Non invasive measurement of hemoglobin using PPGs from light sources of different wavelengths

A Project Report

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THESIS CERTIFICATE

This is to certify that the thesis titled **Non invasive measurement of hemoglobin using PPGs from light sources of different wavelengths**, submitted by **Sunil Tamminaina**, bearing Roll No. **EE11B105**, to the Indian Institute of Technology Madras, for the award of the degree of **MASTER OF TECHNOLOGY**, is a bona fide record of the research work done by him under our supervision. The contents of this thesis, in full or in parts, have not been submitted to any other Institute or University for the award of any degree or diploma.

Prof. V. Jagadeesh Kumar
(Project Guide)
Professor
Dept. of Electrical Engineering
IIT Madras, 600 036

Place: Chennai

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ABSTRACT

KEYWORDS: Hemoglobin; Non invasive; Photoplethysmography.

A novel way to measure hemoglobin content in the arterial blood of human beings, non-invasively is provided here. The method is based on the concept of photoplethysmography. An extremity in a human body, like a finger tip or an earlobe, is illuminated with light of multiple wavelengths and the corresponding PPG signals are obtained. A model describing the PPG signals in terms of their various components is analytically arrived at, giving rise to the contributions from skin, bone, tissue, veins and arteries. Then the relevant arterial blood component is separated and can be further analysed to ascertain the value of the hemoglobin content in the arterial blood of human beings. Apart from the above purpose, computation of several things like heart rate, oxygen saturation in blood, heart rate variability etc. can also be achieved by the knowledge of the data given by multiple PPG signals from monochromatic light of multiple wavelengths.

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ABBREVIATIONS

IITM	Indian Institute of Technology Madras
PPG	Photoplethysmogram
LED	Light Emitting Diode
RBC	Red Blood Cells
WBC	White Blood Cells
CBC	Comprehensive Blood Count
PCB	Printed Circuit Board
VI	Virtual Instrument
DC	Direct Current
AC	Alternating Current
SpO_2	Oxygen saturation in blood
USB	Universal Serial Bus

NOTATION

λ	Wavelength
$I_{i\lambda}$	Input intensity of light of wavelength λ
$I_{o\lambda}$	Output intensity of light of wavelength λ
ε_{λ}	Extinction coefficient of wavelength λ
c	Concentration
$K_{d\lambda}$	Sensitivity of photo detector
$v_{o\lambda}$	Photo detector's output voltage
c_{HbO}	Oxygenated hemoglobin's concentration
c_{Hb}	Deoxygenated hemoglobin's concentration
Q	Ratio of the concentrations of oxy haemoglobin to deoxy haemoglobin
T_F	Path length of light
ε_{HbR}	Extinction coefficient of de oxygenated hemoglobin at red wavelength
v_R	Pulsatile part of the logarithm applied $v_{o\lambda}$ at Red wavelength
v_{IR}	Pulsatile part of the logarithm applied $v_{o\lambda}$ at infrared wavelength

CHAPTER 1

INTRODUCTION

1.1 The constituents of human blood

Many animal species have the most important body fluid, blood, as a carrier for transporting nutrients and Oxygen to all the cells in their bodies and take back the waste products(like ammonia, carbon dioxide) obtained after metabolism from the cells. Humans are no exception to this process. It is an important fluid for the survival of humans. It amounts to $7 - 8\%$ of the body weight in human beings. Apart from supplying nutrients and oxygen to the cells, thus providing them with the energy required to carry all the activities they are involved in, blood also is crucial for providing robust immunity and also to maintain ambient body temperature.

The total number of various individual components in human blood is more than 4000, thus making it a very complex and highly specialized fluid tissue in the body. Among all these constituents of blood, the most important are the plasma, red blood cells, white blood cells and the blood platelets.

Red blood cells(RBC) or erythrocytes constitute about $40 - 45\%$ of the total volume of blood in human beings. They carry oxygen to all the parts of the body from the lungs and carbon dioxide from all the cells to back to the lungs. Hemoglobin, a biomolecule which carries oxygen and contains iron, is present in high amounts in the red blood cells' cytoplasm, thus giving these cells the red colour. Red blood cells are produced in the bone marrow of human beings. An average human being produces about 2.4 million erythrocytes every second.

White blood cells(WBC) are also called leukocytes and play a crucial role in the immune system of the human beings. These cells are present both in the blood and also in the lymphatic system, thus effectively having their presence through out the body.

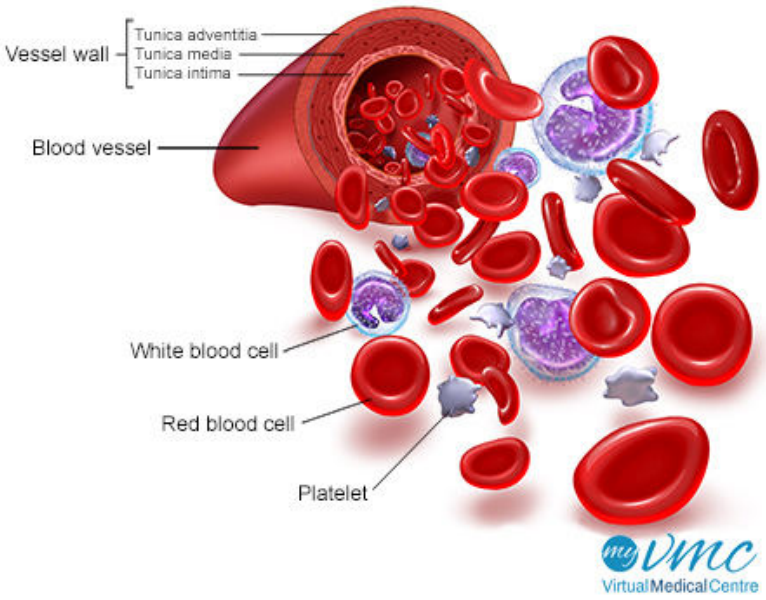

Figure 1.1: Constituents of blood. [image source : virtualmedicalcarecentre.com]

Unlike the red blood cells, these white blood cells do have nuclei in their bodies. Their primary role lies in defending the human body against both foreign invaders and also infections which cause diseases. A healthy adult human being has nearly 1% of the blood volume being made up of these white blood cells. These cells are also produced in the bone marrow of the humans.

Blood platelets or simply platelets are also called thrombocytes are involved in stopping bleeding by clotting the blood. They gather at the site of the injury and plug the hole, thus halting bleeding. These are much smaller in number than red blood cells, making up only about a tenth of the total number of red blood cells in human beings.

Apart from the above three, the other major component of the blood is the blood plasma, which makes up around than 55% of the total volume of the blood. Plasma is fluid in yellow/pale straw colour with more than 90% of it's content being water. All the various cells like erythrocytes, leukocytes, platelets are suspended in this fluid plasma. Apart from water, other major components of blood plasma are proteins such as bilirubin, albumin etc. Thus, it also plays a role of protein reserve in the human body.

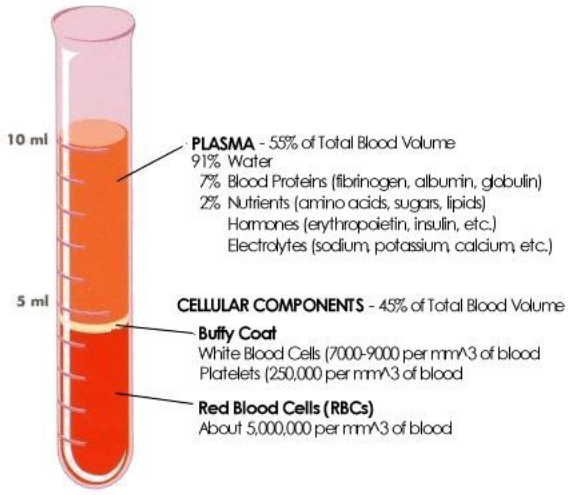

Figure 1.2: Volume proportions of various blood constituents. [image source : pmgbiology.com]

1.2 Role of various components of blood in diagnosing medical conditions

All the above described components of blood and the levels of each of them can be used to reflect the health condition on various fronts, for human beings. Any of the quantity present in abnormal levels may indicate some disease condition and hence the monitoring of these levels might be necessary. Also, as is often the case, symptoms for many different diseases can be the same and hence to diagnose exactly what kind of disease one might be having, it's important to check the levels of various components of blood. Recent innovations have helped proliferate the use of at home medical devices in the health care field and hence it becomes crucial to have methods which can measure these(and other) parameters accurately.

A physician might prescribe various kinds of tests for blood components, depending on the necessity. These include RBC Count, WBC Count, Complete Blood Count(CBC) etc. The first one gives the number and often, size of the red blood cells in a human being, while the second one gives the number of white blood cells in a volume of human blood. CBC test may reveal one or more of parameters like hemoglobin content, mean corpuscular volume, platelet count, haematocrit HCT, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration etc.

1.3 Importance of hemoglobin measurement

As said earlier, hemoglobin is a metalloprotein and a biomolecule, responsible for transporting oxygen from lungs to various tissues in the body. Since the oxygen-binding capacity of hemoglobin is very high, the Oxygen molecules get bound to the hemoglobin thus enabling their transport throughout the body. By weight, hemoglobin makes up more than 90% in the red blood cells.

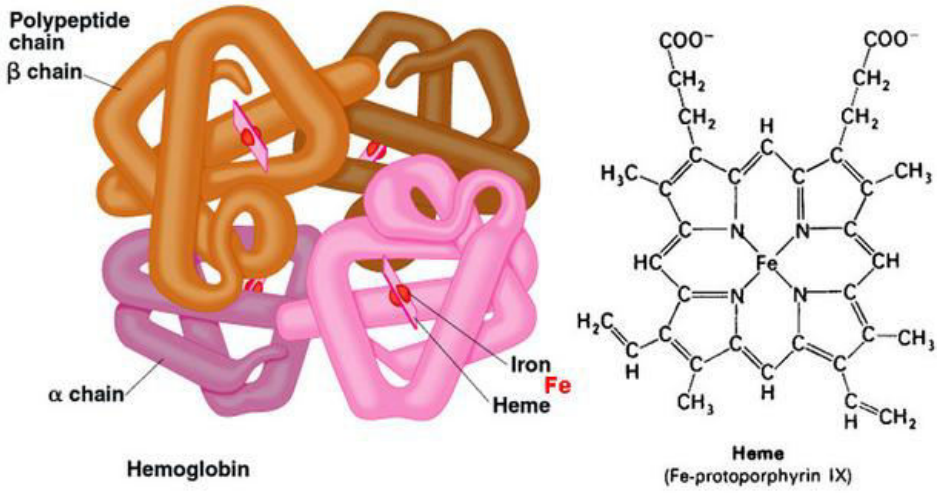

Figure 1.3: Hemoglobin structure. [image source : worldofchemicals.com]

Knowing the levels of hemoglobin in a human being may give insights into various health conditions one might be facing. Since hemoglobin carries oxygen to the tissues of the body and since oxygen is essential for the sustenance of life, abnormal levels of hemoglobin may result in abnormal supply of oxygen to various cells across the body. In extreme cases, it might even result in organ failure and may lead to death. Low levels of hemoglobin results in a condition of anemia, and high levels of hemoglobin might result in a condition called polycythemia. Both the conditions represent ill health among humans and may further lead to medical complications. Apart from these two, many other diseases arise due to abnormal levels of hemoglobin content in human beings. Diagnosis of deficiency of iron and sickle cell disease is also possible with the measurement of hemoglobin content in the blood. Hence, it is important to know, as accurately as possible, the levels of hemoglobin content.

