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GQW content:
The content of the GQW illustrates the process of the algorithm development. From the description of the techniques implemented to process and analyze the biomedical signals, to the method of algorithm assessment.

List of reporting documents: the text of the GQW, thesis defense presentation, algorithm code.

Additional sections: Special aspects of safety

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SUMMARY

Explanatory note 85 p., 52 fig., 04 tables, 53 sources, 01 Appendix

KEY WORDS: Algorithm, ECG, PPG, blood pressure, novel, assertive.

The subject of the research is: Algorithm for joint analysis of Electrocardiogram and Photoplethysmogram.

The target of the GQW

The central objective of this research is based on finding out some assertive and robust PPG & ECG BP related parameters by the implementation of a novel method with innovations in signal processing and analysis.

In order to increase the cuffless blood pressure measurement accuracy, a technique, which involves not only the ECG and PPG joint parameters extraction but also PPG’s morphology features, is proposed. Signal characteristics were studied to be able to extract their correct main information. In the first chapter, the problems that current methods are facing were discussed, within them, motion artifacts and high frequency noises that appear during the signal reading and compromise the purpose of quality, were considered to be reduced or avoided. In the second chapter, a novel technique, which includes wavelet transform and neural networks, was presented to overcome the noise and analyze the data. Additionally, the regression analysis was performed in pursuance of algorithm’s feasibility validation. The third chapter examines the safety aspects that need to be addressed together with the project development and implementation. The results achieved demonstrate the effectiveness of the method for unobtrusive BP measurement.
РЕФЕРАТ

Основной целью данного исследования является нахождение с использованием новейших методов анализа сигналов надёжных и информативных параметров ЭКГ и ФПГ, которые связаны с величиной артериального давления.

С целью повышения точности безмажетного измерения давления была предложена методика, опирающаяся как на определение совместных характеристик ЭКГ и ФПГ, так и на использование отдельных параметров, характеризующих ФПГ. Для получения корректных и достоверных характеристик были исследованы свойства сигналов ЭКГ и ФПГ. В первой главе рассмотрены проблемы, с которыми сталкиваются текущие методы. Среди них рассматриваются вопросы, связанные с устранением помех в сигналах, возникающих на этапе их регистрации. Во второй главе рассматривается применение таких новых методов как вейвлет-преобразование и искусственные нейронные сети для решения задачи помехоустойчивого анализа сигналов. На стадии оценки эффективности разработанных алгоритмов был также использован регрессионный анализ. В третьей главе рассмотрены вопросы безопасности жизнедеятельности, связанные с реализацией данного исследования. Полученные в данной работе результаты демонстрируют эффективность разработанных методов для неинвазивной оценки артериального давления.
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DEFINITIONS, DESIGNATIONS AND ABBREVIATIONS

The present explanatory note uses the following abbreviations and designations:

ADC – Analog to digital converter;
ALC – Ambient light cancellation;
BP – Blood pressure;
CWT – Continuous wavelet transform;
DBP – Diastolic blood pressure;
DWT – Discrete wavelet transform;
ECG – Electrocardiogram;
E-field – Electronic field;
EPIC – Electric potential integrated circuit;
ESD – Electrostatic discharge;
FT – Fourier Transform;
HR – Heart rate;
ICWT – Inverse continuous wavelet transform;
IIR – Infinite impulse response;
PPG – Photoplethysmogram;
PTT – Pulse transit time;
PWV – Pulse wave velocity;
SBP – Systolic blood pressure;
STFT – Short time Fourier transform;
INTRODUCTION

Hypertension is a major risk indicator for coronary heart diseases, which according to the world health organization corresponds to the primary global risk of mortality [1]. Blood pressure (BP) measurement, including systolic blood pressure (SBP) and diastolic blood pressure (DBP) is an important vital sign of health care and represents a fundamental biomedical signal for managing the risks resulting for hypertension.

These days the most common practice for blood pressure measurement is the oscillometric technique. Due to its primitiveness and availability.

One of the problems showed with this practice is the so called ‘white coat effect’, which represents an increase in the blood pressure of the patient in the presence of a physician. While the oscillometric technique can be used at home and in this case it promises to show a more real extent, it requires the use of a cuff that limits the self-recording of BP.

In addition, literature has shown that most cardiovascular parameters (heart rate, blood pressure, artery resistance) are linked with one to another, and may be correlated with the feature in photoplethysmogram signal, which reveals the changes of blood volume during a cardiac cycle [2].

In consideration of the previous observations, nowadays researchers have been developing techniques based on electrocardiogram (ECG) and photoplethysmogram (PPG) signals for the blood pressure measurement.

Although the current methods exhibit high fidelity in terms of BP estimation, they require high sensors synchronization as they are based in pulse wave velocity. Further, they lack applicability in different scenarios.

Consequently, in this work, some tasks are proposed and listed as follows:

1. Acquire ECG & PPG signals recorded using a mobile monitor, as well as SBP & DBP from a sphygmomanometer and translate them to the Matlab workspace.
2. Assessment and improvement of the performance and universality that most of the current cuffless BP estimation methods miss.

3. Develop an algorithm for signal processing and analysis, which is able to obtain reliable BP related parameters.

4. Design and implement a neural network to validate the algorithm feasibility. The aim is to construct the correlation between estimated and reference blood pressure.

Generally, this investigation focus on finding out some certain and robust PPG & ECG BP related parameters and evaluate how they enhance the insufficiencies presented in most of the current methods.
1 PROBLEMS OF THE DEVELOPMENT OF AN ALGORITHM TOWARDS ELECTROCARDIOGRAM & PHOTOPLETHYSMOGRAM JOINT ANALYSIS

1.1 Biomedical Signal

Human bodies are continually radiating data with valuable information about health status. Physicians have determined a group with the most important signs related to general physical health condition of a body, this group with the vital signs (heart rate, blood pressure, respiration rate and blood oxygenation among others) gives clues to identify diseases and track recovery.

In order to measure the signals previously mentioned, there are some medical procedures, which have been evolving for years. This investigation will focus on electrocardiography and photoplethysmography; both have shown good performance in terms of heart condition estimation and more importantly identification of features related to hypertension detection.

1.1.1 Electrocardiogram

Electrocardiogram (ECG) is a diagnostic tool that measures and records the electrical activity of the heart. Conventionally is formed by 12-leads that during a certain amount of time record the heart electrical activity from 12 different angles. Making possible to register heart’s electrical depolarization each moment throughout the cardiac cycle.

The main ECG medical information lays on the QRS complex (Figure 1.1).

![ECG one cycle QRS complex](image1)

Figure 1.1 – ECG one cycle QRS complex
Q, R and S complex present information about the ventricular systole in consequence of the impulse propagation to the ventricles (Q wave), whereas the transmission to the whole tissue is caused by the R and S wave.

Furthermore, the interval between successive heartbeats may be obtained from R-R interval [3].

Despite a normal ECG signal is composed by 12 leads, researchers have found that by using one single channel ECG sensor, the signal still contains feasible information for the identification of many cardiac diseases [4].

1.1.2 Photoplethysmogram

Photoplethysmography (PPG) is an optical procedure to estimate the skin blood flow by using infrared light and a photo detector. PPG can be read from the wrist or a fingertip. Figure 1.2 shows the PPG one cycle waveform.

![PPG waveform one cycle](image)

Some physiological features like, respiratory rate, heart rate, and some vascular and cardiac irregularities can be identified by using PPG signal.

The measurement of blood volumetric changes in the skin perfusion by means of PPG depends on the fact that blood absorbs infrared light many times more strongly than the surrounding tissues. Blood flow in the capillaries raises during systole and decreases during diastolic. PPG uses low-level infrared light to detect small changes in blood volume/content in these regions. Thus, PPG gives a voltage signal that is proportional to the amount of blood present in the blood vessels [5].
Despite this method gives only a relative measurement of the blood volumetric changes and it cannot quantify the amount of blood, it can reflect the dynamics of the blood volumetric changes remarkably well.

PPG waveform involves a pulsatile (AC) physiological waveform attributed to cardiac synchronous changes in the blood volume with each heart beat, and a slowly varying (DC).

Figure 1.3 shows the PPG signal decomposition

![PPG signal decomposition](image)

The DC component has various lower frequency components attributed to respiration, sympathetic nervous system activity and thermoregulation [6].

1.2 Biomedical signal acquisition: Hardware

Biomedical signals ECG and PPG are taken using CardioQvark, which is a mobile monitor shown in figure 1.4. The cardio monitor is commercially available and nowadays have a pilot version with a sensor for PPG recording towards blood pressure estimation.

The device consists of a case for iPhone with two sensors for ECG tracking and one sensor for PPG recording.

Inside the case is a multi-layer shielded printed circuit board with electronic components for the signal pre-amplification, filtering, amplification and control.

