accelerated by medical conditions including renal diseases and diabetes mellitus (6). Premature arterial aging, as determined by an elevated aortic pulse wave velocity is now recognized as a major risk factor for ischaemic heart disease (7).

It has been demonstrated earlier that the contour of the PPG signal contains similar information to that of the peripheral pressure pulse (8). Because the peripheral volume blood flow pulse is essentially due to a propagating pressure pulse, the time course of the signal indicating flow changes bears a relationship to pressure changes

(9). The contour of the PPG signal is determined mainly by the characteristics of the systemic circulation, including pressure wave reflection and pulse wave velocity of the pressure wave in the aorta and large arteries (10). As age increases, pulse wave velocity increases decreasing the time taken for pressure waves reflected from the periphery of the circulation ( mainly from the lower part of the body ) to return to the aorta and then to the upper limb (11). The stiffer the artery the faster the pulse will travel to the periphery- i.e the pulse wave velocity increases. In addition, augmentation of the forward pressure pulse wave by a fast returning reflected wave is another key feature that can be found in subjects with arterial stiffening (5). There has been published data in the literature, which quantify pulse transit timing changes with age (12). Frequency analysis of the PPG signals at different body sites with respect to age has been carried out (13-14) and it has been shown that there is a general reduction in the harmonic components of the pulse in older subjects. Work has also been done using the second derivative of the photoplethysmogram (SDPPG) to study age-related indices and other risk factors for atherosclerotic vascular disease (15-16). This has proved to be particularly useful when the dicrotic notch in the PPG signal becomes less prominent, making it difficult to detect minute changes in the phase of the inflections using the pulse wave contour itself. The contour of the pulsatile component of the PPG has been used for the calculation of certain age related indices using commercial equipments ( 2-3, 8). In this chapter we have described some new parameters related to age using the mean pulse function derived from the PPG signals and have also explained how a few of the already reported age related

parameters were evaluated using our own indigenously developed hardware setup.

## 3.2 PRINCIPLE OF MEASUREMENT

. The contour of the PPG signal exhibits an early systolic peak and a latter peak or point of inflection that occurs a short time ($\Delta T_{BVP}$) after the first peak in early diastole, as shown in fig. 3.1. The systolic component results from the direct pressure wave travelling from the left ventricle to the digit (finger or toe), and the diastolic component results from reflections of the pressure wave by arteries of the lower body back to the finger. The time difference between these two peaks ($\Delta T_{BVP}$) is a measure of the transit time between the subclavian artery and reflection sites and has been used to define a non-invasive measure of large artery stiffness (17).

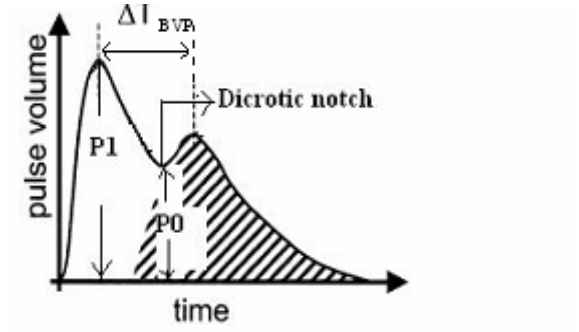


Fig 3.1: BVP recorded by measuring the transmission of IR light through the finger pulp

The PPG signals were recorded from the index finger of the right hand as there is evidence that differences between the age groups are more significant for the right hand compared to the left hand (1). A program was written in MATLAB to determine a mean pulse function from the recording of PPG pulses over a period of 10 sec in the rest condition. The set of measured pulses is optimized for contour similarity in order to minimize the effects of motion and damping artifacts normally present in such data. Also, normalization of the mean pulse function was performed for overall shape assessment and to get rid of variability due to heart rate differences (2, 18). From this ensemble – averaged mean pulse, $\Delta T_{BVP}$ was determined as the time between the first systolic peak and the early diastolic peak in the waveform. The first derivative of the mean pulse function was used to locate the peaks. The systolic peak was identified as the first zero crossing and the subsequent negative zero crossing, or positive inflection nearest to zero determined the time of the diastolic peak or inflection occurrence. It is not necessary that in all the age groups the dicrotic notch be predominantly seen. In such cases the second peak corresponds to the point of inflection itself. Figure 3.2 below shows how the systolic and diastolic peaks are identified for a given PPG signal with or without a dicrotic notch.

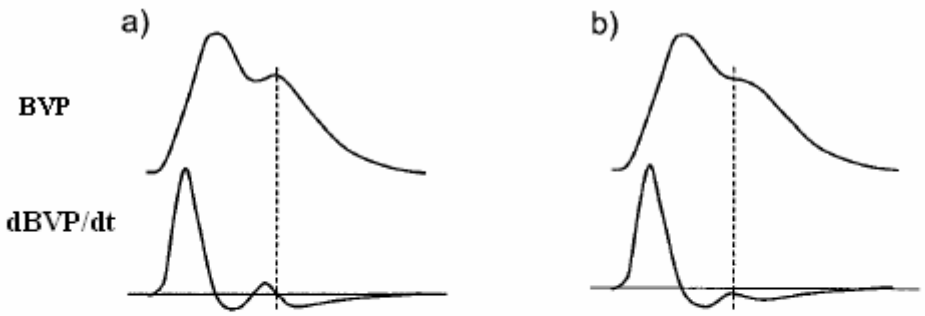


Fig 3.2: BVP and its first derivative dBVP/dt for waveforms exhibiting a) a diastolic peak b) a point of inflection

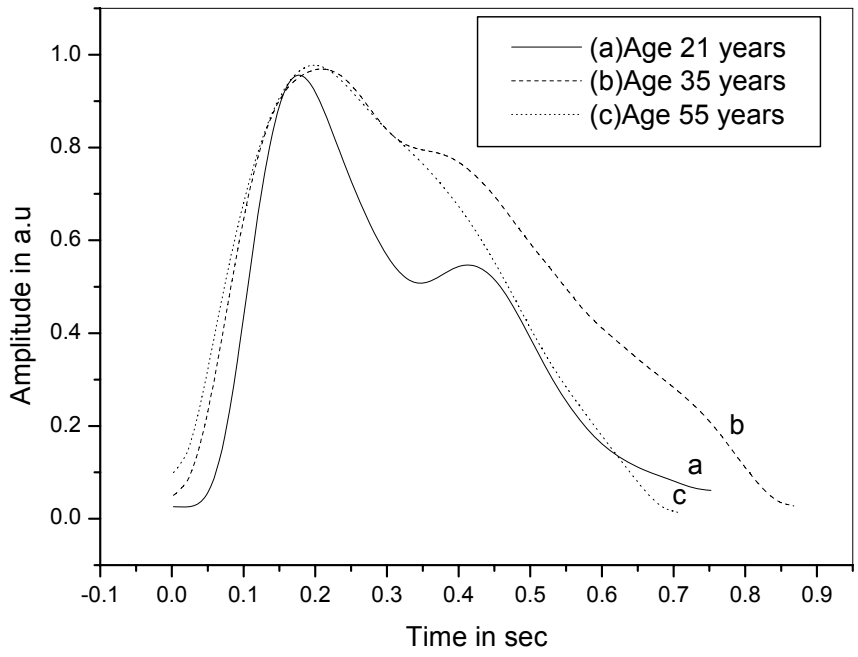


Fig 3.3: Mean pulse function for subjects aged 21, 35 and 55 years

Figure 3.3 shows how the shape of the mean pulse function varies with respect to age. For younger and healthy subjects the dicrotic notch was predominantly seen whereas in older subjects owing to the increase in arterial stiffness and a faster reflected wave augmenting the forward wave the pulse becomes rounded. In our study it was noticed that the peripheral pulse has a steep rise and a notch on the falling slope in younger subjects whereas in older subjects a more gradual rise and fall and no pronounced dicrotic notch . In older subjects the pulse wave velocity is also much higher compared to younger subjects owing to the increase in stiffness index with age.

From the recording of the original PPG, sometimes there is a difficulty in detecting minute changes in the phase of the inflections . So, by double differentiating the PPG, the second derivative of the PPG signal is obtained (SDPPG), which helps in more accurate recognition of the inflection points and an easier interpretation of the original signal. The SDPPG is used as a means to accentuate and locate inflection points and a specific nomenclature has been adopted, such that the five sequential waves are designated as a, b, c, d, and e.( 15). To describe the SDPPG components quantitatively, the height of each wave was measured from the baseline, the value above the baseline being positive, and those under it negative. The a, b, c, d and e waves represent the initial positive, early negative, re-increasing, late redecreasing , and diastolic positive waves, respectively. The normalised mean pulse and its second derivative in the case of a 25 year old subject is shown in Fig.3.4. Absolute values for the height of the waves ‘a’ & ‘b’ were referred to as ‘A’ & ‘B’, respectively (19).

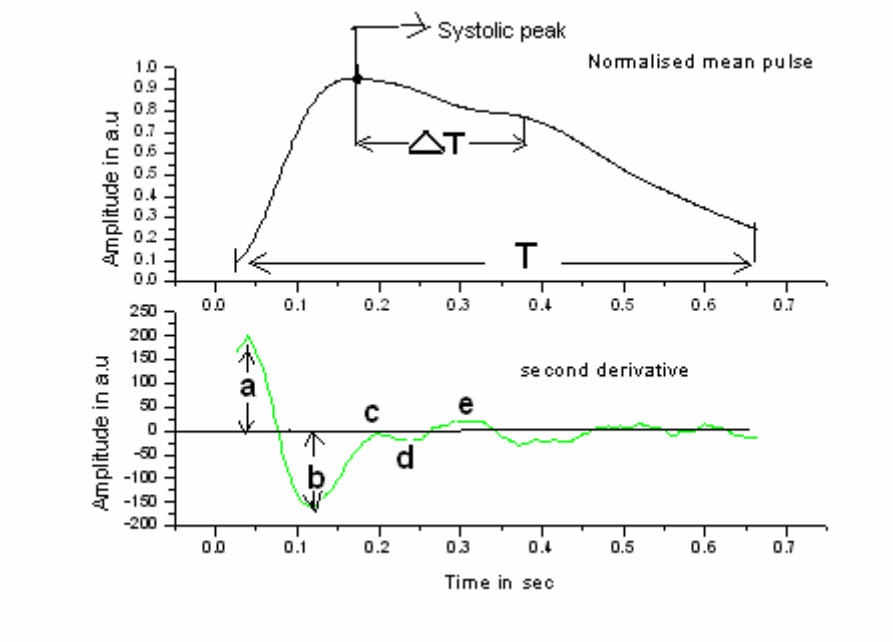


Fig 3.4: Normalised mean pulse and its second derivative (SDPPG) of a 25 year old subject. The waveform of the SDPPG consists of four systolic waves (a, b, c and d waves) and one diastolic wave

## 3.3 MATERIALS AND METHODS

### 3.3.1 Measurement system

A schematic of the recording system used is shown in Fig 3.5. The PPG signals were recorded in the reflection mode with a self designed probe and measurement setup (20). Fig. 3.6 shows the layout of our hardware setup. The source used was a light emitting diode emitting IR light at 940 nm and a photodiode was used as the detector. The

hardware was implemented using FET input and ultralow offset operational amplifiers. The bandwidth of the PPG amplifier was 0.5 to 8 Hz, so as to eliminate low frequency baseline fluctuations as well as the high frequency noise. All the signals were recorded using a Tektronix (TDS5104 B) digital phosphor oscilloscope and the sampling rate used was 500 Hz. All processing and post-processing were done using MATLAB and Microcal Origin software.

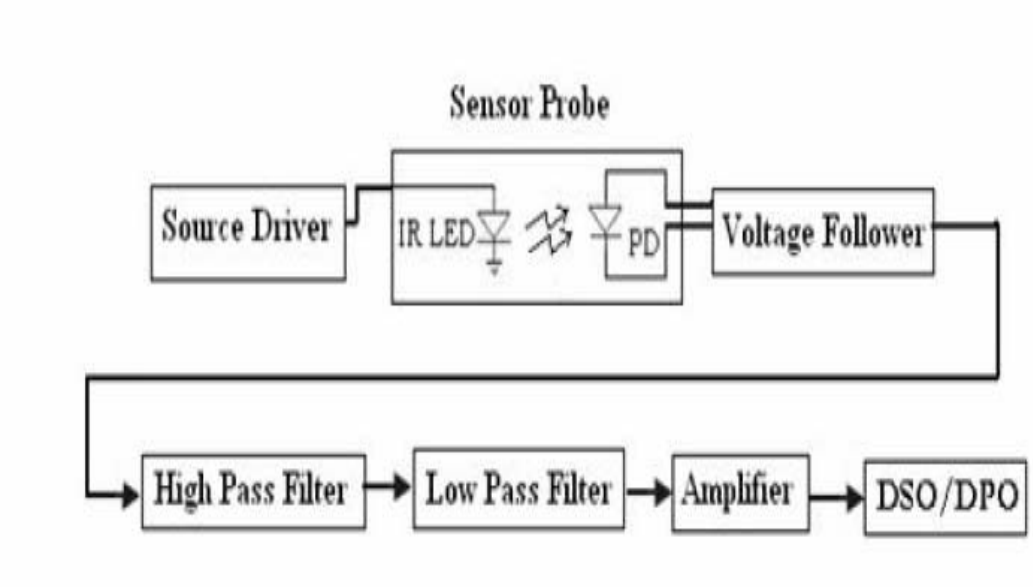


Fig 3.5: Schematic diagram of the experimental setup

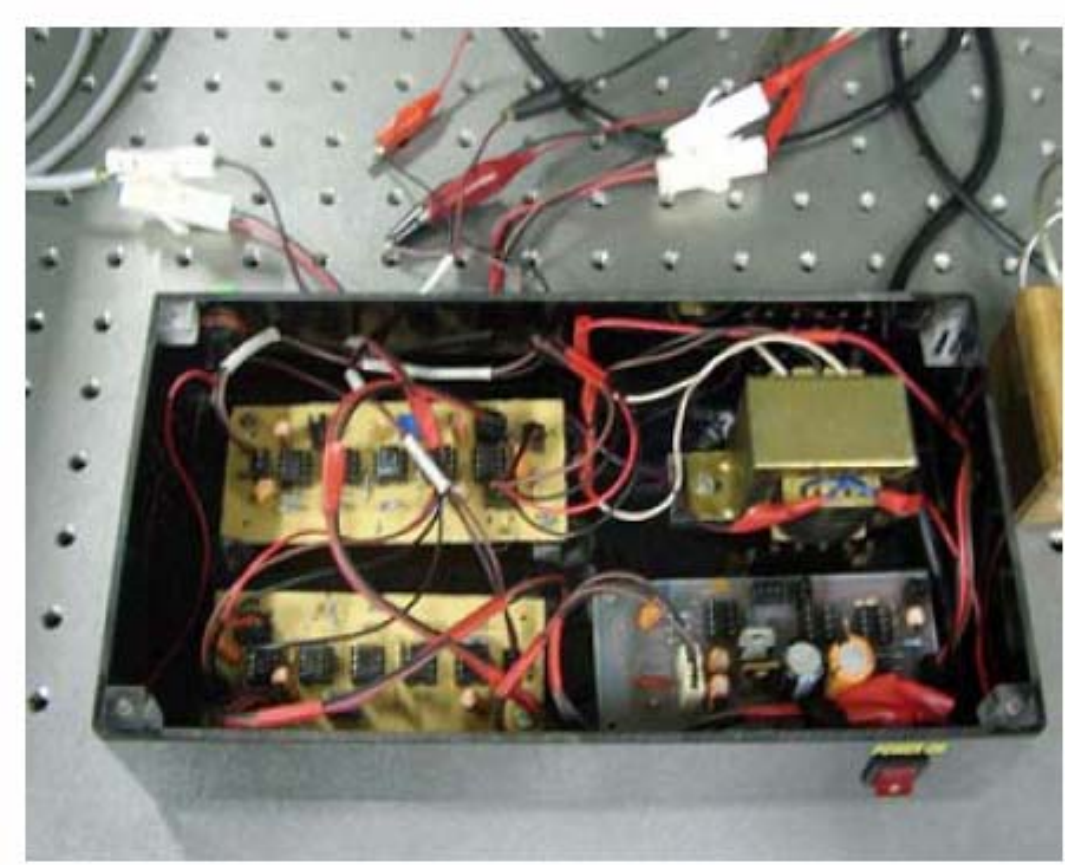

Fig 3.6: Layout of the developed hardware setup

### 3.3.2 Subjects

A total of 30 subjects were involved in the study, with their ages ranging from 20 to 61 years . The demographic data of the subjects are as shown in Table 3.1. The inclusion criteria were: no clinically apparent arterial disease or physical abnormality, not observantly obese or on any medication. Each subject was informed about the details of

the study and their verbal consent was taken before the recordings were made. Peripheral pulse measurements were recorded for 10 sec with the subject sitting on a chair and the arm positioned at heart level with the forearm resting on a table in a temperature controlled room (24±1.5 $^{o}$C). Care was taken to see that the effect of motion artifact was the lowest possible. The subjects were also asked not to undergo strenuous exercise, avoid consuming hot drinks or those containing caffeine, and refrain from smoking for 2 hours prior to recording. It was also ensured that the subjects were relaxed and breathing regularly and gently.