Table 1.1: Normal levels of hemoglobin content in human beings

Category	*Normal Hb levels*
Men	13.5-17.5 g/dL
Women	12.1-15.1 g/dL
Children	11-16 g/dL
Pregnant Women	11-14 g/dL

1.4 Traditional methods of hemoglobin determination (Invasive techniques)

Most of the methods for determination of hemoglobin use invasive techniques which involve taking small amounts of blood from some part of a human body, say from a finger. These are not only painful, but also some times time consuming. The possibility of an infection spreading due to the use of unhygienic needles to prick blood is also present.

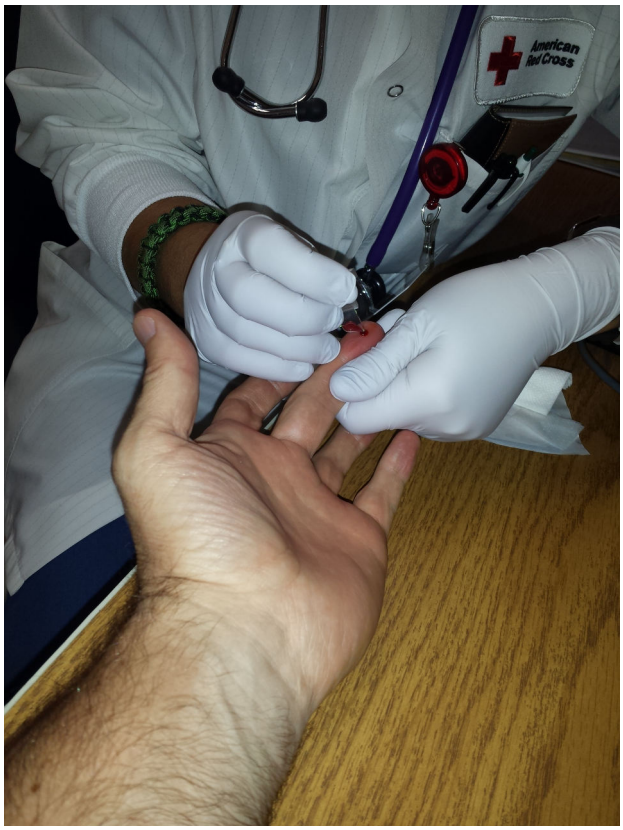

Figure 1.4: Hemoglobin invasive measurement. [image source : en.wikipedia.org/wiki/Hemoglobin]

Some of the invasive methods to determine the levels of hemoglobin content are as follows:

- Azidemetheglobin
- Spectrophotometer based methods
- Haematocrit based methods

1.5 Non-invasive methods

Recent years have seen the increasing prevalence of non invasive techniques in the field of medical diagnosis. Non invasive basically suggests not involving the introduction of any instruments into the human body to test something. As these methods do not involve taking blood samples outside, they do not inflict any pain on the patient and also the possibility of an infection is ruled out. These non invasive techniques are especially helpful for point of care applications. Pulse oximeter is one of the most popular non invasive medical devices that is in vogue currently.

1.6 Objective of the project

In this project, our objective is to explore ways to measure the hemoglobin content in a human being, non invasively, in an accurate manner through obtaining what is called a photoplethysmogram(PPG). A PPG represents an optically obtained waveform via a measurement of organ using volumetric analysis. In our case, the organ would be any extremity like the tip of a finger or even an earlobe. Optical waves of different wavelengths are passed through this extremity and collected and a PPG is obtained. The facts that light of different wavelengths attenuate differently for the same medium and also light of the same wavelength has different attenuation characteristics in different media is exploited to get the desired PPG. An analysis of these PPG waveforms can be done to measure the hemoglobin content in the blood of that particular person.

1.7 Organization of this thesis

In total, this thesis consists of four chapter. The first chapter is an introduction to the the constituents of blood, how various constituents play a role in the diagnosis of various medical conditions, especially of hemoglobin. It gives the traditional invasive methods to measure the content of hemoglobin, and finally talks about the non invasive methods and their usefulness.

The second chapter elaborates on the concept of photoplethysmogram, it's components, and it's applications especially how it can be used for non invasive methods of hemoglobin measurement. The third chapter gives details of how individual parts of the required prototype are developed, and then how the overall setup is put into place. Finally, in chapter 4, the results of the work done for this project are presented and the summary and conclusions are given.

The section on references gives a list of relevant literature that is consulted during the course of this project.

CHAPTER 2

The Photoplethysmogram, it's components, models and applications

2.1 Photoplethysmography

Plethysmographs are those which can measure changes in volume. Photoplethysmography is a method combining optical and electronic features that gives signals which are proportional to the changes in the volume of the blood in a particular part of the body. It is a very convenient non invasive technique. Broadly, there can be two types of photoplethysmograms:

- Reflectance PPG
- Transmission PPG

Reflectance PPG is obtained when we detect the reflected light from the part of the body which is illuminated by with light, while the transmission PPG is obtained when we detect the transmitted light through the particular part of the body which is illuminated. The latter can be obtained from a human body from parts like finger, toe or an earlobe, i.e., an extremity, as light cannot penetrate through very deep body parts. Basically, for both reflectance and transmission type PPGs, the waveform is produced by the emanating photons after passing through a certain body part thus carrying some information about that particular body part. For the former type, both the light source and the detector are on the same side while for the latter, the source and the detector are on the opposite sides of the body part which is being illuminated. Both the types are shown in the figure in the next page, along with an image of a typical PPG waveform for a venous pulsation. Photoplethysmography was first used in the decade of the 1930s by a group led by Alrick Hertzman. Since then, it spread into a wide variety of fields and many applications today use this technique.

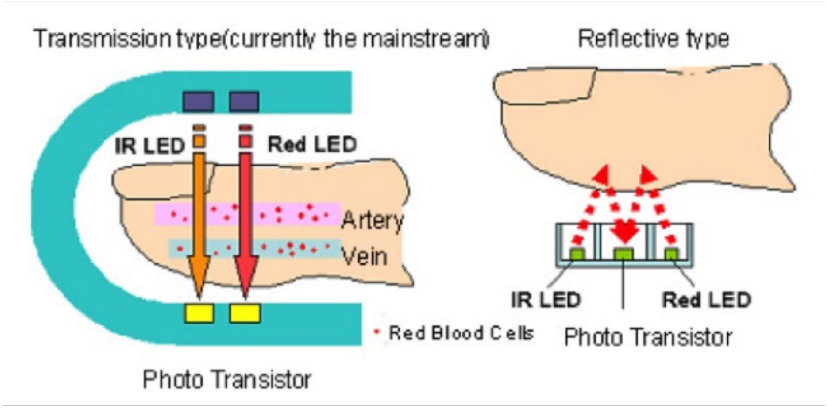

Figure 2.1: Transmission and reflectance type PPG sensors. [image source: www.ee.columbia.edu/]

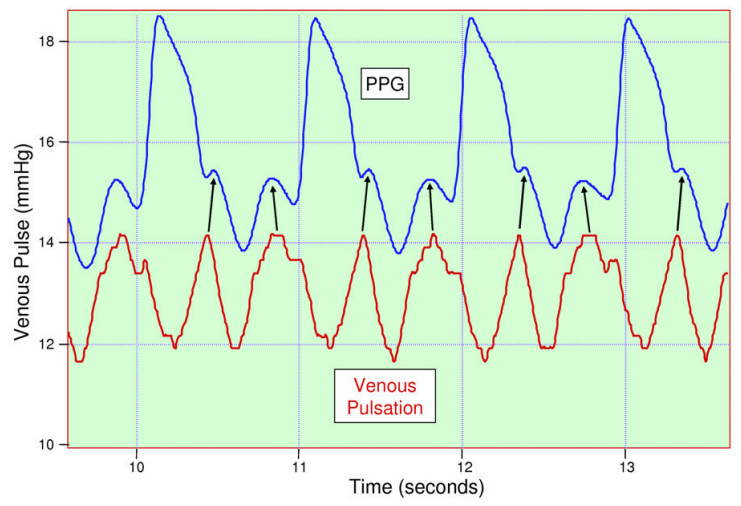

Figure 2.2: Representative venous pulsation PPG. [source: en.wikipedia.org/wiki/Photoplethysmogram]

2.2 Components of a typical PPG

The photons of light that is illuminated on a body part pass through the epidermis and dermis of the skin, the tissue, soft bone, and the blood vessels including veins and arteries. Apart from these blood vessels, the characteristics, primarily the volume characteristics of the rest of the above do not vary anything significantly during the very short period that the light travels through them. Among the blood vessels too, the photons encounter attenuation differently for both the arteries and veins. The part of the signal obtained due to the attenuation in veins has a very low frequency of less than 0.2Hz. On the other hand, the part of the PPG obtained due to the influence of arterial

blood flow has a frequency that is dictated by the rate of heart beat. Thus, it will be pulsatile in nature as the volume changes in the blood flow in arteries is dependent on the heart rate. An increase in volume of blood is seen during systole thus giving a low signal in the PPG as low amount of light reaches the photo detector, and the reverse happens during diastole.

