1. INTRODUCTION

1.1 MOTIVATIONS

The concept of clinical monitoring as been revolutionized in an unprecedented way since the recognition of the pulse oximetry as an indispensable tool to evaluate the clinical status of the patients ensuring is welfare. Since that Takuo Aoyagi introduced the underlying concept of pulse oximetry in the early 70's this technique as progressively evolved from just an interesting concept applied in physiology labs, to a widespread device in operating rooms, general hospital floors, and even domestic application.

Pulse oximetry allows continuous monitoring in a non invasive way the blood oxygen saturation, cancelling the uncomfortable need of blood samples of the invasive procedures. This feature provides a proper surveillance of the oxygen saturation, a physiological parameter that allows the identification of critic situations on the circulatory and pulmonary systems, and provides an overview of this systems state.

The oxygen saturation decrease is usually related with a diminution on the arterial perfusion due to heart failure or to decrease of the oxygen perfusion on the lungs due to a pulmonary failure, this relatively simples reaction chain allows a prompt reaction in critic situations and made the pulse oximetry a reliable tool to evaluate the cardiac and pulmonary function during anaesthesia, in procedures like bronchoscopy, endoscopy, cardiac catheterization, exercise testing and sleep studies, and on general monitoring of patients with cardiac or pulmonary disease.

According to the WHO (World Health Organization) the number of people suffering every day from chronic respiratory diseases is rising and the future trends are not encouraging, the latest studies (2007) points to 300 million patients with asthma, 210 million patients with chronic obstructive pulmonary disease (COPD) and millions of patients with allergic rhinitis and other undiagnosed chronic respiratory diseases. This scenario will drive the pulse oximeter to an even more important place in the future reinforcing the leading role of this tool in health monitoring

In this context this work pretends to highlight the pulse oximeter state of art and point the way to is evolution.[1] [2][3]

1.2 OBJECTIVES

This project main objective is the development of a standalone pulse oximetry device suitable for non invasive measure of the blood oxygen saturation in clinic and home applications. This goal is intended to be achieved developing a prototype of a transmittance probe for data acquisition and an interface device able of acquire and process it, using algorithms for determine the heart rate and blood oxygen saturation. The developed device must be portable, reliable and have a low cost.

The principles of pulse oximetry are well described in the literature, and are already implemented with a remarkable reliability, so our pulse oximetry solution will not certainly revolutionize the world, what is at stake is not to create a whole new device but "only" optimize the available knowledge, using the latest developments in data analysis and hardware.

In the course of the project was established a partnership with the ISA (Intelligent Sensing Anywhere) due to their interest in integrate our oximetry solutions in their broad development of platforms for healthcare solutions.

This document will be mainly focus on the development of interface device for acquire and process data, and on the development of algorithms for data processing

1.3 Team Work and Hosting Entities

This project was carried by the following team work:

Project Coordinator: Professor Carlos Correia
Project Supervisor: PhD João Cardoso
Msc student: Ana Rita Domingues
Msc student: Sérgio Brás

This project was developed as partnership between the GEI and the ISA:

- The Electronics and Instrumentation Group (GEI-Grupo de Electrónica e Instrumentação) is a research group based on the Physics Department of the University of Coimbra that carries research in the field of Atomic and Nuclear Instrumentation, Biomedical Instrumentation, Plasma Physics Instrumentation, Microelectronics, Optical Signal Processing and Telemetry and Industrial Control.[5]

- The ISA (Intelligent Sensing Anywhere) is a company founded in 1990 as a spin-off of the University of Coimbra with more than 15 years of experience developing solutions for the most demanding clients as the Europeans Space Agency and multination industrial companies, the company capitalized the developed Knowledge to request a leading world role as a provider of telemetry and remote metering solutions for gas, fuel, electricity and water. The ISA is an innovative company with a qualified staff and proven merits in the research & development field.

1.4 DOCUMENT STRUCTURE

- In Chapter 1, is presented the document structure and the objectives and motivations are focused;
- In Chapter 2 are described the bases of the theoretical and technical principles of the pulse oximetry applied in the project development , as well as the state of the art of pulse oximetry.
- In chapter 3 are exposed the legal procedures and constraints to commercialize a medical device, such as a pulse, oximeter in Europe and US; are also presented the trends of the oximetry market as well as a brief market study.
- In chapter 4 are weaved brief considerations about the hardware and software bases required to the project.
- Chapter 5 discusses the project evolution and the overall system architecture focusing the acquisition and processing module as well as the algorithms development.
- Chapter 6 presents the obtained results and their contextualized discussion.
- Chapter 7 concludes this document reporting the current status of the project, presenting suggestions for a future work and exposing the team work final project appreciation.

2. THEORETICAL AND TECHNICAL BACKGROUND

2.1 PHYSIOLOGICAL REFERENCES

2.1.1 The blood

Blood is a liquid tissue, produced within the red bone marrow and driven through the vascular system, and its main function is the carrying and delivery of necessary substances, such as nutrients and oxygen, to the body cells and taking back the waste products from their metabolic activities. Blood is a body fluid composed of different types of cells, the solid part representing about 45% of the full volume, suspended within the plasma, the liquid part representing the remaining volume.

Plasma is a yellowish liquid mainly water composed (about 90%), but also containing hormones, proteins (albumin, fibrinogen) and solved minerals, nutrients, gases and metabolic wastes. Plasma is mostly responsible for support, help and intermediate of those components' activity.

The solid part, the blood cells, is composed by: red blood cells or erythrocytes, white blood cells or leukocytes and platelets or thrombocytes. Briefly resuming:

- Red blood cells are the most abundant cells in human's blood as they are the most responsible for oxygen delivery. Due to the hemoglobin presence in these cells they can form a reversible bind with oxygen. The carbonic anhydrase in these cells catalyzes the bicarbonate reaction on the carbon dioxide transportation cycle.
- The white blood cells defend the body against infectious disease and foreign materials (inflammatory response) and also perform an important role on specific immune response.
- The platelets' main function is the formation of clots (platelets and other blood cells clumped together using fibrinogen as a linking agent), thereby inducing the process of blood coagulation.[6]

2.1.2 Hemoglobin

Hemoglobin is a conjugated protein with large dimensions presenting a molecular weight of 67,000 **Da,** composed by a protein part bonded to a nonprotein metallic portion. This molecule structure is organized in four globular polypeptide

subunits, made of constituted by a protein chain (the globin part) each one attached to a heme group presenting a central iron atom (*Fe2*).

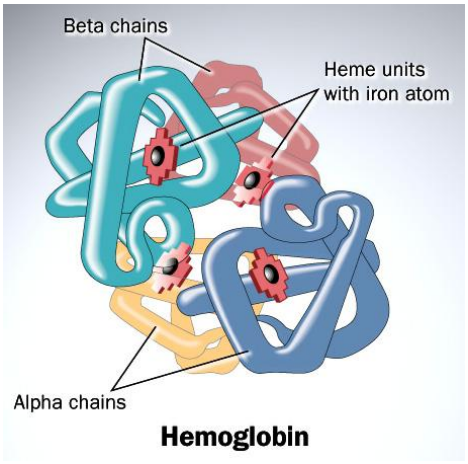


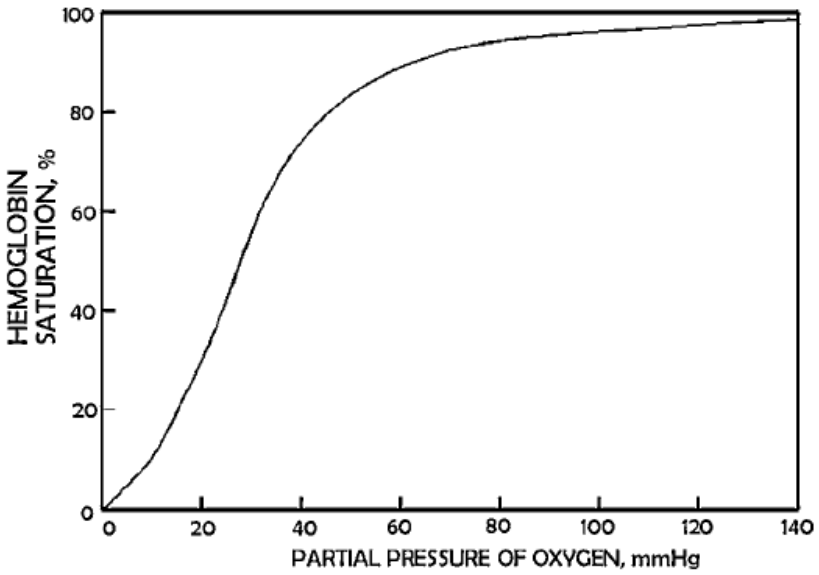
Fig. 1: Hemoglobin structure. [8]

The affinity between the hemoglobin subgroups and oxygen increases with the sequential attachment of an oxygen molecule changing the molecule configuration in a favorable way to increase the free active points, at the heme groups, oxygen affinity, at the heme groups; on the other hand the oxygen unload in one subgroup increases the unload speed on the others; this cooperative relation explains the oxyhemoglobin dissociation curve.

The hemoglobin structure has different active points to bind the oxygen and carbon dioxide, with the heme group part linking up the oxygen molecules, up to four for each hemoglobin molecule, and the globin portion transporting the carbon dioxide molecules, one at each subgroup. This selective interaction allows the hemoglobin to promptly associate and dissociates from oxygen and carbon dioxide, the hemoglobin associated with oxygen is the so called oxyhemoglobin and it is bright red colored, the oxygen disassociate named dioxihemoglobin is bluish purple colored.

Each gram of pure hemoglobin may be combined with 1.34 ml of oxygen, with an average hemoglobin concentration in blood of 15g per 100ml; this provides a total of about 20.8 ml oxygen/100 ml blood for oxygen carrying capacity. The amount of oxygen present in blood is usually expressed by the oxygen saturation under a percentage value and is equal to the amount of oxygen combined with hemoglobin at a given partial pressure divided by the maximum oxygen-carrying capacity. For a reference the oxygen saturation of blood is nearly 75% for breathing air presenting a partial pressure of oxygen of 40 mmHg and about 97.5% with 100 mmHg as partial pressure of oxygen in air.[6][7]

The typical oxygen dissociation curve for humans is presented below:



Grap. 1: Oxygen dissociation curve for humans: at high oxygen concentrations oxyhemoglobin forms, but at low oxygen concentrations oxyhemoglobin dissociates to hemoglobin and oxygen.[7]

2.1.3 Gas exchange and transport

Oxygen diffusion in human tissues occurs when there is a net movement of molecules from an area with high oxygen partial pressure to an area with a lower oxygen partial pressure, this process goes against the initial belief of oxygen secreted into the capillaries by the lungs what would mean that the oxygen would move from the atmosphere to a relatively higher concentration on the lungs trough an active process, because in fact the oxygen transport across the alveolar wall is a passive process, a simple diffusion process.

The oxygen and carbon dioxide move across the blood-gas barrier of the alveolar wall with the transferring rates depending on the diffusion area and the driving pressure (partial pressure difference) in a proportional way and inversely proportional to the wall thickness.

The blood oxygen uptake is mainly limited under normal physiological conditions by the rate of blood flow, the perfusion, through the pulmonary capillaries because the oxygen diffusion through the alveolar wall is enough to provide oxygen to all the red blood cells flowing by the pulmonary capillaries. Only under extreme situations as intense sport or high altitudes the oxygen uptake is affected by the air speed in the lungs and diffusion rate in the alveolar wall.

The oxygen transport includes the oxygen uptake in the lungs, transport through the vessels and delivery to the tissues, this journey begins with the oxygen from the air inspired to the lungs dissolving in the plasma at the alveolar wall, and crossing this passively thanks to the poor oxygen concentration in the pulmonary capillaries were it binds with the hemoglobin heme group forming the oxyhemoglobin.

$$Hb + 4O_2 \leftrightarrow Hb4O_2 \quad (oxyhemoglobin\ reaction)$$

The oxygen is carried through the vessels within blood flow starting to release oxygen when crossing low oxygen concentration areas, this areas high carbon dioxide concentration also stimulates the oxygen release by the Bohr effect where the H^+ ion ,from the carbonic acid,H_2CO_3, (results from the H_2O and CO_2 reaction) dissociation in bicarbonate and H^+ $(H_2CO_3 \leftrightarrow H^+ + HCO_3^-)$ during a carbon dioxide transportation step, reacts with oxyhemoglobin to set free the oxygen which acts as a buffer to decrease the raising acidity caused by carbonic acid dissociation. The higher oxygen concentration in the vessels compared with the surrounding tissues concentration causes the oxygen diffusion, passively, through the vessels walls to the surrounding tissues.[7]

2.2 THE BEER-LAMBERT LAW

The Beer- Lambert relates the attenuation of light with a defined wavelength (λ) crossing an homogeneous medium holding an absorbent substance with the absorbent substance constant concentration (c) in the medium, the length of the optical path,(d,) and the extinction coefficient ($\varepsilon(\lambda)$) or absorptivity of the absorbing substance for that specific wavelength (λ).So when a monochromatic light crosses the medium with an initial intensity, I_0, part of the incidental light is absorbed leading to a decrease of the transmitted light (I) intensity, this descrease in light intensity diminution increases exponentially with the distance,(d,) and is expressed by:

$$I = I_o e^{-\varepsilon(\lambda)cd} \qquad (2.0)$$

The concentration (c) is measured in mmol L^{-1} and the extinction coefficient in L $mmol^{-1}$ cm^{-1} .

Beer's law is based on the assumption that addition of summing the absorbed and the transmitted light is equal to we get equal to the incident light. The scattered light

in the medium and the reflection at the medium surface are despised for this assumption.[9]

2.2.1 Transmittance and absorbance

The transmittance (*T*) of a light that move across a medium with a certain absorbing substance concentration is expressed as the ratio between the incidental light (I_0) and the transmitted light (*I*).

$$T = \frac{I}{I_0} = e^{-\varepsilon(\lambda)cd} \tag{2.1}$$

The unscattered absorbance (*A*) in this process is expressed by the negative natural logarithm of the light transmittance.

$$A = -\ln T = \varepsilon(\lambda)cd \tag{2.2}$$

For multiple absorbers we get that total absorbance (*At*) which is expressed by: [9]

$$A_t = \sum_{i=1}^{n} \varepsilon_i(\lambda) c_i d_i \tag{2.3}$$

2.3 PRINCIPALS OF LIGHT ABSORPTION IN HUMAN BLOOD AT OXIMETRY

The principal responsible for light absorption in human blood in oximeter procedures is hemoglobin, the light absorption properties of hemoglobin depends on the incident light wavelength, and on the chemical binding state. Oxygenated and reduced hemoglobin forms are responsible for the most significant light absorption in blood, however they are not the only hemoglobin forms responsible and hemoglobin also bind substances such as carbon monoxide and hydrogen sulfide.[9]

2.3.1 Functional hemoglobins

Hemoglobin is intended to bind oxygen at the pulmonary capillaries and release it in the systemic vessels; all hemoglobin able to perform this purpose is named functional hemoglobins.

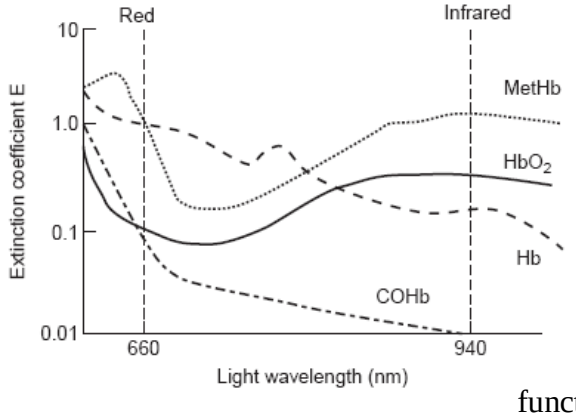
The fully oxygen saturated hemoglobin is called oxyhemoglobin and the non-fully saturated one is the reduced hemoglobin, and the both form the functional hemoglobins. [9]

2.3.2 Dysfunctional hemoglobins

This hemoglobins group is unable to load oxygen to the tissues because of its inaptitude of binding oxygen or because of the interference associated with the oxyhemoglobin oxygen release at the tissues.

The most common dysfunctional hemoglobin are:

- methemoglobin (*MetHb*), carboxyhemoglobin (*COHb*), sulfhemoglobins, and carboxysulfhemoglobins.
- Methemoglobin: is the result of the oxidation of a free heme (Fe^{2+}).
- Carboxyhemoglobin: is formed when hemoglobin binds carbon monoxide.
- Sulfhemoglobins and carboxysulfhemoglobins: results from the oxyhemoglobin reaction with hydrogen sulfide.



Grap. 2: Optical absorption spectrum of different hemoglobin forms. [10]

Focusing in the functional, and most relevant, hemoglobins, it is obvious from the previous chart that in the wavelength ranges of clinical interest for oximetry applications the absorbance of light in the spectral red region (λ<700 nm) is significantly higher for reduced hemoglobin compared with oxyhemoglobin, then at the isobestic point (805 nm) the two species extinction coefficient are equal, and for light incidence in the infrared range (λ>700 nm) the reduced hemoglobin is more transparent than the oxyhemoglobin.[9]

2.3.3 Pulsation of the blood

When light crosses tissues his intensity is attenuated due to different substances absorption; the absorption in the region of interest for oximetry is mainly caused by skin pigmentation, bones, and the arterial and venous blood.

A pulse oximeter relies on the arterial pulsation contrarily to other oximetry procedures as the in -vivo measure of arterial oxygen saturation with an arterial blood sample and spectrophotometer, or the multi wavelengths ear lobe oximeter by Hewlett-Packard.

The arterial pulsation phenomenon is produced by the blood volume variation in the arterial vessels during one heart cycle, during the systole arteries contain more blood because of the arterial vessels diameter increase caused by the pressure increase, at the diastole the pressure decrease leads to the vessels contraction and consequent arterial blood volume decrease. This phenomenon happens only in the arterial vessels, not at the venous vessels. The arterial blood volume increase in systole enlarges the optical path (d) producing, obviously, a light absorbance increase during that cycle in tissues containing those vessels, owing to the larger amount of absorbing substances such as hemoglobins.

This rhythmic component of the total absorbance allows the differentiation between venous blood absorption, constant arterial blood absorption, other non pulsatile absorbing components like skin pigmentation and bones (together, these components together forms the dc absorption component); and the absorption associated with the pulsatile component of the arterial blood (ac component). The rhythmic component of the absorbed light at human tissues does not exceed 1% to 2% of the total dc amount of absorbed light. The measure of the light transmission on the time domain is called plethysmography.

The light transmission through tissues is higher during diastole (I_H), and the responsible absorbing components are the dc components. All components except the nonpulsating arterial blood are collectively represented by ε^{dc}, C^{dc}, and d^{dc}. In this heart cycle step the arterial vessels diameter is minimal d_{min} , thus absorbance thanks to arterial hemoglobin is minimal and therefore the amount of transmitted light is highest (I_H), which represents a peak.

$$I_H = I_0 e^{-\varepsilon dc(\lambda) c_{dc} d_{dc}} \cdot e^{-\left[\varepsilon Hb(\lambda) + \varepsilon_{HbO_2}(\lambda) C_{HbO_2}(\lambda) C_{HbO_2}\right] d_{min}} \quad (maximal\ transmission) \tag{2.4}$$

Moving to next heart step and maintaining the same considerations is perceptive that light absorbance is maximum during systole (I_L) thanks to the arterial vessels diameter increase to a maximum, d_{max} .

$$I_L = I_0 e^{-\varepsilon dc(\lambda) c_{dc} d_{dc}} \cdot e^{-\left[\varepsilon Hb(\lambda) + \varepsilon_{HbO_2}(\lambda)\, C_{HbO_2}(\lambda)\, C_{HbO_2}\right] d_{max}} \quad (minimal\ transmission) \qquad (2.5)$$

From the defined transmitted light per heart cycle it is obvious analyzing each heart cycle equations that the only varying parameter is the optical path length owing to the arterial vessels diameter variation during systole and diastole. So during a cardiac cycle this diameter varies from d_{min} to d_{max}, expressing this variation as $d_{max}=d_{min}+\Delta d$ and starting from the Beer-Lambert law we get the transmitted light (I) expressed as function of I_H: [9]

$$I = I_H e^{-\left[\varepsilon_{Hb}(\lambda) C_{HbO_2} + \varepsilon_{HbO_2}(\lambda) C_{HbO_2}\right] \Delta d} \qquad (2.6)$$

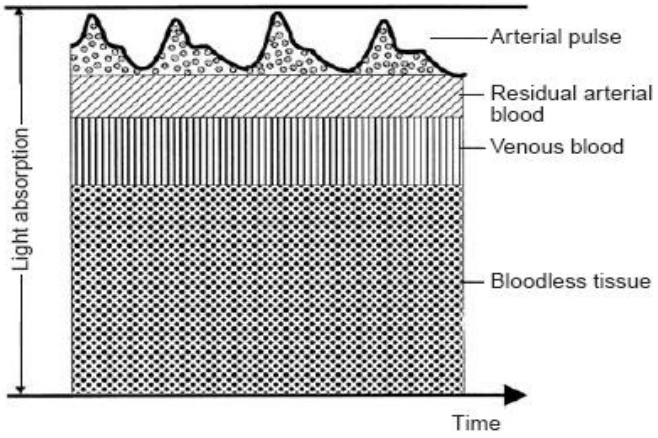


Fig 2: Light absorption rhythmic variation in tissues due to the arterial pulsation effect. [11]

2.4 THE NORMALIZED RATIO (R) AS AN ABSORBANCE FUNCTION

The absorbance through tissues is usually represented as a normalized ratio (*R*) expressed as a function of the absorption due to the non pulsatile component (*DC*) and to the pulsatile component (*AC*) for each of the used wavelengths (red, *R*; and infrared, *IR*), this procedure allows the normalization of the scale between the two wavelengths results, and the ratio is expressed as follows:[12]

$$R = \frac{AC_R / DC_R}{AC_{IR} / AC_{IR}} \qquad (2.7)$$

2.5 MEASURING WITH PULSE OXIMETERS

The oximeters provide an estimate measure of the arterial oxygen saturation using a two wavelengths measuring procedure that allows only the distinction between two blood absorbing compounds (Hb and HbO_2). So without the use of a full set of wavelengths suitable for all the hemoglobins range it's not possible to precisely determinate the Hb and HbO_2 concentrations. However the much higher relative concentration of Hb and Hb02 compared with the remaining hemoglobins decrease the error associated with the two wavelengths measuring procedure to low values. [9]

2.6 USING BEER-LAMBERT LAW TO ESTIMATE THE OXYGEN SATURATION

Pulse oximetry is meant to measure the transmitted light through tissues as the result of the arterial blood effect. As a previously stated, the blood volume in the tissues varies with the arterial pulse that produces a volume increase at systole and a volume decrease at diastole. Blood is the main light absorber in tissues, so the emerging light from tissues is inversely proportional to the blood within tissues. The main absorbing components of the blood are the oxyhemoglobin and deoxygenated hemoglobin.Fortunately these two species have different absorbance coefficients for the most significant wavelengths range, thus indicating the hemoglobin oxygen saturation.

Assuming α is the absorbance of the medium per unit length, commonly named relative extinction coefficient, and relating it with it with the extinction coefficient, and connecting it with the extinction ε, with $\alpha=\varepsilon.C$, where C is the absorptive material concentration, we get a new Beer-Lambert equation for the light intensity (I_n) coming out of a determined medium:

$$I_n = I_0 e^{-\alpha d} \qquad (2.8)$$

I_o is the intensity of the incident light intensity, α is the medium absorbance coefficient per unit length, and d is the medium thickness in unit length.