| ***Parameter*** | ***Mean± Standard deviation*** |
|---|---|
| Age(years) | 34.8 ± 11.6 |
| Weight(kg) | 55.9 ± 7.8 |
| Height(cm) | 161.8 ± 8.3 |
| Systolic Blood Pressure(mmHg) | 108.2 ± 8.4 |
| Diastolic Blood Pressure(mmHg) | 76.3 ± 7.4 |

Table 3.1: Demographic data of the subjects in this study

### 3.3.3 Age related Indices derived from the PPG signal

The following indices were evaluated from the recorded PPG signals using the hardware setup indigenously developed in our laboratory.

**i) Stiffness Index (S.I)**

Assuming the path length to be proportional to a person's height, the stiffness index has been defined as

$$S.I\ (m/s) = \text{Body Length}/\Delta T_{BVP} \qquad \ldots (3.1)$$

Because of the complexities of the formation of the blood volume pulse, S.I cannot be considered as a direct measure of large artery pulse wave velocity. It could be simply considered as an index characterizing the features of the contour of the blood volume pulse that are determined mainly by pulse wave velocity in the aorta and large arteries, and hence by the stiffness of these arteries.

**ii) Minimum rise time**

The minimum rise time (MRT) parameter has been defined (21) as

$$MRT = (dt/dy) \times (\text{Maximum Pulse Height}) \qquad \ldots (3.2)$$

This represents the inverse of the normalized maximum rate of rise of the blood pulse volume. The MRT values for each subject in the experiment were determined using the already derived mean pulse function.

**iii) $P_0/P_1$ Ratio**

The systolic peak of the recorded blood volume pulse was located and the valley point was used to locate the dicrotic notch. From the derived

mean pulse, the foot of the blood volume pulse waveform was located and was taken as the reference. The ratio $P_0/P_1$ was calculated as the ratio of the amplitude from the foot to the valley point ( point where dicrotic notch is located) to the amplitude from the foot to the systolic peak (22).

All the three indices mentioned above were derived from the mean pulse function.

**iv) B: A ratio**

The B:A ratio was determined from the second derivative of the PPG signal (SDPPG). As shown in fig 3.4, the absolute values of the 'a' and 'b' waves of the SDPPG are taken as 'A' and 'B' respectively. This parameter is related to the distensibility of large arteries (7).

**v) Area under the systolic peak**

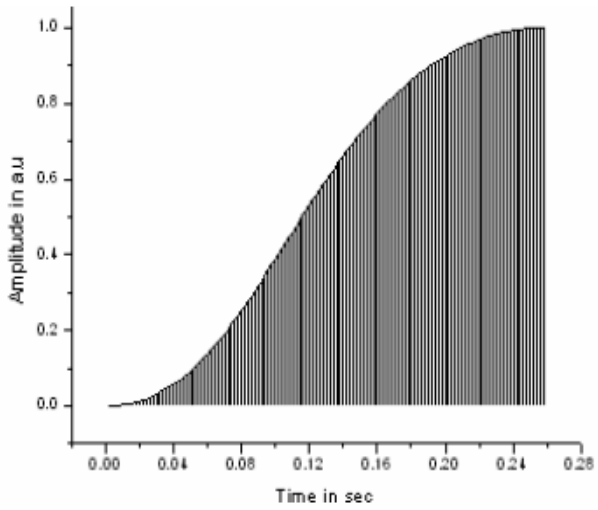


Fig 3.7: Determination of area under the systolic peak

As shown in fig 3.7 above, the area under the systolic peak(shaded area) was calculated as the area lying under the systolic peak and the foot of the wave.

**vi) $\Delta T_{BVP}/T$ ratio**

$\Delta T_{BVP}$ represents the time delay between the systolic and the diastolic peaks and 'T' represents the time period of the PPG waveform.

Indices (v) and (vi) are determined from the normalised mean pulse derived from a set of PPG signals

## 3.4 RESULTS & DISCUSSION

Pulse shapes for normal healthy subjects have been analysed. It is seen from fig 3.3 that the pulse contour exhibits changes in shape with respect to the systolic slope and the demarcation of the dicrotic notch. Figures 3.8, 3.9 and 3.10 show the variation of MRT, $P_0/P_1$ and stiffness index with age respectively.

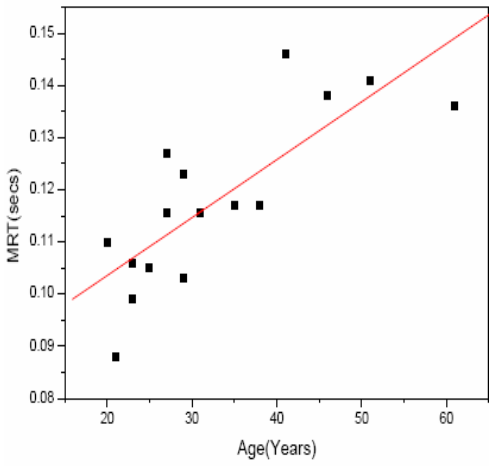


Fig 3.8: Variation of Minimum rise time with age

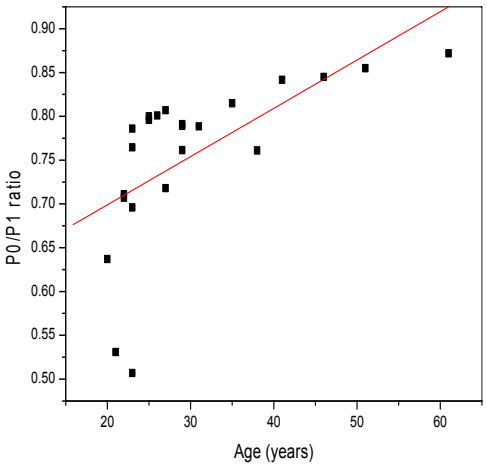


Fig 3.9: Variation of $P_0/P_1$ ratio with age

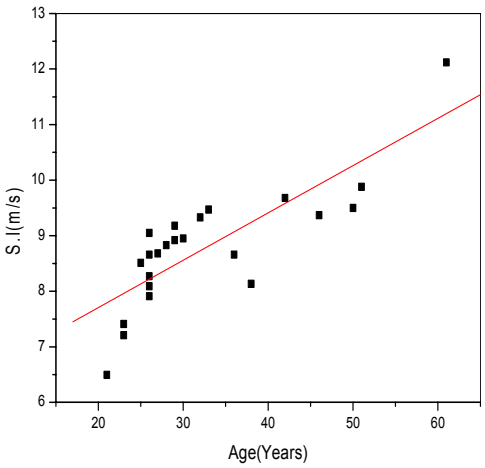


Fig 3.10: Plot of Stiffness index vs age

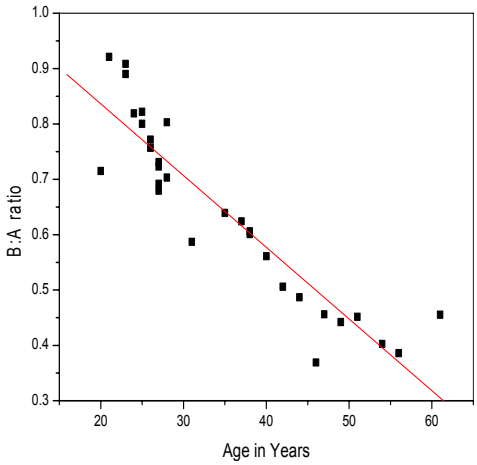


Fig 3.11: Plot of B:A ratio vs age

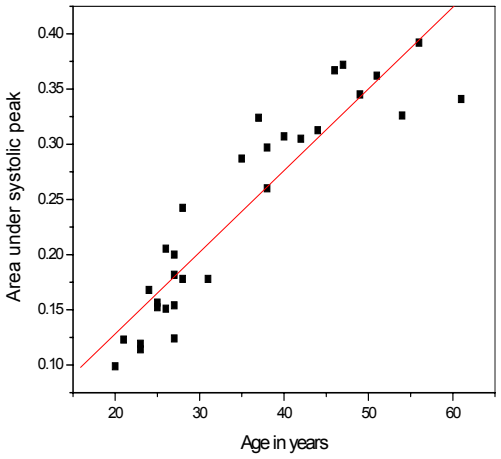


Fig 3.12: Plot of area under systolic peak vs age

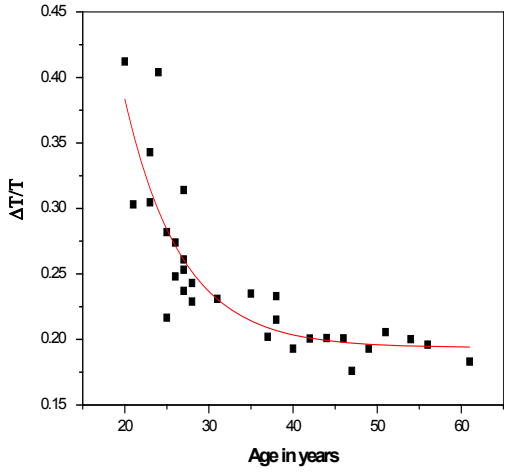


Fig 3.13: Plot showing variation of ΔT/T with age

The stiffness index, minimum rise time and $P_0/P_1$ ratio are derived from measures of distinctive portions of the blood volume pulse, the systolic and diastolic regions, respectively. As seen in Figs. 3.8, 3.9 and 3.10 the older subjects are found to have all the three parameters higher compared to the younger subjects. This agrees well with the

studies conducted earlier (1, 3, 8 ). In older subjects, the pulse can become smoothed, with changes in the blood pressure pulse producing less dramatic changes in the blood volume pulse at the periphery (23). The results show an overall elongation of the systolic rising edge, which could be explained on the basis of changes in resistance & compliance properties of arteries with advancing age. The diminishing of the dicrotic notch in older subjects is mainly due to age related increases in pulse wave velocity resulting in a faster reflected wave augmenting the forward wave. The value of '$\Delta T_{BVP}$' is found to decrease as age increases and $\Delta T_{BVP}$ /T correlates negatively with age. This variation with age may be attributed to the stiffening of the arteries and stiffness index with age.

In older subjects it is difficult to locate the dicrotic notch, thereby increasing the uncertainty in timing measurements related to the reflected wave. Here, by making use of the SDPPG, delicate changes in the waves were emphasized and easily quantified by differentiating twice the original PPG signal with respect to time. The B:A ratio could be considered as a marker of distensibility of large arteries, and hence little affected by the reflection wave (24). The area under the systolic peak is found to increase almost linearly up to the age of 31, and above that there is a slowing down in the rate of increase. The increase in the area under the systolic peak could be attributed to an increase in systolic stress and therefore increased systolic load resulting in part from systemic arterial stiffening. Stiffening of the arterial tree, whether due to aging, diabetes or other cardiovascular risk factors has important

haemodynamic consequences and there is a strong correlation between aortic stiffness and the degree of coronary artery disease (25).

## 3.5 CONCLUSIONS

Our analyses carried out using a cost-effective, self-designed hardware setup showed the overall trend of changes in pulse shape characteristics, with advancing age in a normal study population. In older subjects, the arteries are less distensible, resulting in a lower value of the B:A ratio and a higher value of pulse wave velocity thereby resulting in a rounded pulse. The six parameters, namely the stiffness index, minimum rise time, $P_0/P_1$ ratio, area under the systolic peak, B;A ratio, and the $\Delta T/T$ ratio, that we have determined, can provide a simple non-invasive means for studying the changes in the elastic properties of the vascular system. The obtained results demonstrate that the overall effect of changes in arterial properties, such as relating to arterial stiffness, can be detected non-invasively from the finger tip by examining the mean pulse shape and the SDPPG characteristics.

## References

1. Anne M. Brumfield and Michael E. Andrew, *Physiol. Meas,* **26**, 599-608 (2005)
2. John Allen and Allen Murray, *Physiol. Meas*, **24**, 297-307 (2003)
3. S. C. Millasseau, R. P. Kelly, J. M. Ritter and P.J.Chowienczyk,*Clinical Science*, **103**, 371-377 (2002)
4 Bramwell J C and Hill A V, *Lancet,* **1** , 891-892 (1922)
5. Eliakim M, Sapoznikov D and Weinman J, *Am Heart J,* **82,** 448-457 (1971)
6. Avolio A P, Chen S G, Wang R P, Zhang C L, Li M F and O' Rourke M F, *Circulation,* **68,** 50-58 ( 1983)

7. Hashimoto J, Chonal K, Aokei Y, Nishimura T, Ohkubo T and Hozawa A, *J. Hypertens,* **20,** 2415-2422 ( 2002)
8. Millasseau S C, Guigui F G, Kelly R P, Prasad K, Cockcroft J R, Ritter J M and Chowienczyk P J, *H*ypertension, **36,** 952- 956(2000)
9. Alberto Avolio, *J of Hypertension,* **20,** 2341-2343 ( 2002)
10. Chowienczyk P J, Kelly R P, MacCallum H, Millasseau S C, Anderson T L and Gosling R G, *J. Am. Coll Cardio,* **34,** 2007-2014 ( 1999)
11. O' Rourke M F, Kelly R P and Avolio A P, *The arterial pulse,* london: Lea and Febiger (1992)
12. Nitzan M. Khanokh B and Slovik Y, *Physiol. Meas.,* **23** , 85-93 (2002)
13. Sherebrin M H, Sherebrin R Z, *IEEE. Trans Biomed Engg,* **37**, 313-317 (1990)
14. Oliva I, Isper J, Roztocil K and Guttenbergerova, *VASA,* **5**, 95-100 ( 1976)
15. Takazawa K, Tanaka N, Fujita M, Matsuoka O, Saiki T, *Aikawa* M, Tamura S and Ibukiyama C, *Hypertension,* **32,** 365-370 (1998)
16. Takada H, Washino K, Harrel J S and Iwata H, *Med Prog Technol,* **21,** 205-210 (1997)
17. Kelly R P, Hayward C S, Avolio A P and O'Rourke M F, *Circulation,* **80,** 1652- 1659 ( 1989)
18. Allen John, *Physiol. Meas,* **28,** R1-R39 (2007)
19 Hashomoto Junchiro, Daiserki Watabe, Atsushi Kimnra, Hisaki Takahasi, Takayoshi and Okhubo, *Am J. Hypertension,* **18,** 477-485 ( 2005)
20. Shaija P J, Jayasree V K, Radhakrishnan P, *Proceedings of International cinference on sensors and related networks SENNET -'07,* held at VIT, Vellore, December 12-14 (2007)
21. Gavish B, *Microcirc. Endoth. Lymph,* **3,** 281-296 ( 1987)
22. Irina Illimonenko, Kalju Meigas and Rein Vahisalu, *Measurement Science review,* **3,** 49-52 (2003)
23. Allen J and Murray A, *J. Hum. Hypertension,* **16,** 711-717 (2002)
24. Lopez- Beltran E A, Blackshear S M, Finkel stein and Cohn J N, *Med. Biol Engg & Comput,* **36,** 748-753 ( 1998)
25. Wilkinson I B, MacCallum H, Rooijmans G D, Murray and Cockcroft, *QJM: International Journal of Medicine,* **93 (7),** 441-448 ( 2000)

# *Chapter 4*

## *Investigations on the effect of local cold exposure on the Photoplethysmographic signals*

**Abstract**

Peripheral blood flow at finger tips is influenced by temperature changes and sympathetic activities. Changes in the local temperature of the skin can produce a localized vasoconstriction that can decrease the skin blood flow essentially to zero. Cold exposure test is used to assess vasoconstrictive responses that results from both the local response and the reflex response of skin microcirculation to the cold stimulus. Pulsatile component of the PPG signal decreases when exposed to cold owing to the increase in sympathetic tone. Cold exposure tests are specifically useful for the evaluation of devices that we can wear during long term recording. Studying the changes in the morphology of the PPG signal allows us to detect and characterize the dynamic changes in peripheral vasoconstriction.