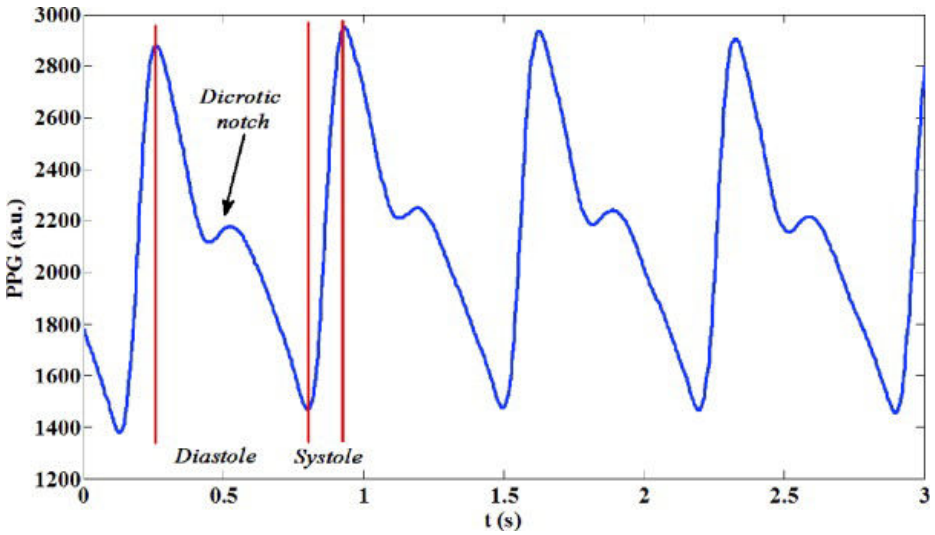

Figure 2.3: Systole and diastole in a PPG. [image source : www.researchgate.net/publication/277027133]

If I_{o_λ} is the output intensity of light received at the photo detector and $I_{i\lambda}$ is the intensity of the light which is being illuminated on a body part, then the former can be expressed as

$$I_{o\lambda} = I_{i\lambda} e^{-[\varepsilon_{\lambda e} c_e l_e + \varepsilon_{\lambda d} c_d l_d + \varepsilon_{\lambda t} c_t l_t + \varepsilon_{\lambda b} c_b l_b + \varepsilon_{\lambda v} c_v l_v + \varepsilon_{\lambda a} c_a l_a]} \tag{2.1}$$

where $\varepsilon_{\lambda e}$ represents the extinction coefficient, at particular wavelength λ, of the epidermis part of the skin, c_e is the concentration of epidermis molecules and lastly, l_e is the light's path length through the epidermis. Like wise, $\varepsilon_{\lambda d}$, $\varepsilon_{\lambda t}$, $\varepsilon_{\lambda b}$, $\varepsilon_{\lambda v}$ and $\varepsilon_{\lambda a}$, c_d, c_t, c_b, c_v and c_a, and l_d, l_t, l_b, l_v and l_a are the extinction coefficients, concentrations and path lengths of light through dermis, tissue, bone, venous blood and arterial blood respectively. Now, the photodetector converts the output light intensity into a proportional

voltage. This voltage can be given by

$$v_{o\lambda} = K_{d\lambda} I_{i\lambda} e^{-[\varepsilon_{\lambda e} c_e l_e + \varepsilon_{\lambda d} c_d l_d + \varepsilon_{\lambda t} c_t l_t + \varepsilon_{\lambda b} c_b l_b + \varepsilon_{\lambda v} c_v l_v + \varepsilon_{\lambda a} c_a l_a]} \tag{2.2}$$

where $K_{d\lambda}$ represents the sensitivity of the photo detector. From the equation 2.2, it is clear that the output voltage has a dc component(arising from light passing through skin, tissue and bone), slow varying ac component(arising from light passing through veins) and a fast varying ac component due to the flow of blood, pulsating at the heart rate, in the arteries.

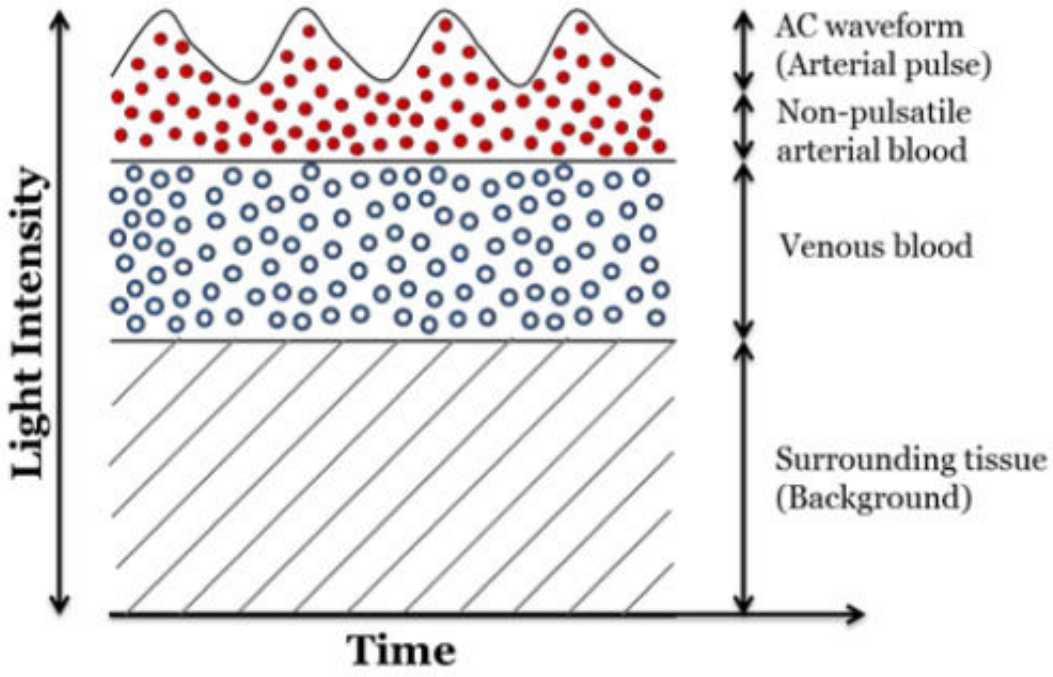

Figure 2.4: Different components of a PPG. [image source : www.osapublishing.org/boe/abstract.cfm?uri=boe-5-7-2362figanchor1]

Figure 2.4 gives a pictorial representation of the determinants of various components of a typical PPG. Thus, we can see that if we can isolate the portion of PPG that was obtained due to a particular body part, we will be in a position to know more about that particular body part in that person and perhaps be able to measure qualitatively certain parameters of that body part.

2.3 Modeling the path of light

For the sake of simplicity, in some methods which use models for path length, the path that light traverses between the source and the photo detector is assumed to be in the form of a cylinder. Various differences can be there in different models after making this assumption too, like bunching all the arteries together or not and so on. In the latter type, based on the method of oxygen saturation, the output intensity can be written as

$$I_{o\lambda} = I_{i\lambda} e^{-[\varepsilon_{\lambda e} c_e + \varepsilon_{\lambda d} c_d + \varepsilon_{\lambda t} c_t + \varepsilon_{\lambda b} c_b + \varepsilon_{\lambda Hb} c_{Hb} + \varepsilon_{\lambda HbO} c_{HbO}] T_F} \tag{2.3}$$

where c_{Hb} and c_{HbO} are the concentrations of deoxygenated and oxygenated hemoglobin, while $\varepsilon_{\lambda Hb}$ and $\varepsilon_{\lambda HbO}$ represent their respective extinction coefficients, and T_F represents the total path length of the light.

2.4 Applications of Photoplethysmography

The following are some of the uses and applications of Photoplethysmography:

- Oxygen saturation measurements
- Various haemo-dynamic measurements
- Heart rate and cariac cycle monitoring
- Monitoring depth of anesthesia
- Monitoring respiration
- Monitoring hyper and hypovolemia

CHAPTER 3

Prototype instrument for obtaining Photoplethysmogram

3.1 A typical pulse oximeter

A non invasive method of measuring hemoglobin through obtaining a Photoplethysmogram is presented in this thesis. A standard pulse oximeter which gives two PPG wave forms has been a popular device worldwide in the recent years. It indirectly measures the oxygen saturation levels in the blood of a person through the PPGs obtained. It uses a standard transmission type PPG sensor and an extremity like the finger is illuminated by two LEDs, one in the red colour range and the other in the infrared wavelength range. The photo detector senses the light that passed through the finger and fell on it and produces a proportional current. The circuitry following that involves a current to voltage conversion, then a demultiplexing unit to separate the currents corresponding to the two wavelengths, an amplifying part, and a filtering circuit, to give rise to the required PPG wave forms. A rough block diagram of a typical pulse oximeter is illustrated in the Figure 3.1.

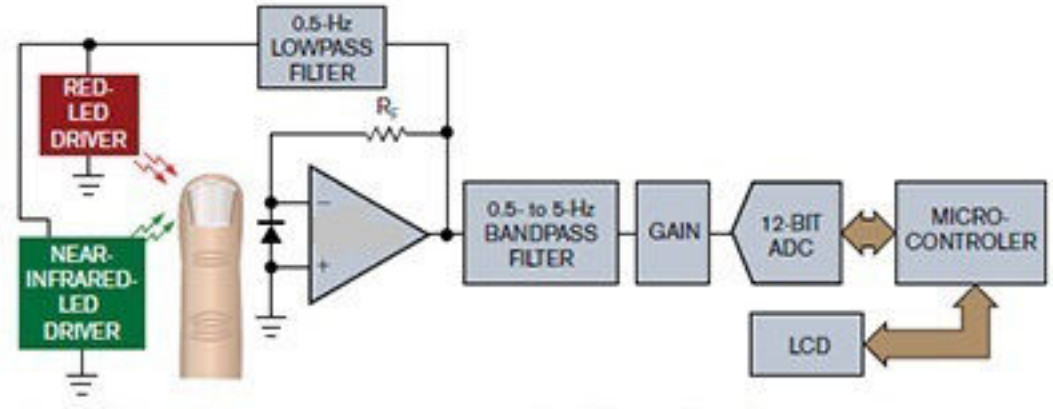

Figure 3.1: A rough schematic of a typical pulse oximeter. [source : http://www.ti.com/ww/en/analog/Amplifiers-eBook/]

3.2 PPG model being used

As described in section 2.3, the intensity of the light received by the photo detector at a particular wavelength is given by

$$I_{o\lambda} = I_{i\lambda} e^{-[\varepsilon_{\lambda e} c_e + \varepsilon_{\lambda d} c_d + \varepsilon_{\lambda t} c_t + \varepsilon_{\lambda b} c_b + \varepsilon_{\lambda Hb} c_{Hb} + \varepsilon_{\lambda HbO} c_{HbO}] T_F} \tag{3.1}$$

and the output voltage of the photo detector is given by

$$v_{o\lambda} = K_{d\lambda} I_{i\lambda} e^{-[\varepsilon_{\lambda e} c_e l_e + \varepsilon_{\lambda d} c_d l_d + \varepsilon_{\lambda t} c_t + \varepsilon_{\lambda b} c_b + \varepsilon_{\lambda v} c_v + \varepsilon_{\lambda a} c_a] T_F} \tag{3.2}$$

From here, proceeding with the calculations as described in [1] in References, we arrive at the following model for the logarithm applied voltages of the highly pulsatile part in the PPG as

$$v_R = [(\varepsilon_{HbR} + \varepsilon_{HbOR} Q) c_{Hb} T_F] \tag{3.3}$$

$$v_{IR} = [(\varepsilon_{HbIR} + \varepsilon_{HbOIR} Q) c_{Hb} T_F] \tag{3.4}$$

where v_R, ε_{HbR} , ε_{HbOR} are the pulsatile part of the logarithm applied output voltage given by the photo detector, extinction coefficient for de oxygenated blood, extinction coefficient of oxygenated blood respectively for red colour PPG and v_{IR}, ε_{HbIR} , ε_{HbOIR} are the corresponding parameters for infra red PPG. Q is given by

$$Q = \frac{c_{HbO}}{c_{Hb}} \tag{3.5}$$

Equations 3.3 and 3.4 show that only c_{Hb} and T_F are the only unknown variables, but since both of them are in a multiplicative form in both the equations, unique solution cannot be found out only with two equations. Ways to estimate or eliminate T_F have been explored before.([1] in References).