The monitor receives power from the smartphone's battery via the Lightning connector, which is also used for data exchange [7].
The ECG trace ideally requires two electrical signals from parts of the body on opposite sides of the heart. By mounting two sensor electrodes on the rear of a Smartphone case, these signals are easily obtained from fingers on both hands just by holding the phone [8]. For the PPG, one sensor is superimposed on one of the ECG sensors.

Figure 1.5 presents a user holding the cardio monitor
Figure 1.6 shows the device’s block diagram configured for ECG recording.

![Block Diagram of CardioQvark for ECG Recording](image)

Figure 1.6 – CardioQvark block diagram for ECG recording

From it, once the signals are received from the sensors, they have two levels of amplification before being digitalized. Besides, the controller in charge of manipulating the digital potentiometer ensures the quality of the system [7].

### 1.2.1 Biosensor for Electrocardiogram recording

The sensor to be used is an electric potential integrated circuit (EPIC). EPIC is a noncontact electrometer, meaning that there is no direct DC path from the outside world to the sensor input. EPIC is a very high impedance sensor that can measure small changes in the ambient Electric field (E-field). This allows it to detect changes in local E-field due to the movement of dielectric objects such as a human body. When a person moves, he disturbs the electric field around himself. The sensors can be configured to detect this change in the E-field and produce a proportional signal that can be used to estimate various information related to position and motion.

A capping layer of dielectric material to ensure that the electrode is isolated from the body being measured protects the electrode. The device is AC coupled with a lower corner frequency (-3dB) of a few tens of MHz and an upper corner frequency above 200 MHz. This response is adjustable and can be tailored to suit a particular application.
Additional gain and filtering can be integrated to the signal from the sensor, prior to being digitalized using ADC with plausible resolution and sampling rate.

In figure 1.7, the block diagram corresponding to the EPIC sensor is shown.

![Figure 1.7 – EPIC sensor block diagram](image)

The EPIC sensor can be used in non-contact, contact and near contact applications [7, 9].

### 1.2.2 Biosensor for Photoplethysmogram recording

Photoplethysmography aims to measure the skin’s blood flow using infrared light and a photo detector to catch the transmitted or reflected light [10].

Normally, a PPG sensor consists of an infrared light emitting diode (LED) and a photo detector (Figure 1.8).

![Figure 1.8 – Light emitting diode & photo detector for PPG](image)

The mobile monitor CardioQVark uses an integrated pulse oximetry module MAX30102 to catch the PPG signal. It includes internal LEDs, photo detectors, optical elements, and low-noise electronics with ambient light rejection.

In figure 1.9, the block diagram for the PPG sensor is presented.
Figure 1.9 – PPG sensor system diagram

The sensor operates on a single 1.8V power supply and a separate 5.0V power supply for the internal LEDs and communication is through a standard I2C-compatible interface.

The SpO2 subsystem of the MAX30102 contains ambient light cancellation (ALC), a continuous-time sigma-delta analog to digital converter (ADC), and a proprietary discrete time filter. The ALC has an internal Track/Hold circuit to cancel ambient light and increase the effective dynamic range.

The SpO2 ADC has programmable full-scale ranges from 2\(\mu\)A to 16\(\mu\)A. The ALC can cancel up to 200\(\mu\)A of ambient current.

The internal ADC is a continuous time oversampling sigma-delta converter with 18-bit resolution. The ADC sampling rate is 10.24MHz. The ADC output data rate can be programmed from 50sps (samples per second) to 3200sps.

The MAX30102 integrates Red and IR LED drivers to modulate LED pulses for SpO2 measurements. The device includes a proximity function to save power and reduce visible light emission when the user’s finger is not on the sensor [11].

1.3 Problems found during Processing of the biomedical Signal

In recent years, biomedical technologies have been developing to allow diagnoses that are more accurate and the subsequent adequate treatments. In contemplation of the high accuracy these new technologies need to accomplish, the
devices should be optimized, meaning by optimization the process of correct signal reading and information delivery to physicians.

There are different factors that influence the accuracy of biomedical signals.

Despite the requirement when performing biomedical signal’s (ECG & PPG) measurements is that, the patient must stay still until the completion of the signal recording. In reality and specifically using mobile monitors, noise caused by motion is imminent.

Due to motion artifacts, the biomedical ECG & PPG signals show a baseline drift which can contribute to errors in the analysis of waveform features.

Motion artifacts frequency is 0.1 Hz; this means it overlaps the ECG and specially the PPG signal, which is in a range lower than 15 Hz. Therefore, the overlapping makes insufficient the use of typical signal processing methods in order to get rid of it [12].

In addition, patient's body can act as an antenna, which picks up electromagnetic interference, especially 50/60 Hz noise from electrical power lines. This interference can obscure the biological signals, making them very hard to measure [13].

In order to obtain the correct information concerning the biomedical signals, the noises previously named must be considered, identified and removed, to help the physician make an appropriate decision.

1.3.1 Signal Detrend and Low Pass Filter

Previous studies suggest a combination of signal detrend and low pass filter to get rid of the noises presented in biomedical signals [14].

In Matlab, detrend removes the mean value or linear trend from a signal represented as a vector or matrix. This action permits to focus on analyzing the fluctuations in the data vector (Figure 1.10).

Unfortunately, biomedical signals (ECG & PPG) rarely show a linear trend but a fluctuating one.
As well, to deal with the noises presented at high frequencies (above usual biomedical signals frequency range), the use of a digital low pass filter has been recommended in some researches.

An infinite impulse response (IIR) low pass filter with a cut off 30 Hz for the ECG signal and a cut off 20 Hz for PPG is designed and used in Matlab (Figure 1.11).

As a result, it is observed that, filtering a signal introduces a delay. This means that the output signal is shifted in time with respect to the input.

In addition, the smoothed signal resultant after filtration presents a reduced amplitude, which may lead to wrong interpretation of the biomedical information.
1.3.2 Fourier Transform and Short Time Fourier Transform

FT offers a useful way to convert any signal that is in the time domain to frequencies. Considering the signal as the resultant of some waves oscillating forever (Figure 1.12). Unfortunately, it does not represent abrupt changes as the ones exhibited by biomedical signals efficiently [15].

![Figure 1.12 – Signal representation for Fourier transform](image)

Short time Fourier transform (STFT) uses a sliding window to take the time domain information into consideration, the frequency resolution depends on the time resolution, or the size of the window. Preventing a zoom in a particular frequency range because the box is uniformly placed (Figure 1.13).

![Figure 1.13 – Short time Fourier transform](image)

In this respect, it should be noted that most biomedical signals of interest include a combination of impulse-like events (spikes, and transients) and more diffuse oscillations, which may all convey important information for the physician. The short-time Fourier transform or other conventional time-frequency methods are well adapted for the latter type of events but are much less suited for the analysis of short duration pulsation.
As biomedical signals, exhibit slowly changing trends or oscillations punctuated with transits, the FT and STFT do not represent the best option for signal analysis [16].

1.3.3 Wavelet Transform

For analysis of non-stationary signals as the ones presented in biomedical engineering, some capable wavelet methods have been developed for the multiscale representation and subsequent analysis of these signals.

Fourier transforms offer a convenient way to reconstruct a signal, from time domain to frequency domain. This signal is decomposed following a sinusoidal function. As the idea is to locate the frequencies in time, the signal can be decomposed inside a window of length L, this window is moved along the time axis. If instead of using a fixed window, a function converging to zero is used, the concept of a wavelet appears.

A wavelet is a rapidly decaying wave like oscillation that has zero mean and which exists for a finite duration [17].

To choose the correct wavelet, there is necessary to take into account the application. As there are many distinctive wavelets, for signal analysis one is free to choose the wavelet, which facilitates the detection of the feature on purpose.

In figure 1.14, some of the most common wavelet families used for biomedical signals analysis are presented [18]:

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For the performance of the wavelet transform, two parameters play an important role.

Scaling: The scale factor is an inherently positive quantity, inversely proportional to frequency, the scale factor strengthens or shrinks the signal in time. The smaller the scale factor, the more compressed the wavelet, this shows the promptly changing details. Contrarily, the larger the scale, the more stretched the wavelet and the easier the identification the slowly changing components. Formula (1.1).

\[
\psi \left( \frac{t}{s} \right) s > 0 \tag{1.1}
\]

In which:

\( \Psi(t) \): corresponds to wavelet function

\( \Psi \left( \frac{t}{s} \right) \): corresponds to scaled wavelet function by \( s \) factor
When scaling the signal by two, results in reducing its original frequency by half (Table 1.1).