The absorbance coefficients for oxygenated and deoxygenated hemoglobin, as previously mentioned, are different for most wavelengths; the exception is the isobestic point, when an incident light reaches a finger and the emerging light on the other side is measured results show that the difference between the two lights intensities is the

amount of absorbed light. That value carries information about the blood content of the finger. The intensity of the incident light on the finger it is not easy to determine therefore it's advisable and desirable to eliminate the effects of the incident light intensity and optical path length. This need requires a Beer-Lambert modification to eliminate those variables.[9]

2.6.1 Eliminating the incoming light intensity (I_0) variable

The intensity of the transmitted light through a finger is a function of the absorbance components, function of the constant components like bone, tissue, hair and skin and of the variant compounds as the blood volume in tissues. It is usually assumed that for a time domain analysis the transmitted light intensity through the tissues may be decomposed in a relatively constant baseline component that varies slightly and is the result of the constant components effect on light, and a pulsatile component with faster and greater variations representing the effect of the blood volume variation in tissues.

The baseline component has a thickness d and an absorbance α, and the pulsatile component has a Δd thickness and a α_A absorbance representing the arterial blood absorbance.

The light transmitted through the baseline component (I_1) can be written according to the incident light intensity (I_0) using the fallowing equation:

$$I_1 = I_0 e^{-\alpha d} \qquad (2.9)$$

In the same way the transmitted light from the pulsatile component (I_2) as function of the incident light (I_0) may be expressed as:

$$I_2 = I_1 e^{-\alpha_A \Delta d} \qquad (2.10)$$

The replacement of the I_1 expression in the I_2 expression lead us to note that the light transmitted through the finger as a function of the incident light intensity Io is expressed by:

$$I_2 = I_0 e^{-[\alpha d + \alpha_A \Delta d]} \qquad (2.11)$$

The effect that arterial blood volume produces on light is formulated from the relationship between I_1 and I_2. Expressing the alteration in transmission from the arterial component as $T_{\Delta A}$, we get:

$$T_{\Delta A} = I_2 / I_1 \qquad (2.12)$$

Replacing the I_1 and I_2 values in the previous equations we have:

$$T_{\Delta A} = \frac{I_2 e^{-[\alpha d + \alpha_a \Delta d]}}{I_0 e^{-\alpha d}} \quad (2.13)$$

In result, it becomes possible to eliminate I_0 (cancelling it in the numerator and denominator) and define the light emerging from the arterial component as:

$$T_{\Delta A} = e^{-\alpha_A \Delta d} \quad (2.14)$$

For a further simplification we apply a logarithmic transformation:[9]

$$lnT_{\Delta A} = \ln(e^{-\alpha_A \Delta d}) = -\alpha_A \Delta d \quad (2.15)$$

2.6.2 Eliminating the optical path length (Δd) variable

The elimination of the Δd variable is possible by using two different wavelengths to measure the arterial transmittance. From each of the two measurements at different wavelengths we get an equation with two unknown variables. The particular wavelengths selection comes partially from a more complete arterial absorbance, α_A, expression.

$$\alpha_A = (\alpha_{OA})(S_a O_2) - (\alpha_{DA})(1 - s_a O_2) \quad (2.16)$$

In the previous expression α_{OA} is the oxygenated arterial absorbance, α_{DA} is the deoxygenated arterial absorbance, and S_aO_2 is the oxygen saturation of arterial *Hb*. The α_{OA} and α_{DA} have significantly different values along all wavelengths within red and near infrared regions; the exception is the isobestic wavelength at 805nm. For a 90% SaO2 the arterial absorbance is 90% due to oxygenate arterial absorbance, α_{OA}, and the remaining 10% is due to deoxygenated arterial absorbance, α_{DA}. The isobestic wavelength represents the α_{OA} and α_{DA} minimal relative importance to the arterial absorbance, α_{OA}, because they are both equal at this point.

The two selected wavelengths are far enough from the isobestic wavelength to ensure the ability to easily differentiate the two signals. It is advisable to place the selected wavelengths in the opposite red and infrared regions.

The ratio from the red and infrared light transmitted through the arterial blood is expressed as:

$$\frac{lnT_{\Delta AR}}{lnT_{\Delta AIR}} = \frac{-\alpha_A(\lambda_R)\Delta d}{-\alpha_A(\lambda_{IR})\Delta d} \qquad (2.17)$$

In the previous equation $T_{\Delta AR}$ is equal to the arterial transmittance variation for incident red light (λ_R), $T_{\Delta AIR}$ is equal to the arterial transmittance variations for incident infrared light (λ_{IR}). Assuming that the two different wavelengths light sources are placed nearly at the same place on the finger we get that the light optical path length through the tissues is approximately the same for the two wavelengths sources. Therefore the optical path length variation, Δd, coming from the arterial blood flow is approximately equal for both wavelengths sources. From this assumption is possible to cancel the Δd term one the right side equation numerator and denominator, this produces the following equation:

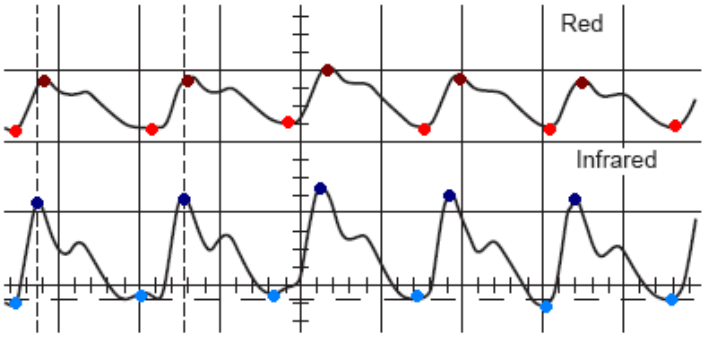
$$\frac{lnT_{\Delta AR}}{lnT_{\Delta AIR}} = \frac{\alpha_A(\lambda_R)}{\alpha_A(\lambda_{IR})} \qquad (2.18)$$

This last equation provides a measuring independence from the incident light intensity and from the optical path length variation with the arterial blood flow. From the complexity of the physiological process it is not possible to directly get a measurement of the oxygen saturation value. The correlation between the measured ratio and the actual arterial blood oxygen saturation is obtained from crossing the measured data with an empirical calibration curve. For simplicity the ratio between the light absorbance at red and infrared wavelengths, R_{OS}, may be expressed as:[9]

$$Ratio = R_{OS} = \frac{\alpha_A(\lambda_R)}{\alpha_A(\lambda_{IR})} \qquad (2.19)$$

2.6.3 The ratio of ratios

The ratio between the light absorbance at red and infrared wavelengths is usually expressed by a variable named as Ratio of Ratios, R_{OS}; this variable is commonly calculated applying the natural logarithm to the ratio obtained from dividing the red signal peak R value by the red sign valley value; and then divide that value by the natural logarithm of the ratio between the infrared peak value and the infrared valley value.



Grap. 3: Red and Infrared light transmission on tissues due to arterial pulse. (R_H, dark red; R_L, light red; IR_H, dark blue; IR_L, light blue).

Moving this concept to a practical field we get that during a measurement the photodiode who records the data records low (R_L) and high (R_H) values in red wavelength, and high (*IRH*) and low (*IRL*) values for the infrared wavelength; from this observation we get that R_{OS} as function of the transmitted light intensity through a tissue may be expressed as:

$$R_{OS} = \frac{\ln\left(\frac{R_L}{R_H}\right)}{\ln\left(\frac{IR_L}{IR_H}\right)} \qquad (2.20)$$

2.7 BEER-LAMBERT LAW VALIDATION FOR USE IN PULSE OXIMETRY

The intensity of the light that crosses a particular medium is not only attenuated by the light absorption due the medium compounds, in fact the incident light will be split in transmitted, absorbed, reflected and scattered light during the journey at the medium.

The light reflection at the skin surface and the absorbance thanks to non pulsating arterial blood are smoothed using the plethysmographic waveform. Nevertheless the skin surface bone, muscle, tissues and mainly the blood produce light scattering that raises the light absorbance. The assumption of the blood as a homogeneous medium is also not entirely true; in fact it is capable of non linear light absorbance due to varying hemoglobin concentration.

The light absorbance varies not entirely thanks to the optical path length variation during a heart cycle, if this was the only factor the variation would much smaller. The co-responsible is the change of the red blood cells axis orientation, these

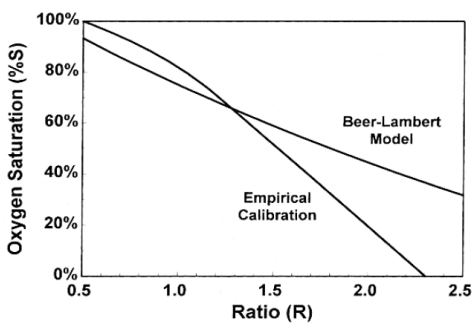
cells are biconcave disks and during the diastole they have the larger diameter parallel aligned with the blood flow, in opposition during the systole they align this side perpendicularly to the blood flow. Thus the optical path length during systole is greater increasing the light absorbance. The light absorbance is also changed by the red blood cells axis reorganization. This space organization condition makes the light transmission and reflection to depend not only from the heart cycle but also from blood speed (Moyle 1994).

These phenomena lead to a difference between the real oximetry measures of light transmission and the theoretical results expected from Beer-Lambert law.

Despite this gap between real and theoretical results, the used assumptions on the theoretical model allow the pulse oximeter to produce accurate enough measurements for most clinical demands. This good reliability on the results is partially obtained with the use of calibration curve based on empirical data.[9]

2.8 CALIBRATION PROCEDURE

The commercial oximeters are nowadays usually calibrated using data collected from in vitro procedures. For a successful calibration procedure it is necessary to collect a large set of data obtained from clinical studies were the ratio of absorbance is calculated, by the oximeter we pretend to calibrate, and associated with a accurate measure of the SaO_2 obtained with an more accurate method such as the co-oximeter. The collected date is then used to identify specific calibration coefficients and create a look up table, that table is then saved on the oximeter memory to convert the optical measurements to SpO_2. Although the major prevalence of the in vitro calibration the in vivo calibration procedure is also an available method to produce a calibration curve, therefore the two methods will be farther discussed above. [Wiley e Webster]



Grap. 4: Relation between the Beer-Lambert expected values and an empirical calibration curve.[14]

2.8.1 In vivo method

The in-vivo calibration method uses the comparison between ratios obtained with the oximeter and the ratio for the oxygen saturation obtained from in-vivo samples collected from human test subjects. This procedure requires a complex clinical apparatus but was the only possible calibration procedure until 1994.

In this procedure the test subjects are punctured in the radial artery with an arterial cannula to provide fast blood samples collection and fitted to one or more oximetry probes. Each patient's breathes a controlled gases mixture to control the blood levels of oxygen and other contents, blood samples are systematic collected to control the desired blood compound concentration determined using the co-oximeter. So the test begins with the test subject breathing a gases mixture who provides a blood oxygen saturation of 100%, the gases mixture is them manipulated (more nitrogen and less oxygen) to produce a controlled hypoxia increase, during this procedure each time the ratio from the oximetry probe decreases to a stable value a blood sample is collected to measure the oxygen saturation using co-oximeter. The blood oxygen saturation decreases only until values that ensure the absence of injuries in healthy subjects, so the minimal oxygen saturation level cannot overcome about 60%.

At the procedure end, the collected data is plotted and a best fit curve calculated. The test subjects are usually selected from nonsmokers with background levels of carboxyhemoglobin between 1% and 2%; this background levels are ascertain collecting blood samples and analyzing them with co-oximeters. [2][9]

2.8.2 In vitro method

This method is based on the application of artificial models that try to ensure a close anatomic and physiologic likeness with the human model. This synthetic model allows to control the concentration of the pretended compounds for a calibration procedure. The market nowadays provides solutions that simulate the optical properties of a human finger and also the pulsatile arterial blood flow. A generic product for calibration in vitro pumps blood across a cuvette acting as a finger model, the pulsatile effect is obtained using a peristaltic pump controlled by a computer and with the ability to produce the desired pulsatile waveform shape. The blood is oxygenated passing through a membrane oxygenator using a gas mixture of O_2, N_2 and CO_2, the composition of the gas mixtures crossing the membrane is controlled with a mixing

pump. Have been tried many models for finger but the one presenting better results is the one formed by a cuvette built with thin (0.5 mm) silicone rubber membranes and a central region of rigid Plexiglass. Using whole blood it's necessary to cover the cuvette with translucent paper that acts as a diffuser. The blood gets in to the cuvette and flows in a thin layer (1mm) through the cuvette circumventing it from side to side.

The silicone membrane is flexible enough to allow that the produced volume variation causes a pulsatile effect, and that this effect produces an *AC/DC* ratio in the physiological range. The readings from the oximeter probe are simultaneously recorded with the data from the collected blood samples measurements obtained with co-oximeter. This calibration procedure allows an accurate calibration for use on a oxygen saturation range from about 50% to 100%, under this values most oximeters have an undetermined accuracy.[9]

2.9 MAIN OPTICAL METHODS OF OXIMETRY

2.9.1 Transmission versus Reflection Oximetry

Any light with a particular wavelength (λ) who crosses a blood sample, which contains hemoglobin (*Hb*), will be absorbed, transmitted or reflected. The value of the transmitted, reflected or absorbed light is related with many factors, such as the type and concentration of the hemoglobins (*Hb*) at the crossed sample. The value of the transmitted light across a blood sample for a particular wavelength is inversely proportional to the amount of light absorbed or reflected. The transmission oximetry is a method to measure the arterial oxygen saturation (SaO_2) by determining the value of the transmitted light for a particular wavelength (λ). In opposition the reflectance oximetry uses the measured value of the reflected light for a particular wavelength (λ) to define the SaO_2. These two procedures are based on the same principles previously exposed, and the main difference between these two techniques is the photodetectors placement; for the transmission method they are placed in the photodetector opposite side and for the reflection method they are placed side by side with the photodetector. [2]

Weaving some more considerations about the reflectance oximetry when are injected photons through a tissue some are absorbed by the different tissues layers however some photons exit from the tissues following a pattern called "banana" pattern, this event is owing to the scattering effect of the tissues, the backscattered photons allow to determine the oxygen saturation because the used light wavelengths are effectively

transmitted through lipids water, as a consequence the detected absorption is produced by the arterial blood. [14]

2.9.2 Co-Oximetry

How was already exposed the blood has a wide range of hemoglobin types, for example: oxyhemoglobin, deoxygenated hemoglobin, carboxyhemoglobin and methemoglobin, each one of them with its own absorption transmission- reflection spectrum and associated extinction coefficient. The typical oximetry that uses only two wavelengths are only able to distinguish between oxyhemoglobin and deoxygenated hemoglobin deleting the other hemoglobins effects, some off that hemoglobins have a very close spectrum to the oxyhemoglobin spectrum taking to masked results. The only way to distinguish between the different types of functional and dysfunctional hemoglobins is using multiple wavelengths lights, using the appropriate wavelength to each hemoglobin type.

A machine able to distinguish the initial exposed four types of hemoglobin would require at least four different wavelengths and is technically close to a regular spectrophotometer. The different wavelengths are obtained with interference filters and the appropriated light source. The procedure to determine the four hemoglobins concentration would include a first step where is performed a reading on a blank solution for all wavelengths, then a reading from a diluted hemolyzed sample is taken for all wavelengths. Hemolyzed solutions without the red blood cells membranes are used instead of simply blood to minimize the scattering effect that decreases the results accuracy. Finally these values will subtract the corresponding measured values with a blank solution to obtain the blood absorbance values at each wavelength. With these absorbencies it is possible to determine each hemoglobin concentration from the fallowing equations:

$$C_{Hb} = K[\varepsilon_{Hb}(\lambda_1)A_1 + \varepsilon_{Hb}(\lambda_2)A_2 + \varepsilon_{Hb}(\lambda_3)A_3 + \varepsilon_{Hb}(\lambda_4)A_4] \quad (2.21)$$

$$C_{HbO_2} = K[\varepsilon_{CHbO_2}(\lambda_1)A_1 + \varepsilon_{CHbO_2}(\lambda_2)A_2 + \varepsilon_{CHbO_2}(\lambda_3)A_3 + \varepsilon_{CHbO_2}(\lambda_4)A_4] \quad (2.22)$$

$$C_{MetHb} = K[\varepsilon_{MetHb}(\lambda_1)A_1 + \varepsilon_{MetHb}(\lambda_2)A_2 + \varepsilon_{MetHb}(\lambda_3)A_3 + \varepsilon_{MetHb}(\lambda_4)A_4] \quad (2.23)$$

$$C_{COHb} = K[\varepsilon_{COHb}(\lambda_1)A_1 + \varepsilon_{COHb}(\lambda_2)A_2 + \varepsilon_{COHb}(\lambda_3)A_3 + \varepsilon_{COHb}(\lambda_4)A_4] \quad (2.24)$$

On this equations C_x is the concentration od the hemoglobin type *x*, $\varepsilon_x(\lambda_y)$ is the extinction coefficient of the hemoglobin type *x* for the wavelength *y*, *Ay* is equal to the difference between the absorbencies values of the blood and blank solution, *k* is a constant defined for the calibration procedure.

These devices are exposed to source errors if at the testing solution are present unwanted particles as cells fragments or lipids that scatter light masking the results, however this method remains the most accurate one to determine the hemoglobin species concentration, being a measure standard.

This accuracy combined with is limitation to make discrete measurement corresponding to only the times to which samples were collected made of this technique mainly a standard for in vivo calibration of oximeters.[9]

2.10 STATE OF THE ART IN PULSE OXIMETRY

The development of pulse oximetry led oximetry to become an accepted and useful standard on the field of non−invasive techniques for arterial SaO2 measurement. This technique is used whether as a safety guard or as a diagnostic tool, being one of the most important developments for a safe patients monitoring. The greatest advantage of pulse oximetry is the ability to produce a continuous and safe bedside monitoring of blood oxygenation on a non invasive and low cost way.

These features are extremely useful on unstable patients with a tendency to rapid or unpredictable oxygen desaturation. The pulse oximeters provide an easy use, with no required calibration by the user, and almost maintenance free require. These features made of the pulse oximeter a widely used method in many clinical practices such as in intensive care units, in anesthesia procedures, and to monitor patients with pulmonary, cardiac and sleep disorders.[11]

The nowadays oximeters, portable or no portable, are based on a oximetric probe, and an acquisition and processing module based on a microcontroller features; this modules properties, features and architecture change from manufacture to manufacture and correspond to industry patents, so it's impossible to us explore and analyze this oximeters component. Relatively to the oximetric probes the available solutions are the transmittance and reflection probes.[2][9]

2.10.1 The probes

2.10.1.1 Transmittance probes

This probe obviously use the light transmitted through an extremity to measure the blood oxygen saturation. This device is basically made of two leds: one emitting in the infrared (usually 940mm) and other in the red (usually 660mm) light spectrum, and a photodetector with a correct response to this light frequencies. These two main components are placed oppositely. These sensors are placed in body extremities such as fingers and ear lobe, these probes are based on the transmitted light detection so the leds are aligned with the photodetector to allow the maximum detection of transmitted light. These probes must ensure a good extremity surrounding and an adequate pressure to place the probe near the skin without cause clots on the on the blood under the tissues. On the market are available reusable and disposal transmittance probes. The advantage in the use of disposal probes is that the single patient utilization eliminates the cross contamination possibility and the adhesive taping provides a better sensor placement providing an nearly zero movement between the sensor and the extremity reducing the signal distortion due to motion artifacts; this probes are recommended for monitoring with a low signal and big surrounding interference. The reusable probes provide a more cost effectively but require a regular clean to avoid cross contamination and are more sensitive to motion artifacts, although their use has acceptable results in most clinical cases.

Relatively to the transmission probe placement the finger allows an easier use and the ear lobe a better transmitted light intensity. [9]

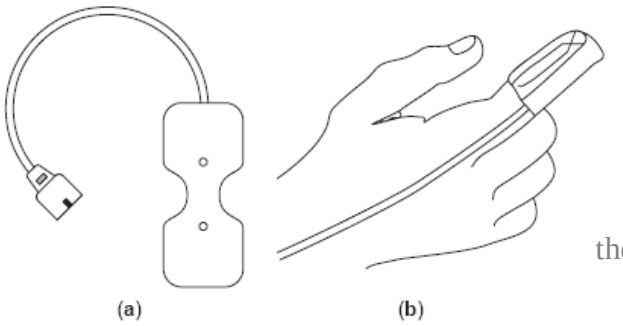


Fig. 3 A typical disposable transmission probe for finger placement (a), the same probe taped to a finger (b).[11]

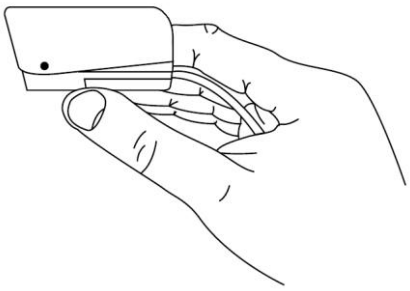


Fig. 4: Typical reusable transmission probe placed on a finger. [Adapted from 15]

2.10.1.2 Reflectance probes

The reflectance probes may be virtually used at any point of the skin surface and are used when the transmission probes cannot be. The oxygen saturation is obtained measuring the pulsatile component of the light scattered by the tissues, light is scattered by the red blood cells and other components on the blood flow, and by the static tissues. The scattered light intensity depends on the skin structure and pigmentation.

These probes are formed by the same main components than the transmittance probes, and they have basically the same features, but on this case the LED'sand the probe are aligned side by side. Where the main issue is on the correct distance between the Led's and the photodetector, and the criteria is that the distance must ensure a good light detection for maximum and minimum pulsatile components.

The market also provides reusable and disposal reflectance probes with the same advantages and disadvantages previously named.

Relatively to the probe placement beside its almost unlimited positioning possibilities, the elected place is normally the forehead or temple.[9][11]

Fig. 5: A scheme of the typical reflectance probe organization and placement.[11]

2.10.2 Pulse oximetry constraints and limitations

2.10.2.1 Accuracy

The pulse oximetry accuracy depends on the oxygen saturation; the accuracy variation along the oxygen saturation range allows the formation of three saturation ranges: low saturation, normal saturation and high saturation, with a related standard accuracy.

- **L*ow concentrations (under 80%):*** due to ethical concerns the in-vivo calibration procedures are limited in hypoxia situations because this clinical situation requires the repeated induction of severe hypoxia states in volunteers, this causes the sample range decrease leading to a potential error increase, the error is attenuated with in vitro collected data. The error associated to these scenarios is also justified by the signal-to-noise reduction at low saturations caused by the transmitted light reduction;

transmission decreases because the hemoglobin red light high absorption reduces the light ability to cross the tissues.

- ***Normal saturation (80 to 97.5%):*** the performance reliability is high for most available oximeters in this range owing to good calibration. This clinical scenario is the most usual, what also leads to the results improvement.
- ***High saturation (97.5% to 100%):*** the oxygen saturation is limited to 100%; this condition at this range high end complicates the accuracy determination due to positive errors (caused by an excessive transmission ratio), and the difficulty in interpreting the origin of these errors decreases the reliability in this range. However patients at this level do not require urgent medical care so it is acceptable.

A brief conclusion about the oximetry accuracy will state that the realized studies show that oximeter have a typical accuracy of about ±4% relatively to the blood co-oximetry measurements. The accuracy is also generically affected by the delay on the response time, with a change on the oxygen saturation of the blood taking from 10 to 35*s* to be displayed. [10][12]

2.10.2.2 Oximetry limitations

- **Motion Artifacts**

Like in other medical devices the motion artifacts induce error increase; in pulse oximetry the problem relies on muscles movement near the oximeter probe, what may cause false pulses similar to real pulses and owing the readiness to get the pretended signal overwhelmed by the remaining plethysmographic signal any motion can cause an artifact.

- **Optical artifacts**

The pulse oximeter uses optical procedures to measure light transmittance in order to define oxygen saturation; this make this devices sensitive to bright external light sources. Artifacts are produced when external bright light hits the photodiode, or when it is reached by light who as not crossed a pulsatile arterial vessel.