3.3 Prototype unit design

The prototype instrument for obtaining different PPGs has, broadly, four major parts, which are:
(i) The sensor head
(ii) The signal conditioning circuitry
(iii) The data acquisition system
(iv) The data processing and display system
The following pages detail the design of each of these units individually and then the assembling of all the four together follows.

3.3.1 The sensor head for PPG

The aim was to obtain four PPGs of different wavelengths of light being illuminated on a finger tip and do the analysis to find out the values of hemoglobin content in blood of a person. So, accordingly, 4 wavelengths were chosen, they being red(wavelength 660 nm), infra red(wavelength 850 nm), blue(wavelength 470nm), and green(wavelength 520 nm). LEDs corresponding to these four wavelengths are embedded onto one side of a soft clip. On the other side, an appropriate photo detector is placed to receive the light. Thus, a custom made probe is designed with a clip type sensor head, cable and a connector, as shown in the Figure 3.2. Figure 3.3 shows a wrap around type sensor head with LEDs on one side and photo detector on the other side.

The LEDs should be chosen such that they do not give very high power output, as it may cause ill effects on the finger of the person being tested on. The photo detector should be such that it is matching to SpO_2 detector responsivity. Also, the area of the photo detector's area should be sufficiently large enough. Care must also be taken to align the photo detector with the four different LEDs in such a way that all four of their light can be detected by the photo detector without any problem. The photo detector also plays the role of a transducer (a photo diode is present inside it), thus it has the capability to convert the incident light into a correspondingly proportional current, i.e., a photo current is generated.

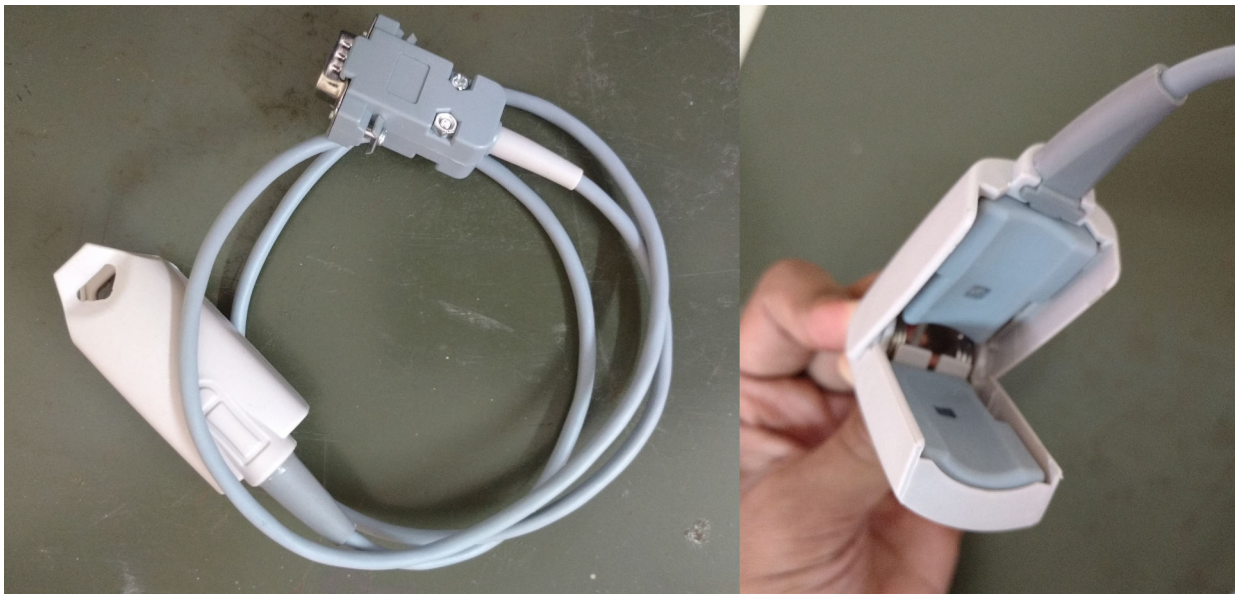

Figure 3.2: A custom made clip-on type sensor head and probe housing LEDs and photo detector

Figure 3.3: A wrap around type sensor head

3.3.2 The analog signal conditioning circuitry

The analog signal conditioning interface circuitry has to, basically, do the jobs of timing and controlling all the four different LEDs, powering them up sufficiently enough, the photo current to an appropriate voltage conversion, filtering and amplifying this particular voltage signal, and to appropriately demultiplex one out of the four signals at one point of time. Apart from these, a data acquisition system should be present which can acquire the final output voltage signal from the interface circuitry and feed it onto an appropriate processing and display unit. These tasks are accomplished in the process described in the following few pages and the final complete circuit is shown in APPENDIX 1.

Photo current to voltage conversion

A logarithmic amplifier, made by Texas Instruments, LOG112, is used for this purpose. It does the job of a trans-impedance amplifier. So, the output current from the photo detector is directly fed into this IC. Appropriate resistors are chosen so that the conversion from the photo current to the voltage is efficient. LOG112 incorporates a logarithmic conversion apart from being an i-v converter. This helps us as we need to separate out the low amplitude but high pulsatile part for the PPG, and so in cases where the amplitudes of unwanted signals is much larger than pulsatile part, doing without logarithmic compression might result in the former just swamping away the latter. The functioning and relevance of the LOG112 IC is tested on a breadboard, along with an appropriate filtering and amplifying circuit (Figure 3.4), before hand and it gave satisfactory results.

LED driver circuit

OPA551 IC is used to drive the four LEDs. The maximum current that can be delivered by this opamp is 200 mA. OPA551 fits the bill perfectly as it is a low cost operational amplifier with capabilities of high current and high voltage. An analog multiplexer ADG409 is used so as to glow one LED at a time and also to enable one output filtering channel at one time, in coordination with the micro controller being used.

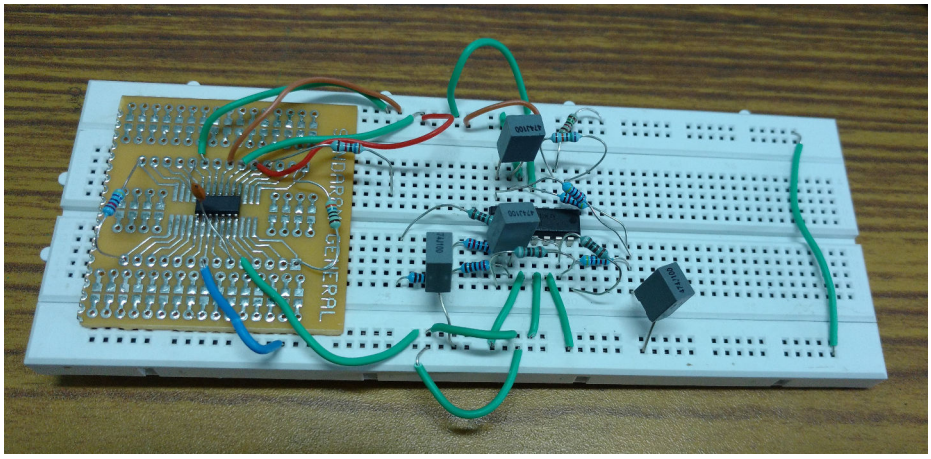

Figure 3.4: Testing for single channel on a breadboard

Circuitry for demultiplexing signals

Since we are using LEDs of four different wavelengths, the photo diode senses all the four different lights coming after traveling through the finger. Nevertheless, at any given point of time, the photo detector's output corresponds to only one wavelength, and there is a need for only one of the four signal filtering channels to be selected at the output of the i-v converter. This is because even the output of the logarithmic amplifier has time multiplexed signals and they need to be demultiplexed. This task is accomplished by using a sample and hold circuit fulfilled by the SMP04 IC. This IC is controlled by a micro controller (described later) appropriately. Thus, say whenever the red LED is on, the corresponding channel will be activated and others are disabled. Similar process is achieved for LEDs of other wavelengths as well.

The filtering circuitry

The output of the i-v converter has all the components like DC, slow varying AC, pulsatile components. However, what we require is only the last one. Hence a filtering circuit is needed to filter out the rest of the components. For this, a series of filters and a subtractor is placed using the IC LF347. The first low pass filter is chosen such that it has a low cut off frequency of 0.3 Hz. The next filter with a DC gain of -1 is made to have a cut off frequency ten times the previous one, to act as a buffer filter. These filters extract the DC and the slow varying components of the PPG. Then a subtractor is used to subtract the residual DC component as well as the slow varying AC component

to give only the pulsatile component. Then, an amplifier is used to amplify the remaining signal. Care is taken that the cut off frequency of this is sufficiently high such that no harmonic of the pulsatile component is lost, at the same time ensuring that there is no noise and interference coming in. All four channels are made similarly to give the pulsatile components of the PPGs corresponding to various wavelengths.

The timing and control logic division

The timing and control section is needed to glow the LEDs one after the other in a circular manner, and also for the demultiplexing for the sample and hold circuitry. Both these jobs need to be done in coordination with one another. This is done by programming the PIC16F628A micro controller. The selection of the said micro controller is done according to the requirement that the number of programmable input/output pins in the selected IC is sufficiently high so as to control four LEDs and the same number of channels at a time. Two control lines corresponding to pins 11 and 12 of the PIC16F628A IC dictate the four LEDs in terms of which one glows and the order and so on. Table 3.1 summarises the sequence of controlling the LEDs.