Table 1.1 – Wavelet scale and correspondent frequency

<table>
<thead>
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<th>WAVELET SCALE</th>
<th>2</th>
<th>4</th>
<th>8</th>
<th>16</th>
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<tr>
<td>EQUIVALENT FREQ (F_{eq})</td>
<td>(\frac{F_{eq}}{2})</td>
<td>(\frac{F_{eq}}{4})</td>
<td>(\frac{F_{eq}}{8})</td>
<td>(\frac{F_{eq}}{16})</td>
</tr>
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Shifting:

Shifting a wavelet is the process of delaying the onset or the wavelet along the length of the signal. Formula (1.2), presents the result while shifting a wavelet.

\[\psi(t - k)\] (1.2)

In which:

\(\Psi(t)\): corresponds to wavelet function

\(\Psi(t-k)\): corresponds to shifted wavelet function delayed by \(k\)

The wavelet shifting responds to the necessity to align the wavelet with the feature in the signal that wants to be identified [19].

Finally, from the point of view of the practitioner, there are two ways for wavelet decomposition: Continuous wavelet transform (CWT) or wavelet frames and discrete wavelet transform (DWT).

**1.3.3.1 Continuous Wavelet Transform:**

CWT uses inner products to measure the similarity between a signal and an analyzing function. The CWT compares the signal to shifted and compressed or stretched version of a wavelet. As a result, CWT presents a description, which is shift invariant (Figure 1.15).
1.3.3.2 Discrete Wavelet Transform:  
DWT helps analyze signals at progressively narrower sub bands at different resolution.

Recommended for denoising and compression of signals and images as it splits up a signal into a low-pass sub band (approximation level), and a high-pass sub band (detail level). The approximation sub band is decomposed at multiple levels for a fine scale analysis (Figure 1.16).

Abrupt changes are presented at high frequencies while, baseline drift occurs at low frequencies. Data compression as well as noise reduction can be achieved by simply discarding certain coefficients that are insignificant [21].
One of the major concerns regarding biomedical objects is the wide variability of signal artifacts, which makes the necessity to operate the wavelet analysis on a case-by-case basis. Furthermore, in the case of biomedical signals, the information uses to be the resultant of some characteristics, as for example spikes and transients, which are well localized in space and time [22].

1.4 Biomedical signal analysis problems
In order to be able to identify feasible parameters presented in photoplethysmogram and electrocardiogram for blood pressure estimation, the identification of features presented in PPG and ECG waveform, which from theory are highly correlated with blood pressure are discussed, in order to consider its workability for the assessment of blood pressure. Considering that, some of the parameters are insufficient or impossible to estimate in the case of several patients.

1.4.1 Pulse transit time
A cuffless and non-invasive blood pressure estimation based on the quantification of the traveling time it takes the blood to move between two points in the body has increased researchers attention in recent years [23-24]. PTT known as the time difference between the R peak in ECG and the systolic point in PPG (Figure 1.17), is usually measured based on the simultaneous monitoring of electrocardiogram and photoplethysmogram, which is a function of pulse wave velocity.

![Figure 1.17 – Pulse transit time](image)
PTT and systolic blood pressure may be inversely related. Since high BP leads to a raise in the stiffness of arterial wall, therefore, the pulse propagation time is shorter and there is a low PTT. On the contrary, low BP accompanies less arterial wall stiffness and consequently, high PTT.

Even though been highly related to blood pressure determination, the PTT based method requires the synchronization of two different signals (ECG and PPG) coming from two different sensors. In this case, even with calibration PTT is not always an unequivocal indicator of BP. Moreover, PTT discloses only one facet of the complex cardiovascular changes produced by blood pressure fluctuation [25].

1.4.2 Dicrotic notch in photoplethysmogram

Besides PTT, several blood pressure related features might be found within the PPG waveform.

PPG single cycle waveform is formed by a first wave commonly recognized as systolic peak and a second one that is the reflected wave, which returns from the periphery, named as diastolic peak (Figure 1.18). Usually there is a downward deflection in the PPG waveform, which separates the systolic from the diastolic phase. This point is the dicrotic notch [26].

![PPG waveform phase separation](image)

Figure 1.18 – PPG waveform phase separation

The major change in pressure and volume waveforms is a decrease in the height of the diastolic component of the waveform and the inflection point preceding
this. Thus, dicrotic notch recognition plays an important role in PPG blood pressure-related features assessment.

For the categorization of PPG waveform in terms of dicrotic notch identification, the wave can be classified into four groups (Figure 1.19):

Type I: An apparent dicrotic notch is visible.

Type II: No evidence of dicrotic notch but a change in the angle of descending is presented.

Type III: No evidence of dicrotic notch but the downward slope becomes horizontal.

Type IV: No evidence of dicrotic notch.

Figure 1.19 – Dicrotic notch types in PPG waveform

The contour of the dicrotic notch differs from patient to patient according to vascular status and with spreading through arterial beds, even in some cases this notch is indiscernible due to different physiological factors [27].

28
Moreover, because of the high frequency nature of the dicrotic notch it is difficult to differentiate it from artificial noises or other high frequency components in the biomedical signal. Consequently, the process for its detection needs to consider the different notch conformation possibilities.

**1.4.3 Diastolic point in photoplethysmogram**

Diverse methods for finding BP-related parameters using a single PPG signal have been submitted. One important factor in these studies includes the diastolic peak.

PPG waveform single cycle appearance is defined by two phases: the rising part related to systole, and the descending part regarding the diastole and wave reflections.

While the systolic segment moves upward from a forward-going pressure wave spreading along a direct path from the left ventricle to the finger. The diastolic component is general derived from the pressure waves transferring along the aorta to the small arteries in the lower body, where they are reflected back along the aorta as a reflected wave that travels to the finger [28]. Diastolic phase starts immediately after the dicrotic notch and is represented with the second peak in the PPG waveform (Figure 1.20).

![Diastolic time PPG one cycle](image.png)
Due to motion artifacts produced during signal acquisition. The pulse height in PPG signal might present inaccurate information and is not reliable for BP estimation. Consequently, the diastolic time, defined as the time from the PPG foot point to its second peak is considered as a feasible feature for the BP estimation.

While systolic peak can be easily identified from the PPG waveform as it represents the maxima within the signal, on the other hand the diastolic peak or inflection is hard to determine. Is known, that cardiovascular parameters and the PPG signal differ from distinct subjects, therefore this variation influences the estimation of the parameter under measurement.

For this reason, a method to reveal diastolic inflections in case there is not observable diastolic peak within the PPG waveform is required.

1.5 Formulation of goal and task

The conception of this project comes from the necessity to enhance the blood pressure estimation, offering a mobile cuffless measurement as an idea to overcome defects and inaccuracy of the current existing methods. The objective of this project is to develop an adaptive algorithm based in Matlab programming which extracts pulse transit time and photoplethysmogram’s reliable BP-related features for the cuffless estimation of blood pressure.

The general structure of this assignment can be formulate in three main phases as presented in figure 1.21.
Figure 1.21 – Bioengineering system structure

1. Data processing

The initial phase corresponds to the reading of the biomedical signals in Matlab workspace and continues with the establishment of the algorithm for signals noise cancelation and preparation for the analysis.

2. Data analysis

This stage comprises the signals waveform description together with feature extraction.

3. Data control

The final part includes the extracted parameters validation in compared with the blood pressure estimated following a conventional process.

As the purpose of this project corresponds exclusively with the conception of the algorithm, is emphasized that the biomedical signal recording corresponds the input of the work and the photoplethysmogram & electrocardiogram parameters, which represent good correlation with blood pressure, mean the output of this project.
In this case, patient represents the object of investigation for the collection and analysis of the biomedical signal. The biomedical data from eleven patients showing different health condition is used to categorize BP changing in wide span, thus grant the BP estimation possible in an extensive range.

Furthermore, for each patient a set with twenty to thirty recordings is adopted. In general an approximate of two hundred sixty trials conform the algorithm goods.

The biomedical signals recorded using the mobile monitor CardioQvark (Figure 1.22) do not have any digital processing before entering the algorithm.

![Figure 1.22 – signal display in smartphone](image1)

In addition, at the time the patients were recording their signals from the comfort of their homes, they were asked to measure their blood pressure using a conventional sphygmomanometer located in patient’s upper arm for the recording of the systolic and diastolic blood pressure (Figure 1.23), which is an important factor to control the algorithm’s quality.

![Figure 1.23 – Upper arm BP measurement by a sphygmomanometer](image2)
During the analysis presented in the previous sections, the different drawbacks that need to be undertaken in the process of ECG and PPG joint analysis algorithm conception where examined.

Therefore, the stages to accomplish the goal of the presented project are presented as follows:

1. Noise removal

   In the interest of motion artifacts and high frequency noises removal, an adaptive process based on continuous wavelet analysis can be implemented to obtain a reliable signal.