- **Temperature effects**

The body exposition to low temperatures changes the peripheral perfusion, what is optically transposed as a reduction on the transmitted *AC* component that causes a greater exposure to motion artifacts, raising the inaccuracy.[2][11]

- **Low peripheral vascular perfusion**

Pulse oximetry depends on a proper arterial pulsation, so an important decrease in peripheral vascular pulsation as the one related with some clinical disorders like: hypothermia, cardiac failure, and hypotension may produce a signal pattern to low to ensure a reliable measure. Generally low perfusion conditions increase the motion artifacts sensibility.[2][11]

- **Venous congestion**

The oxygen saturation measurement relies on a pulsatile signal and on the assumption that it is only due to arterial blood, so if venous congestion happens the consequent venous pulsation will induce artifacts, because the acquired pulse will not only be the result of a single arterial component but the overlap of a venous blood with lower oxygen content component with an arterial component.[2][11]

- **Dysfunctional hemoglobins**

The presence of dysfunctional hemoglobins affects the measuring accuracy masking the results, it is especially dangerous the presence of high concentrations of carboxyhemoglobin because this compound leads to a false increase on the oxygen saturation levels originating a potentially dangerous clinical situation for the patient.[2][11]

3. HARDWARE AND SOFTWARE CONSIDERATIONS

3.1 THE BASIC ARCHITECTURE OF AN OXIMETRY PROBE

3.1.1 The LED's

The necessary light source for the oximetry applications are fulfilled by the light emitting diodes, LED's, due to his features: small size, good drive characteristics, powerful light output and accurate bandwidth selection; about the bandwidth the LED's technology covers the required bandwidth (red and infrared). This features plus the cost effectiveness, low power consumption and good optical properties made the LED the ideal light source for an oximetry probe.

A LED is an optoelectronic semiconductor based on the diode semiconductor that emits light based on an electroluminescence phenomenon, this light emission is produced each time an electron raises is energy state to a level that allows it to cross the forbidden energy gap the electron enters the conduction band (E), to return to the valence band the electron looses energy, corresponding to the two levels energy difference, that is liberated as a photon with a wavelength (λ) expressed as a function of the forbidden energy gap value:

$$E_g = hc/\lambda \qquad (3.0)$$

In the previous equation h is the Plancks's constant, c the light speed in the vacuum, E_g the forbidden energy gap and λ the emitted photon wavelength.

The most relevant specification for the LED's selection is the radiant power and the size. For radiant power the elected reference is 1mW (milliWatt) with 20mA dc current, and usually do not cross the 10mW limit. The Led's size is no longer a constraint due to the manufacturing techniques progress.

Briefly analyzing the other LED's parameters we get that:

- The forward current, current driven from the anode to the cathode, usually varies from 2 to50 mA and is approximately linearly proportional to the radiant power.
- The forward voltage, potential drop across the *p-n* junction, varies typically from 0.9 to 2.5 V. This parameter defines the forbidden energy gap (E_g) and therefore the emitted light wavelength.
- An extremely flexible operating temperature range, from -40 to 85ºC.

- A switching time, time taken to change from an on state to an off state, of low hundreds nanoseconds.
- A narrow bandwidth that varies from less than 20 to 60 nm and ensures the necessary low wavelengths dispersion around the pretended wavelength.
- A beam angle from few degrees to 180º that provides narrowness enough to the incident light beam cross the tissues.[9]

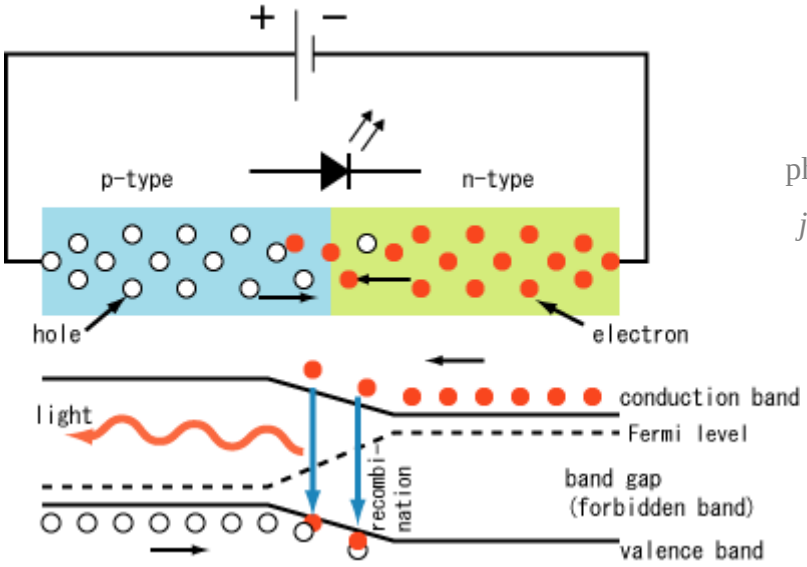


Fig. 6: The light emission phenomenon across the *p-n* junction on a LED driving current.[16]

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3.1.2 The Photodiodes

The decision process to elect a choice from the multiple possible devices available to measure a light source, such as photodiodes, photoresistors and phototransistors, must regard some features. The elected device must have a good spectral response to the particular wavelengths used in the application, a good linearity on the output signal because is highly advisable that this signal presents a linear proportionality to the incident light (illumination E) and a good sensibility that is the ratio between the input and output signal, in this case is desirable that a small change in the incident light intensity produces a visible change on the electrical output.

The use of pulsed LED's also requires a good response time that is the time required to a change on the input signal produce a modification on the output signal. Due to assembling consideration the size is also an important issue, and the commercial goals also demand a cost effective solution. The most balanced choice emerging from all this considerations is unquestionably the photodiode.

A photodiode is a p-n junction semiconductor where the p-n junction is exposed to light; when a light photon hits the junction it is absorbed and his energy produces a

hole/electron pair. The electrons from the p-side move through the depletion zone to the n-side, and the holes swap from n-side to p-side, this charged particles movement produces an electric current.

The photodiode provided current (*I*) is expressed by:

$$I = I_P - I_D \qquad (3.2)$$

With the I_P as the photocurrent expressed as follows:

$$I_P = S.E \qquad (3.3)$$

And I_D as the diode current obtained from:

$$I_D = I_0\left[e^{\frac{qV}{KT}} - 1\right] \qquad (3.4)$$

On the previous equations S expresses the sensibility, E the illumination, I_0 the inverse saturation current, V the voltage at the diode, *K* as the Boltzmann's constant and T the absolute temperature.

Photodiodes may be operated in two modes, the photovoltaic and the photoconductive.

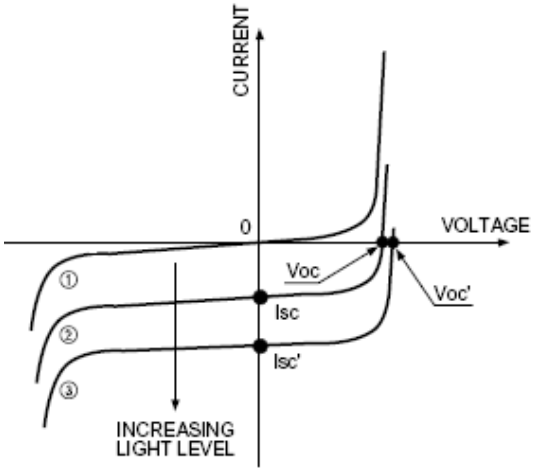
On the photovoltaic mode the circuit is kept open and an incident light produces a voltage modification (V_{OC}) that is not however proportional to the incident light, being expressed by (with *I*=0):

$$V_{OC} = \frac{KT}{q} ln\left(\frac{I_P}{I_D} + 1\right) \qquad (3.5)$$

The photoconductive operating mode requires a power source to ensure that the photodiode voltage is kept constant (usually zero) during the variation of the incident light intensity. On this mode for a *V*=0condition the current output as incident light intensity function is given by:

$$I_{SC} = S.E \qquad (3.6)$$

The photodiode sensibility for a specific wavelength typically varies no more than 0.05% during is operational range, however it varies significantly with the incident light wavelength depending on the assembling process. On the photoconductive mode the photodiodes are quite rugged devices with only a slight variation on the sensitivity, usually about 0.2% / ºC. Briefly analyzing some other features photodiodes present typical response times about 20μs, a radiant sensitive area (the p-n junction exposed to light) from 1 to 7 mm^2, and a low price of about 1 U.S dollar per unit.[9]



Grap. 5: Current versus voltage representation for a photodiode. On an open circuit (I=0) increase the light intensity produces a logarithmic increase on the voltage (photovoltaic mode); for a short-circuit situation (V=0) the photodiodes current varies linearly with the increase of the incident light intensity.

3.1.3 The amplifiers

The photodiode output is a current that has to be converted to a voltage to allow is digital conversion; the typical solution is provided by the transimpedance amplifiers (or current to voltage converters) that have the standard configuration shown above.

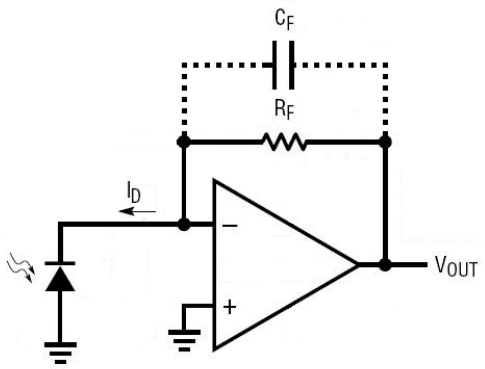


Fig. 7: Typical transimpedance amplifier configuration.

Due to the virtual ground the current through the op-amp is kept at a zero. The current flow across the feedback resistor produces an output voltage that is proportional to the incident light intensity expressed as follows:

$$V_0 = I_D . R_f \qquad (3.7)$$

On the transimpedance amplifier the gain is equal to the feedback resistor (R_f), the gain adjustment is quite important on oximetry applications because the transmittance over the tissues (finger, ear lobe) never exceeds 5% of the incident light

intensity; so even using super bright LED's the transmitted light intensity remains on low values.

Despite is simplicity this circuit is exposed to some constraints, so the optimized circuit should present:

● A photodiode junction capacitance as low as possible because it affects the noise and bandwidth on the circuit.

● The photodiode active area should be as large as small as possible to reduce increase the noise-to-signal ratio.

● A high feedback resistor value, because it is the dominant noise factor on the circuit. The related noise, the Johnson or thermal noise, is expressed as follows:

$$thermal\ noise = \sqrt{4KTBR} \tag{3.8}$$

On the previous equation K is the Boltzmann's constant, T the absolute temperature, B the noise bandwidth (*Hz*) and R is the feedback resistor (Ω).

● The feedback capacitor on the feedback branch reduces the peaking and improves stability so the capacitor value choice becomes a critical issue. For circuits where the junction capacitance is substantially higher than the feedback capacitor and the photodiodes active area is large the capacitor value ay defined from the follows equation:

$$C_f = \sqrt{\frac{C_I}{2\pi R_f f_c}} \tag{3.9}$$

In the previous expression *fc* is the unity gain frequency of the ampop, C_I is the input capacitance (is the sum of the photodiode junction capacitance with the ampop input capacitance), and R_f is the feedback resistance.

For small capacitance photodiodes junction capacitance the feedback capacitor value is obtained from:

$$C_f = \frac{1}{4\pi R_f f_c}\left(1 + \sqrt{1 + 8\pi R_f C_I f_c}\right) \tag{3.10}$$

It is possible to use larger values for capacitance though this produces a reduction on the signal bandwidth that is expressed by:

$$BW = 1.4 f_p \tag{3.11}$$

With f_p being expressed by:

$$f_p = \sqrt{\frac{f_c}{2\pi R_f (C_I + C_f)}} \tag{3.12}$$

3.2 MICROCONTROLLERS: ORGANIZATION AND FEATURES

3.2.1 Microcontroller definition

A microcontroller may be defined in a simple way as a single-chip computer, in other words this means we have a fully functional computer system within an integrated circuit chip whose features are close to the ones found in our personal computers. These features are the result of a set of logic circuits whose connections and states can be specified and later altered if necessary changing the program in his memory; this modularity based in simple programs makes this an extremely adaptable solution.

3.2.2 Microprocessor system organization

The microcontroller structure includes a CPU (central processing unit),RAM(random access memory),ROM (read only memory), I/O (input-output) lines, serial and parallel ports, timers, and depending on the purpose for which it is meant other built-in-peripherals as A/D (analog to digital) and D/A (digital to analog) converters .These components may be embedded in three main modules:[18]

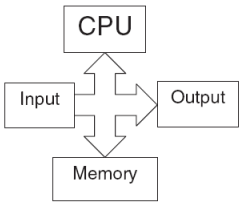


Fig. 8: Block diagram of a basic microcontroller system[19]

- Processor
- Memory
- Input/Output

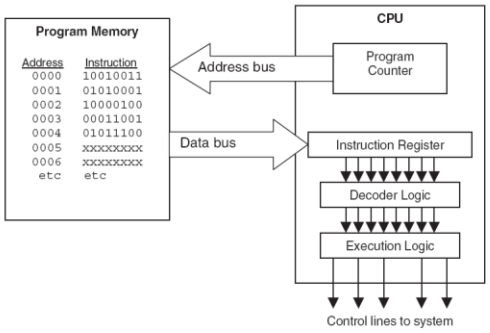


Fig. 9: Program instruction execution [19]

The **processor** (CPU-central processing unit) is responsible for all the input, output, calculations and control; his operation depends on a program, being impossible without it. A program is a list of instructions in binary code that is kept in memory at a numbered location. Each coded instructions are fetched from the memory to the CPU through the data bus; at the CPU they control the operation mode of the control unit.

Each code line is accessed and fetched through an address, corresponds to a specific memory location generated in the program counter, outputted by the data bus. The busses are parallel connections which transfer the address or data information at each operation, being assisted by a set of control lines from the CPU. The code instructions decoding is a hardware operation performed by a block of logic gates.

A CPU is formed by: an Arithmetic Logic Unit (ALU), one or more working registers, a program counter, an instruction register with instruction decoder, a control unit and a stack:

- ALU: performs all arithmetic and Boolean logic operations.
- Work register: small block of memory, as small as a byte, used to temporary data storage during computations.
- Program counter: register who keeps the next instruction to execute address held.
- Instruction register: register that stores the binary data who actually have to be executed at each moment.
- Control unit: controls the necessary time sequence to schedule and execute instructions. While an instruction is running the next instructions is placed in the instructions register after have been fetched from the program memory using the program counter information. The instruction is decoded by the instruction decoder and execute after the previous one end.
- Stack: memory area used to monitor the program counter content when a subroutine is called. Subroutine is a program block that codes an operation repeatedly needed by the main program to avoid the successive inclusion of that block of code at the main program where operation is requested.

Memory may be volatile or non-volatile: at volatile memory the data is lost when power is turned off; the non-volatile retains the memory held when turned off. Memory is an important part of a microcontroller system. According to the type used memory can be classified into two groups: program memory and data memory. The data memory stores the written program and is usually non-volatile; the data memory stores the data used in a program and is usually volatile.

To access the memory is necessary to move two numbers types: the required memory locations address and the data it actually stores. These are connected on two

sets of interconnections: the address bus and the data bus. The way how memory is organized depends on this structures use, the simpler way is the Von Neumann architecture where both buses are single and shared by the data and program memory and also the input/output. At the Harvard architecture where every memory area gets is self address and data bus.

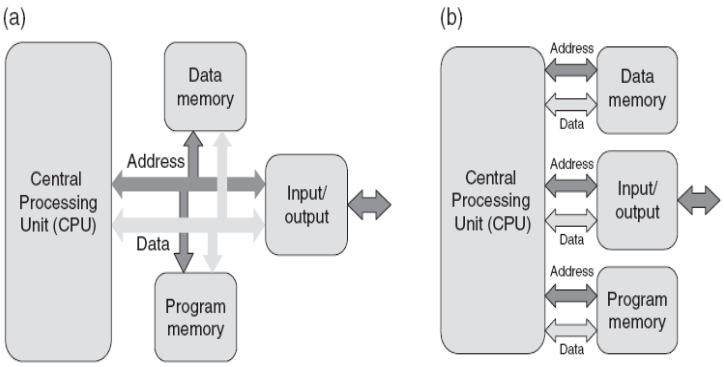


Fig. 10: Memory access organization. (a)The Von Neumann architecture. (b) The Harvard architecture.[20]

The power of a data processing or control system would be useless without an **Input and Output** system to get information and data in and out. Ports perform that operations and are based on a data register controlled by a set of control registers, allowing the data flow in stable and controlled way; the way how it processes depends on the protocol (method of communication).

Ports types are divided in: parallel and serial. The parallel port usually has a data transference rate of 8 bits at a time, while in the serial port it is of 1 bit a time on a single line. The parallel port is potentially faster, but needs more pins, beside that their software drivers is simpler because in the serial port data must be organized in groups of bits.

The ports have to separate internal data bus from the external hardware and temporarily store the data; the data may then be transferred to memory or processed depending on the CPU determinations.

The serial ports may be synchronous or asynchronous. In synchronous mode data transmission is continue, contrarily , in asynchronous mode, data transmission is shifted so it is necessary add stop and start bits to provide the bytes separation at the receiving end, an error check bit is also available to detect corrupt data. In both modes the data must be sent and received at the same speed, so the clock rate has to be equal at the sending and receiving port.[19][20][21]

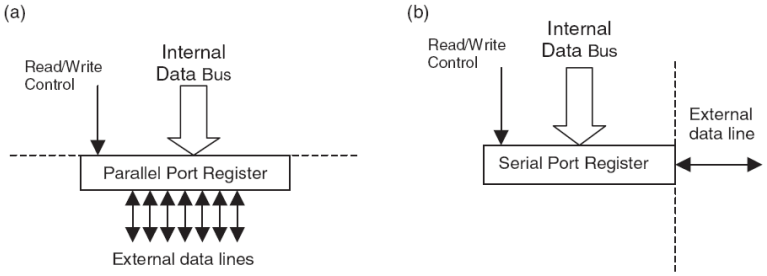


Fig. 11: Parallel and serial data ports: (a) parallel; (b) serial.[19]

3.2.3 Microcontrollers general features

From the large amount of available microcontrollers, with different architectures and capabilities it is possible to define these devices general hardware features:

3.2.3.1 Supply voltage

Usually microcontrollers are operated with a logic voltage of 5V; however some microcontrollers may operate with lower and higher voltages.[25]

3.2.3.2 The clock

It is an indispensable component to any microcontroller; the clock (or oscillator) basically generates a control signal when a crystal and two small capacitors are connected (most accurate), or using resonators or a resistor capacitor pair. The clock may be internal or external. On a PIC an instruction cycle takes four clock cycles; from fetching to execute the instruction.[25]

3.2.3.3 Timers

A timer is basically a counter that uses the clock (or oscillator) signal as a reference

Timers are important parts of any microcontroller. The data flow on the timer may be controlled (started/stopped) by program. This ability allows the program to perform accurate time controlled operations. The timers are of 8 and 16 bits and are found in different amounts in microcontrollers.[25]

3.2.3.4 Watchdog

This components is basically a critical control timer that is refreshed while a program is running, if the program fail, watchdog is not refreshed, is generated a reset.

This mechanism allows the detection of system problems such as endless loops, preventing the execution of unwanted code. [25]

3.2.3.5 Reset input

This input reset the microcontroller, this means it returns to a known state that allows the program execution to start on the 0 (zero) address of the program memory.[25]

3.2.3.6 Interrupts

An interrupt allows the microcontroller to quickly react to an internal or external event, when an interrupt happens the microcontroller moves the program execution to a special part of the program, the Interrupt Service Routine (ISR) .The code inside ISR is executed(starts on a fixed memory address) and them the program returns to is normal flow. In PIC Interrupts may interrupt other interrupts, depending on the priority level of each one; and each interrupt has is vector address.[25]

3.2.3.7 Brown-out detector

The Brown-out detector resets the microcontroller is the supply voltage decrease below a determined value preventing unwanted system problems. [25]

3.2.3.8 Analogue-to-digital converter (A/D) and digital-to-analog converters (D/A)

An A/D is used to convert an analogical signal to a digital form usable by the microprocessor, the D/A do the opposite task. The typical A/D range goes from 8 to 10 bits (from 256 to 1024 quantization levels). A conversion process is usually controlled by an interrupt.[25]

3.2.3.9 Serial I/O

The serial communication (or RS232) allows a microcontroller to connect to other microcontroller or to a PC, the serial communication is usually implement with a built-in-hardware,named USART (Universal Synchronous–Asynchronous Receiver–Transmitter) with the baud rate being controlled by the program.

Some microcontrollers incorporate SPI (Serial Peripheral Interface) or I2C (Integrated Inter Connect) hardware bus interfaces enabling the communication with other devices. [25]

3.2.3.10 Analogue comparator

Analogue comparators are used to compare two analogue voltages [25]

3.2.3.11 Real-time clock

Real-time clock provides continuously date and time information. [25]

3.2.3.12 Sleep mode

This mode stops the internal oscillator and reduces dramatically the power consumption when the microcontroller is not performing any operation; the device wakes with a reset or watchdog time-out.[25]

3.2.3.13 Low power operation

This operation mode is important to save energy allowing the equipment to operate with less than 2 mA with 5 V supply.[25]

3.2.3.14 Current sink/source capability

This feature is important when external devices are connected to a microcontroller because it provides enough current to drive for example small lamps and LEDs. The current may be increased connecting resistor to the ports.[25]

3.2.4 Serial Communication

In a regular microcontroller the communication is performed by synchronous (ex: SPI or I_2C) and asynchronous (ex: UART) interfaces, that differ on the way how information transmission is timed.

3.2.4.1 Synchronous Serial Interfaces

The synchronous communication requires a physical line to carry the clock signal necessary to synchronize the two linked devices; the one that receives the signal is the slave and the other the master.

The I^2C interfaces require two connections between the two linked devices, one for the clock (SCL) and other bidirectional for the data transmission (SDA).

On the SPI interface the data line is separated in two, one for the input (SDI) and one for the output (SDO), this option requires one extra line but provides simultaneous data transfer in both directions.

A multiple devices connection configuration is possible using a I_2C interface and demands a 10bit address (that indentifies the device) to be sent over the data line (SDA) to start the data transference; this procedure slows down the data transference but allows the two connection lines (SCL and SDA) to be used by a maximum of 1000 devices (theoretically).