Table 3.1: Controlling the sequence of turning on LEDs

Control line 1	*Control line* 2	*LED turned on*
0	0	Red
0	1	Infrared
1	0	Blue
1	1	Green

At the same time, according to the LED which is being turned on, a corresponding channel is enabled in the filtering circuitry by controlling the sample and hold IC in coordination via the same micro controller. Care is taken that the transients between turning an LED off and another on doesn't affect the switching in sample and hold circuit. This is done by providing some delay to enable a particular channel after the corresponding LED is turned on, and also by disabling the channel some time before actually turning off the LED. This is to say that, while the LED is turned on for 5ms at one instance, the corresponding channel is enabled only for 3 ms in the middle, i.e., 1ms after the LED is turned on and 1ms before the LED is turned off. All the

other channels are disabled for the entire 5ms time period. This is repeated for all four LEDs and channels, and the logic is repeated until the power supply is turned off, i.e., sufficient time elapsed to get a reliable PPG. The entire logic is programmed onto the micro controller and is the program is tested by building a small circuit with the micro controller and various LEDs on a bread board as shown in the Figure 3.5.

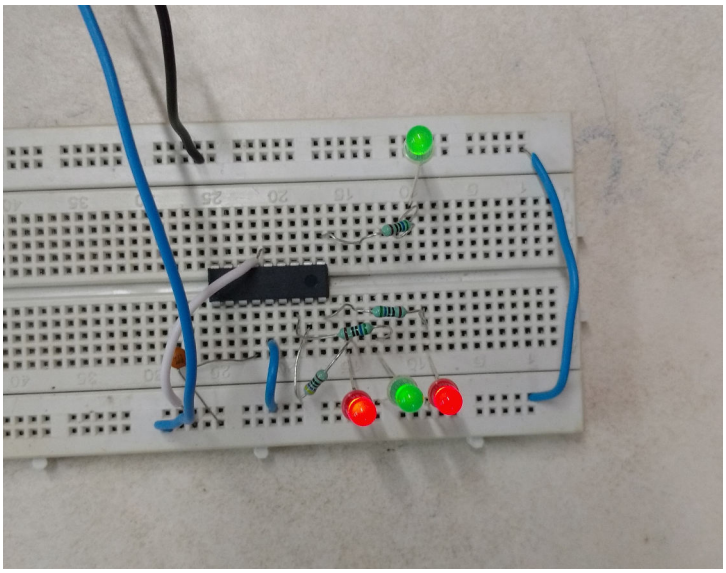

Figure 3.5: Testing the programmed micro controller on a breadboard

3.3.3 The data acquisition, signal processing and display section

The output from the filtering section is given as input to a data acquisition system involving the National Instruments DAQ6008 card. This DAQ card is connected to a personal computer via an appropriate USB cable. Appropriate configuration is set up in the PC through the NI LabVIEW platform by developing a suitable virtual instrument for our requirements. Thus, samples of the signal are collected and displayed via the NI LabVIEW software package. The pin configuration of the DAQ system being used is given in Figure 3.6.

3.3.4 Setting up the hardware

After carefully optimising all the individual sections of the desired prototype, the final analog interface circuit is made into a custom made printed circuit board (PCB). Figure 3.7 shows the manufactured PCB's connection layers and the components. Then, all

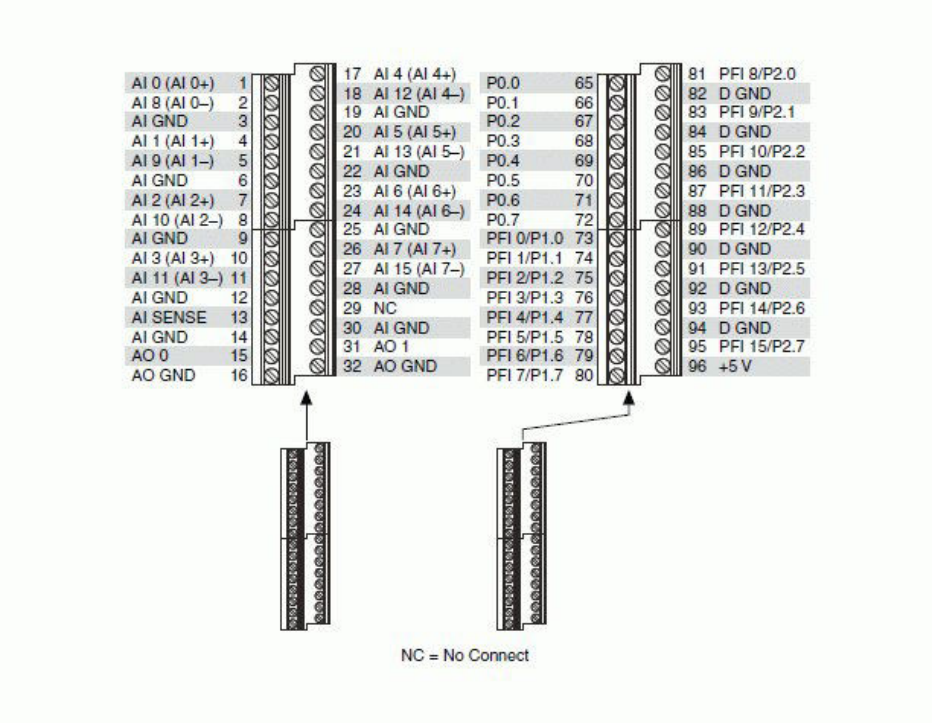

Figure 3.6: Pin configuration of NIDAQ6008. [image source : http://www.koslandtours.com/]

the components are soldered onto the PCB carefully. The PCB populated with all the elements is shown in Figure 3.8. The overall setup is shown in Figure 3.9. PPG signals are obtained and the testing results, which are found to be working as expected, are presented in the next chapter.