## 4.1 INTRODUCTION

Photoplethysmography (PPG) is an optical means to detect the periodic changes in light transmission due to the cardiac-induced changes in the arterial blood volume in the skin. The peripheral blood flow at fingertips is markedly influenced by temperature changes as well as sympathetic activities as the vasculature in finger contains an abundance of alpha-adrenergic receptors (1). It has been reported that changes in the local temperature of the skin can produce a localized vasoconstriction that can decrease the skin blood flow essentially to zero or vasodilatation that can increase skin blood flow to maximal level (2). The changes in the local temperature has been one of the important factors considered by many researchers when developing noninvasive measurements on PPG waveform, since the effects can produce significant errors such as the accentuation of local effects when relating the PPG signal parameters to central large artery properties (3-6).

The cold exposure test is often used to assess vasoconstrictive responses because it simulates the vasoconstrictive challenges commonly encountered in the clinical setting. Cold exposure is likely to introduce vasoconstriction and increased peripheral resistance as a result of which the PPG waveform will change owing to the alteration in vascular wall properties and pulse wave reflection. This response could be attributed to the

vasoconstriction that results from both the local response and the reflex response of skin microcirculation to the cold stimilus (7). The adrenergic responsiveness of the finger is more intense than that of other sites in the body. A technique such as plethysmography may therefore be more influenced by changes in adrenergic tone at the finger than at other sites. In the finger, where the walls of the cutaneous vessels are innervated by the α- adrenoceptors during cold immersion, there is an increase in the sympathetic tone which causes the pulsatile component of the PPG signal to decrease. Although the sensitivity of plethysmography at the finger may give misleading information about stroke volume & systemic flow , it can provide valuable information about changes in sympathetic tone. It may thus be used to detect a vasoconstrictive state & to guide vasodilator therapy. During surgery, the plethysmograph may be viewed as a semiquantitative assessment of the degree of analgesia. It may be used to determine the dose of anesthetic required to block adrenergic response in 50% of individuals who have a surgical skin incision (8). PPG signals reflect a combination of volume and flow changes in skin microcirculation . In normal subjects , the plethysmographic and blood pressure fluctuations are similar and highly correlated , with a generalized synchronization of the low frequency oscillations in different areas of the body.

In this era the emphasis is on wearable device, which is designed to be used in the user's day-to-day life. It is common in daily life that fingers are subject to mild local cold exposure e.g after holding a cold drink , suddenly exposing hands to cold air or washing hands in cold water. A few studies on the PPG signals using the cold

exposure test have been reported in literature , where the emphasis has been given to the pulse transit time and the comparison between the ear and finger pulse oximetry waveform (9). Computerised Photoplethysmography was used in detecting preclinical forms of vascular type vibration syndrome due to its highly specific nature (10). A significant reduction in the pulsatile component of the PPG and its normalized pulse area have been already reported (11) . Nevertheless , to our knowledge no extensive study has been carried out on the PPG pulse characteristics of the same finger before and after a mild cold exposure test. Here, a few new parameters have been arrived at, that could be derived from the finger PPG signal during the cold exposure test- a classic vasoconstrictive stimulus wherein a vasoconstrictive reflex is elicited by immersing a finger in ice cold water ( 4°C ). The morphological features used in this study allow the detection of changes in the pulse characteristics by monitoring how the shape of individual cardiac pulses change with time. Frequency domain techniques can be used effectively to analyse stationary processes, but analysing the morphology of each individual cardiac cycle allows us to detect and characterize the dynamic changes in peripheral vasoconstriction and changes in the dynamics of the blood flow to the periphery associated with the vasoconstriction due to the mild cold exposure.

## 4.2 METHOD.

### 4.2.1 Equipment and sensors.

Plethysmographic monitoring was obtained with a self designed hardware setup using a reflective mode PPG sensing unit. The

reflective PPG sensors comprised of an infrared light emitting diode (LED) with a peak wavelength of 940 nm and a matching photodetector The heat dissipation was less than 0.1 W and does not affect the skin circulation. The pulsatile component of the PPG was obtained from the detector using an analog filter with a passband of 0.5- 13 Hz. The design of the sensor probe is such that the contacting force does not vary with the measurements. During the course of measurement, subjects were asked to put their finger naturally on the sensing unit and maintain the contacting force nearly a constant.

### 4.2.2 Subjects and methods.

Fifteen healthy and normotensive persons (seven men and eight women with age ranging from 22 to 42) without known cardiovascular abnormalities were selected. All subjects gave their informed consent to participate in the study. They were instructed to abstain from caffeine and other known vasoconstrictive compounds for atleast 24 hrs prior to the recording. During the experiment, they were asked to sit firmly and quietly with their forearm lying on the table at the heart level in a temperature controlled room (22 ± 1.5 °C). Subjects were asked to relax for 5 minutes before the measurement. The first trial was performed under baseline conditions. Then the subject was asked to immerse the index finger in ice cold water for 30 sec to elicit a systemic vasoconstrictive response and the PPG signlas were recorded immediately after 30 sec of immersion (period of maximum response) . Finally, the third trial was carried out after 5 minutes of recovery from the cooling. The PPG signals were recorded using a digital storage oscilloscope at a sampling rate of 500 Hz .

## 4.3 SIGNAL PROCESSING AND DATA ANALYSIS

The PPG signals were recorded for a duration of 10 seconds. The set of measured pulses is optimized for contour similarity in order to minimise the effects of motion and damping artifacts normally present in such data. Also, normalization of the mean pulse function was performed for overall shape assessment and to get rid of variability due to heart rate differences (12). All the signals were analysed off-line using MATLAB & Microcal Origin 6.0 software. As has already been reported in (11), there was a significant change in the amplitude of the pulsatile component of the PPG signals before & after cold exposure irrespective of age. This is clearly evident from the figures 4.1 & 4.2 as shown below.

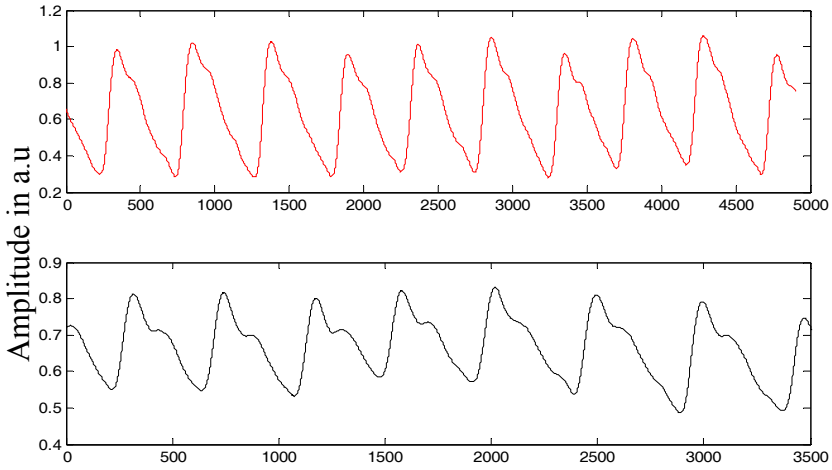


Fig 4.1: PPG signal before (red) and after cold exposure (black) for a subject aged 22 years

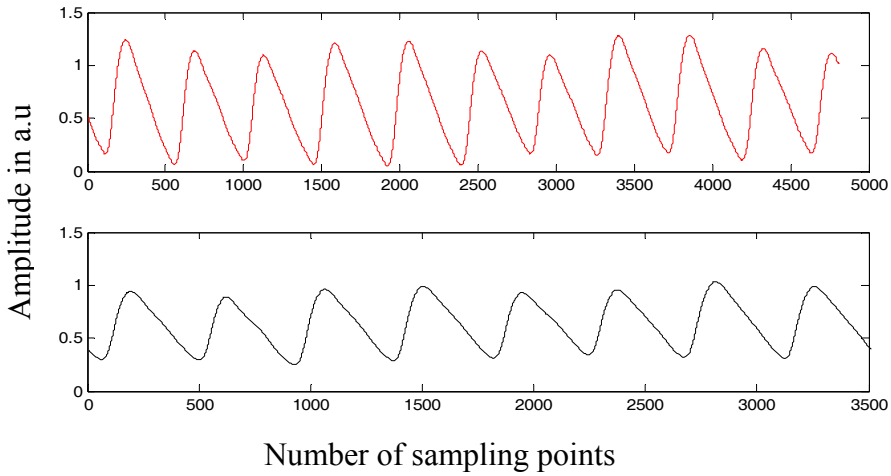


Fig 4.2: PPG signal before (red) and after cold exposure (black) for a subject aged 42 years

## 4.4 PARAMETERS STUDIED

The following parameters have been identified from the morphology of the PPG signal in this work which either show a decreasing or increasing trend with mild cold exposure.

### 4.4.1Normalized pulse width :

As shown in figure 4.3 the pulse height (PH) is the difference between the maximum of a cardiac cycle and the previous minimum. The cardiac period (CP) is the difference in time between the peaks of two consecutive cardiac cycles. The peak

width (PW) is the width of the pulse at a predetermined peak thresold ( PT). A PT value of 10% was selected (13).

Normalized pulse width (NPW) = PW/CP----------(4.1)

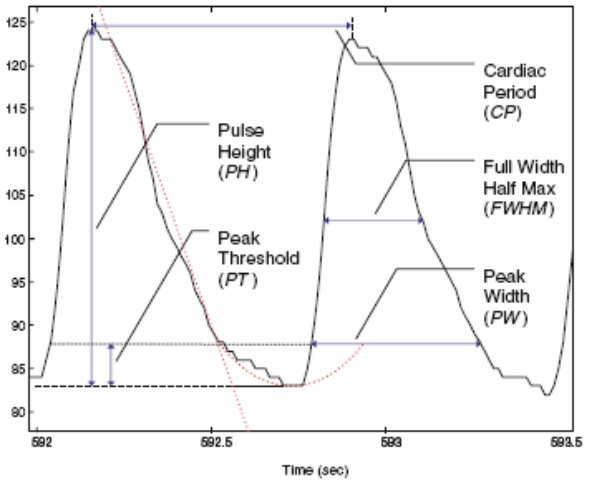


Fig 4.3: Features of the pulsatile component of the PPG used to determine the normalized pulse width

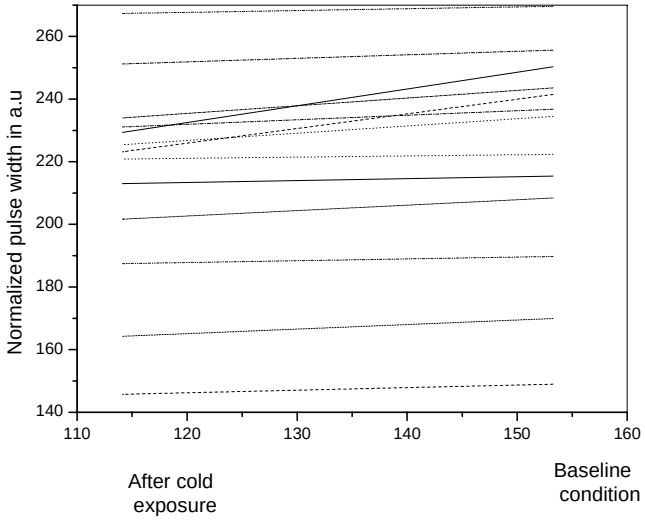


Fig 4.4: NPW before and after cold exposure

In our study it has been found that normalized pulse width decreases with mild cold exposure in all the subjects studied. This agrees well with the reduction in pulse rate with cold exposure ( inversely related to CP ) as reported in (11). Figure 4.4 shows the variation in normalized pulse width corresponding to the baseline and mild cold exposure conditions for the subjects included in this study.

### 4.4.2 Skin vasomotor reflex (SVMR):

Skin (Sympathetic) Vasomotor Reflex (SVMR) is vasoconstriction in response to cold, pain, inspiratory gasp, and other stimuli (14). SVMR is mediated by the sympathetic nervous system and is more intensive in fingers than in other sites in the body. It is useful in the diagnosis of autonomic neuropathies, evaluation of the extent of neuraxial block and depth of the general anesthesia (8). Laser Doppler Flowmetry (LDF) is used to measure SVMR preferably in the research laboratory, but it remains expensive and insufficiently robust for routine use in clinical practice.

The objective evaluation of somatosensory blockade level has been examined using different methods and most of them have proved to be unsatisfactory (8). To perform regional anesthesia effectively and safely in patients with whom communication is difficult for e.g- heavily sedated or mentally retarded patients an objective method for evaluating the level of sensory blockade is of immense help. So a cost effective method to measure SVMR would be of great help to pain clinicians in evaluating the segmental effects attained with various nerve blocks. The level of analgesia determined by the SVMR is

highly consistent with the level determined by conventional methods (15) and this is a clear indication that the SVMR test may be a useful objective indicator of the regional anesthesia level. The merits of the PPG technique are that it is a noninvasive procedure with good reproducibility, reliability and easiness of use in clinical practice. We have used the cold exposure test to assess the magnitude of the SVMR ratio using the equation

$$\text{SVMR ratio} = (BL-MV)/ BL * 100 \text{ ----------(4.2)}$$

where BL refers to the baseline values and MV the minimal values obtained for the recorded PPG signals. Figures 4.5 and 4.6 show a typical PPG signal with BL and MV marked and the variation in SVMR before and after mild cold exposure respectively.