The SPI , also supports multiple devices communication allowing the multiple connected devices to act as masters , and share the bus; but requires an extra connection line, the slave select (SS), between each device. This means that the number of necessary connections increases in a proportional way to the number of connected devices. The main advantage of the SPI interface is its simplicity and provided speed; much higher than the obtained with the I_2C (one order of magnitude higher).[22]

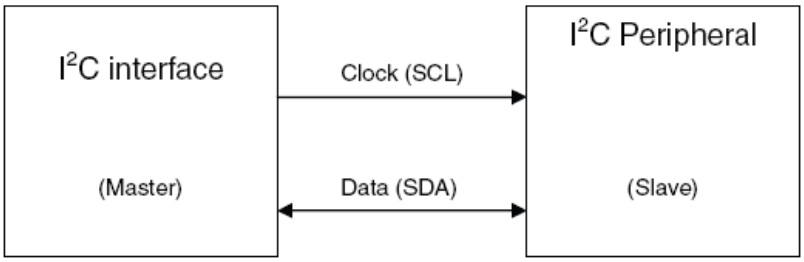


Fig. 12: $_2$ C interface block diagram.[adapted from 22]

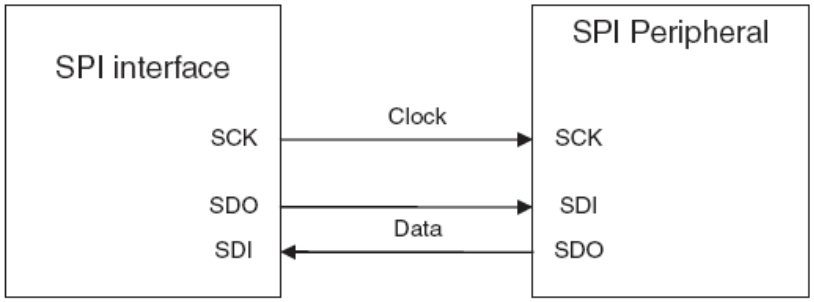


Fig. 13: SPI interface diagram block.[adapeted from 22]

3.2.4.2 Asynchronous Serial Interfaces

In this communication interfaces is not used any clock line; these interfaces usually use two data lines (TX and RX) for input and output and may optionally use more two lines for a hardware handshake. The transference timing is provided by start and stop bits added to the data what enables the synchronization between the transmitter and the receiver; this interfaces demand stable baud rates for reliable transferences.[22]

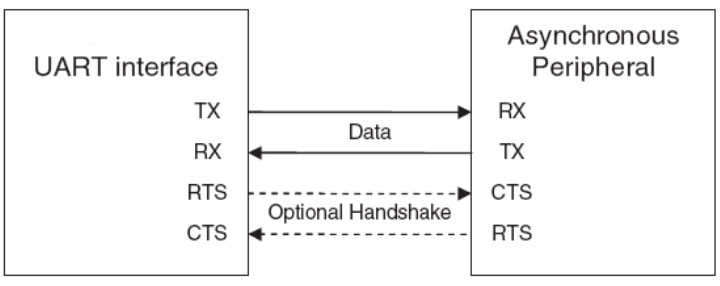


Fig. 14: UART interface diagram block. [adapted from 22]

3.2.5 The Bluetooth protocol

The Bluetooth is a communication protocol that uses unlicensed radio frequencies range (so it is a wireless protocol) presents low power consumption ,short range (from 1 to 100m depending on the power class) and low data transference rates (of 2Mb/s on Bluetooth 2.1 ,may reach the 24Mb/s on new Bluetooth 3.0).

The link between devices is established on the base of a Master/Slave orientation with each master having a maximum number of 7 slaves, this small network is called Piconet. The Master is defined as the first device available for connection in a network and defines the clock rate, jumping sequences access and address for connection, being all the slaves in the Piconet synchronized with the master. Each device may be connected to more than one Piconet and may have at the same time the Slave and Master role depending on the Piconet. A Piconets junction forms a Scatternet.[23]

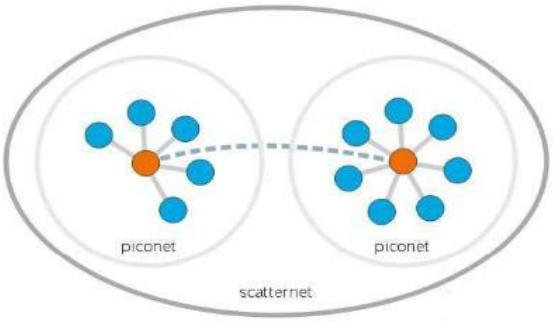


Fig. 15: Scatternet formed by two Piconets (masters in orange, slaves in light blue). [adapted from 24]

3.3 SOFTWARE CONSIDERATIONS

3.3.1 The C language

The *C* language is a compact general-purpose programming language that presents as main features few specific expressions, a modern and reliable data structuring and flow control, and a broad set of operators. In other words when you write a program on *C* language you define precisely what you want the computer to do. The *C* language has not all the powerful features available with the most recent languages and is not specialized to any particular application; however this simplicity and absence of restrictions made it more suitable for many purposes. The *C* language was not meant to run in any specific system or hardware, however is easy to create *C*

programs that ensure compatibility with any machine supporting *C*, increasing the cross platform compatibility.[26]

3.3.2 Creating a program in C language

The process of create a program in *C* language has four fundamental stages:

- ***Editing***

Process of create and modify the *C* source code (*.c) that contains the set of program instructions produced by the user. The editing process is eased by the specific editing solutions provided with some compiler; this solution provides several tools to assist the program management. These solutions are usually provided as complete environments to manage, develop and test the produced *C* programs and are usually called Integrated Development Environments (IDE).

- ***Compiling***

Compile is to convert the source code (source file,*.c) into machine language with a control routine that detects and reports errors during the process.

- ***Linking***

Link is combine the different modules produced by the compiler (object file,*.obj) from the source code, this process adds the required code modules present on the program libraries supplied as part of the *C* language; after collect and gather all the necessary module the linker welds everything into an executable whole (executable file,*.exe). As the compiler the linker also has a routine that detects and reports error during the process, for example if a requested library component is unavailable.

- ***Executing***

Execute is to run the program after all the previous stages get successfully completed. However this stage may also produce several errors, for example as the wrong output or system crash.[27]

3.3.3 Structuring a C Program

The *C* programs follow a rigid structure with different modules that allow a simplified and organized programming process. On the structure of a *C* program each module is responsible to hold specific information. A *C* program structure is organized as follows above.

- ***Pre-processor Directives***

The pre-processor directives are the commands that invoke the *C* pre-processor. The pre-processor is an independent program called by the compiler when a compiling process starts. This procedure allows the directives to be considered during the compiling process.

The most frequent directives are: #define that replaces a text for a specific identifier, and #include that the content of another file into the program, it's usually used to include libraries.

- ***Declaration***

The declarations perform the task of define the name and type of variables and functions in a C program. The nature of the variable or function is defined by many attributes as the basic type and the size, or declaring specific features as pointers or arrays. For example:

- Basic type: char, int, float and double.
- Size: short, long.
- Pointer declaration: using the * type declarator.

- ***Definition***

Define is the process of assign a contents to a declared variable or function. The assigned content depends on the declaration type. During the defining process is established the allocated storage size for the given variable or function.

- ***Expression***

Expressions are the main element of a *C* program, and are basically pieces of code that combine operators and operands to obtain the desirable value.

- ***Statements***

The statements control the flow of a program during the execution. These statements are reserved *C* words with a specific syntax associated. This feature requires the statements Knowledge to achieve the programming objectives.[28]

4. OXIMETERS CERTIFICATION AND MARKET ANALYSIS

4.1 OXIMETERS CERTIFICATION

All medical devices (except the ones custom made or the ones made for clinical investigation) have to be approved to use the mark *CE* for be sold on the European market, if the objective it to trade the device on the American market it has to obtain the license FDA (510K) emitted by the Food and Drugs Administration, an American governmental agency. The approved products must place the corresponding marks on a readable and viewable way. The approval processes for this marks is regulated by specific legislation, with a well defined steps. The regulatory legislation follows attached.

4.1.1 CE marking

The authorization to use the *CE* mark on a product is synonymous of the fulfillment by that product of the requirements imposed by the provisions contained in the European legislation, this marking process results from the European Directives to ensure the quality of the traded products. The pulse oximeters are governed by the Medical Devices Directive 2007/47/EC.

The products that get approval under the European legislation beside the *CE* mark also present a four digits code that identifies the organization that conducted the evaluation process requested by the manufacture intending to get the product granted. The requested organization is responsible for verify the fulfillment of the related Directives by the device, and in case of approval emit the correspondent authorization to allow the use of the *CE* marking on the approved device.

The licensing procedure at Portugal is conducted by the INFARMED that is the authority responsible for the implementation and verification of the Medical Devices Directive 2007/47/EC.

The certification process requires the elaboration of a dossier with a defined structure and obligatory documents, the dossier delivered to the regulatory authority must contain a signed declaration by the applicant manufacture stating that it has not required an evaluation procedure to any other regulatory organization, and all the requested the technical and scientific documentation accordingly the procedures prescribed by the Directive 93/42/EEC [30][31][32]

4.1.2 FDA (510k)

The FDA (510K) is the required license to introduce a product and medical device in the U.S.A market. This licensing procedure is controlled by the Food and Drug Administration (FDA), an American agency under the United States Department of Health and Human Services (HHS) dependence. Some Class 1 and Class 3, and most Class 2 medical devices need to get the 510k license granted. So the first step is to determine the device classification using the online database available at the FDA site. Focusing on the oximeters they are classified as a Class 2 medical device and are included on the cardiovascular monitoring devices.

To obtain the 510(k) license it is necessary to prove that the product requesting licensing is widely equivalent to another product already licensed to market introduction, this criterion by comparison should ensure that the device under licensing process, is has safe and efficient as the previous products. A device meets the minimum requirements to obtain equivalence to the compared product if presents the same technical features or in case or diverging features it after presented for assessment , to the FDA the submitted documentation ensure it is has safe and efficient has a previous marketed product.

The FDA does not provide a guiding document to ease the conduction of the requirement procedure so the licensing procedure is not as linear as the European equivalent, but the applicant entity must compile a dossier with all the possible technical information about the submitted product. The assessment period to the FDA lead a licensing procedure is of 90 days after the application for license, during this process the FDA may request additional documentation to the applicant entity this outages are not counted for the licensing period term; this means that during this events the licensing procedure time stops, "freezes". In case of approval the applicant entity is notified by the FDA to complete the licensing procedure with the product listing and registration using the FURLS system available at the FDA website. After this final procedure the company and the product are finally registered by the FDA. This procedure depends on some taxes payment. [31]

4.2 ISO 9919:2005

The ISO 9919:2005 is a document that defines the guiding directives for the development processes and procedures of a pulse oximeter device intended for use in humans, this standardization procedure intends to ensure the safety and performance of a pulse oximeter device. These standards also cover the pulse oximeter equipment, including pulse oximeter probes, pulse oximeter monitors and reprocessed probe cable extenders.

The first 11 pages of the ISO 9919:2005 (attachment A) are freely provided as a preview by the International Organization for Standardization (ISO) and fallows attached to this document. Analyzing the ISO 9919:2005 index it is possible to identify the document orientation, it provides a broad set of guidelines to the manufacturing process containing specifications to the device classification, components and their assembling, technical description, calibration procedures, and demands for the accuracy tests.

In Portugal the Instituto Português da Qualidade is responsible for the implementation, control and verification of the ISO provisions.

4.3 MARKET ANALYSIS

Any oximeter currently on the market shall provide the ability to measure oxygen saturation on the arterial blood and the heart rate; in such a competitive market the products must assure the effective answer to different demands, the attempt to answer this demands leads to a dispersion on the offered solutions, with many differentiating factors between products; nevertheless it is possible and suitable to roughly differentiate the products offer from now on in two product families:

- Continuous monitoring of the vital parameters in stake.
- Discrete monitoring of the same parameters.

Establishing the product price in this market is a hard task, however defining two reference products within these families we get:

- For a discrete monitoring equipment usable between the limit values for vital parameter we pretend, compatible with children and adults, light weighted, power sourced with conventional batteries with autonomy for approximately 20h of use, two digits precision for a oxygen saturation range from 70% to 100%, useable under

a relatively broad temperature and humidity conditions range for general purposes, and with an acceptable reliability; for this product it is possible to announce a reference price of 150€.

Fig. 16: Nonin 9570B-EN [43]

- For a continuous monitoring equipment reliable on the possible range of physiologic conditions for the parameters in stake, with 2/3 digits precision, useable in children and adults, power sourced by regular batteries with an equivalent use range of 20h and able to record the data equivalent to that period, useable under a relatively broad temperature and humidity conditions range for general purposes; for this product it is possible to announce a reference price of 350€.

Fig. 17: Nonin 8500 Digital Handheld Pulse Oximeter[43]

For this market analysis were only considered the products available under non specific distribution channels.

Despite this effort to normalize the product offer, in such a competitive and versatile market were all manufactures try to differentiate their products with new and improved features, were each one focus his purposes on factors as the autonomy increase, portability reinforcement , data storage capacity expansion , multiple patients record ability, reliability and precision increase in particular conditions as in newborn use, and finally with the emphasis on the remote monitoring possibility with the implementation of Bluetooth communication for example. The improvement of the previous reference products with any of the previous features would inflate the market value of the product; depending on the improvement the price may double. [33][34]

4.3.1 Pulse oximetry market trends and numbers

Historically pulse oximeters have been bought for intensive care units and operating rooms, although in the last years these products began to move on to new and different hospital areas such as intermediate care step-down units, general floors and

post-anesthesia units. This new trend on the oximetry target market is occurring due to hospitals new policies to reduce costs effectively by moving patients out of the most expensive areas, although this patients distribution rearrangement most patients still need monitoring, what opened a new window of opportunities to oximetry products.

Year	Units	Revenues(million dollars)	Revenue growth rate (%)
1986	17.900	97.5	----
1987	23.000	118.0	21.1
1988	28.000	129.5	9.7
1989	32.700	84.3	34.9
1990	35.000	89.0	5.6
1991	36.000	92.0	3.4
1992	37.000	94.2	2.3
1993	38.000	95.6	1.5
1994	40.000	96.5	1.0
1995	40.000	96.9	0.4
1996	41.700	96.6	0.4

Tab. 1: Pulse oximeter blood gas monitor market (1986-1996).[35]

The reality is that pulse oximetry has become a standard of care in patients monitoring market due to his reliability and contribution to the patient's safety; in fact his solid results claimed the title of fifth vital sign to the oxygen saturation. Nowadays almost every multiparameter patient monitor includes or may link an oximetry module. The rising interest with healthcare of the regular citizen is changing the way how the health treatments and overall health was meant to be on a recent past, the nowadays patient demands to have decision power and wants the health monitoring by his side, this new attitude is taking oximetry products out from hospital and putting them side by side with daily life, simple use products may be found in places such as physician's offices, clinics, wellness/prevention centers, health fairs, employer-based nursing stations, and even the home.

The report titled "Pulse Oximeters: A Global Strategic Business Report" published by Global Industry Analysts states that the oximetry market will exceed the 438 million dollars by 2010 with the USA and Europe representing about 80% of that

value and Asia-Pacific region with the highest expected market growth for 2000/2010 and an expected market income of 6.9 million dollars on standalone devices at the end term.

The report "Pulse Oximetry Monitoring Equipment Market" published by Frost & Sullivan's estimates at 201 million dollars the oximetry market revenue on 2006 for USA market and projects a growth to 310 million dollars by 2013 pushed by the hospital and alternative markets expansion. For Europe the expected market income was of 150 million in 2008 and estimates total revenues of 246 million dollars in 2015 .This report also states that the decreasing price of some oximetry products and the reduction on the equipment substitution rate in hospital due to the high maturity of the coverage level combined with budget limitations may influence negatively the market results. On other hand the non conventional market is growing, with the home market presenting a great boost on the simpler oximetry products demand and the open possibility of improved miniaturized products with telemetry and data storage features may produce interesting profits in this segment. The low cost and ease of use is also opening the market doors to fire rescue and military markets, for example on fire rescue oximetry may prevent carbon monoxide poisoned fireman to keep at critical scenarios by means of a rapid diagnosis.

On the year 2004 one of the principal industry's sensor technologies patent expired and opened a window of opportunities for new rising companies wishing for a market slice. Expert predicted a collapse on the oximetry device pricing due to a competition increase, though things have changed they had not take such a dramatic way and the monitoring equipment and sensors prices have not come down much on last years, this price stability is due to the technological progress toward customers needs and the enough value added to the product. However the emergent low-cost manufactures will continuously maintain the market under pressure, so the price erosion is a real possibility with companies such as the leading Chinese Mindray offering an average product price of 300 dollars against the average price of 400 to 800 dollars of an American brand product; these price policies are guiding Mindray boost on European market. The fight for global market share against low price brands growth may lead to downward the current selling prices, decreasing the expected profitability potential, to stop low cost brands market penetration. The after sales service will certainly be a critical element on the market share evolution.[35][36][37][38][39][40]

4.3.2 Principal market players

Dominant players in the pulse oximeters market include:

- Nellcor Puritan Bennett Inc.,
- GE Healthcare Ltd.,
- ALARIS Medical Systems Inc.,
- Criticare Systems, Inc.,
- CAS Medical Systems Inc.,
- Masimo Corporation,
- Nihon-Kohden Corp,
- Nonin Medical, Inc.,
- Philips Medical Systems,
- Respironics, Inc.,
- Spacelabs Healthcare, Inc.,
- Welch Allyn, Inc.;
- Agilent, Inc. [38]

4.3.3 Future

The demand increase in developing countries and the growth on the prevalence of respiratory diseases, with asthma and chronic obstructive pulmonary disease as the main cause of infant mortality and about 300 millions of asthma carriers and 14.2 millions of chronic obstructive pulmonary disease, shall support market stability.

The best market opportunities will be at the emerging giants China and India were the healthcare investments are on an increasing trend, other densely populated countries such as Indonesia will join the range of opportunities.

It is possible that non conventional markets overlap the traditional markets, the clinic interest and commodity will put wireless developments in focus. [42]

5. PROJECT OVERVIEW

5.1 PROJECT REQUIREMENTS

This project is set to comply by the defined guidelines proposed by the project promoters, the CEI and ISA, and lead to a work development towards a transmittance oximeter prototype. The prototype developments are focus on two complementary modules with different features and objectives; the modules are a finger transmittance oximeter probe and an oximeter interface.

The transmittance probe should be simple, reliable, robust, economic and ensure a correct switching between the red and infrared emitting channels; a process that will be controlled by a simple signal (as a square wave) to allow correct data acquisition and processing. It must also ensure a correct signal acquisition for the both emitting spectra, producing a pre-amplified signal to the ADC (analogical to digital converter) input.

The switching frequency in the emission spectra (the LED's emission is pulsed) should be much higher than the frequency of the arterial pulse to ensure a good description of the signal evolution. The circuit is powered with a 5V to allow an easy portability because most low cost general battery voltage is within that range.

The oximeter probe must be able to interface with the pulse interface that includes an acquisition and processing module. The acquisition module must provide an acquisition rate high enough to fulfill the sampling theorem, which states that the acquisition rate should be at least twice the frequency of the event we want to detect.[44] The processing module must have a processing and memory capacity that allows the implementation of algorithms used for determining the heart rate and oxygen saturation in the blood and storage of the process data. The implemented algorithm must ensure a pre-processing of the data to reduce the noise, preventing erroneous results. The portability requirements also demand that the module may be powered by a regular commercial battery, and ensures minimum power consumption to extend the device's autonomy.

5.2 WORK EVOLUTION OVERVIEW

This project went through some goal and planning changes, due to different issues and constraints that forced some rearrangements on the intended strategy and methodology,

and lead to a delay on the project‘s goal persecution. The project’s evolution will be overviewed bellow.

The initial step of this project was the market analysis, to collect information about the project’s viability in terms of commercial interest, and the identification of a guideline on the oximetry devices’ features to provide us with the ability to define our project’s features. The market was briefly characterized and it was decided that our prototype should be a standalone device able to measure, in a discrete way, a heart rate and produce a peripheral oxygen saturation value (S_pO_2). At the same time, information about the process of market certification of the oximetry devices was gathered, and so, we identified the requirements and main steps to achieve commercial authorization to trade a device on the European and American market, in other words was studied the authorization procedure to use the CE and FDA (510K) marks.

After defining the prototype features, were collected some usual information that in a later analysis proved to be useful providing us with the necessary knowledge about the oximetry technical background. All these procedures were conducted nearly until the end of October.

After this step, the development of a transmittance oximetry probe that was assembled over an available and referenced CEI’s SMD circuit was initialized. This circuit’s elements were dimensioned using the literature-suggested solutions, and, after the assembling, the first data acquisition was conducted, using a NI-DAQ 6009 board as an acquisition interface. The data viewing and critical analysis was conducted using the NI provided software, LabView. The circuit definition went through some difficulties and the SMD circuit proved to be not flexible enough for a testing and development process, so, despite the first encouraging results, the final results never achieved the pretended goals, and so, this development platform was abandoned and replaced by a bread board (parallel to this process, some competences in C language were developed and the data collection and analysis of the oximetry background was kept). This development platform was left on late January and by that time the project’s tasks were rearranged and Sergio Bras became responsible for the interface device development and algorithm definition and implementation. Based on the available material and it being the newer member of the large PIC microcontroller’s family, it was decided to adopt the PIC32 as our interface device core component.

This solution began to be analyzed with the study of this platform's features and properties, collecting the necessary information to be able to get familiarized with a completely new reality; due to the lack of knowledge and experience in this field, the learning process was a bit slower. This platform approach was made using the PIC32 starter kit, available on CEI. This is a good choice to get started in programming microcontrollers', although it is not interactive enough and does not own the necessary features to develop the interface. It was necessary to get an I/O expansion board, provided as a complementary starter kit device; this board would provide the necessary tools to attach prototype circuits or monitor signals with logic probes, precisely what we needed to develop our independent processing and acquisition platform; however, despite the intention of buying a board to pursue the objectives, and even after requesting budgets, the board was not acquired and the standalone device objective was bypassed in late March.

This change on the project orientation happened due to the recognition, by ISA, of our project's interest to their vital signal's acquisition project. From these interests' alliance a new project orientation was born, with ISA providing us their hardware and firmware solutions (the Leonardo® board synchronized with the Bioplux® acquisition module), and us becoming responsible for developing a functional transmittance oximetry probe and a reliable algorithm to identify the heart rate and the peripheral oxygen saturation (S_pO_2). From this new orientation the algorithms implemented by ISA began to be analyzed so that it could be rearrange later to process other vital signals, the firmware was also overviewed for when becomes necessary implement our detection algorithm on their platform. Nevertheless after the initial periodic with reciprocal information exchange with the ISA providing us a Leonardo® board, the corresponding firmware, brief technical information about the platform and help with the information understanding was not possible to get the necessary Bioplux® module.

On late May from these constraints become impossible to move to a real time acquisition with an independent platform and the acquisition platform remained the NI-DAQ 6009 board, due to the limitations in use the MPLAB IDE to analyze the external data from the NI-DAQ 6009 board was decided to move to a more flexible solution to keep developing the detection algorithms. The chosen solution was to use a general purpose C language IDE to implement, test and validate the results, because the developed code would be compatible with the hardware firmware (are both written in C language) with just the necessary adaptations to the hardware processing and memory

limitations. The elected C IDE was the NetbBeans IDE 6.7 because it is a free, intuitive software adapted to low end user. The algorithm development process produces some encouraging results with the continuous acquired signal for both emitting spectra.

5.2.1 The first probe prototype

The first probe circuit was assembled using mainly SMD (the circuit may be found at the attachment B) components, and was basically formed by: a red and an infrared LED, two polarization resistors, a transimpedance amplifier, a photodiode, a feedback resistor, a feedback capacitor and two resistors to the voltage divider. Was included a Darlington transistor on the circuit to prevent possible damages from current peaks crossing the circuit due to any abnormal event.

The sizing of the components, and their features selection took in account the probes architecture considerations exposed on the chapter 4.1, to maximize the required bandwidth and signal-to noise ratio.

The chosen LEDs had emission spectra with a wavelength (λ) of 635 nm for the red LED and a wavelength of (λ) 940 nm for the infrared LED; these values are in line with the constraints from the oxyhemoglobin and reduced hemoglobin specific extinction coefficients curves. To maximize the value of the transmitted light intensity across the finger tissues were used super bright LED's, to maximize this issue were also conducted tests to define the polarization resistors values to which the LED light emission has a higher value. This way the determined value was of 100Ω. The coupling capacitor is not a much significant component, so was suggested the reasonable value of 10nF that proved to be suitable for the application. The transmitted light across the finger tissues was detected using a photodiode on the photoconductive mode; the amplification and conversion (from current to voltage) of the photodiode output was performed by a transimpedance amplifier. Though this is the standard configuration implemented in pulse oximetry applications, the transimpedance configuration is exposed to some constraints so it is necessary to take in account the methodologies and considerations presented in chapter 4.1.3 to define the components features and dimensions, from these considerations the defined values for the feedback capacitor was of 33KΩ and for the feedback capacitor 10nF. Therefore important considerations must be taken in account on the components selection. The value for the resistors of the voltage divider was of 1kΩ to ensure that V^+ is 2.5 V.