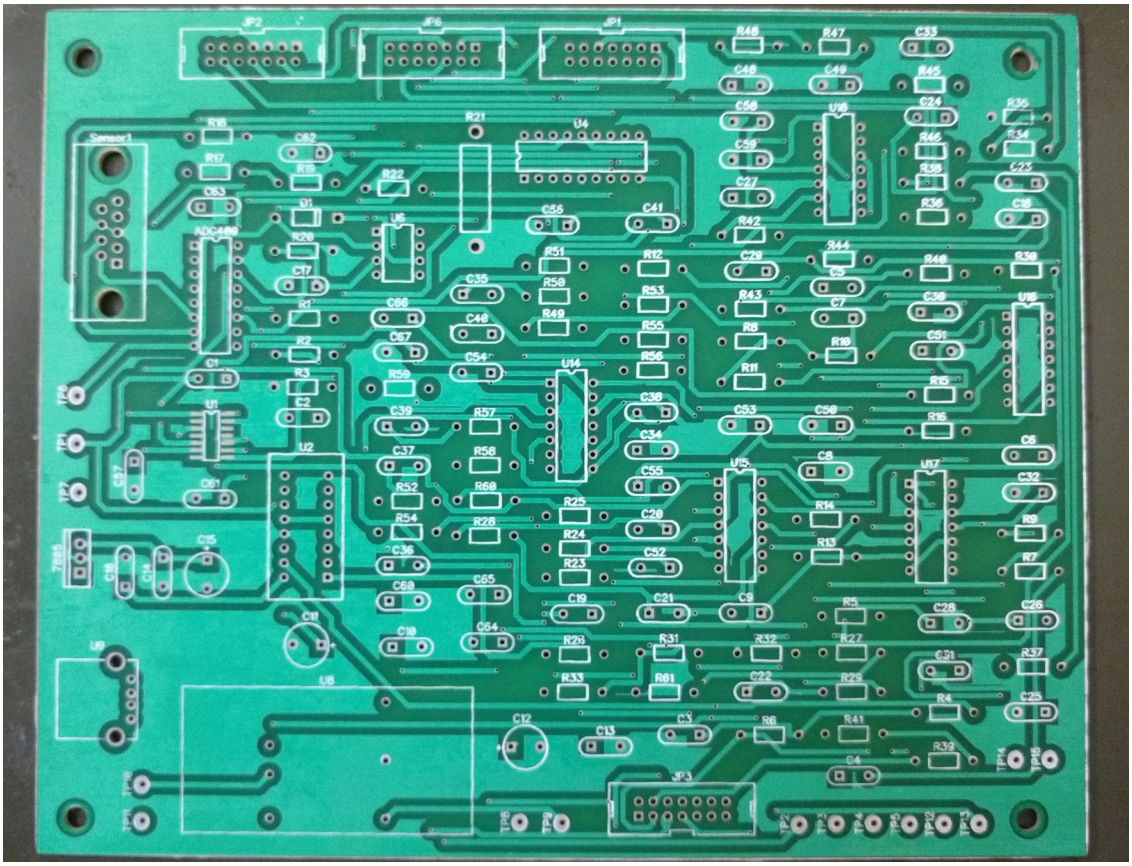

Figure 3.7: The PCB for analog signal conditioning electronics

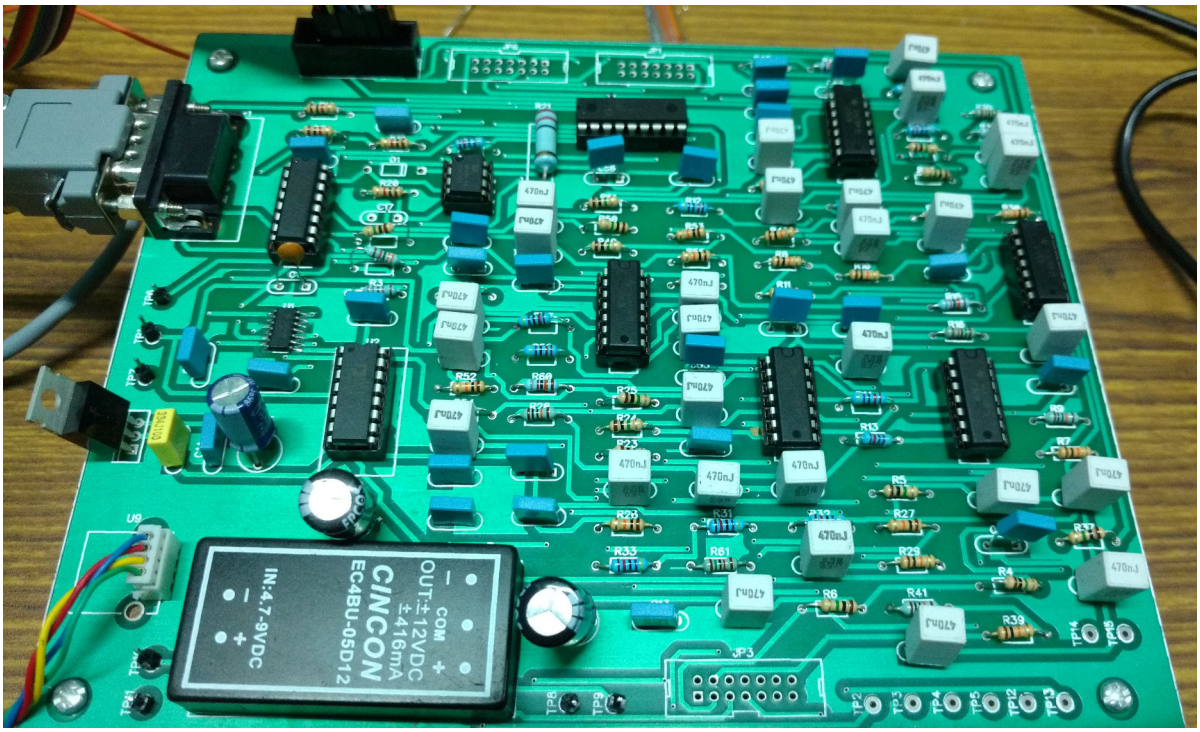

Figure 3.8: The PCB for analog signal conditioning electronics

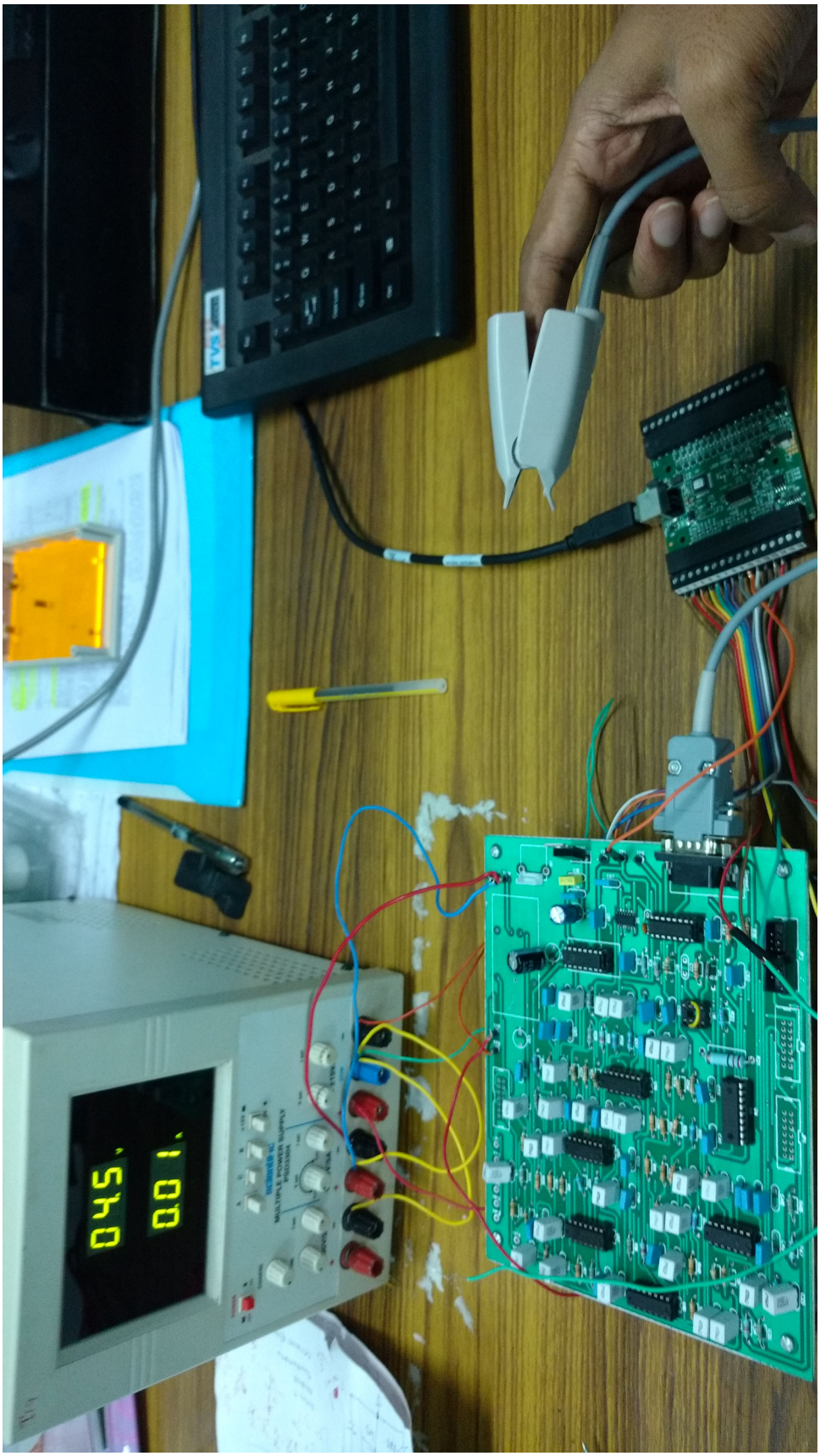

Figure 3.9: The overall setup of the hardware

CHAPTER 4

The results, summary and conclusions

4.1 The results

After carefully testing and debugging the prototype unit, as described in the previous chapter, the final results, in terms of the PPG signals desired, are obtained. These PPG signals are presented a series of images in Figure 4.1, Figure 4.2, Figure 4.3 and Figure 4.4. These correspond to the red and infra red wavelengths. The systole, diastole and the dicrotic notch can be seen in each of these figures, thus confirming the wave forms obtained do represent the PPGs from arterial blood fairly well enough. But, unfortunately, from the blue and green LEDs, the PPG wave forms could not be obtained satisfactorily.

Now, the parameter of concern to us would be the peak-to-peak voltage in one cycle of both the red and IR PPGs. Let us now define a parameter $\Re$ as

$$\Re = \frac{v_R}{v_{IR}} \tag{4.1}$$

Where v_R and v_{IR} can be said to be the peak to peak voltages in one cycle of the red and IR PPGs that we have obtained. Now, from section 3.2 and especially equation 3.3 and equation 3.4, we can say that,

$$\Re = \frac{(\varepsilon_{HbR} + \varepsilon_{HbOR}Q)}{(\varepsilon_{HbIR} + \varepsilon_{HbOIR}Q)} \tag{4.2}$$

Rearranging equation 4.2,

$$Q = \frac{\varepsilon_{HbR} - \Re\varepsilon_{HbIR}}{\Re\varepsilon_{HbOIR} - \varepsilon_{HbOR}} \tag{4.3}$$

From equation 4.3, we can compute the value of Q. Thus, the number of unknown variables in the equation 3.3 and equation 3.4 in the model presented in section 3.2, now become only two, those being c_{Hb} and T_F.

We also know that,SpO_2 as a fraction can be calculated from the relation,

$$SpO_2 = \frac{Q}{1+Q} \tag{4.4}$$

From this value of SpO_2, we know that,

$$c_{Hb} = (1 - SpO_2)Hb_{tm} \tag{4.5}$$

where Hb_{tm} is the value of hemoglobin obtained by traditional measurement methods. Thus, if we know the data on hemoglobin measurements from a training set of volunteers, then, T_F remains the only unknown in the model summarised by equation 3.3 and 3.4. From the training set data, it will be possible to frame an empirical model via a direct relationship between the path length T_F and one of the peak to peak voltages obtained from the PPGs. From this empirical model, we will be able to measure the levels of hemoglobin content on any other person non invasively, by illuminating an extremity and obtaining a PPG, thus getting the value of the peak to peak voltage from that PPG. It would be advisable to derive the two different empirical models for both the genders separately to get more accurate results.

4.2 Summary of the work done

The objective of the efforts put in this project are to develop a novel, non-invasive technique to measure the hemoglobin content in the arterial blood in human beings. In this method, an extremity in the human body, like a finger tip is illuminated with monochromatic light of different wavelengths and the transmitted light is detected by a photo detector on the other side of the extremity. The attenuation characteristics in different parts within the finger tip, i.e., skin, bone, tissue, veins, arteries are analysed and for our purpose, suitable hardware is developed to filter out the unwanted signals and get only