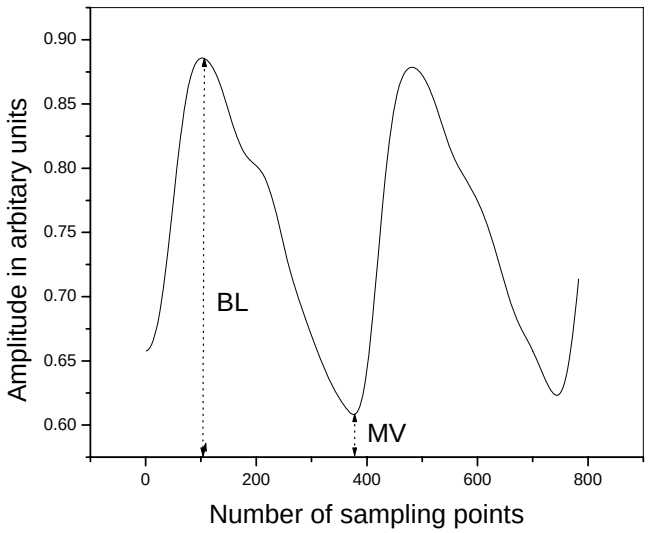


Fig 4.5: Typical PPG signal showing baseline and minimal values

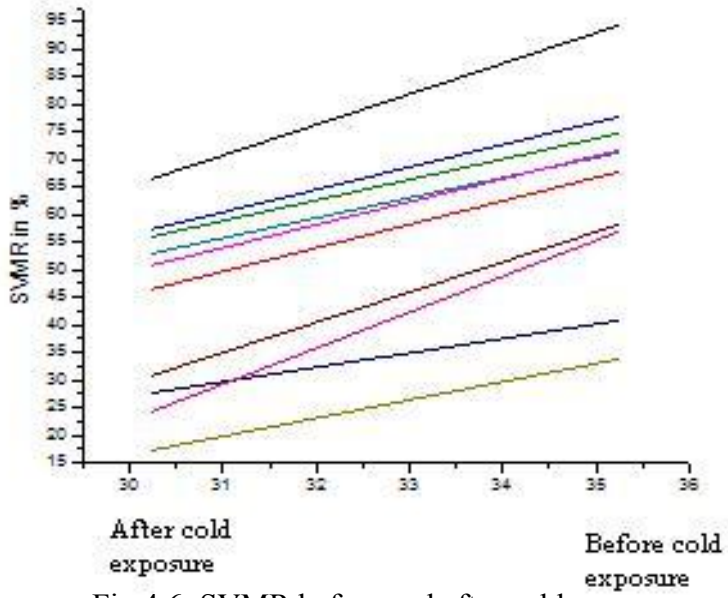


Fig 4.6: SVMR before and after cold exposure

As shown in figure 4.6, SVMR is found to decrease with cold exposure. This could be attributed to the reduction in skin blood flow owing to the vasoconstriction that occurs as a result of cold exposure.

### 4.4.3 Area Index

The pulsatile component of the PPG signal recorded from the finger tip precipitously declined immediately after cold water immersion. In this study we have investigated the variation in the areas under the systolic peak and the remaining portion of the cardiac cycle under baseline and cold exposure conditions and have arrived at an area index that is found to be different in both the cases. This

parameter could be of use in the early diagnosis of traumatic vasospastic disease (10).

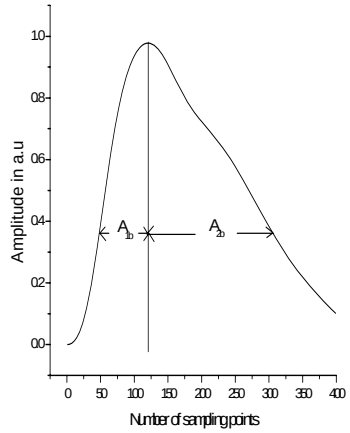


Fig 4.7: Area under Systolic peak & the remaining cardiac cycle under baseline condition

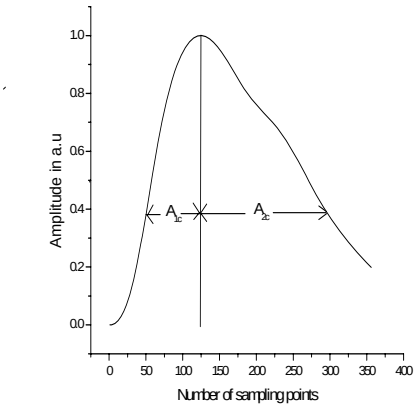


Fig 4.8 : Area under systolic peak & the remaining cardiac cycle under cold exposure condition

As shown in figures 4.7 and 4.8 , $A_{1b}$ and $A_{1c}$ represent the areas under the systolic peak under the baseline and cold exposure conditions respectively and $A_{2b}$ and $A_{2c}$ represent the areas under the remaining cardiac cycle under baseline and cold exposure conditions respectively. The area indices under the two conditions were calculated using the formulae given below.

$$AR_{cold} = A_{1c} - A_{2c} / A_{2c} \text{----------(4.3)}$$

where $AR_{cold}$ represents the area index after cold exposure.

$$AR_{baseline} = A_{1b} - A_{2b} / A_{2b} \text{----------(4.4)}$$

where $AR_{baseline}$ represents the area index under baseline condition.
It has been observed that in except two subjects, the area index under baseline condition is greater than that under cold exposure condition irrespective of age. This result seems to agree well with the one already reported in literature (11) where a significant reduction in the normalized pulse area has been found on mild cold exposure.

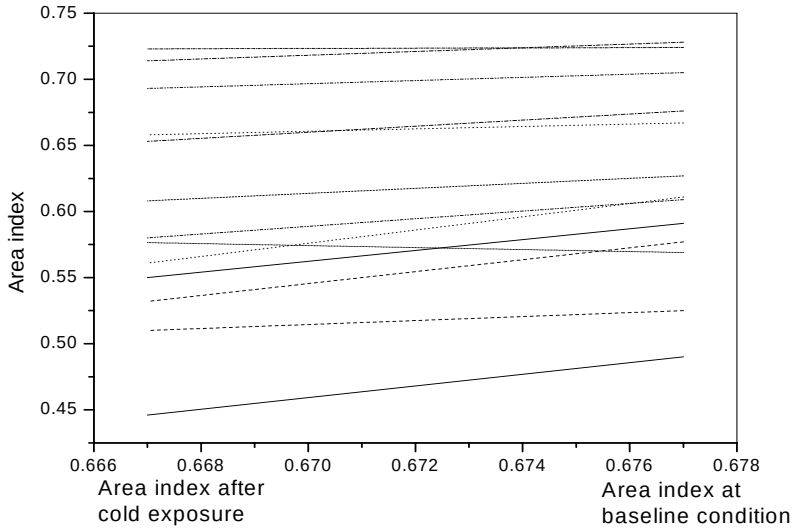


Fig 4.9: Area index under baseline and cold exposure condition

### 4.4.4 Half Width Amplitude

Half width amplitude (HWA) is defined as the width of the PPG pulse at the half of the peak amplitude.PPG can be used extensively to estimate vascular compliance and arterial blood oxygen saturation. To ensure accurate measurement in various applications, it is of interest to

study the changes in the photoplethysmogram under different conditions. It is however known that the PPG waveform changes with factors such as the contacting force between the PPG sensor and the contact part of the human body, aging and vasoconstrictive drugs and with local cooling of the body part around the PPG sensor (11,16). Though changes in the width ratio of the PPG pulse after exercise has been studied previously, the changes in the half width amplitude of the PPG pulse after cold exposure has not been reported so far . So the objective of this study was to examine the change in the width of the PPG waveform at half its peak amplitude at baseline and after cold exposure. It has been found that the half width amplitude decreases immediately after mild cold exposure in all the subjects irrespective of their age. This could be attributed to the reduction in the pulsatile component of the PPG and the normalized pulse area after cold exposure (11). Figures 4.10 and 4.11 show the PPG pulse with half width amplitude marked and the variation in HWA before and after cold exposure respectively.

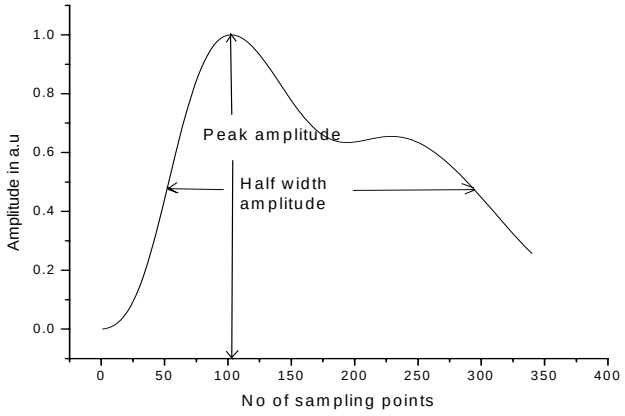


Fig 4.10: PPG pulse showing the half width amplitude

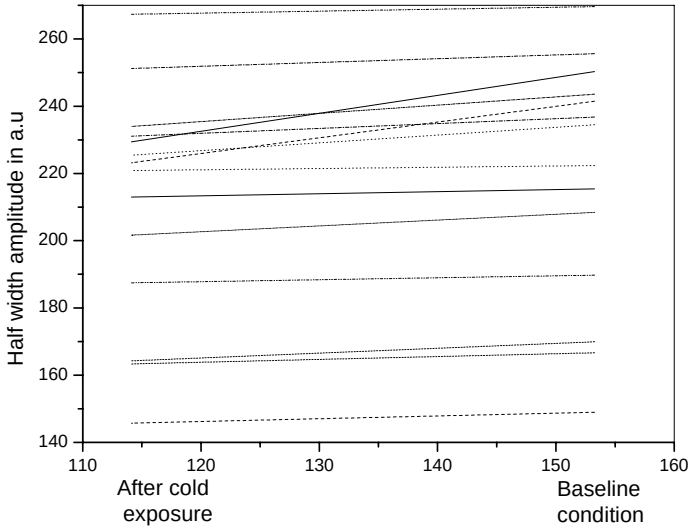


Fig 4.11: Variation in Half width amplitude before and after cold exposure

### 4.4.5 Latency between systolic and diastolic peaks ( ΔT )

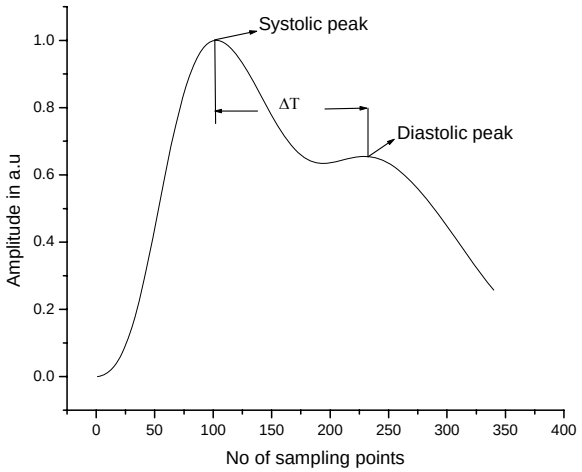


Fig 4.12: Typical PPG pulse showing the latency between the systolic and the diastolic peaks

The contour of the PPG signal exhibits an early systolic peak and a latter peak or point of inflection that occurs at a short time (ΔT) after the first peak in early diastole as shown in fig 4.12. As age increases the PPG pulse becomes more and more rounded and the dicrotic notch becomes less predominant. The time difference between the two peaks (ΔT) is a measure of the transit time between the subclavian artery and reflection sites and has been used to define a noninvasive measure of large artery stiffness (17). As shown in fig 4.13 the latency between the peaks is found to decrease with cold exposure irrespective of age for the subjects studied. As the arterioles get vasoconstricted when exposed to cold, they are likely to become stiffer thereby increasing the pulse wave velocity resulting in a faster reflected wave following the forward wave which could be the probable reason for the reduction in 'ΔT'.

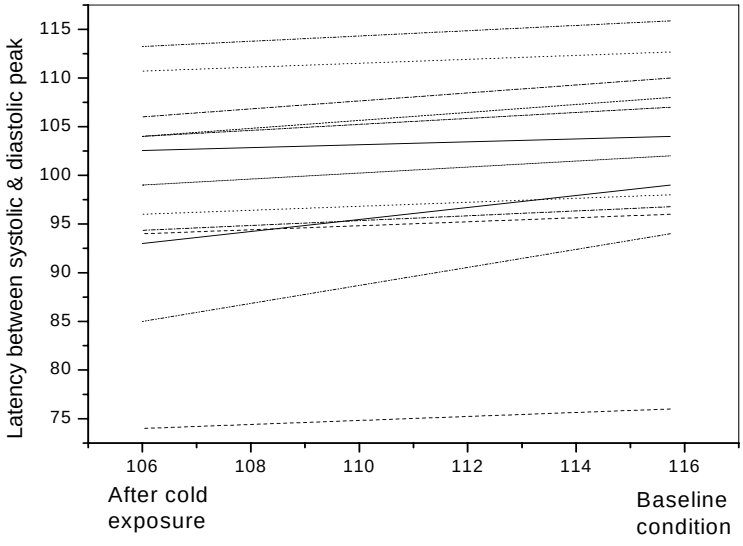


Fig 4.13: Plot showing 'ΔT' varaiation under baseline and cold exposure condition

## 4.5 CONCLUSIONS

Photoplethysmography in combination with cold exposure test provides an economic, noninvasive method to diagnose cold-induced vasospastic disorders and to evaluate therapeutic success. Although ample evidence is available in literature supporting the existence of a difference between males and females in vascular reactivity, in our study we have found no significant differences between genders based on the changes in finger temperature, amplitude of the pulsatile component of the PPG signal and any of the parameters studied. The changes in the PPG waveform features varied from subject to subject probably due to inter-subject's differences in sensitivity to finger vasculature response to temperature variation as well as the measuring site on the finger. The parameters studied here gives us an insight into what happens to the features of the PPG signal when the recording site is exposed to cold.

### References

1. Hertman A B and Orth L W, *Am. J. Physiol. Meas,* **136,** 669-679 (1942)
2. Bergersen T K, Eriksen M and Walloe L, *Am. J. Physiol. Regul. Integr. Comp. Physiol,* **269**, R325-330 (1995)
3. Wesseling K H, Settles J J, Hoeven G M, Nijober J A, Micelle W T and Dorlas J C, *Cardiovas. Res,* **19,** 139-145 (1985)
4. Imhol B P, Wieling W, van Montfrans G A and Wesseling K H, *Cardiovas. Res,* **38,** 605-616 (1998)

5. Millasseau S C, Guigui F G, Kelly R P, Prasad K, Cockcroft J R, Ritter J M and chowienczyk P J, *Hypertension,* **36,** 952-956 (2000)
6. Raamat R, Talts J, Jagomagi K and Kingisepp P H, *Proc. 22nd Annual EMBS Int. Conf,* 2223-2226 ( 2000)
7. Hahn M, Hahn C, Junger M, Steins, Zuder D, Klyscz T, Buchtemann, Rassner G and Blazek V, *Microvascular research,* **57,** 187-198 (1999)
8. Kand 0, Shimoda O, Higashi K and Sadanaga M, *J. Auton. Ner. Sys,* **48,** 257-266 ( 1994)
9. Aymen A. Awad, Ashraf M Ghobashy, wagih Ouda, Robert G Stout, David G Silverman and Kirk H. Shelley, *Anesth Analg,* **92,** 1483-1486 (2001)
10. Andrzej Dyszkiewicz and Michal Tendera, *Physiol. Meas,* **27,** 353-369 (2006)
11. Zhang X Y and Zhang Y T, *Physiol. Meas,* **27,** 649-660 (2006)
12. Jayasree V.K, Shaija P J, Manu P John and Radhakrishnan P, *Sensors & Transducers,* **87(1),** 39-45 (2008)
13. Stephen P Linder, Suzanna M Wendelken, Edward Wei and susan P McGrath, *J. clin. Monit. Comput,* **20,** 151-158 (2006)
14. Yoshihiro Ikuta, Osamu Shimoda, Kozuo Ushijimo and Hidenori Terasaki, *Anesth Analg,* **86,** 336-340 (1998)
15. Bengtsson M, Nilsson G E and Lofstrom J B, *Acta Anaesthesio.Stand,* **27,** 206-210 (1983)
16. Teng X F and hang Y T, *Physiol.Meas,* **25,** 1323-1335 (2004)
17. Millasseau S C, Kelly R P, Ritter J M and Chowienczyk P J, *Clin.Sci,* **103,** 371-377 (2002)

# *Chapter 5*

# *Photoplethysmographic studies on blood volume pulse signals based on body posture and lower limb height*

**Abstract**

The variation in the characteristics of blood volume pulse detected via Photoplethysmography signals detected from toe, while the lower limb is passively raised to different heights, has been studied. The changes that are detected in the PPG signals due to passive leg raising could help in the study of regulation of lower limb blood perfusion, which is an important factor in the assessment of peripheral occlusion arterial disease of the lower limbs especially in the case of diabetic patients. As passive leg raising can predict preload responsiveness, PPG could become an ideal noninvasive and less time consuming method in studying the haemodynamic response to fluid loading in patients with acute circulatory failure.