   Wavelets are considered a dominant tool for the representation and analysis of signals, which have varying frequency component during time, as the physiological signals ECG, PPG. A wavelet-based technique is able to localize signal information in the time-frequency plane. In particular, is capable of trading one type of resolution for the other, which makes it especially suitable for the analysis of non-stationary signals [16].

   One mayor concern regarding biomedical information is the variability of the signals and the necessity to operate on a case-by-case basis. Often, is not possible to know a priori at which scale the pertinent information is located. Consequently, the emphasis is more on designing a robust method that works in most circumstances.

2. Feature extraction

   With regard to the extraction of biomedical signal’s one-cycle waveform, and considering that during the three minutes of signal recording, the physiological signal experiences a process of stabilization, the registered PPG signal is segmented in terms of single cycles and an average one-cycle waveform is extracted as the model for feature recognition. Secondly, the corresponding ECG’s one-cycle is chosen to confirm signals synchronization.

   Last but not least, pulse transit time and PPG’s systolic time are obtained among other components that are going to be discussed further.
3. Parameters validation

In order to evaluate the feasibility of the proposed ECG and PPG BP-related features, the regression line and coefficients between the prospective parameters and the reference systolic and diastolic blood pressure are determined using an artificial neural network.

1.6 Conclusion

In this chapter, the drawbacks that assessed in the accomplishment of the stages for the development of the algorithm for joint analysis of electrocardiogram and photoplethysmogram have been analysed.

In the first place, it was needed to study the characteristics of the biomedical signals, to be able to extract their correct main information. Supplementary the process, starting from signal processing to continue with the features identification and understanding. Consequently, different aspects, which appear during the signal reading and compromise the purpose of quality, were considered to be reduced or avoided. The proposed algorithm dedicates attention into the conception of a robust method that works in most cases. As well, the evaluation of different ECG’s and PPG’s joint features besides some individual PPG’s parameters can successfully overcome the deficiencies that most of the current algorithms lack. Subsequently, the use of an artificial neural network for evaluation of the parameters feasibility in terms of blood pressure estimation is going to be used. For this project, Matlab represents the software that is going to be implemented.
2 PROCESS OF ELECTROCARDIOGRAM & PHOTOPLETYSMOGRAM AUTOMATIC ANALYSIS ALGORITHM ESTABLISHMENT

2.1 Biomedical signals examination and preparation for study

Valuable medical information concerning heart status and blood pressure is obtained from ECG and PPG. Unfortunately, in most of the cases, these signals contain noises related to the measurement methods, patient’s movement and environment’s interference. As a result, the quality of the medical interpretation might be compromised and physicians might not be able to correctly recognize diseases or track recovery.

Consequently, previous signal interpretation, a process to get rid of the unwanted information is demanded. Although, the primary method for signal processing focus on the use of digital filters to remove noises [29], it was discussed in the previous chapter the drawbacks it implies. Thus, this research proposes a technique using wavelet transform to understand the time – frequency aspects of signals. Additionally, the recognition of the beat-to-beat cycle presented in raw ECG signal serves as a classifier previous spectral analysis.

In the purpose of this research, the biomedical information of eleven patients randomly selected from the cardioQVark database is obtained [11]. The selection of patient do not discriminate age and aims to consider several health conditions. In general, for each patient an estimate of thirty recordings were selected to build the algorithm’s directory.

Once the data is collected it is organize in tables in which the patient’s ID, blood pressure measurements, ECG and PPG recordings are gathered (Figure 2.1).
Consequently the course of signal processing opens.

2.1.1 Electrocardiogram synchronization points recognition

Several methods of computer electrocardiography involve identification of QRS complexes (Figure 2.2) by determining the position of their maximums (R wave). The obtained sequence of R-waves is used for segmentation of the cardio cycle [30].

Figure 2.2 – QRS complex in raw ECG signal
Since QRS complex is the most remarkable waveform within the electrocardiogram, its detection has been a research topic for several years and a lot of effort has been applied to the development of an algorithm for its correct identification.

While it was the computational load, what conditioned the algorithms operation in the early years (about 30 years ago). Nowadays due to the advancement in computer technologies, the computational load is less significant and the most effort is placed into detection effectiveness [31].

Generally, algorithms for QRS detection are divided into two distinctive stages: 1) Preprocessing or feature extraction. 2) Decision making implicating peak detection. In preprocessing stage, different techniques are applied to the signal, such as linear and non-linear filtering or smoothing to attenuate P and T waves as well as noise. In this step the QRS frequency components range is considered (Figure 2.3). In decision stage, the essential task is the establishment of thresholds and usually the use of techniques to discriminate T waves [31].

![Typical algorithm stages for QRS identification](image)

Figure 2.3 – Typical algorithm stages for QRS identification

Considering that, most of the proposed methods for QRS complex identification propose a preprocessing step using signal filtration, which may introduce signal distortions in frequency or temporal components. In this research, a method preserving the signal information contents and particularly R wave positions, in the presence of noise is presented.

In the first place, the first algebraic derivative of the raw ECG signal is obtained (Figure 2.4) with the aim to accentuate the R wave slope [32].

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Secondly, an amplitude threshold is set on account of the first derivative’s maximum and mean values. So then, the peaks exceeding the limit are going to be considered as R peaks. Using a threshold permits to adjust the signal changing conditions automatically since thresholds float over the noise.

The cardiac cycle rate range commonly is from 60 to 120 beats per minute [33]; thus once the first R peak is identified it is expected that a minimum amount of time is needed until the subsequent R peak arises. Therefore, a sliding window in time domain is implemented besides the amplitude threshold (Figure 2.5).

Consequently, the peak candidate that exceed the magnitude threshold and the time dead zone are denoted as R peaks (Figure 2.6).
The QRS complex detection accuracy obtained is sufficient for the purpose of this research (Figure 2.7).

Figure 2.6 – R peak identification steps

The QRS complex detection accuracy obtained is sufficient for the purpose of this research (Figure 2.7).

Figure 2.7 – ECG signal with R peaks identified
Although in some cases, the R peak is not exactly identified, the imprecision do not exceed a ten samples difference. This project do not aim to deeply study the QRS complex but just to use the R peak to obtain an R-R interval which will give enough information to segment the signal in cycles.

2.1.2 Electrocardiogram & photoplethysmogram time frequency analysis

Wavelet analysis is arising as a powerful tool for the processing of non-stationary signals. They describe the temporal characteristics of a signal by its spectral components in frequency domain.

Wavelets are a signal description in which an analysis window that is long at low frequencies and short at high frequencies is used to evaluate a signal. Therefore, they overcome the time – frequency resolution deficiency presented in the STFT method.

The wavelet transform (WT), is a signal decomposition onto a set of basic functions. For the design of the WT procedure, there are two important functions, which need to be described. The scaling function and the primary wavelet function.

The scaling function is the one, which dilates or narrows the signal and is related to the levels of decomposition of the signal. For instance, in the first decomposition level, a scale of two is applied and the signal sampling frequency is divided in two.

Then in the second decomposition level, the signal sampling frequency is scaled by a factor of four.

There are some steps to a continuous wavelet transform approach [34]:

1. Select a wavelet and compare it to the start segment in the raw signal.
2. Obtain the correlation factor C between the wavelet and the fragment of the signal.
3. Shift the wavelet to the right and repeat steps 1 and 2 until reaching the end of the signal.
4. Scale the wavelet and repeat steps 1 to 3.
5. Repeat the previous steps for all the scales.
While finishing the process, we obtain the resultant coefficients from different decomposition levels (which can be displayed in terms of scale or frequency) at different sections of the signal.

Figure 2.8 shows the scalogram of the ECG signal. From it is observed that the fluctuating features which contains the important ECG information lays in the frequency range between 8 to 32 Hz. Therefore, the components exhibited at lower frequencies are considered as the artifacts related to patient’s movement and the ones exposed at higher frequencies, noises from power lines. Both require to be removed in order to obtain a denoised and baseline corrected ECG signal.

![ECG Scalogram](image)

**Figure 2.8 – ECG scalogram**

The continuous WT is as well applied to the raw PPG signal and the results are presented in figure 2.9. Applying the same interpretation as the one for ECG signal, the main PPG information is found between the frequency range 2 to 10 Hz. Lower and higher frequencies features are taken as noises.
Although some investigations \cite{35,36} suggest that, the main ECG information lays in a predetermined frequency range. In this research, we contemplate that as the patient heart rate (HR) changes so does the ECG beat – to – beat interval. For that reason, we are going to use an adaptive frequency range to extract the signal information, in which the boundaries are set in terms of the HR retrieved from the R – R interval that we got in the preprocessing step.