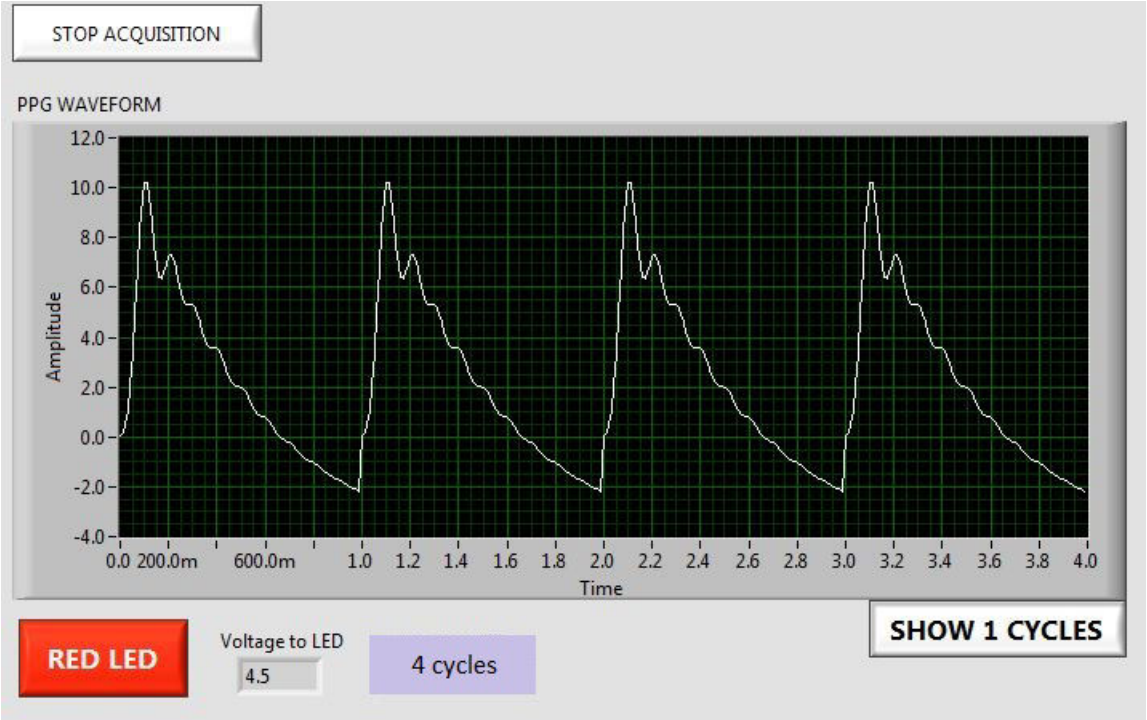

Figure 4.1: Red PPG showing 4 cycles

Figure 4.2: Red PPG showing a single cycle

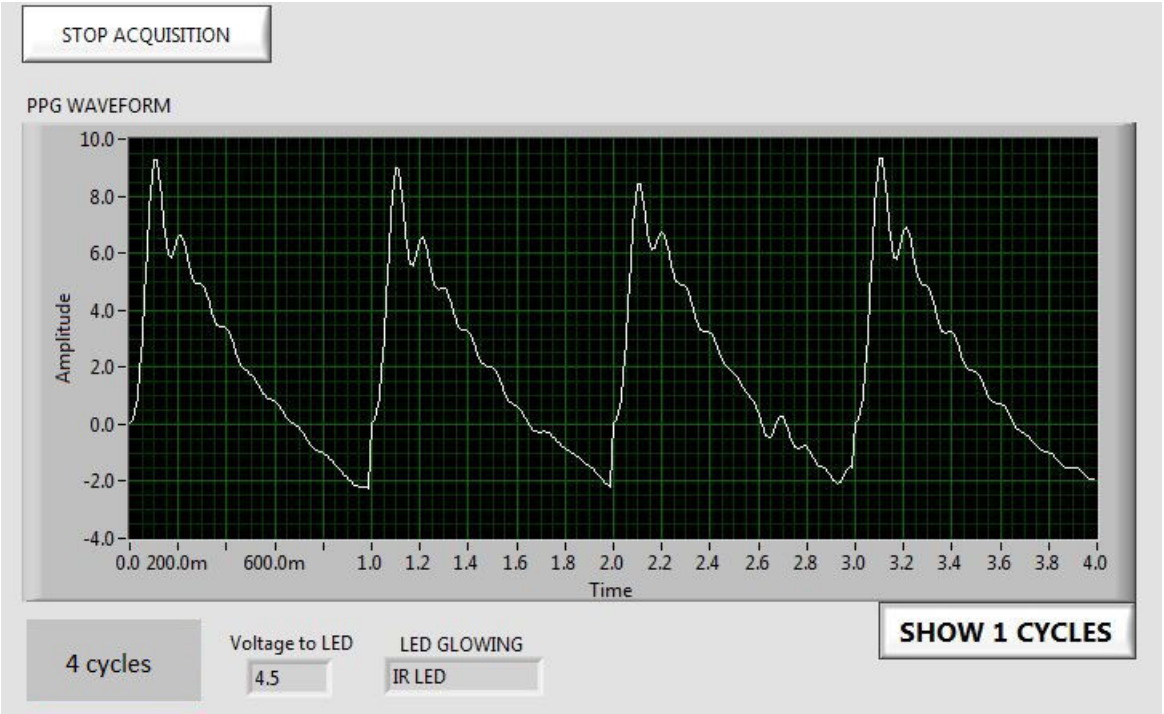

Figure 4.3: IR PPG showing 4 cycles

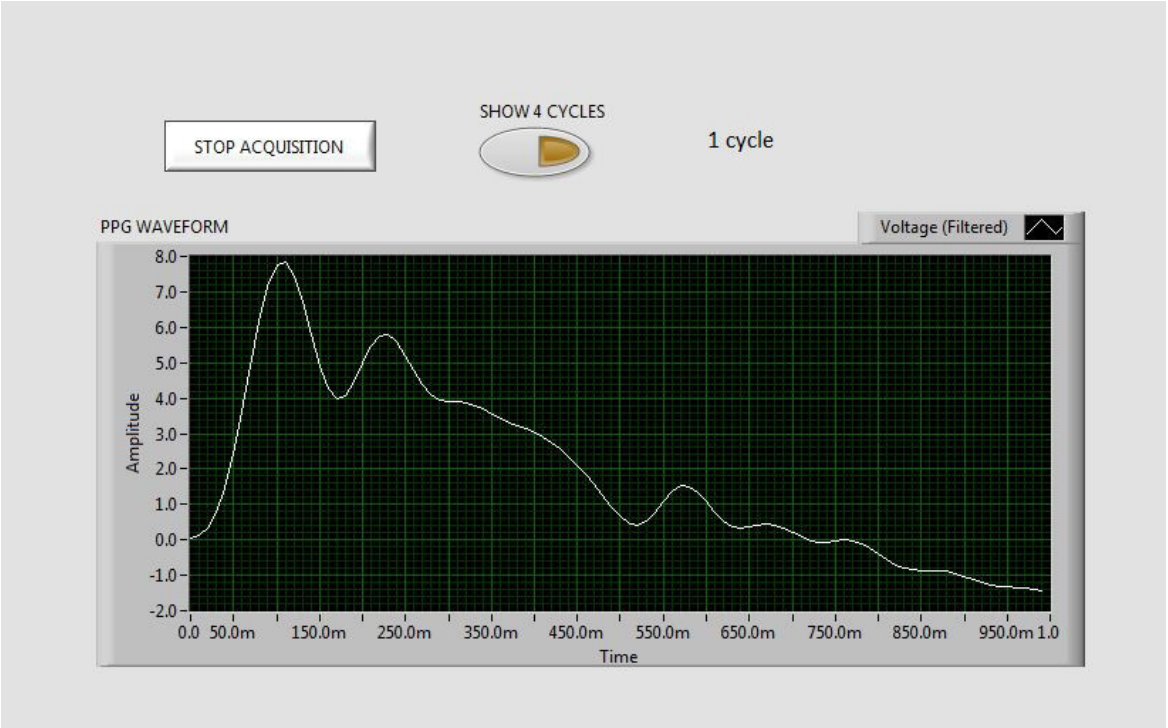

Figure 4.4: IR PPG showing a single cycle

the part of the PPG corresponding to the arterial blood. This portion gives information about the blood volume changes in the arteries, thus having the potential to reveal a lot of characteristics of the arterial blood. Appropriate overall setup is developed with a custom made PPG sensor head, a PCB with all the signal conditioning electronics, a relevant data acquisition system, and a signal processing and a display section. Thus, PPGs corresponding to red and IR wavelengths are achieved, from which by further analysis and a use of an empirical model for the path length of the light, we can calculate the levels of hemoglobin content in blood.

4.3 Conclusions

- The method of photoplethysmography can be applied satisfactorily to measure hemoglobin content in blood satisfactorily.
- This method is far less time taking and eliminates the possibility of any infection, when compared with the traditional invasive methods.
- The value of path length is required for the method being proposed here.
- The path length value can be calculated empirically, thus enabling the calculation of the hemoglobin content in arterial blood.

4.4 Scope for future work

There can be different sections in this project, where there is scope for further research and improvement. The empirical equation for the path length can be accurately found out. Various different combinations of wavelengths can be used to get the PPG wave forms. Also, the number of wavelengths being used to give the PPG wave forms can be increased to research it's viability. Attempts can also be made to make the overall hardware set up more compact, and perhaps ways to make the instrument portable by using, say a tablet for the signal processing and display unit, can be further explored.