## 5.1 Introduction

The human autonomic nervous system modulates heart rate (HR) and blood pressure (BP) in order to maintain homeostasis and there are current interests in the response of the human autonomic nervous system that moderate the autonomic and local autoregulation to maintain homeostasis (1). To facilitate investigation of the reflex responses of the autonomic nervous system, relative changes in HR and BP have been used as the assessment parameters. A change in posture could induce changes in HR and BP and therefore facilitate the investigation of reflex responses. The PPG technique utilizes an optical or infrared sensor which produces a signal associated with a change in the volume of red blood cells in the peripheral microvascular bed with each pressure pulse initiated by the heart (1,2). Two common peripheral sites where there is a high degree of superficial vasculature are at the fingers and toes. The associated PPG pulse signal can be obtained through tissue pads at the various sites (3). The simplicity of the PPG technique has attracted much interest as a possible clinical investigation tool to assess cardiovascular information from patients ( 4,5,6). The time related derivations from the PPG signals have shown to be confounded by a postural change (7). This variation in PPG timing characteristic is mainly due to the sympathetic responses as a new posture is adopted.

In emergency medicine, acute circulatory failure is frequently caused by hypovolemia, either absolute (dehydration or hemorrhagic shock) or relative (septic shock). In the case of circulatory failure, one

of the most important initial therapy used for patients is volume expansion (8). So aggressive fluid loading (FL) is often necessary to maintain adequate cardiac preload and output, and early volume expansion has been shown to be an indicator of improved survival in studies on sepsis therapy in emergency departments (9,10). Though there are a few usual clinical variables like tachycardia, mean arterial pressure, lactate levels, and skin mottling, which can give an indication of the inadequacy of cardiac preload they are not very reliable (8). In the intensive care units (ICUs) there are many tools to evaluate FL responsiveness such as Doppler echocardiography, Esophageal Doppler and respiratory variations in invasive arterial blood pressure etc (8, 11-14). But all these specialized tools are invasive, sources of complications, time consuming and commonly not available in emergency departments (ED). Although respiratory variations in arterial systemic pulse pressure (ΔPP) is found to be a predictive marker of FL responsiveness (13), unfortunately it has been evaluated only in patients receiving mechanical ventilation and sedation ( ie. not breathing spontaneously). Also the determination of ΔPP requires intraarterial catheterization, which is not a common procedure in emergency departments (15). Furthermore, determining expiration and inspiration is difficult in spontaneously breathing subjects and so there is a need for a less time consuming, noninvasive tool in the emergency departments that could predict FL responsiveness. The PPG waveform is readily available in the Pulse oximeter equipment found in intensive care units, operation theatres and emergency departments. The PPG waveform depends on arterial pulsatility and a strong correlation has

been observed between the respiratory ΔPP and respiratory variations in PPG waveform (16-19).

Passive leg raising (PLR) is a simple reversible maneuver that mimics a rapid fluid loading by shifting venous blood from the legs towards the intrathoracic compartment. It also increases right and left ventricular preloads, thereby increasing stroke volume and cardiac output (20). Fluid responsiveness in critically ill patients induced by PLR has been already studied using Esophageal Doppler by evaluating the changes in aortic blood flow (21). Studies on the variations in the PPG waveform amplitude based on respiratory variations in spontaneously breathing subjects during PLR has been reported (22). The shape, amplitude and rhythm of the PPG pulsations have been studied based on the parameters derived from the dynamic component of the signal (23-25). But for a quantitative assessment of the heamodynamic changes, the ratio of the a.c component of the PPG signal to its d.c component is more appropriate than using the PPG pulsatile component amplitude itself because this ratio is proportional to the relative arterial blood volume increase during systole (23). Furthermore, it has been shown that this ratio is less prone to fluctuations caused by the incident light intensity and total absorption of the tissue (26). The objective of the present study is to use the noninvasive PPG technique to assess the changes in the haemodynamics by mainly concentrating on the d.c and a.c components of the signal, and their ratio which are blood volume related parameters induced by sympathetic responses on the lower extremities by postural changes. Since this ratio can be closely related

to the arterial compliance, we can extract information regarding the effects of the induced sympathetic activity on the circulatory system.

## 5.2 Materials and Methods

### 5.2.1 Subjects

This study included 15 healthy adults (9 male, 6 female) with their mean age ± standard deviation 29.5± 4.3 years. Their mean weight was 52.6± 2.7 Kg, and their mean height was 161± 5.9cm. The recruited population had a mean heart rate of 69.5 ± 3.7 beats/min, and the systolic and diastolic BP were 112.5 ± 2.2 mm Hg ,and 63.4 ± 7.2 mm Hg respectively. The inclusion criterion was the absence of clinically apparent arterial disease or physical abnormality. In addition, they were not observantly obese or on any medication, stimulants (including coffee) or on strenuous exercise 24 hours prior. All the measurements were done in a dim and tranquil environment at a controlled ambient temperature of 25°C. The BP related parameters were manually recorded from the subjects using a sphygmomanometer before the commencement of any test activity. The signals were recorded with informed verbal consent from all the recruited subjects.

### 5.2.2 Experimental setup

The details of the hardware setup used for recording the PPG signals has been described in detail elsewhere (27). We have used an indigenously developed system for the recording as there was no or

very little control of the raw PPG signals acquired from commercial systems. Since in commercial pulse oximeters both infrared and red light emitting diodes are used as sources , it is difficult to assess independently the acquired PPG signal characteristics from a single source. The customized PPG acquisition unit has a bandwidth from 0.5-15 Hz and was constructed using discrete electronic devices. The PPG pulse reflectance mode transducers employed for the present investigation had an infrared LED operating at 940 nm as the source and used low level tissue illumination (output power less than 3mW). The probe was used to record the PPG signal from the subject's second toe of the right foot. The signals were recorded using a digital phosphor oscilloscope and sampled at 500 Hz. The post processing and analysis of the recorded signals were done using MATLAB and Microcal Origin 6.0 software.

### 5.2.3 Experimental Protocol

The subjects were requested to measure their SBP and DBP just before the trial. They were asked to rest for 5 minutes prior to any measurements to give room for cardiovascular stabilization and familiarization with the environment. The laboratory trials in this study were conducted using two protocols which are mentioned below.

**Protocol 1:**

(i) Semirecumbent (baseline) (ii) Passive leg raising (iii) Semirecumbent (Recovery) position

In the baseline condition the subject was breathing spontaneously with his back reclining at an angle of 60° with the floor and the lower limbs parallel to the floor ( referred to as the semirecumbent position). The first set of measurements was obtained in the baseline condition after the subject rested for 5 minutes. This was followed by passive leg raising where the lower limbs of the subject were lifted keeping them straight to an angle of 60◦ with the floor while the trunk was lowered in a supine position. Since the maximal effect of PLR is observed within 1 min of elevation of the legs (28), a second set of recordings were made during leg elevation for 5 minutes. Finally the third set of measurements were taken after a 5 minute rest period in the semirecumbent position as in the baseline condition ( referred to as recovery position). The procedure used in this protocol is summarized in Fig 5.1.

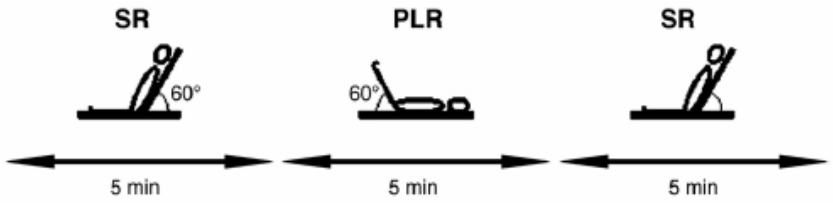


Figure 5.1: Subject positions during the study. SR indicates semirecumbent position and PLR indicates Passive leg raising.

**Protocol 2:**

(ii) Supine position (ii) passively raising the right foot in steps of 5cm upto a height of 30cm using wooden blocks (iii) recovery back to supine position.

Using this protocol the subject was asked to lie on a trial bed ( supine position) and relax for 5 min. During the period of the successive trial, the right foot was passively raised using a wooden block to a height of 5,10,15 20,25 and 30 cm respectively whilst the left foot was kept still. The order of the height was random. During the execution of this protocol , the PPG signals were collected from the subject's second right toe in the supine position for 10seconds which is considered to be the baseline condition (step1). After that, wooden blocks of 5cm height each were gently added up below the subject's right foot one by one upto a height of 30 cm. Each time a block was added , the subject was requested to relax for 10seconds after which the PPG signals were recorded for 10seconds (step 2). The wooden blocks were gently moved out and the right foot was returned to the baseline condition. After 10sec of relaxation the PPG signals were recorded for 10sec again (step3) . Figure 5.2 shows a subject in supine position and with the right foot passively raised as mentioned in step(2). The duration of recording was selected such that unnecessary strains to the raised foot could be reduced. Also this was to minimize possible motional artifacts that could affect the recorded PPG signals and thereby complicate the acquired results.

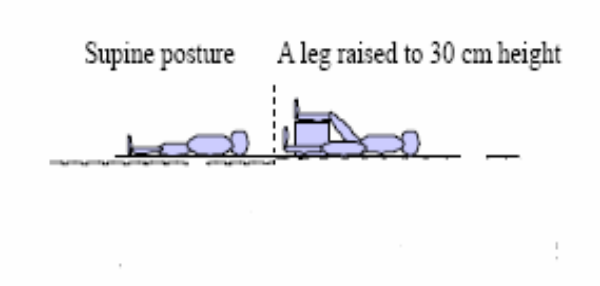


Fig 5.2: Supine posture and passive leg raising with a wooden block introduced under the right foot

### 5.2.4 Arithmetical Protocols & Data analysis

Figure 5.3 shows the maximal (MAX) value of the PPG signal that is proportional to the light irradiance transmitted through the tissue at the end of diastole when the arterial blood volume is at the minimum. During the normal cardiac cycles , there is a reduction in the PPG amplitude at systole, and the absolute value from the peak to the trough of the PPG signal which is the pulsatile component of the PPG signal is taken as the amplitude ( AMPL). If we assume the sympathetically induced blood volume change to be homogenously distributed in the illuminated tissues ( $\Delta V_{blood}$ ), then its corresponding absorbance (A) can be related to the absorption coeffecient of blood ( $\alpha_{blood}$ ) using the modified Beer- Lambert's law as

$$A = \alpha blood * \Delta Vblood \qquad \text{-------} \qquad (5.1)$$

It has been shown that the MAX and AMPL parameters are related to the arterial blood volume modulation (29), and equation (1) can be rewritten as

$$AMPL/MAX = \alpha_{blood} * \Delta V_{blood} \qquad \text{--------} \qquad (5.2)$$

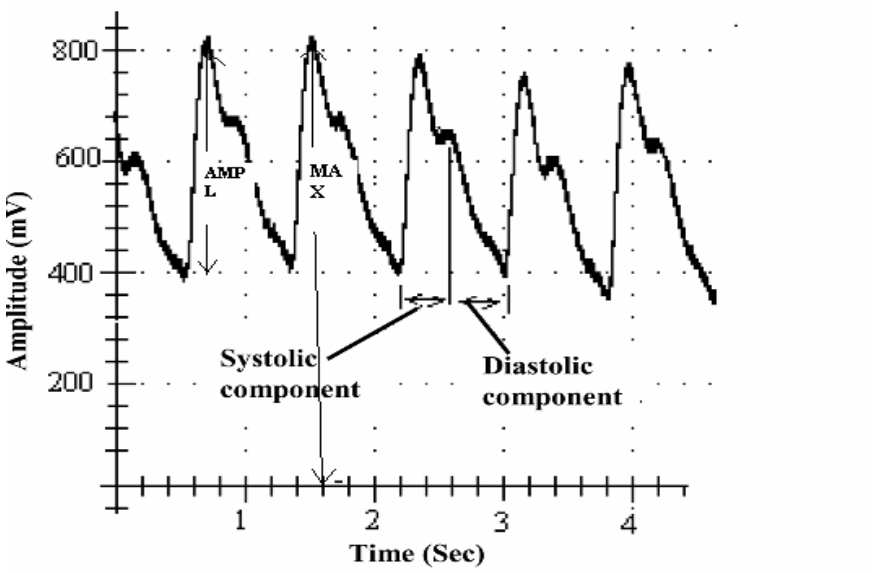


Fig 5.3 Typical PPG signal showing AMPL & MAX values

The digitised PPG MAX and AMPL values collected from the trial were analysed using Microcal Origin 6.0 software. The pulse to pulse AMPL was first measured, from which the mean AMPL of each

subject was calculated. The mean MAX value was calculated by averaging over 10 s recording and for each individual postural trial height, the mean value of the MAX and AMPL were calculated by averaging mean AMPL and MAX over all the 15 subjects. Due to the possible intersubject differences, all the derived parameters were compared relative to the baseline value of each subject. Table 5.1 below shows the mean values of the normalised amplitude in the supine position

| Height (cm) | AMP (Mean) | MAX (Mean) | MAX/ AMPL | Standard Deviation (MAX/ AMPL ) |
|---|---|---|---|---|
| 5 | 1.0 | 2.02 | 2.02 | 0.1 |
| 10 | 0.92 | 1.96 | 2.13 | 0.12 |
| 15 | 0.70 | 1.76 | 2.50 | 0.13 |
| 20 | 0.59 | 1.67 | 2.84 | 0.13 |
| 25 | 0.49 | 1.58 | 3.22 | 0.15 |
| 30 | 0.38 | 1.47 | 3.86 | 0.13 |

Table 5.1 : Normalised PPG amplitudes in the supine postural trial

## 5.3 RESULTS & DISCUSSION

PROTOCOL 1: The PPG signals recorded from the subject's second

right toe while performing the first protocol mentioned above for the subjects studied is shown in figure 5.4.