After finish the assembling of all the components on the circuit it was encapsulated into a black box to protect the circuit and reduce the exposure to light pollution. The result is presented on the following images.

Fig.18: The first developed probe encapsulated in a black box.

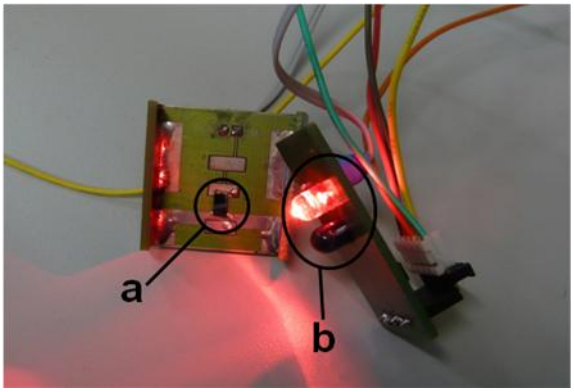
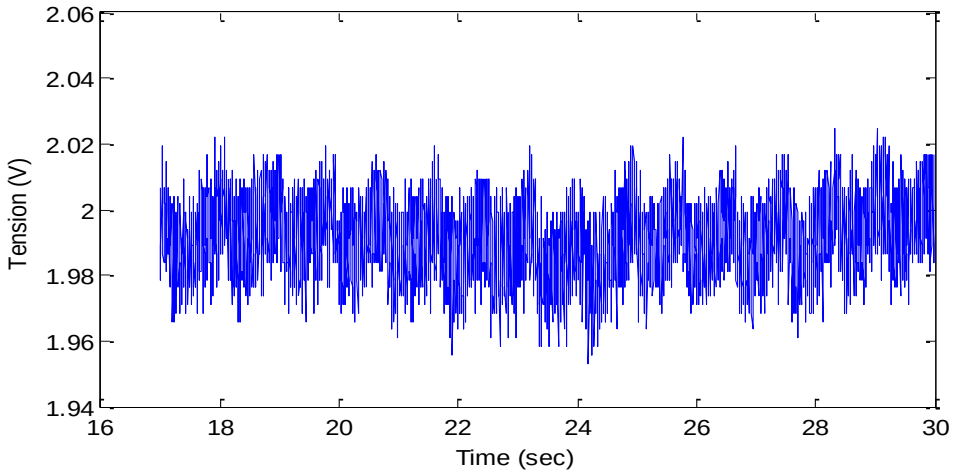


Fig. 19: The first prototype circuit: a) photodiode, b) Led's.

After the assembling procedure was conducted a test period using the NI-DAQ 6009 board as acquisition interface, the transmittance through the finger was obtained for each LED continuously emitting, the obtained data for a sampling rate of 300 Hz was stored in a text file. The selected frequency is much higher than the frequency of the event we want to detect (equivalent to the heart rate) and allows describing the signal evolution.

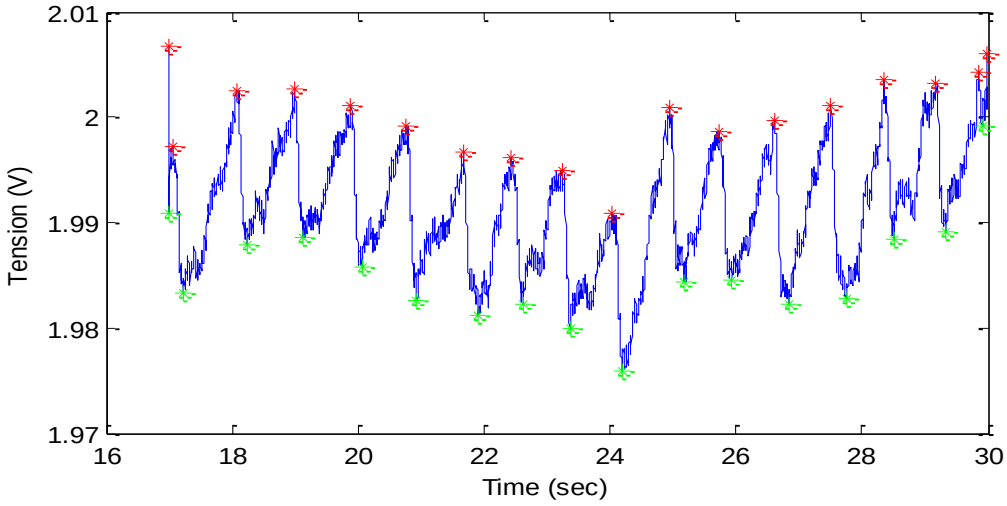
The signal analysis was done using a simple Matlab program develop over a simple algorithm for peak detection already implemented in Matlab and licensed for public use by the author[46]. The Matlab program [45] was able to read the stored data from a text file, apply a smoothing filter to the data to reduce the noise, find the maximums and minimums to determine the heart rate, and plot the results.

Some of the results produced during the test period for the light transmittance through a finger, with the use of each LED operating in a continuous way are presented ahead.



Grap. 6: Graphical representation of the data acquired using the red LED, between the 17 and 30s (before the Matlab processing).

It is notorious the presence of noise on the acquired data, this constraint difficults the determination of the maximums and minimums so was performed a signal smoothing using the developed Matlab program. From this process results a better defined signal where is easier to observe the desired pulsatile pattern and determine the maximums and minimums to find the heart rate. This maximums and minimums determination is performed by the implement Matlab program that marks the maximums with a red dot, and the minimums with a green dot, allowing the heat rate determination from summing the peaks in a time period. The result is presented below.



Grap, 7: Signal after being smoothed with the Matlab. The maximums are marked in red and the minimums in green.

Thwarting our initial hopes after repeatedly tested the probe revealed a lack of repeatability and an abundance of contradictory results becoming clear for all the team that the adopted architecture was not suitable for the project goals. It was necessary to find new solution and the SMD platform did not provide the necessary flexibility to a test new solution, so this platform was abandoned in favor of a more suitable platform for test: the breadboard.

This change in our orientation coincided with the rearrangement of the work division. Sergio Bras become responsible for the development of an interface device for data processing and acquisition, as well as for the development of the necessary algorithms for signal treatment, and pulse rate and oxygen saturation determination.

5.2.2 Overall Architecture of the System

The architecture defined initially was based upon the PIC32 starter kit attached to the I/O expansion board that would ensure the data acquisition and processing; this module would be connected to a transmittance oximetry probe with a time-controlled switching circuit for the LED's emission and a pre-amplifying circuit.

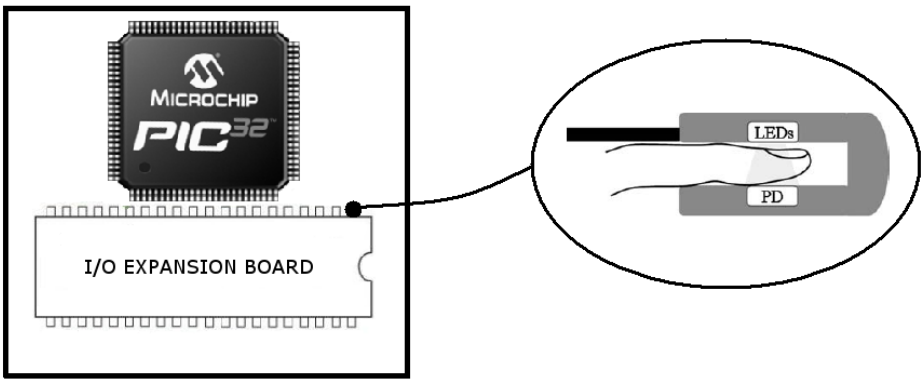


Fig. 20: Initial project architecture.

How already said regarding the new goals proposal the initial aim of a standalone oximeter was bypassed, not overwhelmed, thanks to the knowhow available and used in other similar projects by ISA. So from that moment on our objective became the integration of our previous results and developments on the ISA platform. The ISA platform is formed by the Leonardo® board synchronized with a Bioplux® module (by Bluetooth connection with 100m range), the Bioplux® module has 6 analog channels with 12bits and a maximum sample rate of 1000Hz, and 2 analog channels with 12bits and a maximum sample rate of 125Hz available to connect the

oximetric probe and perform signal digitalization. All the firmware to board initialization (configuration bits for CPU and bus speed (Hz), timers, ISR) and communications protocols (I^2C, SPI, UART, Bluetooth) were already developed and operational.

Fig. 21: The final system architecture: (a) Leonardo® board, (b) Bioplux® module and (c) transmittance oximetry probe.

- ***The Leonardo® module***

This project uses the Leonardo® module main board based on a microcontroller PIC24HJ128GP306 and the Bluetooth module based on a PIC 18F25J10, the communication between the two modules uses the SPI serial communications protocol. The necessary firmware was already implemented.

Parameter Name	Value
Architecture	16 bits
CPU Speed (MIPS)	40
Flash Program Memory (Kb)	128
RAM Memory (Kb)	16
Operating Voltage Range (V)	3 to 3.6
Internal Oscillator	7.37 MHz, 512 kHz
Digital Communication Peripherals	2xUART, 2xSPI, 2xI2C
I/O Pins	53
Analogical Peripherals	1x12 bits
Timers	9 x 16-bit 4 x 32-bit

Tab. 2: The PIC24HJ128GP306 (main board) principal features.

- ***Bioplux® module***

The Bioplux module is a compact and portable device intended for biosignals acquisition on a continuous way. This device uses a short range wireless communication protocol Bluetooth) for send and receive data, being possible to integrate it on a previous system.

This device was projected to acquire a large range of biosignals with different features, from the ones that have high oscillation rates and small amplitudes as the electrocardiogram signals, to signals more rigorous concerning the sampling rate and signal amplification as the temperature signals.

Technical information

- Short range, until 100m, wireless connectivity (Bluetooth protocol)
- 6 analogical channels with a 12 bits resolution and maximum sampling rate of 1000Hz
- 2 analogical channels with a 12 bits resolution and maximum sampling rate of 125 Hz.
- 1 digital port configurable, with may be used as input or output port.
- 12 hours autonomy

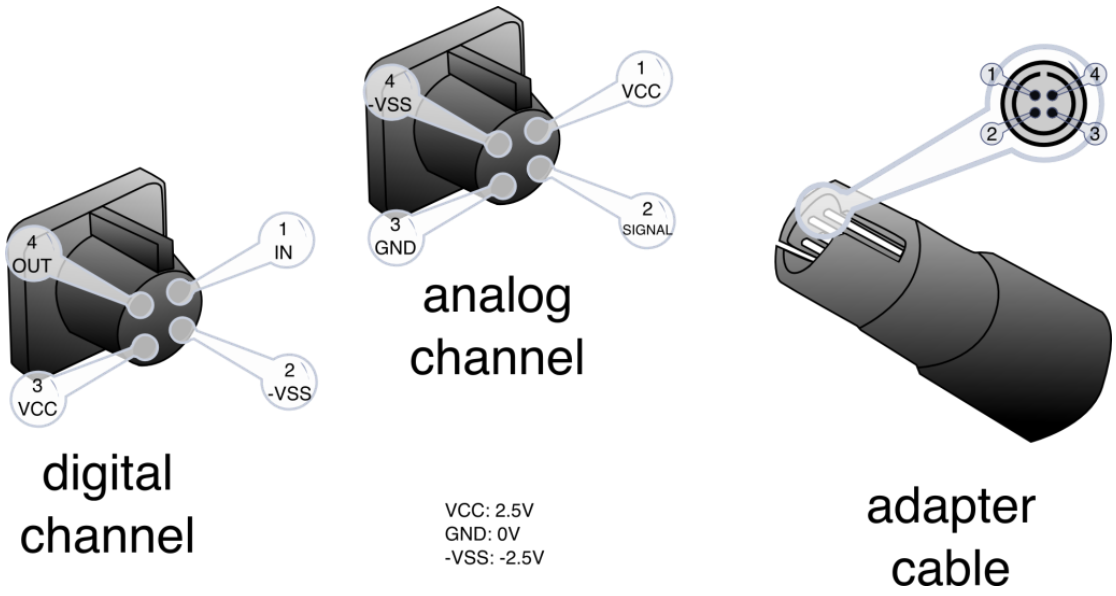


Fig. 22: Pinout of the Bioplux® module connectors.

- ***The transmittance probe***

The probe has a pre-amplifying circuit that amplifies and converts the signal from current to voltage. It presents a pulsatile LED's light emission, with the red LED emission alternating with the infrared LED emission. This switching process is controlled by a timing circuit.

5.2.3Algorithms for signal processing

5.2.3.1 Signal treatment

The signal treatment was carried using simple techniques to reduce the processing requirements, so the treatment was performed using averaging techniques and simple considerations to reduce the noise and the amount of data to process. The use of averaging techniques was possible because the measured variable varies slowly and the present noise is random. Beside that this techniques are suitable to time domain analysis, although it is not the best technique his simplicity worth the drop in the results quality.

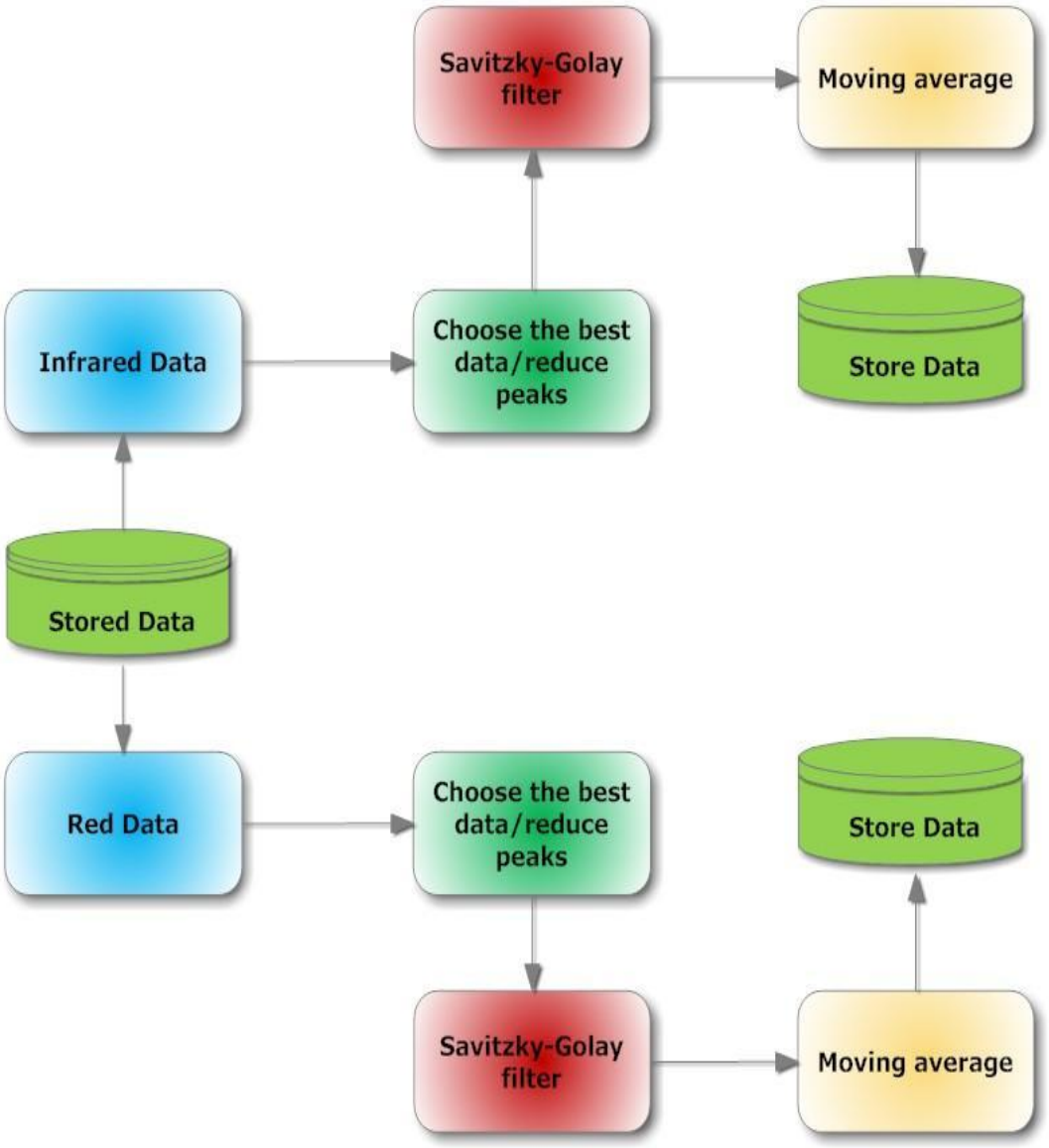


Fig. 23: Signal treatment workflow

The signal was first divided in red and infrared data, that have the same treatment but in independent processes. To fulfill the sampling theorem was used a sampling frequency that is twice the frequency of the event we want to detect, this lead us to have two samples per event; strangely it was frequent one of the samples present a really low value that was too close to the photodiode baseline; this phenomenon was strange because the probe architecture supposedly ensures that there is no time delay between the LED' switching. However the option was to use this event as an opportunity to reduce the amount of data to treat and remove the exposed artifacts, was only selected the highest sample value of each set of two samples, this removed the

artifacts and reduced the amount of data to treat, was conclude that the new samples number was enough to describe the signal evolution as we want. Next the reaming values were compared sequentially, and each time that was verified a big jump between the consecutive values the value correspondent to the peak was withdraw and replaced by the previous sample value.

The next step was use a Savitzky-Golay (attachment C) filter; this is not more than an averaging technique that uses specific coefficients to preserve the higher moments, despite is constraints this technique allows to render visibly the heights and widths of spectral lines in noisy data. The averaging techniques are based on the assumption that considering a reference point the surrounding points measure approximately the same, so a point may considered as a function of the surrounding points; is this case the Savitzky-Golay filter tries to perform this operation approximating the signal evolution to a polynomial.

The use of averaging techniques flattens the signal, however in this case the objective is to calculate a ratio between the two data channels, so applying the same procedure in the two channels will induce the same bias canceling the filter effect and safeguarding the pretended ratio. The use of this filter blocks a recursive calculation procedure raising the processing requirements, so was just used a second order filter with 5 elements. Was also performed a second averaging process in this case using a simple moving average, that is based in the same principles than the previous filter but uses a linear approximation that allows a recursive calculation procedure.

On the end of these steps the signal is free of spikes and retains only small irregularities.

5.2.3.1 The first approach to peak detection

Continuing the first attempts to analyze the signal was conducted an effort to develop a simple algorithm to identify the maximums and minimums on the acquired data, to allow the determination of the heart rate and the ratio of ratios (R_{os}) , which subsequently allows the determination of the oxygen saturation on the blood. The first approach to the problem will be discussed ahead. The corresponding code is in the attachment *D*.

This first adopted algorithm was based in quite simple considerations, starting directly from the maximum and minimum definition, as respectively the highest and lowest value of a variable for a particular time interval. To simplify the algorithm

explication it is considered that the stored data was already treated to reduce the noise. To determine an inflection point and the consequent maximum or minimum situation are required at least three points that in this implementation are named $Reference_x$,

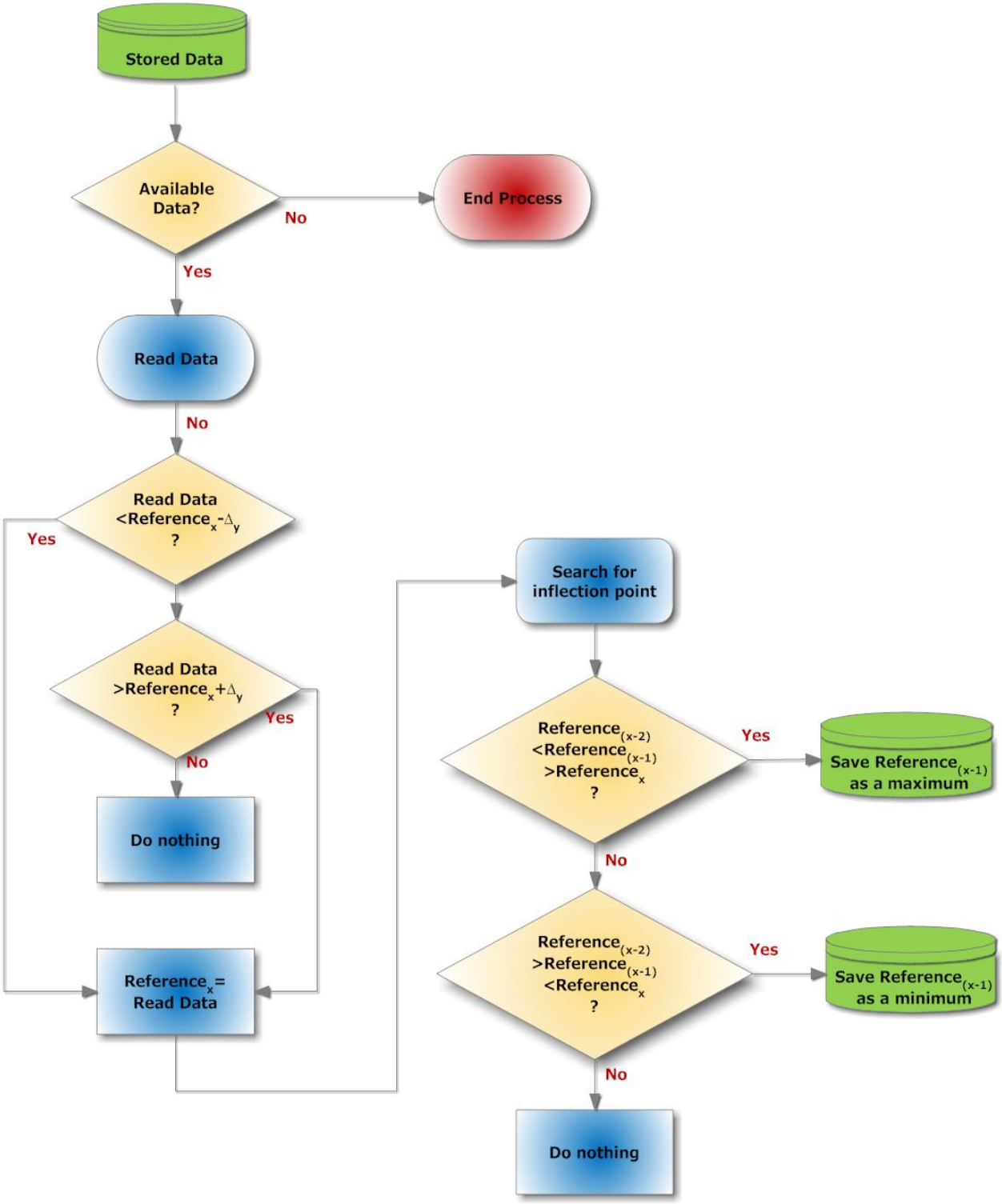
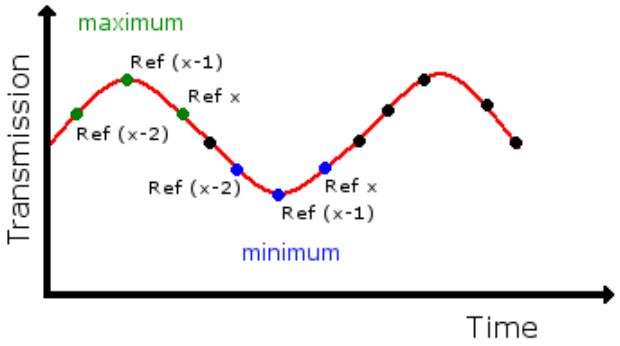


Fig. 24: Workflow of the first implemented algorithm for peak detection.