APPENDIX A

APPENDIX 1

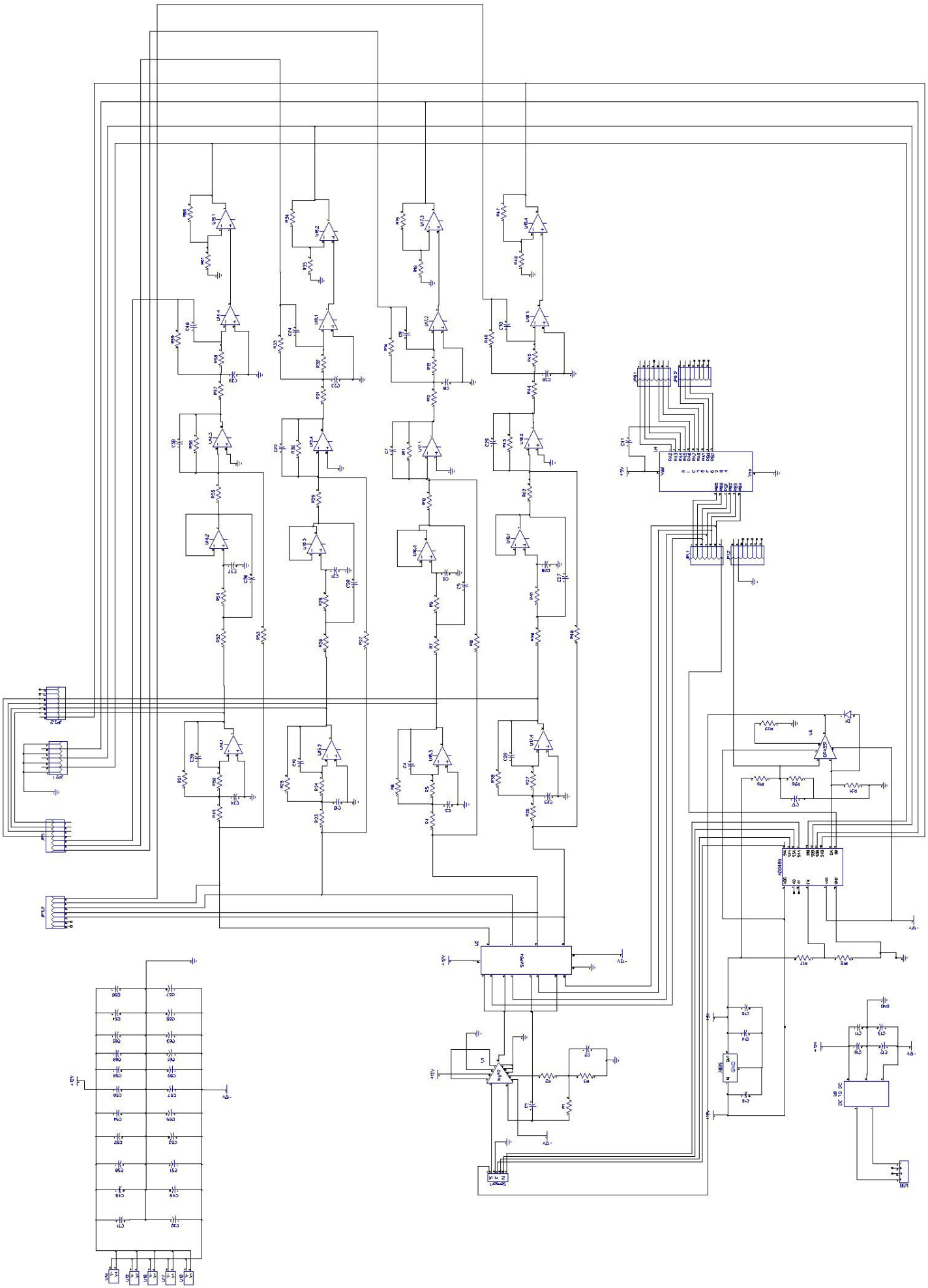

Figure A.1: The schematic of the overall analog signal conditioning circuit

APPENDIX B

APPENDIX 2

The following is the C code used to program the PIC16F628A micro controller for timing and controlling the LEDs and also to correspondingly enabling and disabling appropriate sample and hold channels.

```
#include <16F628A.h>
#fuses MCLR, INTRC_IO, NOWDT, NoPROTECT
#use delay (clock=4000000, RESTART_WDT)

int8 int_count;

int8 int_innercount;

#INT_Timer1

void isr()

{
  switch (int_count){
  case 0: if (int_innercount == 0)
          {
            output_low(PIN_B5);
            output_low(PIN_B6);
            output_low(PIN_B1);
            int_innercount = 1+int_innercount;
            set_timer1(60535);
          }
          else if (int_innercount == 1)
          {
            output_high(PIN_B1);
```

```
26            int_innercount = 1+int_innercount;
27            set_timer1(65035);
28          }
29          else
30          {
31            output_low(PIN_B1);
32            int_count = 1+int_count;
33            int_innercount = 0;
34            set_timer1(65035);
35          }
36        break;
37
38  case 1: if (int_innercount == 0)
39          {
40            output_low(PIN_B5);
41            output_low(PIN_B6);
42            output_low(PIN_B2);
43            int_innercount = 1+int_innercount;
44            set_timer1(60535);
45          }
46          else if (int_innercount == 1)
47          {
48            output_high(PIN_B2);
49            int_innercount = 1+int_innercount;
50            set_timer1(65035);
51          }
52          else
53          {
54            output_low(PIN_B2);
55            int_count = 1+int_count;
56            int_innercount = 0;
57            set_timer1(65035);
58          }
59        break;
60
```

```
61  case 2: if (int_innercount == 0)
62          {
63            output_low(PIN_B5);
64            output_low(PIN_B6);
65            output_low(PIN_B3);
66            int_innercount = 1+int_innercount;
67            set_timer1(60535);
68          }
69          else if (int_innercount == 1)
70          {
71            output_high(PIN_B3);
72            int_innercount = 1+int_innercount;
73            set_timer1(65035);
74          }
75          else
76          {
77            output_low(PIN_B3);
78            int_count = 1+int_count;
79            int_innercount = 0;
80            set_timer1(65035);
81          }
82       break;
83
84  case 3: if (int_innercount == 0)
85          {
86            output_high(PIN_B5);
87            output_high(PIN_B6);
88            output_low(PIN_B4);
89            int_innercount = 1+int_innercount;
90            set_timer1(60535);
91          }
92          else if (int_innercount == 1)
93          {
94            output_high(PIN_B4);
95            int_innercount = 1+int_innercount;
```

```
96              set_timer1(65035);
97            }
98            else
99            {
100             output_low(PIN_B4);
101             int_count = 0;
102             int_innercount = 0;
103             set_timer1(65035);
104           }
105         break;
106
107   default: output_low (PIN_B5);
108           output_low (PIN_B6);
109           break;
110           }
111 }
112
113
114 void main()
115 {
116 set_tris_b(0x00);
117 int_count = 0;
118 int_innercount = 0;
119 setup_timer_1 (T1_INTERNAL);
120 enable_interrupts(INT_TIMER1);
121 enable_interrupts(GLOBAL);
122 for( ; ;)
123    {
124    }
125
126 }
```

APPENDIX C

APPENDIX 3

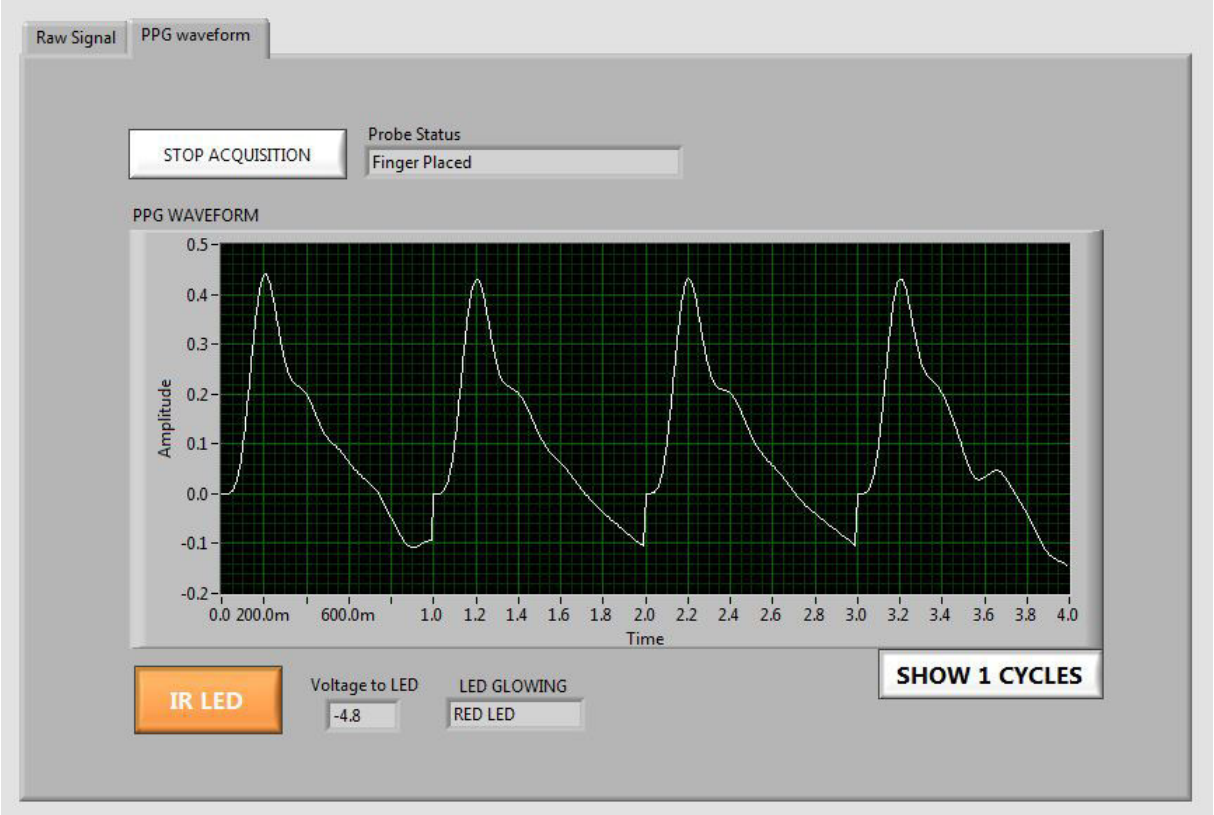

Figure C.1: Front panel of the VI used

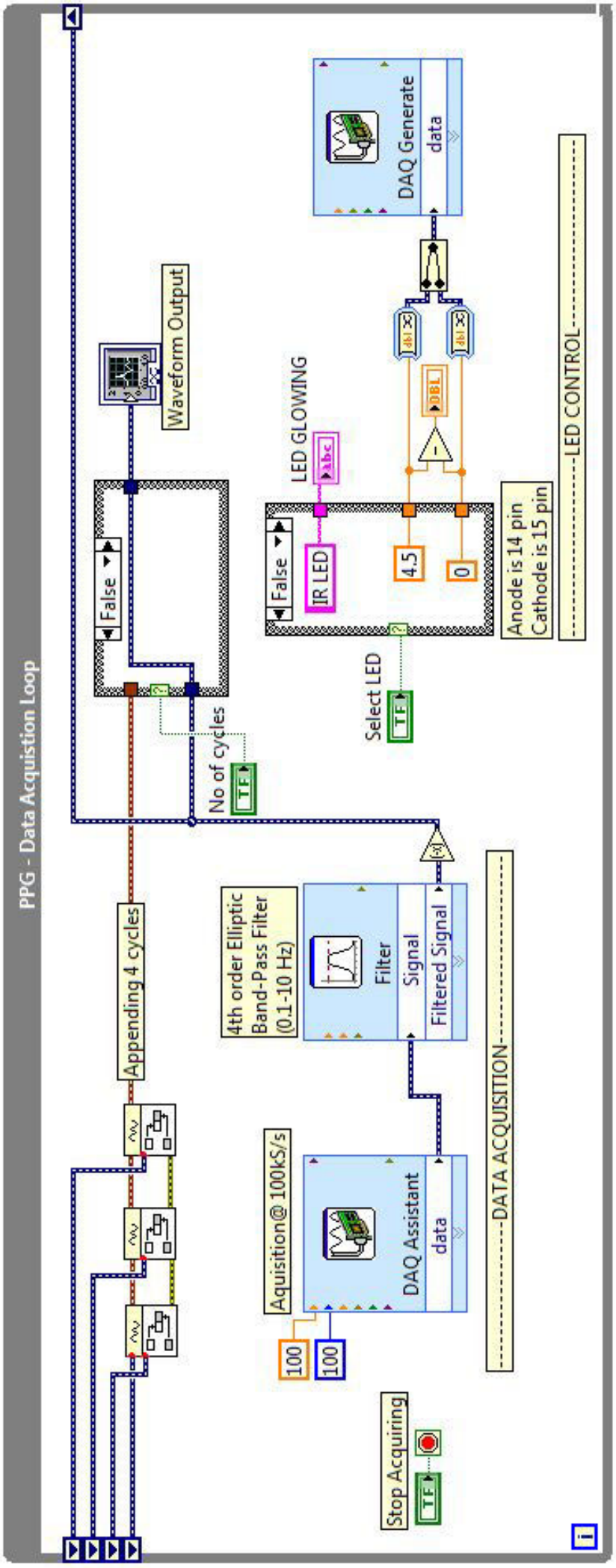

Figure C.2: Block diagram of the VI used

APPENDIX D

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