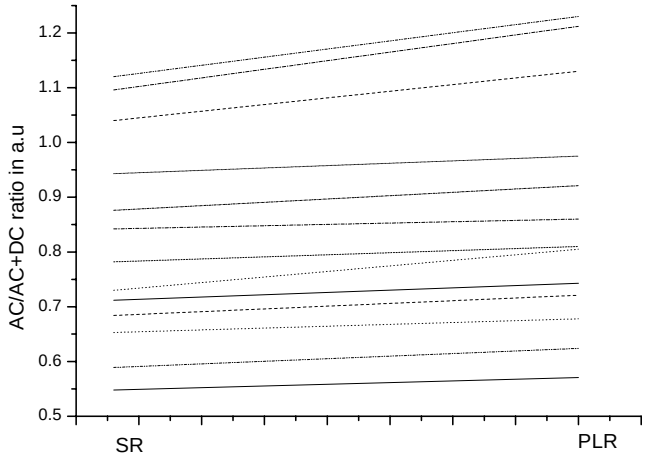


Figure 5.4 : Variation in AC/AC+DC ratio during the execution of protocol 1

It can be clearly seen that as the right foot is passively raised , from the baseline condition which is the semirecumbent position the ratio of the AMPL (AC) to AMPL + MAX (AC+DC) component of the PPG signal increases. The ratio parameter can be closely related to the change in arterial compliance resulting from the lower tonus of its wall muscle induced by the onset of sympathetic activities. Since the MAX and the AMPL parameters show significant changes during the execution of the first protocol, there is an implication that the induced sympathetic activities may have affected the mean systolic and diastolic blood pressure .

PROTOCOL 2 : The PPG signals recorded from the subject's second

right toe while performing the second protocol mentioned above for a subject aged 28 years is shown in figure (5.5)

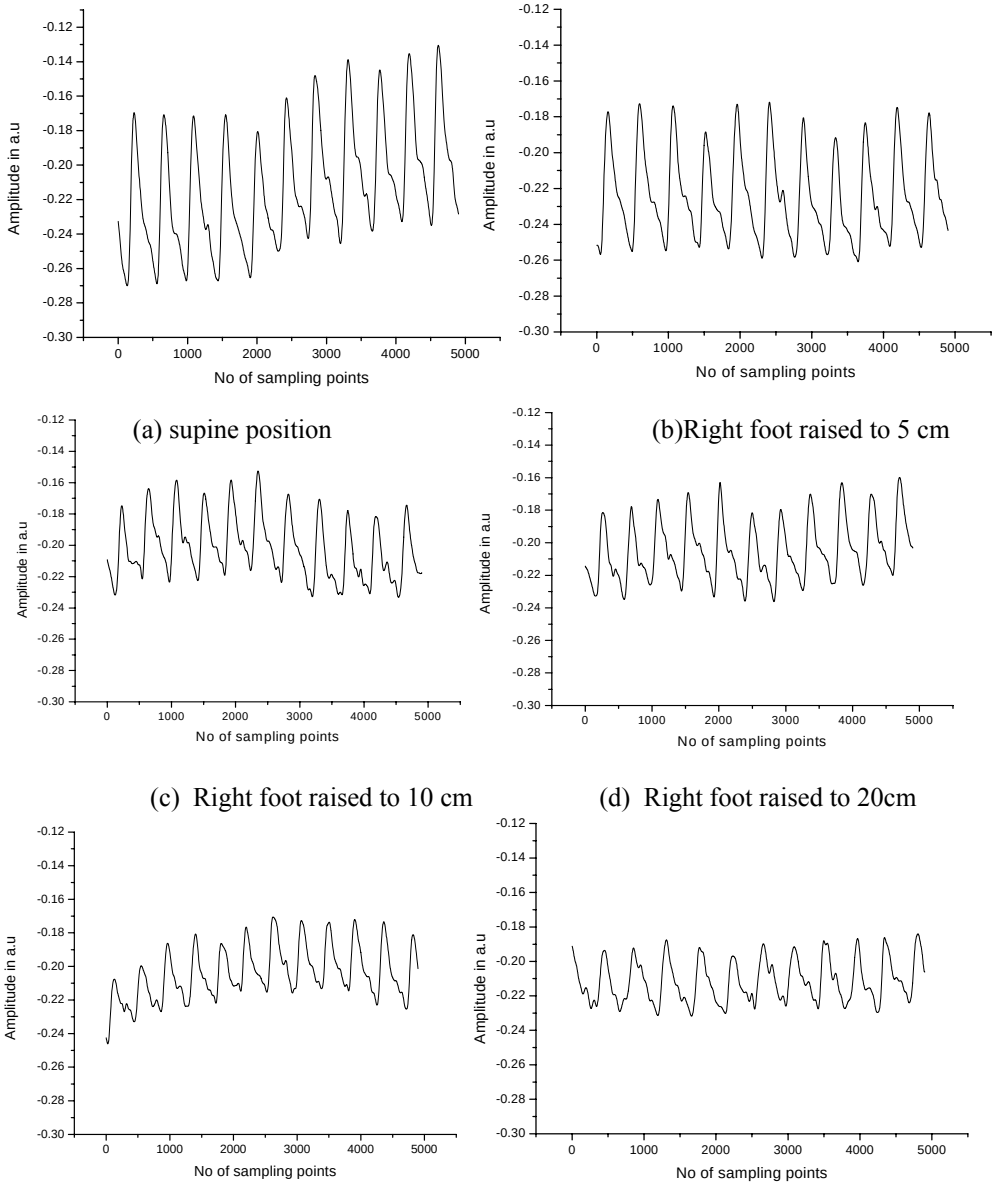


Fig 5.5: PPG signals of a subject aged 28 years with foot in normal position and raised to various heights in supine position

It can be clearly seen that as the right foot is passively raised , the amplitude of the pulsatile component of the PPG signal decreases. Figure 5.6 shows the variation in the normalised mean of the AMPL of the subjects studied as a function of height of the passively raised right foot as mentioned in the second protocol. It is found that as the height of the passively raised leg increases, the AMPL value decreases.The MAX and the AMPL parameters are known to be associated with changes that occur during the cardiac cycle (30,31) .

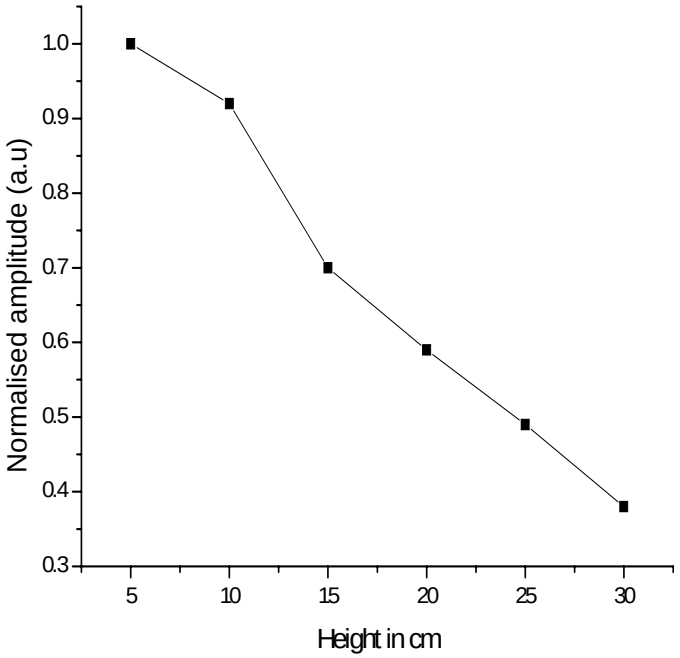


Fig 5.6: Average normalised AMPL (AC component) vs height plot for passive leg raising in supine position

Figure 5.7 below shows the variation in the mean value of the MAX amplitude as a function of height of the passively raised foot and figure 5.8 shows the peripheral vascular response of the AMP/MAX ratio in the lower limb as the height of the foot varies. From the results obtained, it can be suggested that the parameters derived from the PPG signal are dependent on arterial BP and hence be affected by the sympathetic activity. Also when a foot is passively raised from a low to high position , the venous blood in the lower limb can return to the heart as a result of which the end-diastolic volume, the stroke volume and the cardiac output could be increased (32) . The baroreceptor reflex is found to be activated when the relative height of the raised foot and the heart level changes (33). The effect of blood pulse regulation with the postural change in our study agrees well with the theory of blood flow dynamics (34) .

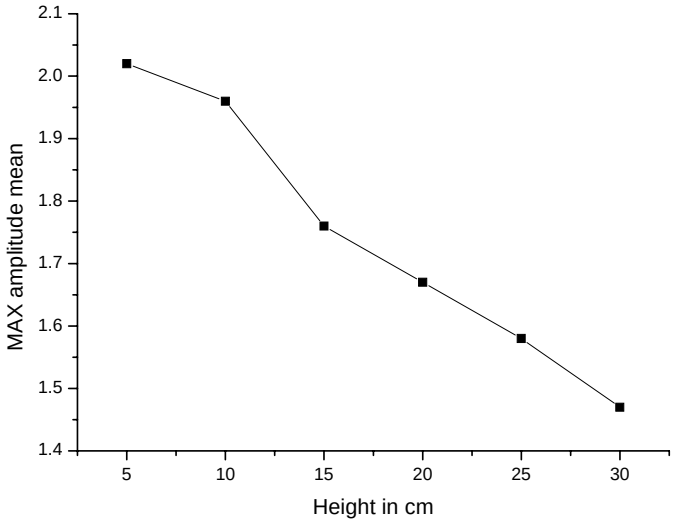


Fig 5.7: Average MAX amplitude vs height plot for Passive leg raising in supine position

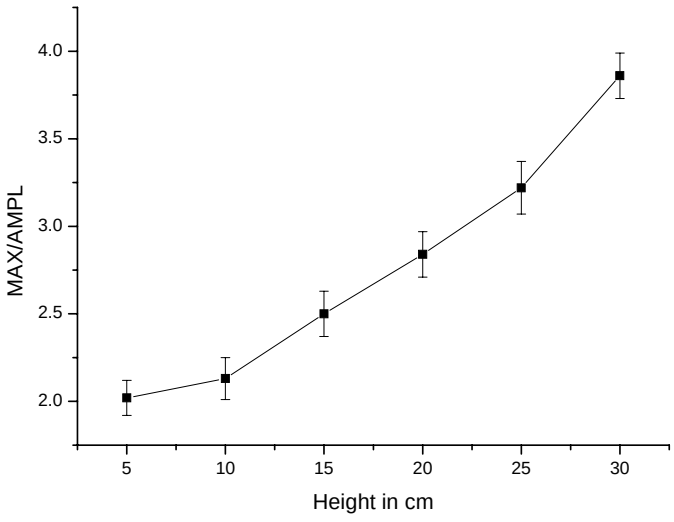


Fig 5.8: Peripheral vascular response of the lower limb in supine position (MAX/AMPL) ratio

## 5.4 CONCLUSIONS

The PPG amplitude related parameters derived from the study conducted on the lower extremity show significant changes.The monitoring of these parameters help in evaluating the change in arterial compliance and tissue blood volume of the selected periphery could be estimated. The execution of protocol 1 gives us an idea of how the body posture affects the PPG signal and protocol 2 gives a picture of how the PPG signal gets affected when the relative height between the heart and the raised foot changes. The PPG-derived heamodynamic parameters can provide information on the effects of the induced sympathetic activity on the circulatory system which could be of help in screening diabetic patients. PPG being a noninvasive and convenient method shows potential to become a clinical tool for assessing the reflex response of the autonomic nervous system .

## References

1. Lopez-Beltran E A, Blackshear P L, Finkelstein S M and Cohn J N, *Med. Biol. Engg. Comput*, **36**, 748- 753 (1998)
2. Johansson A and Oberg P A, *Med. Biol. Engg. Comput*, **37**, 42-47 (1999)
3. Tur E, Tur M, Maibach H I and Guy R H, *J. Invest. Dermatol* , **81,** 442-446 (1983)

4. Allen J and Murray A, *J. Hum. Hypertens,* **16**, 711-717 ( 2002)
5. Drinnan M J, Allen J and Murray A, *Physiol. Meas*, **22,** 425-432 (2001)
6. Foo J Y A, Wilson S J, Williams G, Coates A, Harris M.A and Cooper D M, *Physiol. Meas,* **26**, 317-328 ( 2005a)
7. Foo J Y A, Wilson S J, Williams G, Harris M A, Cooper D M, P*hysio. Meas,* **26,** 1093-1102 (2005)
8. Task force of the American College of Critical Care Medicine, Society of Critical care medicine, *Crit Care Med,* **27**, 639-660 (1999)
9. Micek S T, Roubinian N, Heuring T, *Crit Care Med,* **34**, 2707-2713 (2006)
10. Rivers E, Nguyen B, Havstad S, *N. Engl J Med,* **345** , 1368-1377 (2001)
11. Feissel M, Michard F, Mangin I, *Chest,* **119, 867-873** (2001)
12. Pinsky M R and Vincent J L, *Crit Care Med,* **33,** 1119-1122 (2005)
13. Michard F, Boussat S, Chemla D, Anguel N, Mercat A, Lecarpentier Y, Richard C, Pinsky M R and Teboul JL, *Am J Respir Crit care Med,* **162,** 134-138 (2000)
14. Tavernier B, Makhotine O, Lebuffe G et al, *Anesthesiology*, **89**, 1313-1321 (1998)
15. Bedford R F, Wollman H, *Anesthesiology,* **38**, 228-236 (1973)
16. Dorlas J C and Nijboer J A, *Br J Anaesth,* **57**, 524-530 (1985)
17. Patridge B L, *J Clin Monit,* **3,** 263-268 (1987)
18. Shamir M, Eidelman L A, Floman Y et al, *Br J Anaesth,* **82,** 178-181 (1999)
19. Cannesson M, Besnard C, Durand P G et al, *Crit care,* **9,** R 562-568 (2005)
20. Boulain T, Acard J M, Teboul J L, Richard C, Perrotin D, Ginies G, *Chest*, **121**, 1245-1252 (2002)
21. Lafanechere A, Pene F, Goulenok C, Delahaye A, Mallet V, Choukroun G, Chiche J D, Mira J P and Cariou A, *Crit Care,* **10(5),** R 132 (2006)
22 Samuel Delerme, Robin Renault, Yannick Le Manach, Virginie Lvovschi, Mouhssine Bendahou, Bruno Riou and Patrick Ray, *Am J. Emer Med,* **25,** 637-642 (2007)
23 Foo J Y A, Lim C S and Wilson S J, *Angoilogy,* **(**2008)
24 Allen J, *Physiol. Meas,* **28,** R1-R39 (2007)

25 Erts R, Spigulis J, Kukulis I and Ozols M, *Physiol Meas,* **26,** 865-874 (2005)
26 Nitzan M, Babchenko A, Khanokh B and Landau D, *Physiol. Meas,* **19,** 93-102 (1998)
27 Jayasree V K, Shaija P J, Manu P John and Radhakrishnan P, *Sensors & Transducers Jl,* **87** ( Issue 1), 39-45 (2008)
28 Monnet X, Rienzo M, Osman D, *Crit care Med,* **34,** 1402-1407 ( 2006)
29 Nitzan M, Babchenko A, Khanakh B and Landan D, *Physiol Meas,* **19**, 93-102 (1998)
30 Webster JG, *Medical Instrumentation : Application and design,* 3rd ed. Newyork, NY: John Wiley & Sons Inc, 1998
31 Zourabian A, Siegel A, Chance B, Ramanujan N, Rode M and Boas D A, *J. Biomedical Optics,* **5** , 391-405 2000
32 Berne R M and Levy M N, *Physiology,* St Louis Mosby, London 1998
33 XIN Shang-Zhi, HU Sijung, Crabtree Vincent P, ZHENG Jia, AZORIN-PERIS Vincent, ECHIADIS Angelos and Smith Peter R, *J. Zhejang University Sci A,* **86** , 916-920 2007
34 Liu Z R and Li X X, *The theory and method of blood flow dynamics,* Fu Dan University Publishing House 1997

# *Chapter 6*

## *Photoplethysmographic assessment of haemodynamic variations in diabetics affected by diabetic retinopathy*

**Abstract**

The characterisation of the PPG pulses of diabetics affected by diabetic retinopathy and nondiabetics gives us an idea about how the activity of the autonomous nervous system is affected by the disease. Bilateral symmetry studies help in detecting the inadequacy of the sympathetic nervous system. The right-left baseline or amplitude correlation coefficient, being less dependent on age , provides a parameter for the assessment of diabetic retinopathy. The correlation coeffecient is found to be low for diabetics compared to the normals and this has been verified using a statistical signal processing approach. Another parameter which is related to the distensibility of the arteries has been derived from the second derivative of the PPG and it has been found that diabetics have a lower value of this parameter when compared with age matched normal subjects.