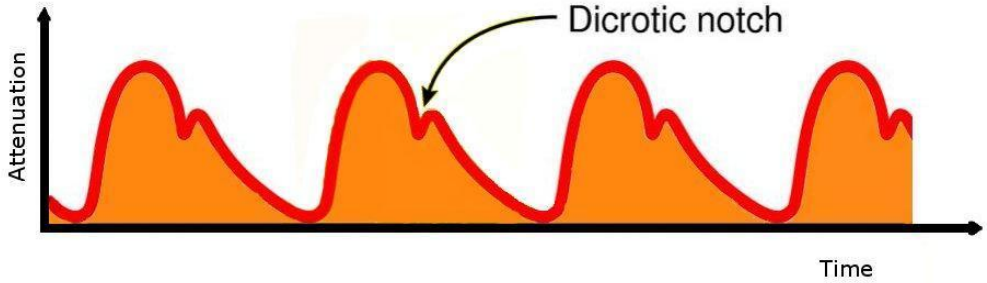
While there is data available to read from the file that holds the acquired data each read value is tested against two simples conditions. If the read value is higher than the last Reference value plus a constant Δ_y the read value is stored in $Reference_x$ place, $Reference_x$ becomes $Reference_{(x-1)}$, and $Reference_{(x-1)}$ becomes $Reference_{(x-2)}$. To the contrary if the read value is lower than the last Reference less a constant Δ_y the read value is stored following the some procedures than the previous condition. If none of the conditions is satisfied the algorithm continues reading data. Each time a new Reference value is added the algorithm verifies if an inflection is fulfilled, in this case is simply verified is the $Reference_{(x-1)}$ value is higher or lower than both the surrounding reference values, to validate the $Reference_{(x-1)}$ respectively as a maximum or a minimum.



Grap. 8: The algorithm detects reference points (the dots on the image), and verifies the inflection condition (maximum in green, minimum in blue).

The Δ_y constant is the principal issue to successfully implement this algorithm and was the reason that lead to abandon this algorithm. The signal obtained in pulse oximetry application is how expected irregular with the presence of many small peaks and valleys along the typical curve, although this irregularities become softened after the signal treatment they are enough to produce many false maximums and minimums detections using a simple comparison between two consecutive points to determine if the curve is rising or falling, and consequently define inflection points. The solution was to introduce the Δ_y factor to stifle this problem. Introducing this factor is created a constant gap between the reference points used to determine an inflection point; this procedure makes the reference points independent from the small signal variation due to a greater spacing between them, and focuses the attention on the general evolution of the signal and not on the small local variations. For achieve this objective is necessary

that the Δ_y overlaps the amplitude of the small variations on the signal, is this weighting procedure that derailed this algorithm due to the difficult to define a universally applicable value for Δ_y without the risk of decrease the peaks and valley detection accuracy. This difficulty in define the Δ_y value comes from the dicrotic notch. The dicrotic notch it is a very common physiological phenomenon produced due to an increase on the arterial pressure after the aortic valve closure; during the systole when the pressure on the aortic artery goes beyond the pressure on the left ventricle the aortic valve closes producing an increase on the arterial pressure due to a decrease on the aortic artery contraction, this pressure increase raises the blood flow producing an increase in the arterial vessels diameter that has a visible effect on the light transmission through the tissues, the result is a secondary peak on the ascending branch of the curve considering the transmitted light signal, or on the descending branch of the curve considering the attenuated light.[6]



Grap. 9: The dicrotic notch on an attenuated light signal[adapted from 42]

The amplitude of the dicrotic notch is not constant from subject to subject and may not even be present; from the conducted tests was also possible see that it is not even constant for the same subject. So to use a Δ_y value covering all the possible dicrotic notch amplitudes values is necessary to use a large value that potential induces a dangerous lack of accuracy; that due to the small variation on the peaks and valleys values is even more important.

Grap. 10: Errors associated to the Δ_y definition, in this case the Ref 2 would be mistakenly considered a maximum.

So how is visible in the previous figure increase the Δ_y is potentially reduce the accuracy due to the decreasing of possible valid reference points per curve that may cut the true peak or valley.

5.2.3.1 the final approach to the peak detection

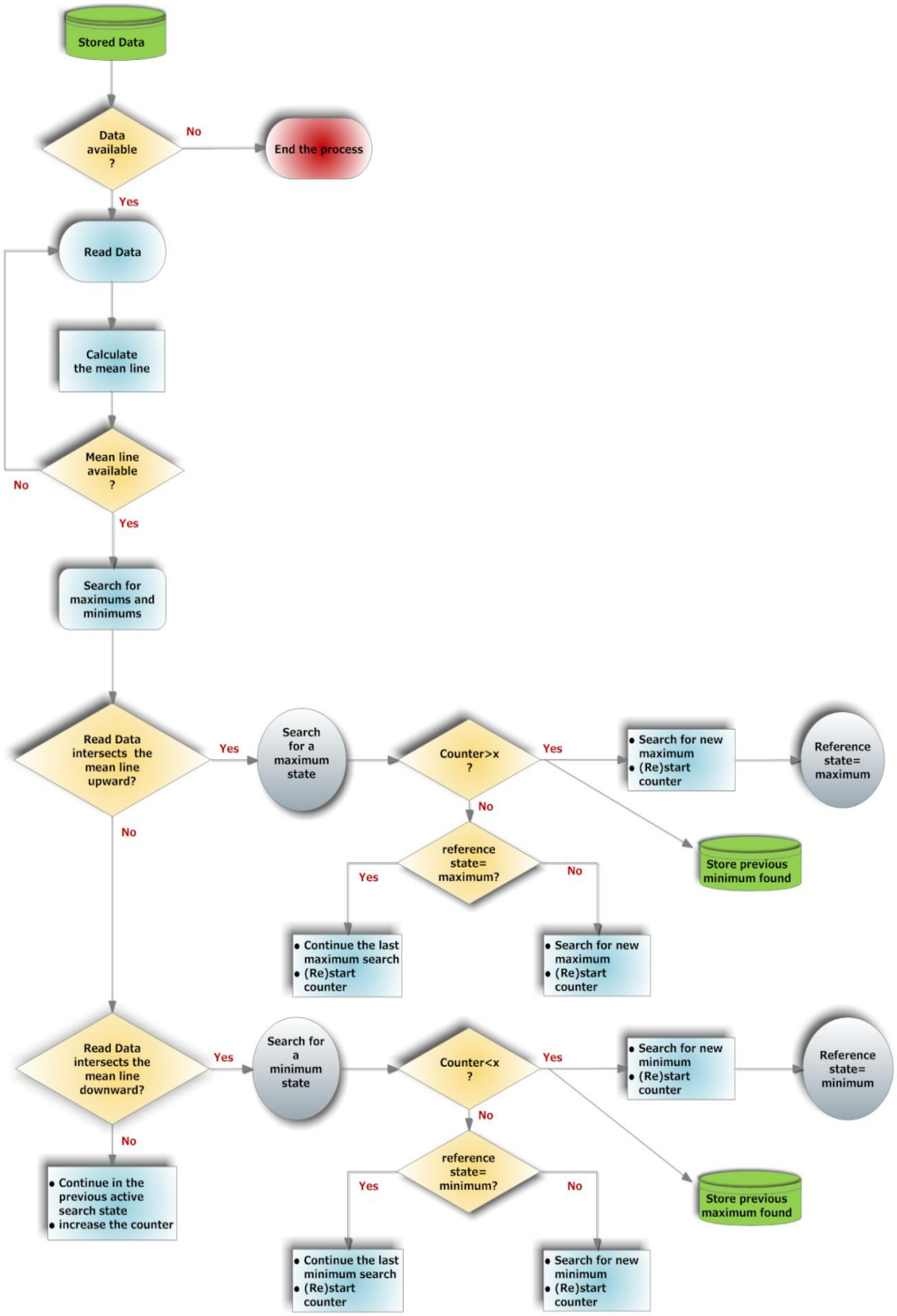
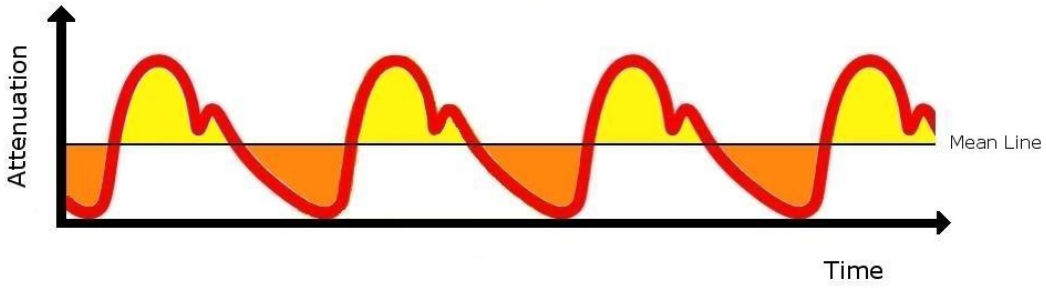


Fig. 25: Workflow overview of the final approach to the peaks and valleys detection.

The final approach is based in three simple considerations: the mean value of an acquired set of data separates the intervals where is possible to find a maximum from the intervals where is possible to find a minimum; the time interval where is possible to find an absolute or local maximum (or minimum) lasts much more than the false intervals for maximum or minimum search produced by irregularities on the signal; and final the validation of an event is done by the opposite event, in other words a maximum is validated when the next minimum is found and a minimum is validated when the next maximum is found. These assumptions were exposed on the previous workflow where the algorithm was briefly exposed. (The respective Code is in the attachment *E*.)

The advantages of this approach to the peaks and valleys detection issue is that the mean line independently of the signals variation will always separate the intervals where is possible to find a maximum from the ones where is possible to find a minimum allowing the use of a simple functions for search for maximums and minimums, this function only compares the consecutives data values and holds the higher or lower value depending on if it is being searched a maximum or a minimum. This approach taking in account the duration of the defined search intervals becomes quite independent from the signal irregularities (after a signal treatment to smooth the noise), reacting very well to the dicrotic notch event. The dicrotic notch is usually placed above the mean line, however even if it crosses the mean line downward the event would have such a brief time duration that the minimum found on the time interval would be discarded and the algorithm would continue searching for a maximum using the value of the previously found local maximum. If on the contrary the dicrotic notch crosses the mean line upward the found maximum would be also discarded and the algorithm would keep searching for a minimum.



Grap. 11: Are visible on the picture the time intervals where is possible do find a minimum (orange intervals), and the time intervals where is possible to find a maximum (yellow intervals)[adapted from 42]

The dicrotic notch as quite variable amplitude however has always a small time duration compared with the entire pulsatile event, allowing the definition of a standard duration to consider an event meaningful or disposal without the risk of loose accuracy. The definition of the search intervals is formalized bellow. Being y (t) the sequence of stored data and N the size of the window used to calculate the mean line, we get:

$$mean\ line(t) = \frac{1}{N}\sum_{t=0}^{N} y(t)$$

An interval where is possible to find a maximum is defined if:

$$[y(t) < mean\ line(t)] \wedge [y(t+1) > mean\ line(t+1)]$$

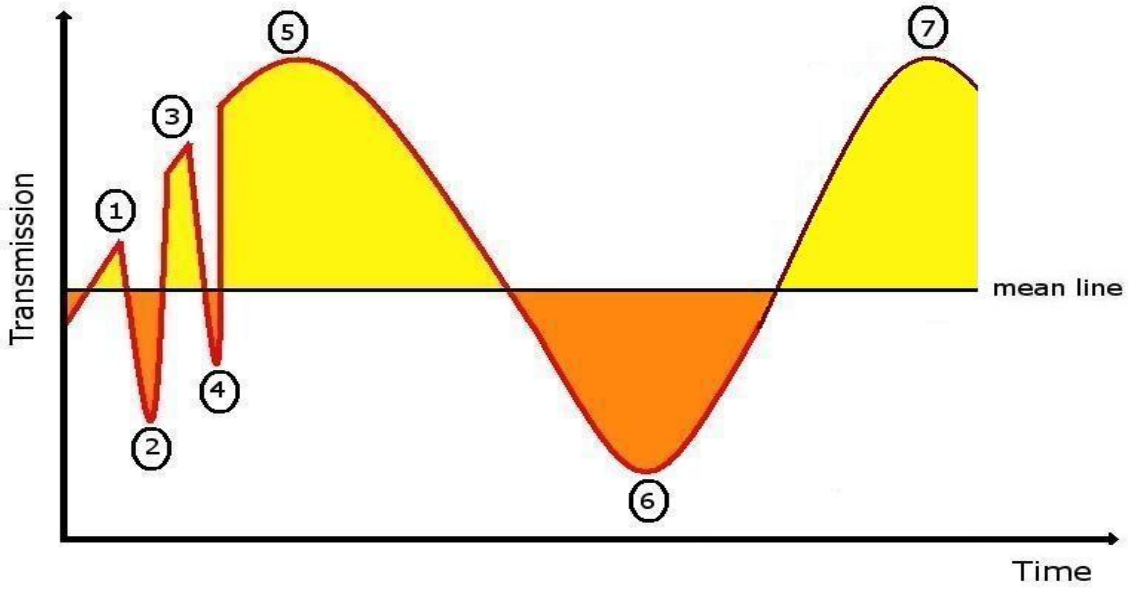
And an interval where is possible to find a minimum is defined if:

$$[y(t) > mean\ line(t)] \wedge [y(t+1) < mean\ line(t+1)]$$

(Note: on the c implementation the mean line was not calculated recursively, it was calculated for small discrete intervals to simplify the processing.)

After define the duration of a valid event (that is verified by the counter on the work flow) that depends on the sampling frequency in use, it is necessary the introduction of a control variable to watch the occurrence of exceptions. An exception will be considered a disposal event. This control process was not considered on the workflow to ensure a better overview of the algorithm.

Each time that two exceptions occur sequentially is generated a critic event that is controlled by the exceptions control variable. The exceptions will be analyzed ahead in the context of the program execution.



Grap. 12: A simulated signal with four consecutive positive exceptions

.

The algorithm iterations for the signal evolution on the previous figure will be presented on the next table considering that the active state on the beginning of the interval 1 is the find minimum state, and that the intervals 1,2,3 e 4 do not last time enough to be considered valid intervals.

The maximums and minimums are stored on separated vectors, each vector with a pointer pointing to the next space where data will be stored (maximum and minimum head). The other aspects will obey to the previous workflow.

Interval	Counter	search State	Reference state	Action	Minimum/ Maximum head	Exceptions Counter
1	>x	Search maximum	Minimum	Search a new Maximum	Stop/Stop	0
2	<x	Search minimum	Minimum	Search a maximum using the previous as reference	Recoils one position/ Stop	1
3	<x	Search maximum	Minimum	Search a new maximum	Stop/Stop	2

4	<x	Search minimum	Minimum	Search a maximum using the previous as reference	Recoils one position/ Stop	1
5	<x	Search maximum	Minimum	Search a new maximum	Stop/Stop	2
6	>x	Search minimum	Maximum	Search a new minimum	Advances one position/ Stop	0
7	>x	Search maximum	Minimum	Search for a new Minimum	Stop/ Advance s one position	0

Tab. 3: The work flow during a critic situation without use the exceptions counter.

From the previous table analysis is possible to observe that each time that at least two exceptions take place consecutively without the introduction of a control variable is produced loss of data. This happens in this case because the minimum found on the interval 6 will overlap a previous minimum, due to the previous decrease on the minimums storage vector. So it is necessary to use a control variable that is a simple exceptions counter; each time that the counter is equal to two it decreases the head increased on the last exceptions preventing loss of data. The exceptions counter is restarted each time it reaches the value two, and every time that a meaningful event is validated.

With all this verification procedures the algorithm has produced good results that will be presented and discussed ahead.

6. RESULTS/DISCUSSION OF RESULTS

6.1 TESTS

To validate the probe and the processing algorithms, a set of tests that tried to simulate different physiologic states were performed. The performed test and their protocols will be exposed ahead.

Due to some constraints, this test was set using only one test subject: a 23 year-old healthy female with a height of 1.70 m, weighing 63 kg, and with no history of cardiac or pulmonary disease.

The signal was acquired using the NI-DAQ 6009, and the results were stored in text files. Given the probe's operation mode, tests using the time control circuit were conducted, to produce a pulsatile light emission switching the LED's emission, as were tests using continuous emission in each light channel. The sampling rate used depended on the operation mode of the probe, so the continuous emission mode was used at a 800 Hz frequency and the pulsatile mode was used at a 1400 Hz to comply with the Nyquist Theorem which states that the sampling rate (f_c) for an analogical signal should be at least twice the maximum frequency of that signal's spectrum (f_w) to ensure the signal reconstruction with minimum information loss. [44]

$$f_c = 2f_w \qquad (6.0)$$

The used sampling rate was 1400 Hz because the signal we wanted to acquire, the pulsatile light emission, had a 700 Hz maximum frequency.

Performed tests' protocols:

Test1: In this test, our subject was kept in a resting situation to ensure that his heart rate and oxygen saturation levels were within the typical values for these situations. Then, the probe was placed around the subject's finger using a Velcro tape; finally the signal was acquired using the probe in different operation modes:

- Test 1A: continuous red light emission.
- Test 1B: continuous infrared light emission.
- Test 1C: pulsatile light emission.

Test2: In this test, our subject was kept on an aerobic physical activity situation (going up and down stairs during 3 minutes) to ensure that his heart rate and oxygen saturation levels were within typical values of the simulated situation. Then, the probe was placed around the subject's finger using a Velcro tape; finally the signal was acquired using the probe in different operation modes:

- Test 2A: continuous red light emission.
- Test 2B: continuous infrared light emission.
- Test 2C: pulsatile light emission.

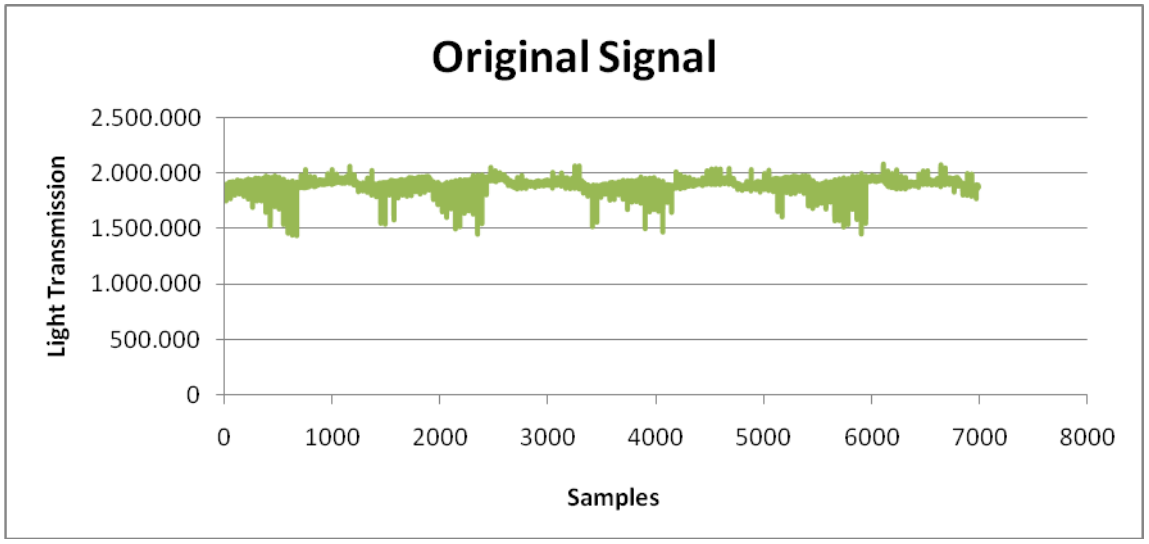
We wanted to perform another test, simulating a hypoxia state; however this clinical scenario is not reliably reproduced by having a subject holding his breath during a pre-evaluated time. As this was the best available mechanism to test this situation, the obvious option was to discard the study of this state.

A reliable hypoxia state requires a clinical environment and can be simulated when the test subject is breathing an air mixture with a controlled amount of oxygen, to reduce the oxygen saturation levels in a controlled way. So, in the future, it is necessary to proceed with this test.

6.2 RESULTS

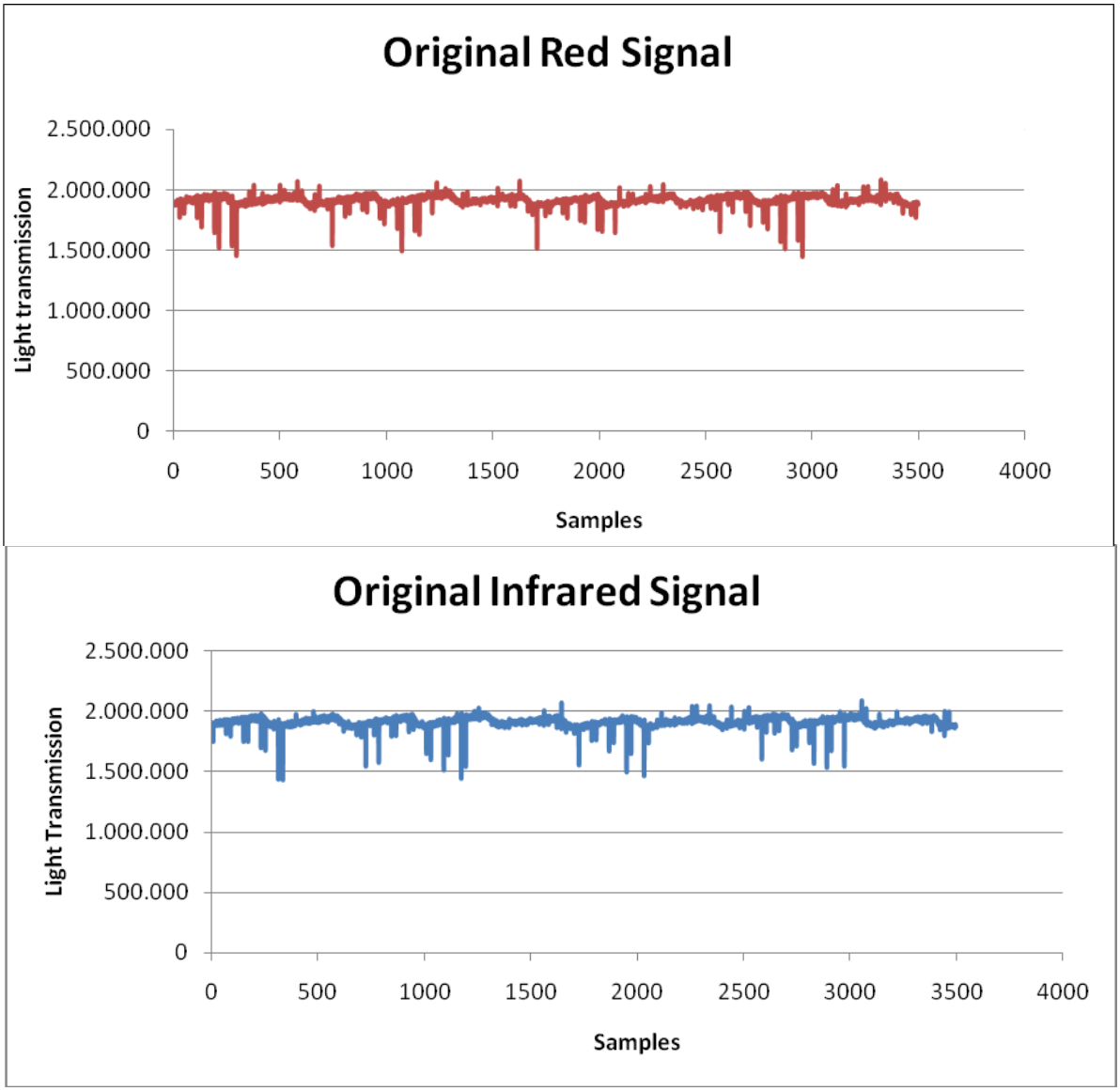
6.2.1 Signal treatment results

To illustrate the results of the applied steps to treat the signal, its evolution during a treatment procedure sample of 5s will now be presented. The selected signal was acquired during the physical activity test using pulsatile emission (test 2C); this choice is justified because of the worst quality of the signal, which presents more irregularities than the signals sampled for the other test.