The same concept applies for the PPG signal. In order to consider the effect of the HR in the peak – to – peak interval, the algorithm to extract the denoised signal contemplates patient HR to determine the limits for the spectral analysis (Figure 2.10).
After the time – frequency representation of the biomedical ECG and PPG signals, and the identification of the spectral range where the meaningful information stays. The reconstruction process starts. In this step, the inverse continuous wavelet transform (ICWT) is used to assemble selected signal components back into the original with no loss of information.

In Figure 2.11 the reconstructed and the raw ECG, signals are presented.

For the assembly of the signal, the baseline drift is corrected by removing the frequency components, which coincide with motion artifacts or low frequency noises. Additionally, artifacts coming from power lines or high frequency noises were identified and discarded for getting a denoised and baseline corrected signal.

![Figure 2.11 – ECG signal after WT and Raw ECG](image)

In the case of PPG signal, after the time – frequency representation and analysis, the reconstruction signal is done using the ICWT and establishing the reconstruction frequency range in such way that the identified baseline wander components and captured high frequencies noises are extracted (Figure 2.12).
2.2 Electrocardiogram and photoplethysmogram feature extraction

After processing the biomedical signals, corresponding single cycle waveform model needs to be selected for the intent of features extraction.

2.2.1 Photoplethysmogram waveform model selection

In order to obtain the PPG waveform single cycle which best describes the whole signal, the R-R interval discussed in the previous sections is used to reshape the signal in terms of one period (Figure 2.13). In other words, the signal, which initially was described in a vector, is organized in a matrix in which one row represents the data for one signal period. The number of rows depends on the length of the signal and the R – R interval magnitude.

Figure 2.12 – PPG signal after WT and Raw PPG

The removal of those components permits to obtain a denoised baseline drift corrected signal.
Secondly, a matrix with the correlation coefficients between the cycles is obtained (Figure 2.14) to be able to evaluate which cycles are strongly correlated. The diagonal in this matrix represents the correlation coefficient of the signal with itself and is not considered in the evaluation. For assessment of correlation coefficient, a threshold is set, thus the waves which correlation coefficient is higher than the threshold are considered as possible models.

Figure 2.14 – Correlation coefficient matrix between cycles

Additionally, another step in which the prospect models are evaluated is added. Following the aim to consider those cycles which are not only strongly correlated from the beginning to the end of the signal but also, are accepted as a proper description of the fragment of signals in which they are located. The
correlation coefficient matrix is divided in a number of groups, and its values are compared with a threshold.

Finally, the group of signals that are highly associated is gathered in the signal group models as presented in figure 2.15.

![Figure 2.15 – PPG best correlated waves](image)

As a result of the process, the single cycle PPG waveform presented in figure 2.16 is obtained.

![Figure 2.16 – PPG Single cycle model](image)

The biomedical signal model presented in figure 2.16 opens up the next step for signal parameters extraction.
2.2.2 Electrocardiogram waveform model selection

In contemplation of the synchronization requirement between the PPG and ECG biomedical signals.

Posterior the identification of the cycles, which best describe the PPG signal or group models, the process to extract the same time localized cycles corresponding to ECG starts. The same process as the one done in the case of PPG models, the group of ECG models is average and the single cycle ECG waveform displayed in figure 2.17 is obtained.

![ECG Single Cycle Waveform Model](image)

Figure 2.17 – ECG Single cycle model

Once the ECG and PPG models are obtained their corresponding parameters extraction starts.

2.2.3 Hybrid Electrocardiogram & photoplethysmogram blood pressure – related features

Pulse transit time (PTT) is the measurement of the travelling time of blood between two points inside the body, and is known to be linearly related to pulse wave velocity (PWV), therefore a function of BP [37,38].

PTT is mostly measured based on the continual and synchronal monitoring of ECG and PPG.

Commonly is defined as the time difference between the R-peak in the ECG signal and the next following peak of the corresponding PPG cycle.
Even though, the defined PTT has the potential for continuous and cuffless monitoring of arterial BP because of its linear relation with BP [39], most of the current PTT – BP models could provide only one BP parameter.

From a physiological perspective, BP is mainly affected by four factors: arterial compliance, cardiac output, peripheral resistance, and blood volume [23]. Arterial compliance and cardiac output can be evaluated by PTT but some of the other parameters that affect the BP still are not being considered.

Following the idea to enhance the accuracy of BP estimation. In the present work, three different proposals for PTT definition are presented and explained as follows:

a. Peak – to – peak PTT

The peak-to-peak PTT proposed in this research is the time difference between the R-peak of the ECG and the first peak of the PPG. Both signal models obtained after WT.

From the ECG model, the R peak is easily observed due to its unique shape. Therefore, by locating the local maxima in the ECG model, the R-peak index is determined (Figure 2.18).

![Figure 2.18 – Peak-to-peak PTT](image-url)
The position of the first peak of the PPG model demonstrates the same characteristics as the R peak. Subsequently, is detected using the local maxima approach

b. Peak – to – foot point PTT

The Peak – to – foot point PTT is the time delay between the R peak of ECG model and the foot point of PPG model (Figure 2.19).

![Figure 2.19 – Peak-to-foot PPT](image)

For identification of the foot point in PPG, we search for local minima.

c. Peak – to – Maximum slope point PTT

Peak – to – Maximum slope point PTT is determined as the time interval between the R peak of ECG and the peak of the first derivative of PPG in the same cardiac cycle (Figure 2.20).
Figure 2.20 – Peak-to-maximum slope PTT

At this step, the first derivative of the PPG model is obtained and the identification of local maxima gives the position of the peak. The time location of this point is transferred to the PPG signal to obtain the amplitude in the model therefore use it to determine the point for PTT.

2.2.4 Photoplethysmogram waveform blood pressure – related parameters

BP estimation methods based on PTT have several challenges in order to be accepted as a feasible method for cuffless monitoring. In terms of implementation, they require the synchronization of two different sensor data (ECG and PPG) coming at different sampling rates in real time. Additionally, it has been studied [39] that PTT is strongly related with SBP, but do not exhibit the same performance while talking about DBP. This is perhaps one reason to decrease the accuracy of predicted BP depending only on the PTT.

Information within the PPG’s waveform is hardly taken into consideration for measurement of BP. In [34] researches discovered that the second peak presented in
A photoplethysmography signal would influence the position and the amplitude of the main peak of the original PPG signal and consequently influence the PTT. Consequently, by introducing the information of the PPG second peak in the estimation of BP, the correlation coefficient between the measured and the predicted BP might increase [40-43].

It was discussed in section 1.4.2 that in some cases the secondary peak from the PPG signal cannot be easily identified. Nevertheless, in the case of this research, the process of wavelet transform performed in signal processing, allows us to obtain a PPG model in which the first and second peak are clearly represented (Figure 2.21).

Accordingly, in this project is hypothesized that the second peak in the PPG model might be useful for BP estimation.

![Figure 2.21 – PPG first and second peak](image)

Normally, within one period of the PPG signal there are two main peaks. In between of the two peaks is what is known as dicrotic notch.

Dicrotic notch is recognized as a representation of the pressure transiently produced when the aortic valves close at the end of left ventricular ejection. As vasodilation develops, the notch descends towards to the baseline [44,45].

The existence of dicrotic notch in PPG signal is mostly accompanied by the presence of a second peak. Secondary peak or diastolic peak is caused by the reflection of the blood in the vessel.
The time span between the first and second peak inside the PPG signal, is related to the transit time of pressure waves from the root of the subclavian artery to the apparent site of reflection and back to the subclavian artery [2].

Therefore, in addition to the recognition of the first peak in the PPG signal to evaluate the PTT towards BP estimation, the analysis of the two peaks inside the PPG signal might be useful to understand arterial stiffness, which is a parameter to consider in BP assessment.

In consideration, the properly identification of the dicrotic notch and the PPG’s second peak is included in the development of the algorithm for ECG & PPG analysis.

PPG first derivative is used to locate inflection points within the PPG signal. The dicrotic notch is identified as the point where the PPG first derivative crosses the zero value from the negative to the positive region (Figure 2.22).

Figure 2.22 – Second peak identification, a – PPG waveform model. b – PPG First derivative. C – PPG Second derivative
Additionally, the diastolic peak is established as the subsequently point in which the PPG first derivative crosses the zero value from the negative to the positive region (Figure 2.23).

![Figure 2.23](image)

Figure 2.23 – Second peak identification, a – PPG waveform model. b – PPG First derivative. C – PPG Second derivative

Finally, once the dicrotic and secondary peak points are spatially and time located, we proceed to establish the PPG’s waveform features for the BP estimation.

a. \( \text{Ra} \)

Is the amplitude ratio between first and second peak in relation to the foot point in one cycle of the PPG signal (Figure 2.24).