## 6.1. Introduction

PPG provides a qualitative measure of the tissue blood volume increase during systole by measuring the light attenuation through the tissue as a function of time. The PPG signal oscillates with the heart cycle period, due to the systolic increase in the tissue blood volume resulting in a lower transmission of light ( 1-2). The different components of the PPG signal, such as the amplitude of the pulsatile component of the PPG signal (AM) and the baseline (BL) mainly fluctuate in the low-frequency region and these are mediated mainly by the sympathetic nervous system ( 3-4).The fluctuations in the finger blood volume are due to the constriction and relaxation of the tissue blood vessels which are predominantly affected by the sympathetic nervous system.

Microvascular blood flow in the human skin is subjected to rhythmic variations reflecting the influence of heartbeat, respiration, intrinsic myogenic activity, neurogenic factors and endothelial activity. The available noninvasive diagnostic methods for the evaluation of blood flow through cutaneous microcirculation are venous occlusion plethysmography (VOP) and laser doppler flowmetry ( LDF) (5). Though laser Doppler flowmetry is a popular diagnostic method, vasomotion in adjacent vessels under its probe does not consist of a single rhythmic component. Hence spectral analysis has to be performed to detect periodic components within the complex signal and obtain a detailed insight into the mechanism involved in peripheral blood flow regulation (6). Hence a

simple, noninvasive, economic and less time consuming method is desired to assess microcirculation and that is where PPG has proved its worth.

Diabetes Mellitus is a chronic, systemic, life-threatening disease that can affect the eyes & nervous system, as well as the heart, kidneys and other organs. It is a major risk for vascular disorders affecting both microcirculation and macrocirculation. Diabetic retinopathy (DR) is the complication caused to retina due to diabetes and may lead to blindness if untreated. It is an ocular manifestation of systemic disease which affects up to 80% of all patients who have had diabetes for 10 years or more. Previous works on diabetics and nondiabetics available in the literature were mainly focussed on the effects of diabetic neuropathy, especially related to foot problems ( 6- 9). Recently work has been done on the identification of diabetic retinopathy stages using the non- linear features of the higher order spectra using support vector machine classifier based on image signal processing (10). The nature of fluctuation of each PPG parameter can be determined by simultaneously measuring the PPG signal in both the hands and evaluating the synchronisation of the variability of the PPG parameter in the two hands (11). The PPG pulse becomes more dampened with almost no dichrotic notch in the case of diabetics. Measurement of the right-left correlation coeffecient can detect the inadequacy of the sympathetic nervous system (12). The right-left amplitude (AM) correlation coeffecient only slightly depends only slightly on age and so it is a parameter for retinopathy assessment. This parameter does not require the

use of age-adjusted normal ranges and is therefore advantageous over age-dependent parameters.In our proposed work we have compared the correlation coeffecient of the amplitude of the PPG signal for the diabetics and nondiabetics for assessing the bilateral symmetry and verified the same using statistical signal processing. Correlation functions were estimated to measure the similarity of signals.The second derivative of the PPG (SDPPG) has also been used to arrive at a parameter which is closely related to the distensibility of arteries. The method employed in the present studies is simple, economical, reliable and less time consuming and could become an effective screening tool for the early diagnosis of diabetic retinopathy.

## 6.2 MATERIALS AND METHODS

### 6.2.1 Subjects

PPG examinations were performed on the index fingers of 15 healthy subjects ( 8 males and 7 females) aged 38-61 years ( mean age 45.8 years) with no known vascular disease and of 15 diabetic patients ( 6 male and 9 female) aged 38-78 years ( mean age 45.0 years). The duration of the diabetes was 2-25 years. The recordings were done at Ranjini eye care clinic, Vyttila under the supervision of a medical practitioner. Subjects on anti-hypertensive therapy were excluded from the study due to the potential influence of the same on the SDPPG components. Subjects with liver and renal dysfunction and gastrectomy were also excluded from the

study. The non-diabetic patients had no known neurological or cardiovascular disease. Patients treated with beta-blockers were excluded from the study, because beta- blockers pharmacologically reduce sympathetic activity. The clinical characteristics of the diabetic patients and the non-diabetic subjects are given in Table 6.1.

All the subjects were instructed to refrain from coffee consumption for 3 hours before the examination. The PPG examination was performed with the subjects in the sitting position , with their forearm resting on a table and the finger at heart level. All the subjects were asked to relax for 5 minutes before the recording to allow for cardiovascular stabilization. Subjects were asked to breathe regularly, to relax and to stay still during the measurement period.

| Sl. No | | Diabetic (Retinopathy) | Non-diabetic |
|---|---|---|---|
| 1. | Total Number | 15 | 15 |
| 2. | Sex (M/F) | 6/9 | 8/7 |
| 3. | Age, Years | 45.8.1± 6.2 | 45.0± 6.3 |
| 4. | Systolic Blood Pressure,mm Hg | 124.3±7.5 | 120.8±6.5 |
| 5. | Diastolic Blood Pressure, mm Hg | 77.8±9.8 | 78.5±3.2 |

Table 6.1: Demographic data of diabetic and non-diabetic subjects

### 6.2.2 PPG Measurement System

The PPG acquisition unit is a self designed portable unit which consists of two amplifiers which are matched in pair,each with a bandwidth of 0.5-15 Hz The system was designed such that the PPG pulses from the right and left index fingers could be collected simultaneously. Both the PPG probes were of the reflection type with an LED in the infrared region as the source and a matched photodiode as the photodetector. The PPG signals were sampled at a rate of 500 samples/s. A dedicated digital storage oscilloscope(Tektronix TDS 5104B,1GHz,5Gs/s) was used for data capture and for further offline analysis of the captured data. Care was taken to see that the effects of phase differences due to mismatching of the electronic measurement system were small relative to the right–left differences for the physiological data. Atmost care was also taken to apply similar right–left side pressure with the Velcro straps and also to have symmetrical positioning of the probes relative to the measurement sites. The gains of the two PPG amplifiers were set individually to utilize the dynamic range of the recording system. Subjects were asked to breathe regularly, to relax and to stay still for the 5 minute pulse measurement period. The block level diagram of the PPG measurement system is shown in figure 6.1.

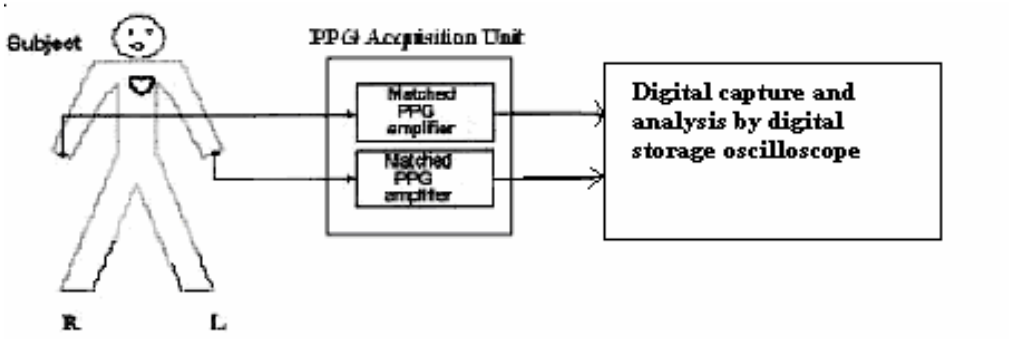


Fig 6.1: PPG measurement system for bilateral study

### 6.2.3 System Validation

Electronic matching of the right-left PPG pulse channels is indispensible for bilateral symmetry assessment. A 1 Hz signal derived from a stable signal generator was used to externally drive the current simultaneously in the infrared LEDs of the two PPG probes causing reflected signals to arrive at each photodiode. The simulated pulse waveforms were captured by the digital storage oscilloscope at 500 Hz.

### 6.2.4 Pulse wave analysis

6.2.4a Bilateral symmetry measurement

Similiarity in pulse waveform shape at the two index fingers for the diabetics and nondiabetics was assessed using two types of analyses- (i). Right-left correlation coeffecient for the very low frequency fluctuation of the amplitude of the PPG pulse which provides a measure of the degree of similiarity and (ii) Determination of autocorrelation and crosscorrelation functions using statistical signal processing approach.

The pulse was analysed off-line using MATLAB based utilities. The obtained pulses were suitably filtered and digitally analysed for the detection of the maximum and mimimum of each PPG pulse. The first 25 sec of recording free from movement artefacts was divided into ten 2.5 sec epoch and the peak to peak amplitude for each of them was normalized to unity. This was further used to determine the right-left correlation coefficient for the amplitude in both the classes of subjects. Using the statistical signal processing approach the Autocorrelation Function (ACF) and the Crosscorrelation function ( CCF) were determined from which an inference regarding the degree of similiarity between the PPG pulses recorded from the right and left index fingers could be obtained. Autocorrelation was used to measure the self-

similarity of each signal and CCF was employed to show the correlation between the right and left side PPG signals.

6.2.4b Analysis of Second derivative of the photoplethysmogram

Diabetes is associated with endothelial dysfunction and increased arterial stiffness, both of which may contribute to excess cardiovascular mortality in such patients. Arterial stiffening increases pulse wave velocity and wave reflection, which augments central systolic pressure and stress (13). Increased arterial stiffness is a characteristic feature of both type1 and type 2 diabetes and can be detected using a variety of techniques (14).Current methods of assessing arterial stiffness, such as measurement of pulse wave velocity (PWV) or the use of ultrasound-derived indices, only provide information about compliance within a specific artery or arterial segment, and hence tend to be time-consuming or operator dependent. The technique of pulse wave analysis provides information about systemic arterial stiffness.

Using PPG the wave contour itself is not usually analysed because of the difficulty in detecting minute changes in the phase of the inflections. The delicate changes in the PPG waves can be easily quantified by quadratically differentiating the original PPG signal with respect to time. Several epidemiological studies have demonstrated that the information extracted from the SDPPG waveform is closely associated

with age and other risk factors for atherosclerotic vascular disease ( 15-17). Although the clinical significance of SDPPG measurement has been thoroughly discussed, there is still lack of sufficient studies focussing on the SDPPG waveform pattern in diabetes afflicted with retinopathy. The PPG signals recorded were double differentiated using Microcal Origin software. The SDPPG waveform consists of a, b, c and d waves in systole and an e wave in diastole as mentioned in Chapter 3. Since the b/a ratio is also dependent on age, it was calculated for the diabetics and the age matched normal subjects and there was found to be a significant difference between them.

Figures 6.2(a) and 6.2(b) show the normalized mean pulse function for a diabetic and a nondiabetic of the same age respectively. The lack of dicrotic notch in the case of a diabetic as already mentioned in literature is clearly evident.

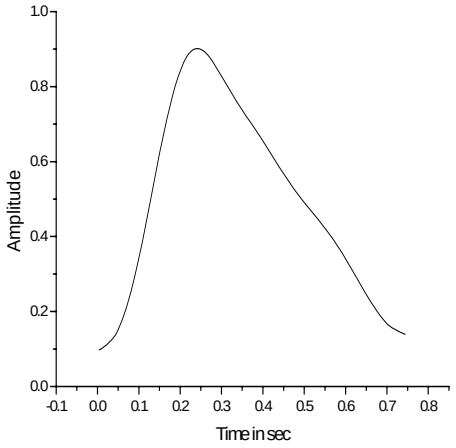


Figure 6.2(a): Normalized mean pulse of a diabetic aged 38 years

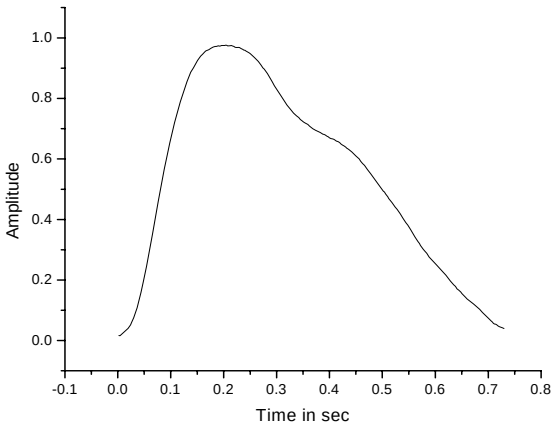


Figure 6.2(b): Normalized mean pulse of a nondiabetic aged 38 years

## 6.3 RESULTS & DISCUSSION

The plot of right-left correlation coefficient for the PPG amplitude vs age for both diabetics and nondiabetics is shown in Figure 6.3. It is clear from the graph that diabetics owing to the lack of bilateral symmetry have low values of right left correlation coeffecient when compared to nondiabetics. The amplitude of very low frequency fluctuations showed high right-left correlation ( 0.93±0.05) for nondiabetic subjects and significantly lower correlation ( 0.38±0.16) for the diabetic patients.

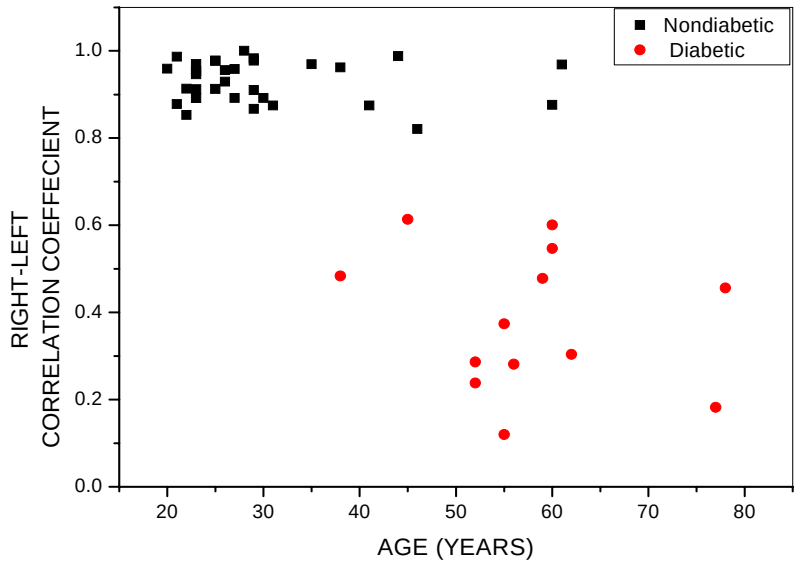


Figure 6.3: Right left correlation coeffecient vs age graph for diabetics and nondiabetics

The PPG signal is known to vary from patient to patient and even from measuring site to site (18). The average and correlation of signal are not independent of time, which means that the signal is not stationary and ergodic. Hence to apply the statistical signal processing tool it was assumed that the measured time series data were locally stationary in a wide sense. The post processing of the PPG signals were done using MATLAB tool. The autocorrelation function for the left and right hand signals for a normal subject showed high correlation as shown in Figures 6.4 & 6.5 ,while in the case of diabetics there was less correlation which is clearly evident from Figure 6.6 & 6.7. The superposition of the autocorrelation functions of the two PPG signals recorded simultaneously from the left and right hands gives a clear illustration of this.