Grap. 13: The original signal with both emitting channels overlapped, merged on a single graph. (The signal was acquired with a sample rate of 1400 Hz, so 1400 samples represent one second).

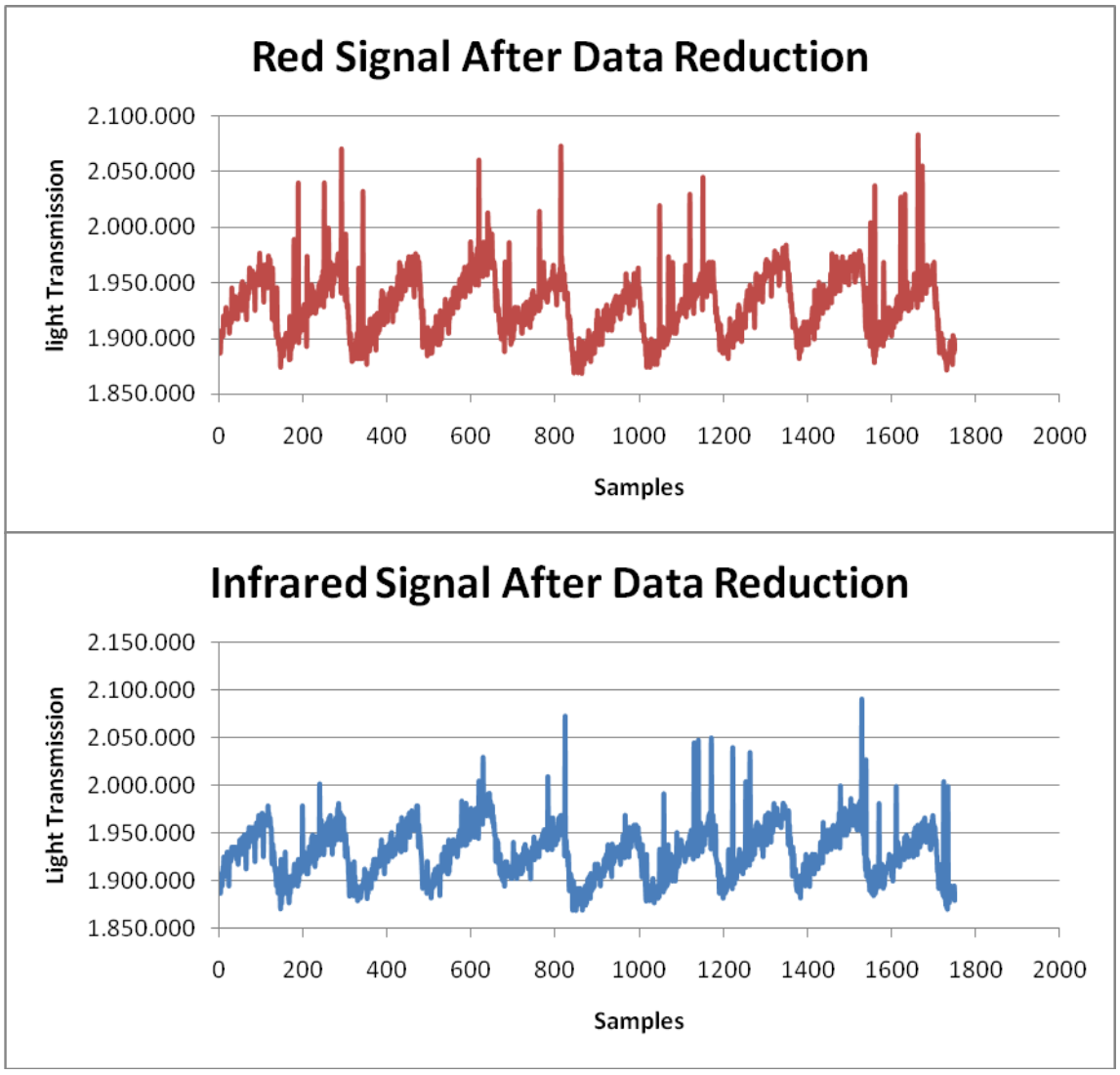
It is not possible to distinguish any periodic pulsatile event with the current graph, so it is obviously necessary to underline the original signals of each channel, separating them into different vectors, in this case different graphs.



Grap. 14: Representation of the separated channels (each 700 samples represent 1s).

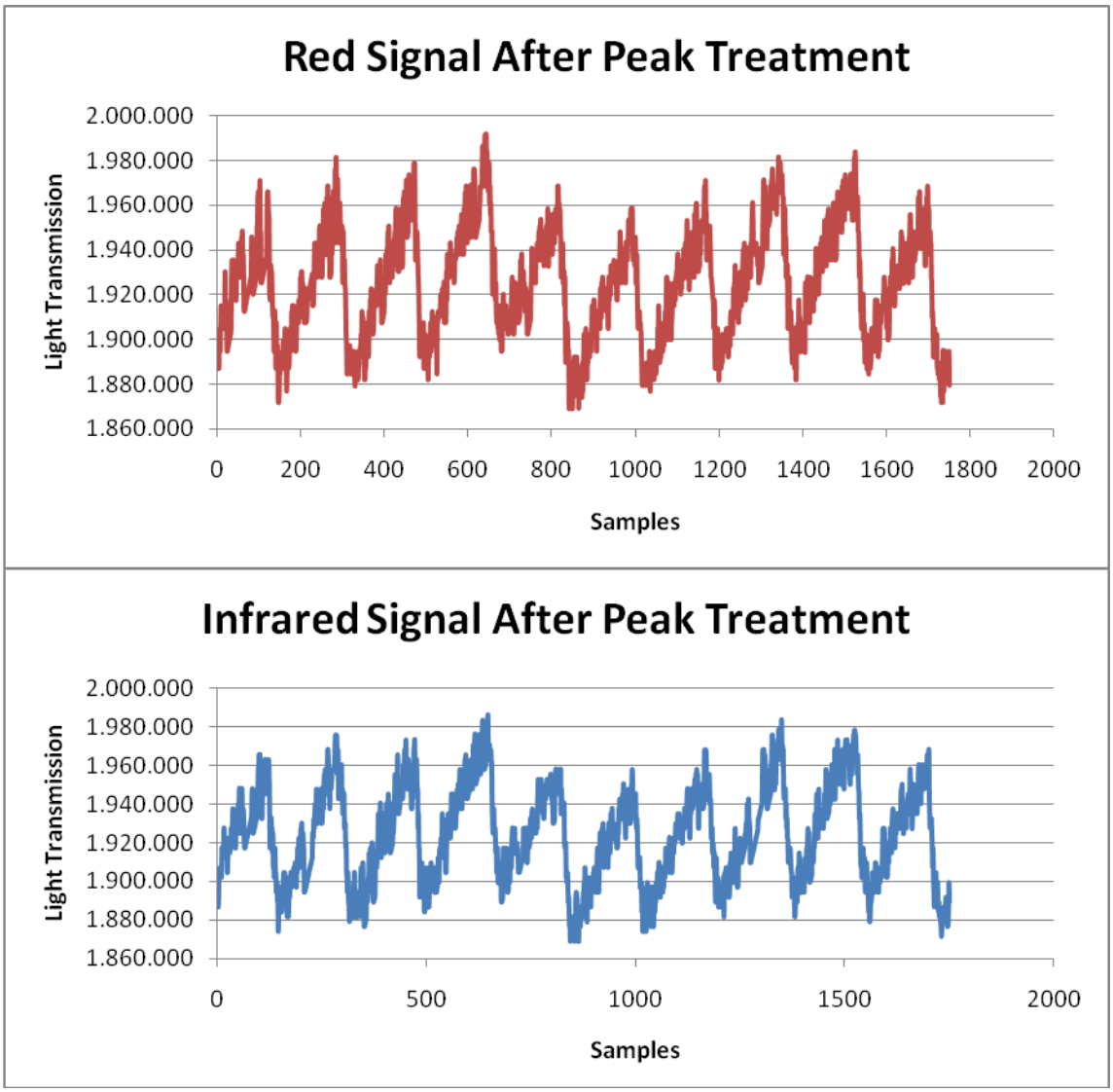
With two separate channels, it is possible to identify the required pulsatile pattern, however, the presence of many spikes and their tendency to down toward the

photodiode baseline is visible. This strange trend is possibly explained by the time response of the photodiode, because theoretically, at least, the probe architecture should ensure that there is always one LED emitting, even if there is any delay during the LED's switching; because of the LED's turning on time period, it would be minimal. So, without the possibility of testing other options, the photodiode time response is the most valid cause for the spikes pattern. Considering just the highest sample of the two acquired samples for each LED emission cycle, it's possible to eliminate these spikes and reduce the amount of data to treat, without compromising the necessary description of time evolution.



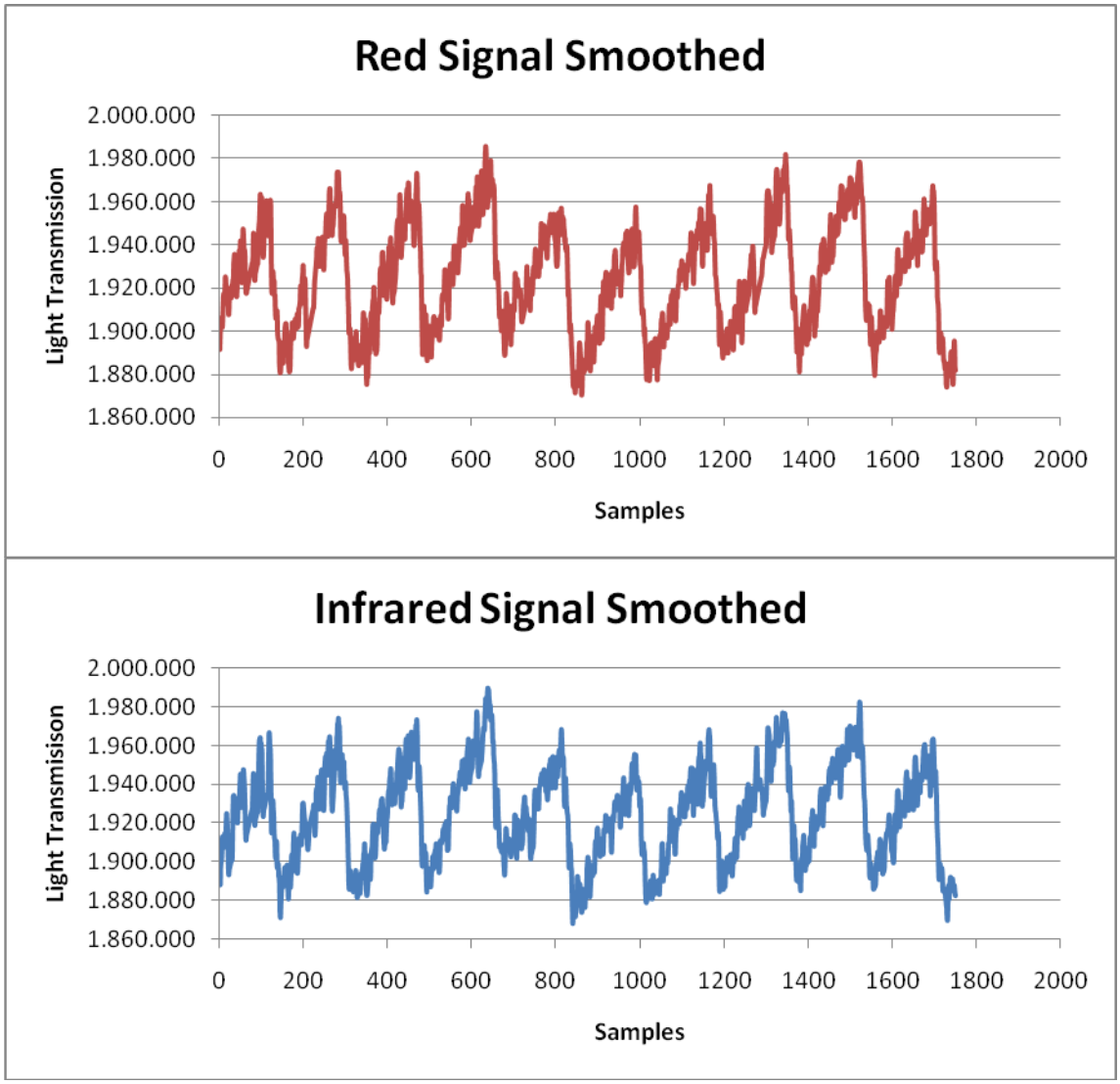
Grap. 15: both channels representation after the downward spikes' elimination using data reduction (each 350 samples represent 1s).

The absence of downward spikes and the conservation of the minimum values after the previous treatment is obvious, however, the persistence of upward spikes requires a peak treatment in order to eliminate them.



Grap. 16: Representation of both channels after the peak treatment (each 350 samples represent 1s).

As we can see, the peak treatment eliminated the upward spikes and maintained the maximums values; however, the signal still presents some irregularities that may be smoothed using a Savitzky-Golay filter and a simple moving average.

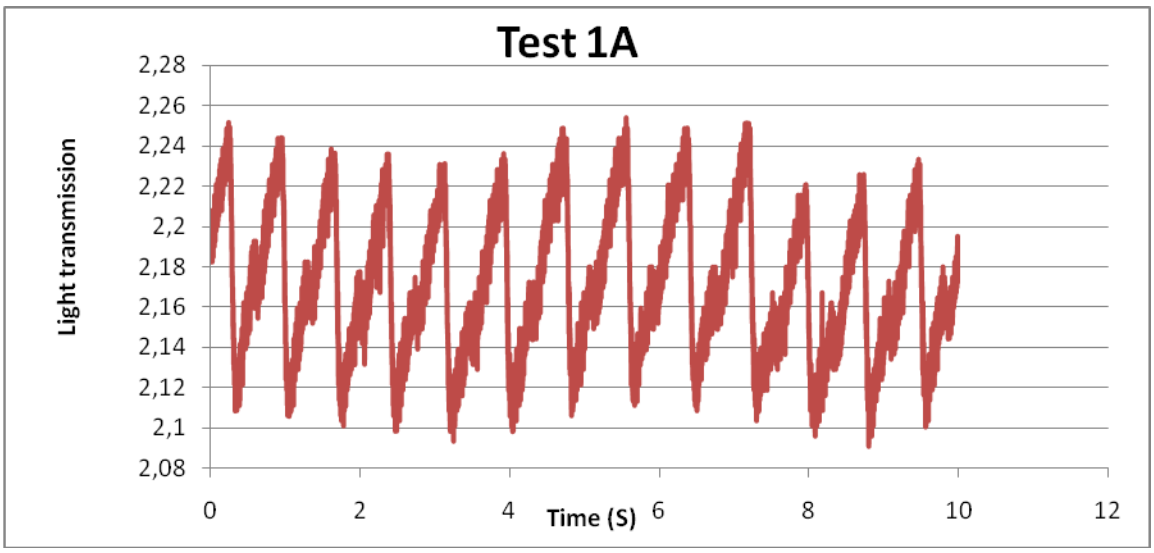


Grap. 17: Representation of both channels after the smoothing treatment (each 350 samples represent 1s).

The smoothing procedure produced an improvement on the signal quality, conserving the signal features. The complete signal treatment procedure allows the use of the peaks and valleys detection algorithm with an improved accuracy.

6.2.2 Signal Processing Results

The implemented algorithm returns the heart rate and ratio each 10s, with a variable initial delay to calculate the mean line value.

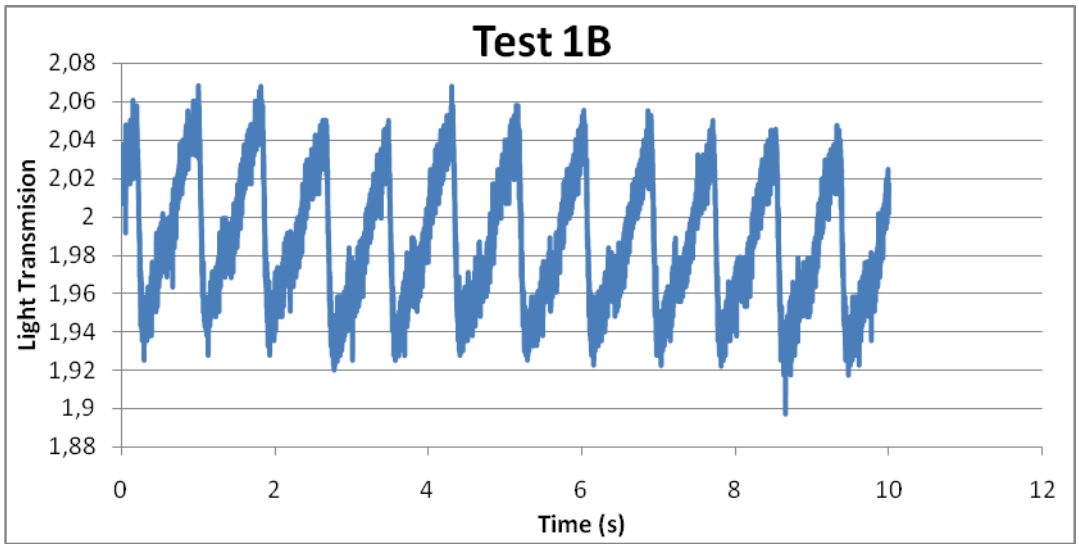


Grap. 18: Representation of the signal acquired with the red LED on, for a resting situation.

Time interval(s)	Partial Ratio(min/max)	Heart Rate (bpm)
[0,10]	0.948851	78
[10,20]	0.958524	78

Tab 4 : Test 1A results.

Analyzing the graph, it's possible to see that the signal represents a regular pulsatile pattern with the calculated heart rate and partial ratio confirming the signal trend.

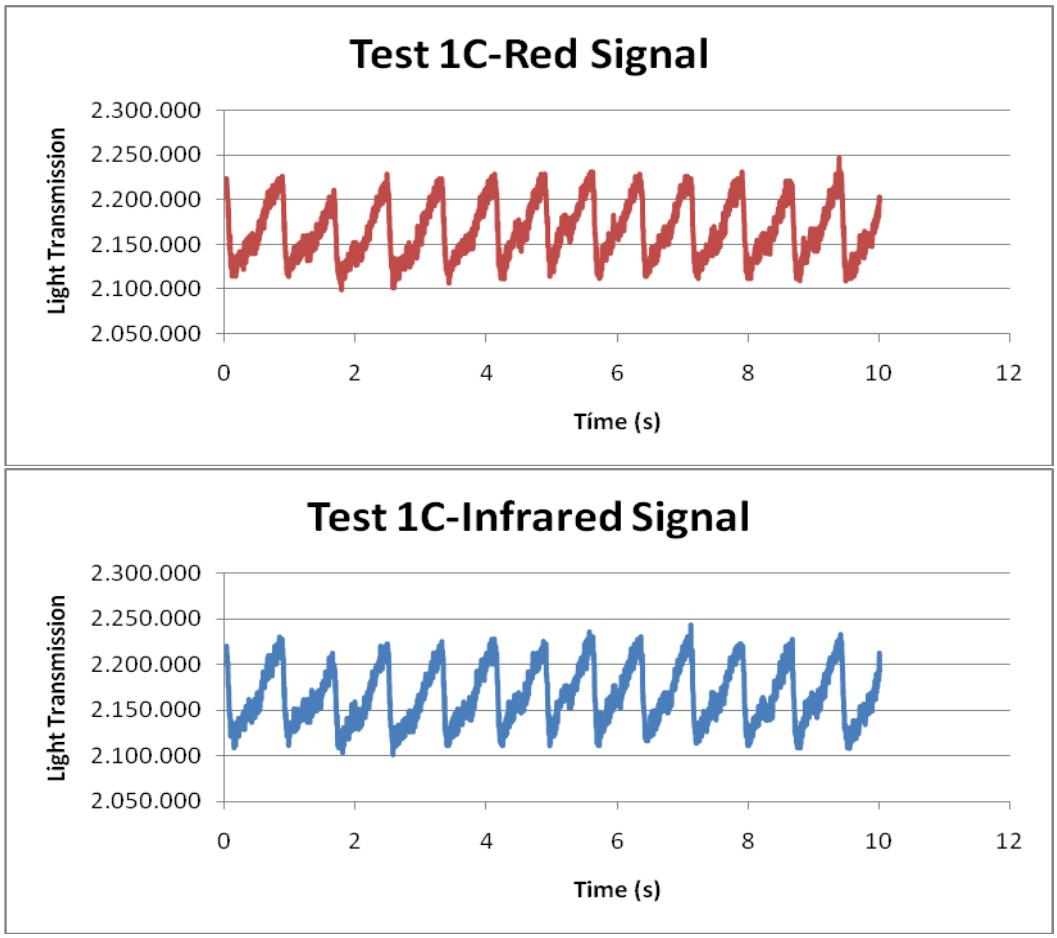


Grap. 19: Representation of the signal acquired with the infrared LED on, for a resting situation.

Time Interval (s)	Partial Ratio (min/max)	Heart Rate (bpm)
[0,10]	0.947009	72

Tab. 5: Test 1B results.

From the graph analysis, it's possible to identify a pulsatile pattern, and verify that the calculated heart rate and partial ratio respect the signal trend.

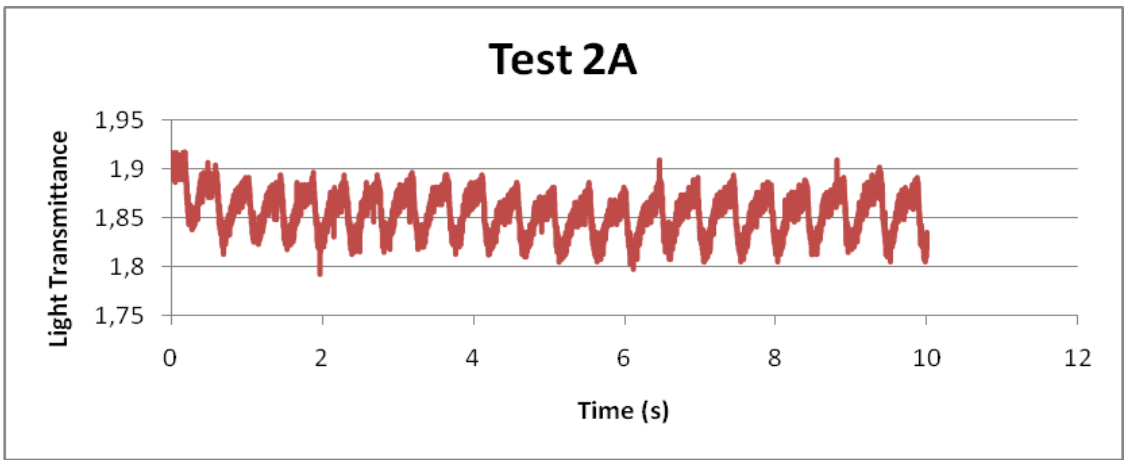


Grap. 20: Representation of the signal for the separated channels; the signal was acquired using pulsatile light emission, obtained from a resting situation.