Defined in formula (2.1):

\[
R_a = \frac{Y}{X} \quad (2.1)
\]

In which:

\( Y \): corresponds to the amplitude of the first peak with respect to the foot point of the PPG

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X: corresponds to the amplitude of the second peak respecting PPG foot point

First peak

Figure 2.24 – Ra representation

b. \( T_{sd} \)

\( T_{sd} \) represents the time span from the first peak to the dicrotic notch (Figure 2.25).

c. \( T_{fd} \)

\( T_{fd} \) identifies the time span between the PPG foot point and the dicrotic notch (Figure 2.25).

First peak

Figure 2.25 – \( T_{sd} \) and \( T_{fd} \) representation

At this point three individual PPG’s features have been propose for the BP assessment.
2.4.5 Photoplethysmogram & electrocardiogram blood pressure related parameters retrieval

It has been discussed through the development of this section that considering some PPG’s morphology features in addition to the PTT, the task of SBP and DBP assessment might be improved.

In this part, the selected ECG and PPG parameters which are considered BP related are presented as follows:

1. Peak – to – peak PTT
2. Peak – to – foot point PTT
3. Peak – to – Maximum slope point PTT
4. Ra
5. Tsd
6. Tfd
7. T1

In addition to the well studied first six parameters, a new feature called T1 is added to the features group. This new index represents the time span from the PPG foot point to the PPG maximum slope point in the same cardiac cycle.

T1 is graphically obtained constructing a line, which best represents the PPG wave before the systolic point and crosses the maximum slope point, the intersection point between this line and the PPG foot point amplitude line is obtained. Therefore, T1 is defined as the time interval between this intersection point and the foot point time (Figure 2.26).
Summarizing, six time span indices and one amplitude index are gathered in a data set to build the group of ECG and PPG BP related parameters.

For each patient a dataset is created, within each of them, columns represent the seven features separately, and rows the recorded trials.

### 2.3 Feasibility validation

In this section, the seven PPG and ECG parameters studied in the previous part are correlated with the reference SBP and DBP. Both components of BP were measured using a standard sphygmomanometer located in patients’ upper arm. For this, an artificial neural network is designed for fitting the parameters dataset and the measured blood pressure.

The method chosen to assess the adequacy of the parameters in terms of blood pressure measurement is regression analysis.

#### 2.3.1 Linear regression

Regression analysis is an approach for the study and modeling of the relationship between a variable of interest and a set of related predictor variables.

The process of regression analysis involves the construction of a model based on the predictors and the response variable. In this, the collected data plays an important role considering that the resultant model is as good as the data on which
it is based. In other words, a good data set can ensure a more generally applicable model [46].

The most common method for fitting a regression line is the method of least-squares. This method calculates the best-fitting line for the observed data by minimizing the sum of the squares of the vertical deviations from each data point to the line, if a point lies on the fitted line exactly, then its vertical deviation is zero.

A linear function known as linear regression model is described in formula (2.2):

\[ a_q = m \cdot t_q + c + \varepsilon_q \]  \hspace{1cm} (2.2)

In which:
- \( m \) and \( c \) are the slope and offset respectively of the linear function
- \( t_q \) is the regressor variable
- \( a_q \) is the response variable
- \( \varepsilon_q \) represents the residual error of the regression

An example of linear regression representation is showed in figure 2.27

![Figure 2.27 – Linear regression](image-url)
In it, the blue line represents the linear regression, the thin black line represents the perfect match, and the circles represent the data points.

2.3.2 Correlation Coefficient

Correlation coefficient is used to evaluate the strength and the direction of the relationship between the BP and the BP-related parameters from ECG and PPG signal.

Following the nomenclature used in formula (2.2), the following formula (2.3) describes the correlation coefficient.

\[
R = \frac{\sum_{q=1}^{Q} (t_q - \bar{t})(a_q - \bar{a})}{(Q-1)s_t s_a} \tag{2.3}
\]

Where

\[
s_t = \sqrt{\frac{1}{Q-1} \sum_{q=1}^{Q} (t_q - \bar{t})^2}
\]

and,

\[
s_a = \sqrt{\frac{1}{Q-1} \sum_{q=1}^{Q} (a_q - \bar{a})^2}
\]

The R value can generally range from -1 to 1.

If \( R = 1 \), it means all the data points fall exactly on the regression line. If \( R = 0 \), then the data will not be concentrated around the regression line, but will be randomly scattered. Is expected for the correlation coefficient to be close to 1.

While the correlation R is only suitable for linear regression, the correlation \( R^2 \) can be used to evaluate both linear and nonlinear regression. \( R^2 \) provides information about the goodness of the regression curve in fitting the model, that is, it represents the proportion of the variability in the data set that is accounted for by the linear regression, and is referred to as the coefficient of determination.

For our interest, is hypothesized that the parameters and BP are not linearly related. For this, the \( R^2 \) represent the correlation coefficient in this study.
2.3.3 Artificial neural network

Artificial neural networks are based on biological structure of brain function. Their principal aim is to enable a computer to learn from data.

The artificial neural networks process is listed in the following workflow:

1. Collect the data
2. Chose network architecture and build the network
3. Configure the network (Arrange the network – so it is compatible with the problem)
4. Initialize the weights and biases
5. Train the network
6. Validate the network
7. Use the network

Regarding data selection, it is generally difficult to incorporate prior knowledge into a neural network. That is, the network can only be as accurate as the data that is used to train the network.

For this, it is important that the training data span the full range of the input space (the network do not have the ability to accurate extrapolate beyond the range of inputs).

Consequently, the determination of network architecture is case based. The process of building the network architecture starts with the establishment of number of neuron layers.

Most commonly, a network uses to have more than one Layer to perform the process. In the case of the present work, three layers are selected organized as input, hidden and output layer.

Additionally, the number of neurons for each layer is fix. Firstly, input neurons number depends of problem units that in this case is seven. For the output layer the number of neurons corresponds to the number of problem outputs (two). The number of neurons in the hidden layer corresponds to the mean value between the problem units and problem outputs.
Figure 2.28 shows the network architecture; in this case, a feed forward backpropagation net is used. The BP related ECC & PPG parameters are used as inputs and the hidden layer with five neurons. Further, the output layer with its two neurons and the output or targets SBP and DBP.

![Network architecture diagram]

**Figure 2.28 – Network architecture**

In the second place, the transfer function is determined, in figure 2.29 the commonly transfer functions and their characteristics are presented [47].

<table>
<thead>
<tr>
<th>Name</th>
<th>Input/Output Relation</th>
<th>Icon</th>
<th>MATLAB Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hard Limit</td>
<td>( a = 0 \quad n &lt; 0 ) &lt;br&gt;( a = 1 \quad n \geq 0 )</td>
<td>![Hard Limit Icon]</td>
<td>hardlim</td>
</tr>
<tr>
<td>Symmetrical Hard Limit</td>
<td>( a = -1 \quad n &lt; 0 ) &lt;br&gt;( a = +1 \quad n \geq 0 )</td>
<td>![Symmetrical Hard Limit Icon]</td>
<td>hardlims</td>
</tr>
<tr>
<td>Linear</td>
<td>( a = n )</td>
<td>![Linear Icon]</td>
<td>purelin</td>
</tr>
<tr>
<td>Saturating Linear</td>
<td>( a = 0 \quad n &lt; 0 ) &lt;br&gt;( a = n \quad 0 \leq n \leq 1 ) &lt;br&gt;( a = 1 \quad n &gt; 1 )</td>
<td>![Saturating Linear Icon]</td>
<td>satlin</td>
</tr>
<tr>
<td>Symmetric Saturating Linear</td>
<td>( a = -1 \quad n &lt; -1 ) &lt;br&gt;( a = n \quad -1 \leq n \leq 1 ) &lt;br&gt;( a = 1 \quad n &gt; 1 )</td>
<td>![Symmetric Saturating Linear Icon]</td>
<td>satlins</td>
</tr>
<tr>
<td>Log-Sigmoid</td>
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<td>![Log-Sigmoid Icon]</td>
<td>logsig</td>
</tr>
<tr>
<td>Hyperbolic Tangent Sigmoid</td>
<td>( a = \frac{e^{n} - e^{-n}}{e^{n} + e^{-n}} )</td>
<td>![Hyperbolic Tangent Sigmoid Icon]</td>
<td>tansig</td>
</tr>
</tbody>
</table>

**Figure 2.29 – Neural network transfer functions**

Summarizing, a two layer feed forward network with sigmoid hidden neurons and linear output neurons, is designed to fit and solve the data.

60
At this time, the training process start. Firstly, the dataset is divided. In this degree, some data is use to train the network and some other for validation and testing.

For instance, seventy percent of the data is for training, fifteen and fifteen percent for validation and testing (Figure 2.30).