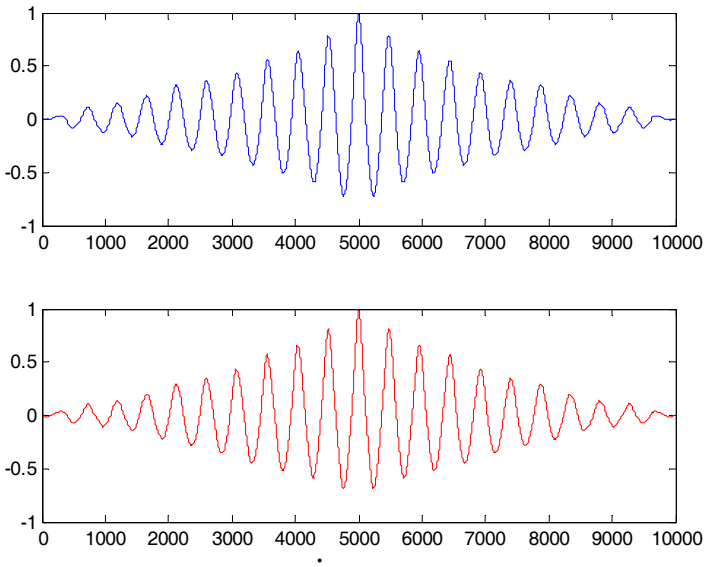


Figure 6.4: Auto correlation function corresponding to the left and right hand signal of a healthy person

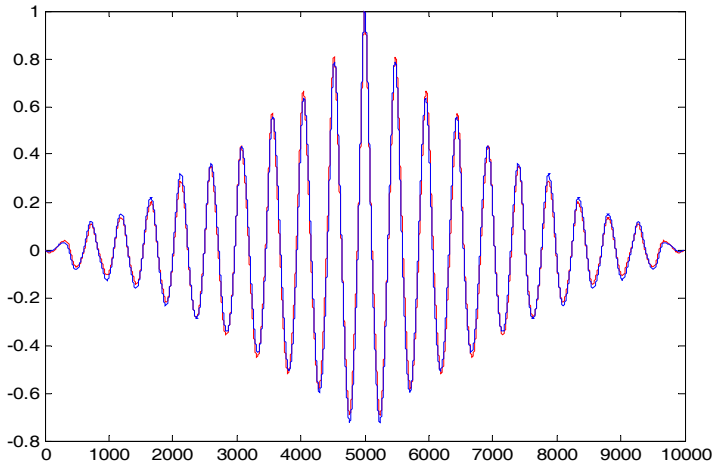


Figure 6.5 **:** Superposed autocorrelation functions of plots shown in Figure 6.4

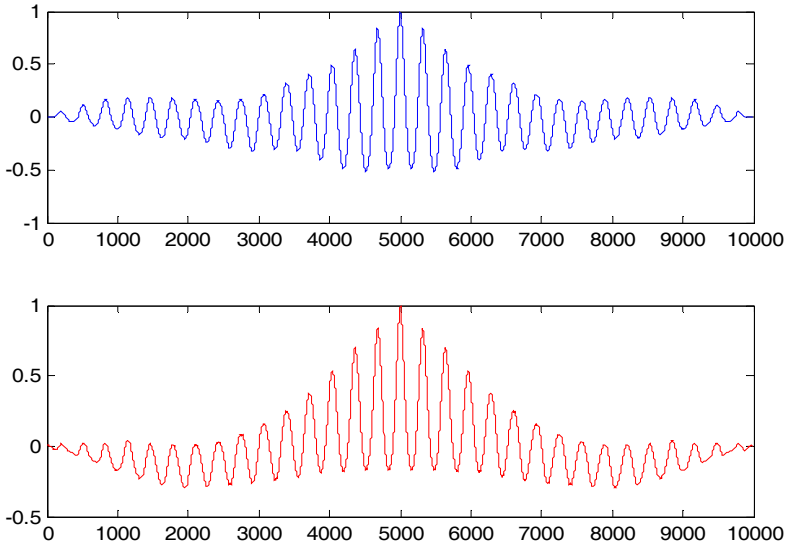


Figure 6.6: Auto correlation function corresponding to the left and right hand signals of a diabetic subject

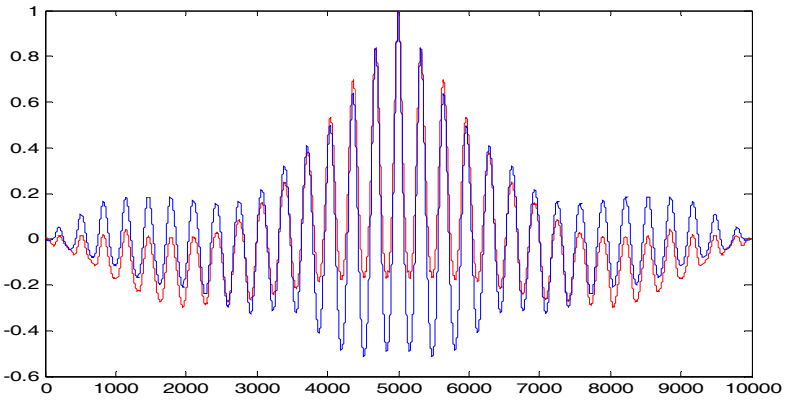


Figure 6.7: Superposed autocorrelation functions of plots shown in Fig 6.6

Similarly cross correlation functions of simultaneously recorded left and right fingers were plotted and its correlation coefficient was calculated . Figures 6.8 and 6.9 show the cross correlation function of normal and diabetic subjects..

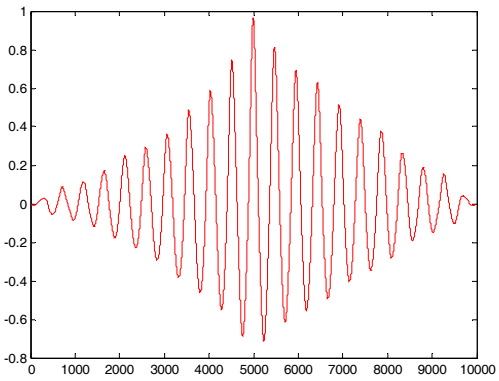


Figure 6.8: Cross correlation function of signals recorded from left and right index fingers of a normal subject

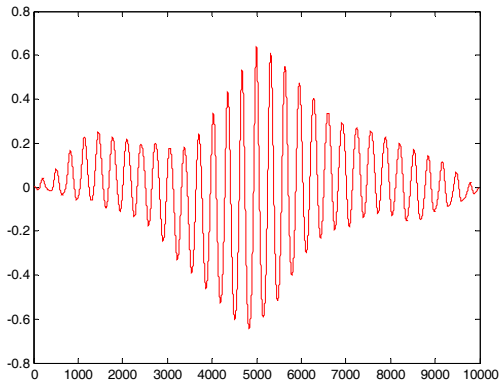


Figure 6.9: Cross correlation function of signals recorded from left and right index fingers of a diabetic patient

Using the SDPPG the b:a ratio for age matched controls and diabetics was determined. Since the b:a ratio of only 8 matched controls and diabetics could be obtained this study is only a pilot study. The range of age for the study was from 38-60. The average b:a ratio for subjects with diabetic retinopathy was found to be -0.773±0.2 and that for normals -0.477±0.1. The differences in mean values between the two groups were analysed by a one-tailed student t-test. $p < 0.05$ was considered to be statistically significant.

The similarity of pulse timing, amplitude and shape of the high frequency pulses between the right and left sides of the body were expected in normal subjects since the anatomical structures are similar (19), the peripheral vascular beds are innervated symmetrically by the autonomic nervous system ( 20) and the blood vessels will have incurred the same levels of age-related reduction in arterial compliance (21).

The similarity in peripheral pressure at each level influences the pulse arrival times and therefore relative pulse wave velocities. Any differences in vessel properties can affect the times and shapes of the rising edge (anacrotic phase) and falling edge ( catacrotic phase) of the PPG pulses. By having studied the pulses obtained simultaneously, the right-left characteristics allows important information about the peripheral circulation to be extracted. Simultaneous measurements are also likely to be better than sequential measurements in detecting right–left differences with confidence, especially if there are changes in key cardiovascular

parameters such as heart rate, body temperature, peripheral resistance or systemic blood pressure.

## 6.4 CONCLUSIONS

The present study shows that PPG can provide a potential tool for evaluating the role of the sympathetic nerves in the regulation of the microcirculation. The high right-left correlation coefficient for amplitude shows that the spontaneous fluctuations in the tissue volume and the systolic blood volume increase are of central origin. The lower values of the right – left correlation coefficient for diabetic patients indicates the deterioration of the sympathetic nervous system which results in asynchronous sympathetic activity in the two hands inspite of its central origin. So the PPG signal variability shows promise for the objective assessment of autonomic retinopathy. Though Photoplethysmography is not appropriate for quantitative measurement of tissue blood flow or the systolic blood volume pulse in absolute terms it can still be used as a simple and convenient means to assess the fluctuations of tissue blood volume, the systolic blood volume pulse , and the temporal relationship between them. The simplicity of the PPG measurement technique, the speed with which peripheral PPG assessments can be made and the valuable cardiovascular information contained within it could make this a useful clinical investigation tool.

## References


1. Nitzan. M, De Beer. H, Turivnenko. S, Babchenko. A and Sapoznikov .D, *J. Basic Clin. Physiol. Pharmacol*, **5**, 269-276 (1994)
2. Nitzan. M, Babchenko. A, Khanokh. B and David Landan, *Physiol. Meas*, **19**, 93-102 (1998)
3. Akselrod. S, Gordon. D, Madwed. J.B, Snidman N C, Shannon D C and Cohen R J, *Am. J. Physiol*, **249**, H867-75 ( 1985)
4. Malliani A, Pagani M, Lombardi F and Cerutti S, *Circulation*, **84**, 482-92 ( 1991)
5. Nitzan M, Turivnenko S, Milston A, Babchenko A and Mahler Y, *J. of Biomedical Optics*, **1(2)**, 223-229 (1996)
6. Arora S, Freeman R, Smakowski P, LoGerfo FW, Frykberg RG, Veves A and Simeone, *Diabetes Care*, **21(8),** 1339-1344 (1998)
7. Flynn MD and Tooke JE, *Diabet Med*, **12**, 298-301 (1995)
8. Wigington G, Ngo B and Rendell M, *Arch Dermatol*, **140(10),** 1248-1250 (2004)
9. Sung Woo kim, Soo Chan Kim, Ki chang Nam, Eun Seok Kang, Jae Jung Im and Deok Won Kim, *MedBio Engg Comput*, **46**, 61-67(2008)
10. Rajendra Acharya U, Chua Kuang Chua E, Y.K. Ng, Wenwei Yu and Caroline Chee, *J. Med Syst*, **32**, 481-488 ( 2008)
11. Allen J and Murray A, *Physiol. Meas*, **21**, 369-377 (2001)
12. Buchs A, Slovik Y, Rapoport M, Rosenfeld C, Khanokh B and Nitzan M, *Med. Biol. Engg.Comp*, **43**, 252-257 (2005)
13. Wilkinson I B, MacCallum H, Rooijmans D F, Murray G D, Cockcroft J R, McKnight J A, Webb D J, *Q J Med*, **93**, 441-448 (2000)
14. Arnett D K, Evans G W, Riley W A, *Am J Epidemiol*, **140**, 669-82 (1994)

15. Takada H, Washino K, Harrel J S, Iwata H, *Med Prog Technol*, **21**, 205-210 (1996)
16. Imanaga I, Hara H, Koyanagi S, Tanaka K, *Jpn Heart Jl*, **39**, 775-784 (1998)
17. Takazawa K, Tanaka N, Fujita M, Matsuoka O, Saiki T, Aikawa M, Tamura S, Ibukiyama C, *Hypertension*, **32**, 365-370 (1998)
18. John Allen , *Phys.Meas***, 28**, R1-R39 ( 2007)

19. Anderson J E, *Grant's Atlas of Anatomy* 7th edn (Baltimore, MD: Williams and Wilkins), (1978)
20. Rowell L B, *Human cardiovascular control ( New York: Oxford University Press)* (1993)
21. Nichols W W and O'Rourke M F, Mcdonald's Blood flow in arteries: Theoretic experimental and Clinical principles 3rd edition ( London : Arnold) (1990)

# *Chapter 7*

## *Summary and future prospects*

**Abstract**

A summary of the work presented in this thesis is given in this chapter. General conclusions arrived at and the future scope of work in this field are also presented.

## 7.1 GENERAL CONCLUSIONS

The previous six chapters present the design and fabrication of a PPG sensor head and selected cardiovascular studies based on the PPG signals recorded.

With the advancement in optical technology, noninvasive assessment of cardiovascular functions by the peripheral arterial pulse has gained substantial research and clinical interest and PPG is one such technique which has gained popularity during recent decades. The PPG signals have been used to carry out studies related to vascular diseases. There has been a resurgence of interest in this technique in recent years, driven by the demand for low cost, simple and portable technology for the primary care and community based clinical settings. The wide availability of low cost and small semiconductor components, and the wider acceptability of computer- based pulse wave analysis techniques have facilitated advancement in this area. In the present work a low cost, low power, transmission mode PPG sensor head was developed for short term monitoring purposes. The effect of contacting force on the measuring site was also studied and the sensor head was used to implement a heart rate meter. The performance of the same was also compared with that of a commercial equipment and was found to be satisfactory.

Age-related changes in the PPG pulse shape characteristics can yield valuable diagnostic information about the cardiovascular system. PPG being a simple, noninvasive technique could provide a means for

studying the changes in the elastic properties of the vascular system as a function of age. We have conducted studies using the systolic and diastolic characteristics of the resting peripheral volume pulse and have arrived at a few parameters that could be correlated with age. The observations made clearly show that arteries become more and more stiffer as age increases.

The variation in the local temperature at the measuring site is one of the important factors to be considered while performing noninvasive measurements on subjects using the PPG waveform as these local effects can introduce significant errors . The effect of mild cold exposure on the PPG signals has been studied and we have also arrived at a few parameters using the cold exposure test that could be of use to diagnose vasospastic disorders and thereby evaluate therapeutic success. The PPG signals are also affected by variations in body posture and the position of the recording site. Studies based on these factors have also been conducted and the obtained results obey the theory of basic blood flow dynamics.

One important study was conducted using the PPG signals recorded from diabetics affected by diabetic retinopathy. Lack of bilateral symmetry in diabetics when compared to normal subjects, was confirmed using a statistical signal processing approach and using a parameter derived from the second derivative of the PPG. All the studies from chapter two onwards were conducted using reflective type PPG sensor probe.

In conclusion, the versatality and utility of the photoplethysmography technique for the evaluation of certain parameters based on selected cardiovascular studies have been experimentally demonstrated.

## 7.2 LOOKING FORWARD

Though PPG technology can be found in a wide range of commercially available medical devices for measuring oxygen saturation, blood pressure and cardiac output, assessing autonomic function and detecting peripheral vascular diseasecs, challenges still remain with the technology, including the standardization of measurements, improving repeatability, and establishing comprehensive normative data ranges for comparison with patients and for evaluating responses to therapy. PPG imaging, simple endothelial dysfunction assessments and home diagnostics are areas where future research in this area needs emphasis.