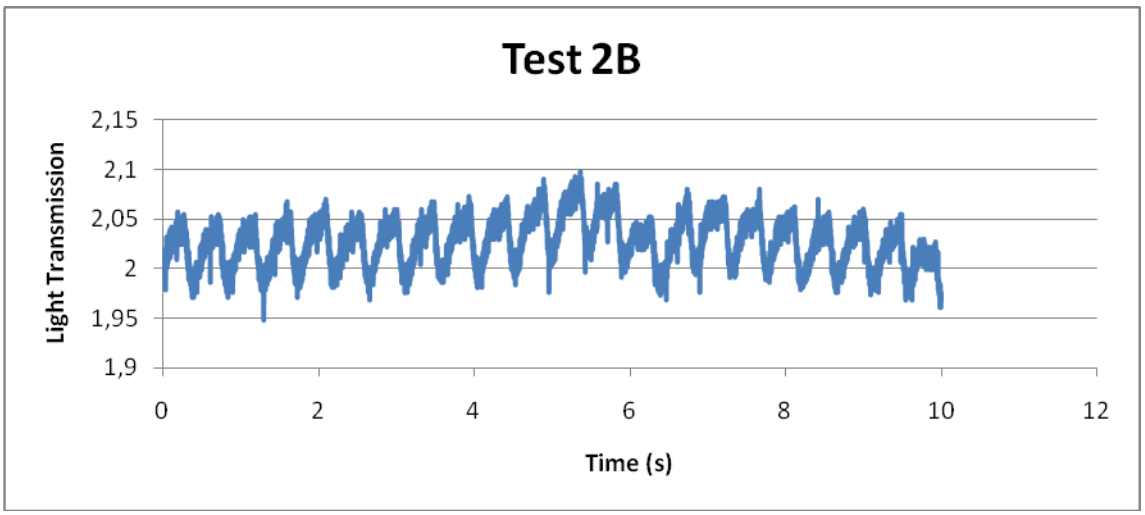
Time Interval(s)	Heart Rate(bpm)	Ratio of Ratios
[0,10]	72	1,02627
[10,20]	78	0,990736
[20,30]	72	0,994225
[30,40]	78	1,005511

Tab .6: Test 1C results.

Analyzing the chart, it's possible to identify a pulsatile pattern and confirm that the calculated heart rate and Ratio of Ratios respect the signal evolution trend. It is also possible to note that the representation in both channels is coherent.



Grap.20: Representation of the signal acquired with a red LED emission for a situation of physical activity

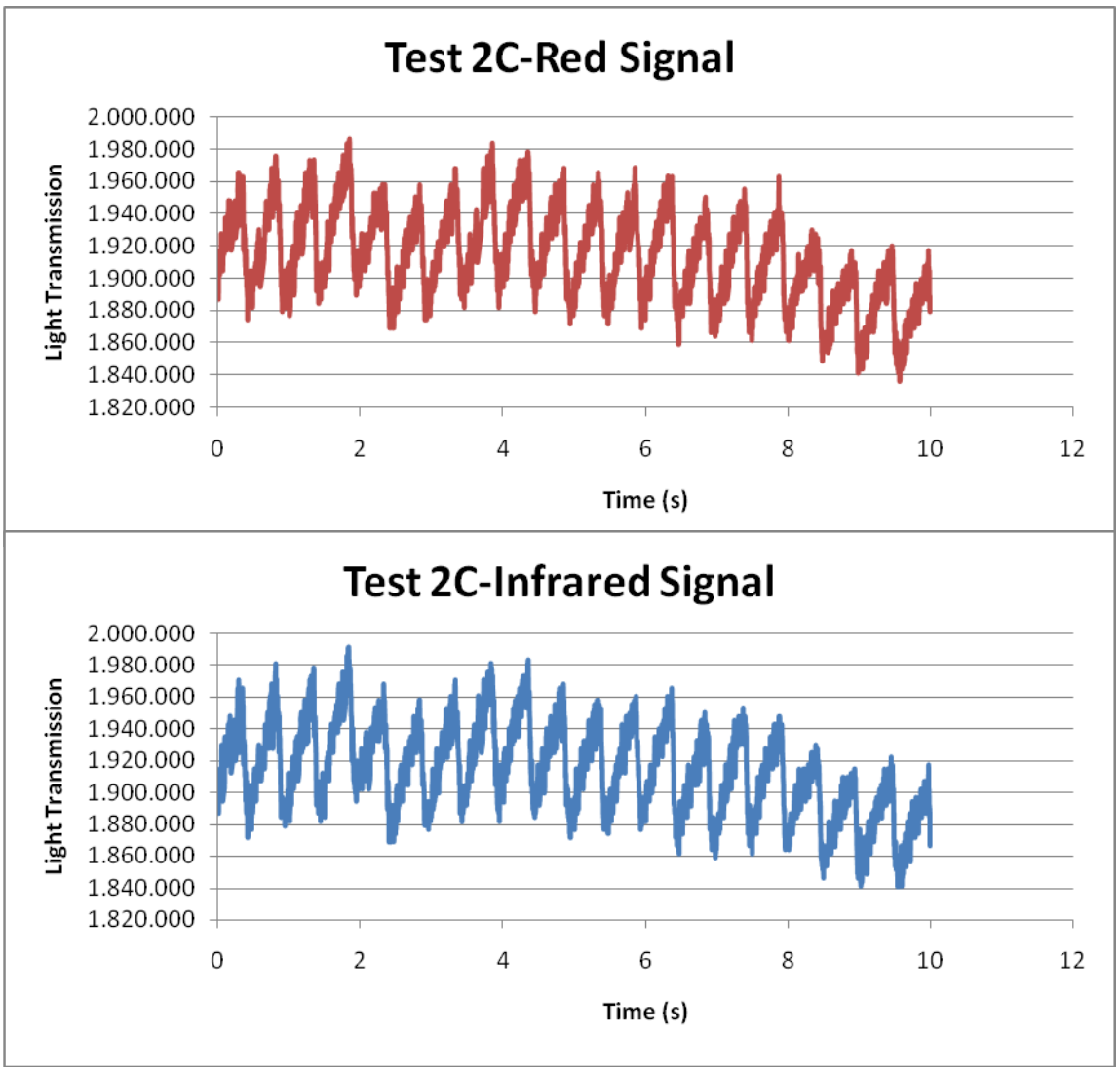


Grap. 22: Representation of the signal acquired with an infrared LED emission for a situation of physical activity.

Time Interval (s)	Partial Ratio (min/max)	Heart Rate (bpm)
[0,10]	0.967682	126
[10,20]	0.964248	126

Tab. 7: Test 2B results.

Analyzing the previous two graphs, the desired pulsatile pattern is visible, and we can verify that the calculated heart rate and partial ratio (if available) fit on the signal evolution trend.



Grap. 23: Representation of the signal for the separated channels; the signal was acquired using pulsatile light emission, obtained from a physical activity situation.

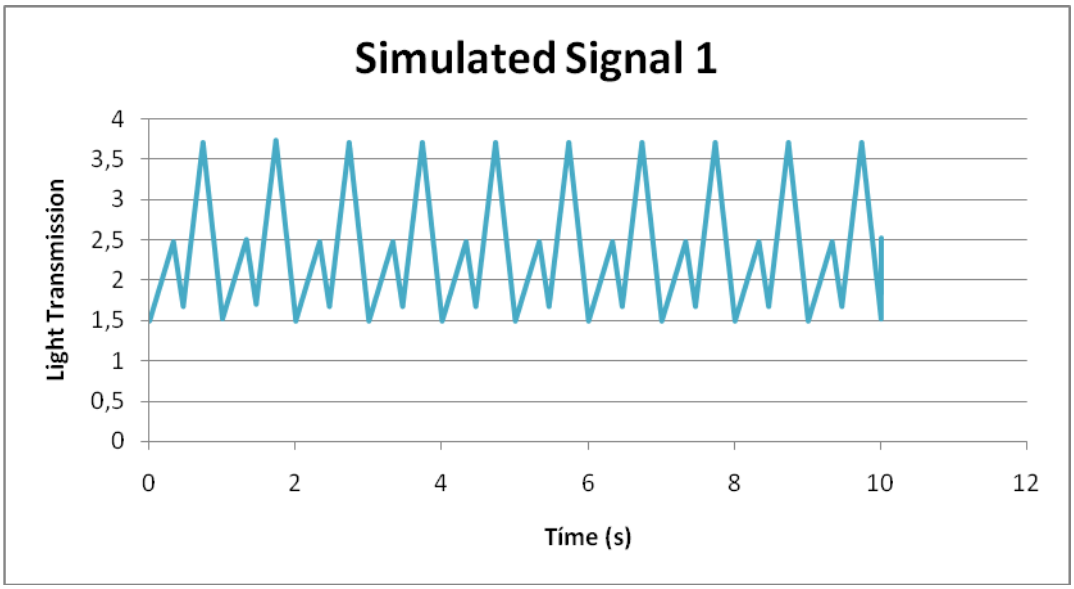
Time Interval(s)	Heart Rate (bpm)	Ratio of Ratios
[0,10]	114	1,005601
[10,20]	114	1,011159
[20,30]	114	0,980245

Tab. 8: Test 2C results.

From the analysis of the previous graph, it's possible to identify a pulsatile pattern and verify that the signal representation in both channels is coherent. It also confirms that the calculated heart rate and ratio of ratio is in accordance with the signal evolution trend.

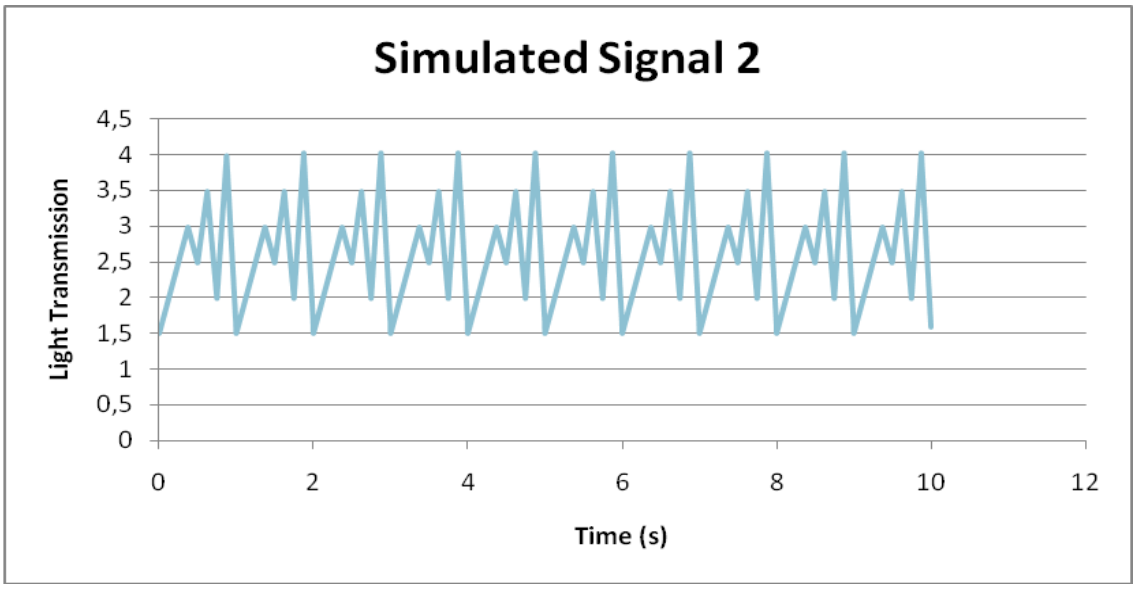
➢ ***Testing the algorithm with a simulated signal***

In order to proceed to the algorithm testing in adverse situations and due to the limited number of tests performed for real data were conducted some more tests using simulated signals. The used signals were intended to simulate critic situation that potentially lead to erroneous results.



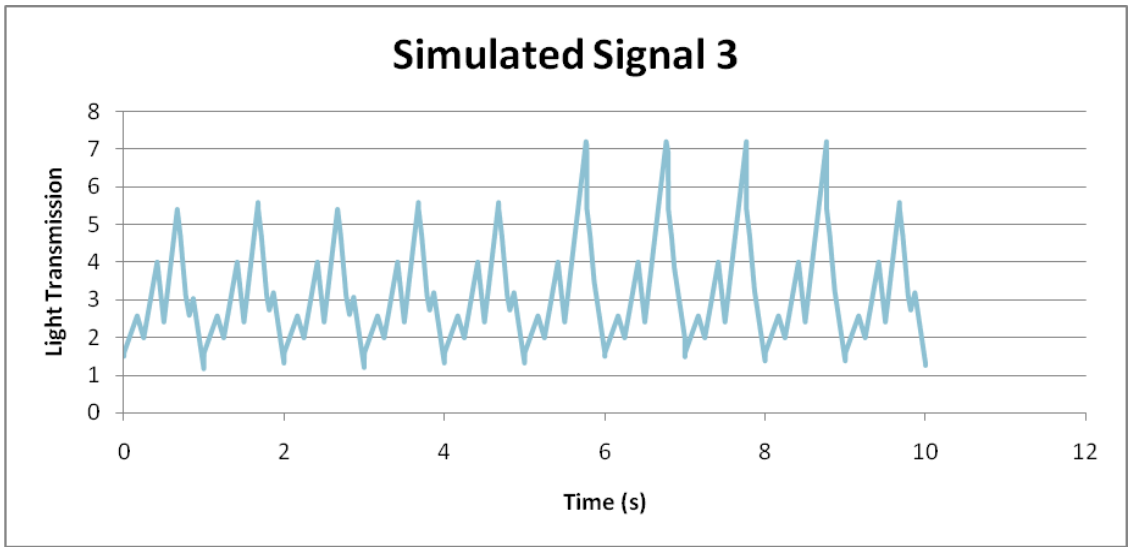
Grap.24: Simulating a signal with extreme dicrotic notches.

The algorithm returned a constant value for the maximums (3.653333) and minimums (1.528958) in this interval as would be expected, the obtained values are according the graphic. The calculated heart rate was 60bpm and also agrees with the expected. So it is correct to say that the algorithm performs wells in a scenario with secondary sharp peaks, this situation was intended to simulated an extreme dicrotic notch and demonstrates the algorithm independence from this event.



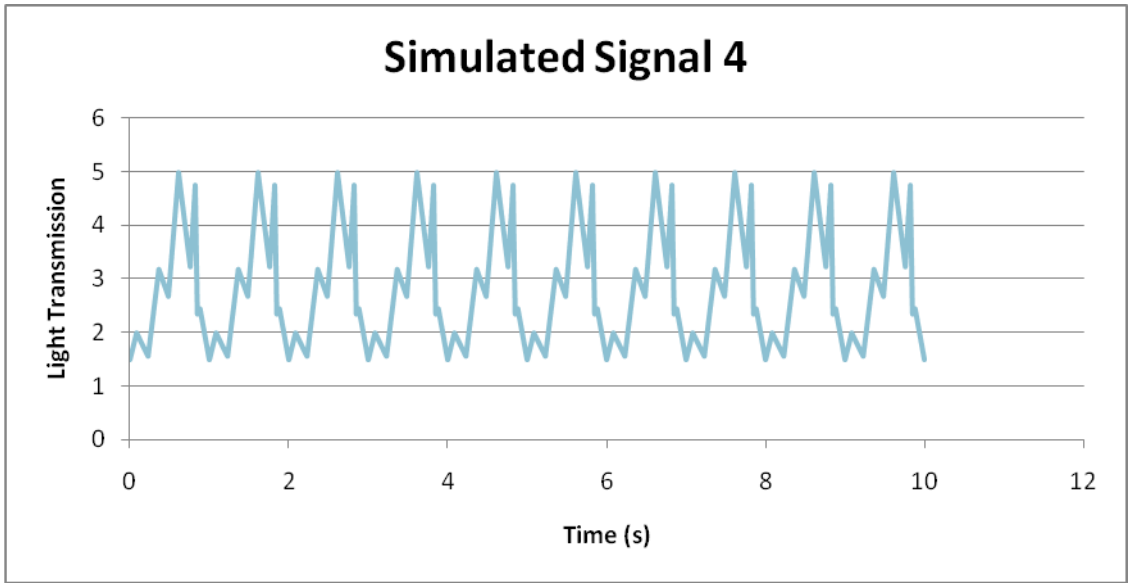
Grap. 25: Simulating a noisy signal with two consecutive exceptions.

The algorithm returned a constant value for the maximums (3.943382) and minimums (1.537534) thus is according the layout of the graphic. The calculated heart rate was 60bpm and also corresponds to the simulated situation. This performance allows to state that the algorithm has a reliable answer to this critic situation, according the previously predicted.



Grap. 26: Simulating a very noisy signal.

The maximums (about 7.1 and .4) and minimums (about 1.4 and 1.6) returned by the algorithm for this noisy situation present a significant accuracy. The returned heart rate value was 54bpm, a value that respects the graphic layout and produces very good indications about the algorithm performance in extreme situations.



Grap. 27: Simulating a regular noisy signal.

For the previous simulated signal the algorithms returned the maximums (4.9435) and minimums (1.517595) values with the necessary accuracy, being possible trace a parallel with the graphic representation. The determined heart rate value was 60bpm, a result that matches perfectly with the expected from the signal graphical representation. These results show the algorithm reliability in noisy scenarios.

6.3 RESULTS DISCUSSION

The results presented in the previous sections allow us to trace the reliability of the developed solutions, in order to process and identify a pulse oximetry signal, stating an appreciable complementarity between the developed probe and the implemented algorithms.

A weighted analysis of the results produced by the implemented algorithms for signal treatment reveals a good performance on the treatment of noisy data and a balanced compromise between efficiency and simplicity, that lead to the ability to

provide data, free of relevant artifacts, as a valid input to the peaks and valleys detection routine, preventing the detection of the, always unwanted, false events.

Concerning the calculation of the heart rate and R_{os} the previous results are encouraging and unveil a comprehensive set of achieved goals with the considerations done to adjust the algorithm being suitable for peak detection, was considered a meaningful event an event with time duration of at least 30 samples.

The tests performed for a resting situation the heart rate returned by the algorithm for the infrared channel signal was 72 bpm and for the red channel signal was 78bpm, these values are valid according the signal evolution and fit in the carried resting scenario, especially considering that the test subject do has a history of regular sport practice.

For the tests carried under a physical activity is visible as expected an increase on the heart rate returned by the algorithm, the calculated value for the infrared channels signal was 126 bpm, this value is slightly below the signal evolution trend, although is possible to verify that some of the represented peaks had a dramatic decrease of amplitude inducing a little work delay due to the need of readjust the mean line value; this happens because the algorithm was meant mainly to not validate false events, so it is possible that due to the tight criterion some meaningful events become discard in situation of rapid signal amplitude variation. Anyway the returned results are suitable for a physical exercise situation and present a good accuracy comparing the obtained results with the graphical representation of the signal.

The graphics presented the separated channels on the tests 1C and 2C were obtained from the signal acquired with pulsatile light emission using the implemented algorithm to separate the merged channels.

Concerning the returned heart rates is possible to once again observe a correlation between the returned values, the graphical signal representation and the carried situation; for the test 1C the heart rate value varies between 72 and 78 bpm fitting a resting situation, finally on test 2C the returned heart rate value is 114bpm that once again is according with a physical exercise situation.

Focusing on the returned R_{OS} (that acts as a pointer of the oxygen saturation levels) it is possible note a similarity in the results against the initial expectations of obtains a higher value for the test 2C R_{OS} compared with the test 1C R_{OS} values, due to an intended decrease on the oxygen saturation levels. [6]

However a further analysis revealed that despite the great alterations on the oxygen consumption and carbon dioxide production during physical activity the mean values of P_{O_2}, P_{CO_2} and pH of the blood remain constant near the values at rest for an aerobic exercise situation, unfortunately go up and down on stairs during 3 minutes is classified as an aerobic exercise and do not produce significant changes on the oxygen saturation values.

Concerning the results for the simulated signals the algorithm revealed a very acceptable performance in critic situation that used signal features much more irregular than the present in real signal; this good accuracy reinforces the algorithm reliability for use in regular physiologic situations.

Weaving a brief consideration to the operation of the probe it is possible identify a great noise increase using the pulsatile light emission, this is an undesirable effect of the absence of a "black" period without light emission between each LED active state, this feature would save energy and prevent crossed interferences between the two used light wavelengths reducing the noise presence.

7. CONCLUSIONS

The developed efforts to develop a pulse oximetry device have been exposed in this document as an account of the academic project conducted during the last year.

The academic project was intended to compromise the development of a suitable system architecture and of robust algorithms for data processing in an device able of acquire and process spectrometry data for further correlation with an physiological state. These goals are the central theme for this thesis and this chapter will present the prudent balance of the developed work.

7.1 PROJECT STATUS

The initial aim was develop a standalone pulse oximeter based on a transmittance probe connected to a hardware interface equipped with the capacity to acquire and process the probe signal, and return as final result a heart rate and a blood oxygen saturation value.

However as previously mentioned this objective was bypassed due to the ISA interest in integrate our oximetry solution in the development of their vital signals monitoring platform.

This new project approach would require the development of a transmittance oximetry probe compatible with the Bioplux module that would acquire and transmit the data to the Leonardo module, where would be implemented the necessary algorithms for signal processing.

Concerning the probe development the current prototype already produce produces consistent data, although it is limited to some constraints as the bad light pollution isolation and the consequences of not perfect connections isolation in the probe circuit.

However the tested solutions are consistent and many of these constraints are not insurmountable, in fact a simple careful assembly of the final architecture should eliminate many of these “noisy” constraints.

The developed algorithms have shown to be reliable producing consistent results and presented a good indifference to false events resulting from the noise interferences. The algorithms implemented in C allow separating the merged infrared and red channels

from the acquired signal using pulsatile emission, reduce the present noise, and return the value of the heart rate and of the R_{OS} (ratio of ratios).

Although it was not possible to test the module, the Bioplux® module is ready to acquire data from the developed probe requiring just the adjustment of the sampling frequency.

This acquisition tool communicates with the Leonardo® module using a Bluetooth protocol; the both devices firmware was already developed and operational according to the ISA information.

7.2 FUTURE WORK

Any development project always remains an open book with each new analysis producing improvement possibilities. In this section will be presented some improvement possibilities that may be become useful guidelines for the recipients of this thesis.

In terms of hardware this project development will require the development of a final probe architecture assembled using SMD technology to reduce the noise produced from the bread board use constraints. It is always important that the final probe ensure a good isolation from surrounding environment light, this requires a probe adaptable to the finger shape.

To improve the acquisition detection would be interesting study the signal evolution trend white a third LED cycle in which the two LED's are off, this state between each active state should prevent the crossed interferences reducing the noise, and will enlarge the final device autonomy saving energy.

The introduction of analogical filters was not tested and is an interesting open possibility.

Would also be interesting the probe produce a control signal identifying the current emissions channels, this control mechanism may prevent erroneous data processing.

Concerning the implemented algorithms will be necessary after obtain the necessary data develop a weighing algorithm to validate the data in critic situations as fast oxygen saturation increase or decrease taking in account the previous signal evolution , will be also necessary reinforce the signal treatment and develop additional security mechanism against false events.

The obtained data is clinic valid only after a calibration procedure, so it is necessary to develop a calibration procedure to relate the obtained values with a precise physiological state.

Finally after maturate the probe and the processing algorithms would be quite challenging and interesting return to the initially aimed development of a reliable standalone device with good autonomy features.

7.3 FINAL APPRECIATION

This final section intends to be the condensed overview of the developed worked, presenting the final balance and considerations.

The balance of the actual status of the project reveals the need of continue improving the developed work, with many unexplored possibilities, however and despite of this the balance is still very positive and the work consider that was developed a meaningful work that produced consistent results for the probe and implemented algorithms.

This project has produced more than technical improvements; it was the first approach to the scientific environment and allowed the development of competences on the electronics and programming fields. It was also an opportunity to develop team work habits, with the developed work spirit promoting the development of common ideas and goals that required a good team work planning.

Analyzing this project as the last formative stage before the beginning of a professional life it is possible to affirm that this year was an opportunity to apply the knowledge acquired during the academic pathway and provided the tools to an effective professional evolution.

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ATTACHMENTS