![Figure 2.30 – Validation and test data](image)

Validation vectors are used to stop training if the network performance on the validation vectors fails to improve or remains the same. Test vectors are used as a further check that the network is generalizing well, but do not have any effect on training.

The network will be trained with Levenberg – Marquardt backpropagation algorithm that is a supervised algorithm to update weight and bias values according to Levenberg – Marquardt optimization (Figure 2.31).
To start with regression analysis. The regression line for the training, validation and testing process is built between the input and target data.

Figure 2.32 shows the regression line for the training, validation, testing and the resultant overall process.
Figure 2.32 – Regression line results, a – Training, b – Validation and testing, c – Overall performance

Once the correlation coefficients and regression lines are obtained they will be gathered for analysis.
2.3.4 Results

In this part, the detailed information about the dataset used to evaluate the algorithm and the blood pressure estimation results is presented (Table 2.1).

The data collection involves the recording of the ECG and PPG signals from the mobile cardio monitor CardioQvark for three minutes. This device obtains the biomedical signals at a sample rate of 1000 Hz. Additionally, the SBP and DBP are measured from a sphygmomanometer and its information retrieved with the ECG and PPG signals.

For the algorithm, an average of twenty recordings is measured from each patient. Patient's age range is within thirty to seventy years (30 to 70) and the overall health condition varies among them.

Table 2.1 – Patient’s heart rate and blood pressure

<table>
<thead>
<tr>
<th>Patient ID</th>
<th>Heart rate [bpm]</th>
<th>Systolic Blood Pressure SBP [mmHg]</th>
<th>Diastolic Blood Pressure DBP [mmHg]</th>
<th>BMI [Kg/m²]</th>
</tr>
</thead>
<tbody>
<tr>
<td>P01</td>
<td>54 ± (4.10)</td>
<td>146 ± (16)</td>
<td>76 ± (5.18)</td>
<td>22.9</td>
</tr>
<tr>
<td>P02</td>
<td>56± (5.39)</td>
<td>123 ± (13)</td>
<td>75 ± (5.6)</td>
<td>21.7</td>
</tr>
<tr>
<td>P03</td>
<td>58 ± (7.29)</td>
<td>131 ± (11.209)</td>
<td>84 ± (7.075)</td>
<td>28.4</td>
</tr>
<tr>
<td>P04</td>
<td>64 ± (8.49)</td>
<td>126 ± (11.647)</td>
<td>79 ± (8.709)</td>
<td>34.3</td>
</tr>
<tr>
<td>P05</td>
<td>78± (9.14)</td>
<td>112 ± (11.087)</td>
<td>72 ± (11.538)</td>
<td>27.8</td>
</tr>
<tr>
<td>P06</td>
<td>67 ± (4.47)</td>
<td>121 ± (14.423)</td>
<td>68 ± (4.745)</td>
<td>30.7</td>
</tr>
<tr>
<td>P07</td>
<td>71 ± (7.36)</td>
<td>135 ± (10.524)</td>
<td>85 ± (10.277)</td>
<td>32.1</td>
</tr>
<tr>
<td>P08</td>
<td>78 ± (9.66)</td>
<td>119 ± (11.856)</td>
<td>86 ± (7.269)</td>
<td>26.4</td>
</tr>
<tr>
<td>P09</td>
<td>88 ± (6.83)</td>
<td>123 ± (12.043)</td>
<td>86 ± (7.869)</td>
<td>25.6</td>
</tr>
<tr>
<td>P10</td>
<td>86 ± (8.35)</td>
<td>141 ± (9.961)</td>
<td>92 ± (5.371)</td>
<td>30.8</td>
</tr>
<tr>
<td>P11</td>
<td>98 ± (13.6)</td>
<td>134 ± (13.485)</td>
<td>90 ± (8.765)</td>
<td>27.7</td>
</tr>
</tbody>
</table>
The algorithm is tested against eleven patients and the correlation coefficient between the ECG & PPG BP – related parameters and the SBP and DBP is gathered in table 2.2.

Table 2.2 – Correlation coefficient measured and estimated blood pressure

<table>
<thead>
<tr>
<th>Patient ID</th>
<th>Training</th>
<th>General</th>
</tr>
</thead>
<tbody>
<tr>
<td>P01</td>
<td>0.99758</td>
<td>0.95383</td>
</tr>
<tr>
<td>P02</td>
<td>0.99563</td>
<td>0.96674</td>
</tr>
<tr>
<td>P03</td>
<td>0.99168</td>
<td>0.9583</td>
</tr>
<tr>
<td>P04</td>
<td>0.99655</td>
<td>0.97548</td>
</tr>
<tr>
<td>P05</td>
<td>0.99322</td>
<td>0.95556</td>
</tr>
<tr>
<td>P06</td>
<td>0.98298</td>
<td>0.95701</td>
</tr>
<tr>
<td>P07</td>
<td>0.99099</td>
<td>0.95449</td>
</tr>
<tr>
<td>P08</td>
<td>0.98426</td>
<td>0.96341</td>
</tr>
<tr>
<td>P09</td>
<td>0.99782</td>
<td>0.80218</td>
</tr>
<tr>
<td>P10</td>
<td>0.99772</td>
<td>0.94722</td>
</tr>
<tr>
<td>P11</td>
<td>0.997</td>
<td>0.97556</td>
</tr>
</tbody>
</table>

In appendix A, the resultant code corresponding to the algorithm designed in this research is showed.

Conclusion

In this chapter, the algorithm for ECG and PPG analysis was developed. Figure 2.33 presents the flow work of the approach.
With the aid of three supporting levels:

a) Acquisition

b) Processing

c) Analysis

The bioengineering system outcome is exhibited granting the study for model and parameters recognition.

Consequently, we have presented a method to study ECG and PPG signal in order to obtain some reliable BP related parameters. The feasibility of the method was evaluated by obtaining the regression analysis between the measured blood pressure and the proposed parameters.
3 SPECIAL ASPECTS OF SAFETY

The development of the algorithm for ECG and PPG joint analysis have several steps that combined build the Project workflow. Each step is characterized for having a group of implicit inputs, processes and outputs. In the case of our concern, the acquisition, processing, analysis and control of the biomedical signals integrate the support levels to accomplish the conception of the algorithm. Additionally, some internal and external factors affect each of the phases of the project in terms of safety and performance.

In consideration of the task goal and being aware that the internal and external aspects that might compromise the project effectiveness need to be addressed and controlled. The group of safety factors that were considered during the design and development of the present project are organized as follows [48]:

1. Device accuracy
2. Biosensors
3. Communication protocols
4. Electrical safety
5. Stability
6. Ergonomics

3.1 Device Accuracy

In order to evaluate the adequacy of the method presented in this research, in terms of BP measurement. For each trial, the estimated BP is compared with a reference BP, the second one taken using a conventional sphygmomanometer. The process is repeated for the group of patients and the regression analysis is performed in pursuance of obtaining the correlation coefficient between the cuffless BP and the reference BP (Figure 3.1).
Figure 3.1 – Estimated BP validation process, a – Recording of ECG and PPG signals. b – Recording of SBP and DBP. c – Typical results for the analysis of biomedical signals. d – Correlation agreement of estimated and reference BP.
The process of measuring the SBP and DBP using a sphygmomanometer was taken following the recommendations set in the standard for clinical use of non–invasive sphygmomanometers [49-50]. Additionally, the reference BP is measured immediately after finishing the recording of the biomedical signals ECG and PPG.

3.2 Biosensors

In this part are studied the standard requirements that the sensors used to obtain the ECG and PPG signals shall meet.

In section 1.2, the hardware system used to measure the biomedical ECG and PPG signal was presented. There it was said that two EPIC sensors and one integrated pulse oximetry module MAX30102 are the selected sensors to record the ECG and PPG signals respectively. These sensors have a combination of LEDs, photodetectors, optical elements and low-noise electronics with ambient light rejection to provide a complete system solution to ease the design-in process for mobile and wearable devices [11]. Additionally, some amplifiers and ADCs are placed within the cardio monitor.

Several external and internal factors can affect the accuracy or performance of the sensors and other electronic components used to measure the biomedical signals, from the strength of cardiac signal generated by the individual being measured, the clothing, and the surrounding environment conditions in which temperature, humidity, electromagnetic fields, among other factors might affect the signal quality.

In order to safety the effectiveness of the electronic components, which constitute the system’s hardware. The environmental conditions in which it is recommended to measure the biomedical signals are specified as follows:

3.2.1 Temperature, humidity and atmospheric pressure ranges

For electronic components, temperature represents an important aspect. High or very low temperatures can destroy the components or affect its operation. In order
to establish the adequate temperature to obtain the biomedical signals, the
temperature ranges within the electronic components shall operate are presented in
Table 3.1.

Table 3.1 – Recommended operation temperature range for the components

<table>
<thead>
<tr>
<th>Component</th>
<th>Temperature range [°C]</th>
</tr>
</thead>
<tbody>
<tr>
<td>EPIC sensor</td>
<td>0–50</td>
</tr>
<tr>
<td>MAX30102</td>
<td>(-40)–85</td>
</tr>
<tr>
<td>Amplifiers</td>
<td>(-40)–85</td>
</tr>
<tr>
<td>ADCs</td>
<td>(-40)–85</td>
</tr>
<tr>
<td>Controller</td>
<td>(-40)–85</td>
</tr>
</tbody>
</table>

Additionally, in the cardio monitor user’s manual regarding the operation of
the device, a temperature range from +15 to +35 °C is suggested.

The electronic components contained in the device used to record the
biomedical signals are affected by high humidity. Humidity might affect static build
up and sometimes prevent the biomedical signals from being seen clearly. For our
concern, the humidity range recommended in the place where the biomedical signals
are going to be recorded is 35 to 65 %.

Regarding atmospheric pressure, the IEC 60601–1 says that it is not recommended
to operate any medical electrical equipment with an atmospheric pressure higher of
600 mm Hg [50]. In the case of the cardio monitor, the fabricant recommends to
operate the device at an atmospheric pressure of (750 + 30) mm Hg [51].

3.2.2 Indoor or outdoor operation

According to the cardio Qvark user’s manual, there is a standard procedure
recommended to properly record the biomedical ECG and PPG signals. Within the
considerations, the patient’s hands shall be dry and clean. Patient is asked to seat or
lie down and hold the device into both hands ensuring proper contact with the
biosensors but avoiding strong pressure. The START button located in the user
interface needs to be pushed and the calibration of the biomedical signals start. This process normally takes ten seconds. Manufactures recommend patients to breath calm and normally, trying not to move during the measurement. Measurement of the biomedical signals commonly takes three minutes.

Figure 3.2 presents the correct way to hold the monitor while recording signals [51].

Subsequently, some recommendations regarding operation of the device are presented:

- Do not try to open or repair the device on your own.
- Do not drop the device as it may operate incorrectly.
- Do not overheat or overcool the device, avoid penetration of dirt or water into sensors.
- The device, including sensors, may be cleaned with dry natural fabric or alcohol wipe. Do not use household chemicals or abrasive materials.

3.3 Communication Protocols

Once the biomedical signals are measured with the cardio monitor, they are automatically send to the server for processing via mobile internet or Wi-Fi and then returned to the patient. In the case when the patient does not have internet or wants to send the recorded data manually, it can be done from the screen of the interface where the list of recording with dates can be find.
Additionally, patient can send the recording results to the doctor, in the case they consider something strange happened and need a professional opinion. This allows the doctor to control patient’s health status in real time remotely.

Figure 3.3 shows the data recording process.

Figure 3.3 – Biomedical signals communication process

Finally, all the recorded biomedical signals from the device’s users are gathered in the server and are able to be studied for research and medical purposes.

3.4 Electrical Safety

The cardio monitor is powered from the iPhone via the lightning connector and does not require additional charging.

Figure 3.4 shows the cardio monitor’s electrical specifications visible and available for the user according to the recommendations in IEC 60601-1.

Figure 3.4 – Cardio monitor electrical specifications
The power consumed by the cardio monitor ranges from 17 mW in the standby mode to 90 mW in the active mode, this does not affect the energy balance of the phone's battery.

### 3.4.1 Protection against electrical hazards

Every equipment connected to electricity is exposed to electrostatic discharge (ESD) which might affect the device’s operation.

ESD is an electrostatic phenomenon that causes an unexpected current to circulate between two objects at different electrical potential. There are several situations that initiate an ESD, such as friction between two different materials or in the cases when an electrical charged object is placed near a conducting object isolated from ground. In this case, the presence of the charged object creates an electrostatic field that creates electric charges distributed across the surface of the other object.

Among the effects ESD can carries for the device’s operation we can find:

- The device continues to operate in a normal performance pattern.
- The device demonstrates a temporary functionality loss or performance degradation, which stops after the incident of the electrostatic discharge stops. Afterwards, the device continues to operate in a normal performance pattern.
- The device demonstrates a temporary functionality loss or performance degradation which imposes a specialist involvement to retrieve or improve the occurred damage.
- The device demonstrates functionality destruction, performance degradation or software and hardware deterioration, which is not retrievable [52].

As in can be noticed, ESD might lead to poor operation or destruction of the device. For this reason, manufactures of electronic components set several recommendations in order to avoid the effects of ESD. In the case of the biosensor used to record the ECG signal, the producer says that the sensor is manufactured using a high performance analog CMOS process. As for all CMOS components, it is essential that conventional ESD protection protocols be applied for the handling
of this device [9]. Additionally, in the cardio monitor user’s manual a recommendation regarding ESD claims that cardio monitor sensors may accumulate static electricity, which may influence signal quality. In the case user see any noise instead of usual ECG signal, they are asked to wipe the sensors with an antistatic tissue [51].

3.5 Stability

Stability refers to the characteristics of the system to maintain its performance and safety attributes over the life of any battery within the system and over the life of the device, measured in terms of full – scale cycles.

For the cardio monitor, manufacturer talks about not less than 1000 hours of use of the device before failure. Considering an average intensity of operation of 6 hours per day, this would comprehend device’s service life of 5 years.

3.6 Ergonomics

Through the development of this chapter, the study of its subsections have focus mainly in the safety aspects connected to the device used to gather the biomedical signals. Considering the importance of the proper software development for the enhancement of the complete algorithm performance, the present ergonomics subsection will discuss the steps recommended to optimize the software design and conception.

Ergonomics is a discipline that generally studies humans and its relation with machines in a specific environment. Its objective is to design the work situation so that it is appropriate for the psychophysiological capabilities and needs of the human being; increase the efficiency, effectiveness and productivity of work.

The aim is to optimize the three elements of the system (man-machine-environment), for which methods of study of people, technique, and environment are elaborated.

Interactive systems or systems, in which humans and machine cooperate, have several requirements to be considered in terms of ergonomics. The system design in
accordance with those requirements will help to minimize the common usability problems in which we can find: unnecessary steps, unexpected response of the interactive system or inefficient error readjustment [53].

The algorithm for ECG and PPG joint analysis aims to provide the adequate interface for the analysis process. In consideration, some aspects regarding interactive systems ergonomics are organized and studied as follows:

3.6.1 Suitability for the task

An interactive system is suitable for the task when it supports the user in the fulfillment of the assignment. Avoiding the presentation of not necessary information.

Figure 3.5 shows the functional progress of the algorithm.

The algorithm for ECG and PPG joint analysis, involves the use of biomedical signals as inputs coming in form of audio signals. In this case, the Matlab software offers several functions for the proper understanding of this information, allowing us to translate the biomedical information to the Matlab workspace for the purpose of processing and analysis. Regarding the output information it is storage in the form of numeric matrixes and available to be gathered for posterior uses.

3.6.2 Self – descriptiveness

An interactive system is self-descriptive when, at any time, the dialogue guides the user in accomplishment of the assignment. For example is an input is expected and the user is keep informed about any changes happening within the
interactive system. For the ECG and PPG algorithm the process of analysis do not start until the input is charged in the Matlab workspace, additionally the process finishes with the display of the resultant analyzed parameters or outputs.

3.6.3 Conformity with user expectations

In order to correspond with the standards, which regulate the development of CL blood pressure monitors such as the IEEE 1708-2014 [48]. The appropriate linguistic conventions, which the standard recommends are adopted in the algorithm design.

3.6.4 Controllability

Matlab interface offers several functions to debug the execution program; as a result, user has the control over the steps and the outputs of the algorithm until the achievement of the main goal.

3.6.5 Error tolerance

Error tolerance relates to the operation of the interactive system although some errors in the input are found. In this case, the strength of the system to control, correct or manage the errors is assessed. In this case, Matlab interface offers two kinds of errors, the ones in form of warnings that the program can automatically correct, and the severe ones that stop the program execution and require user’s mediation. In both cases, explanation is given about the type of error, the address and the possible causes. As a result, the actions needed to correct the failure are minimized.

3.7 Conclusion

In this chapter, the internal and external factors that might affect the design and development of the algorithm for ECG and PPG joint analysis were studied. These aspects include the accuracy of the system and the proper use of the involved devices, in addition to the selection of the steps for the algorithm advancement, which might enhance its resultant performance. Consequently, the user requirements established in the standards, which regulate the development of medical enterprises were studied and considered.
GENERAL CONCLUSION

The development of the bioengineering system includes certain steps. The process arises from the study of the biomedical signals in order to identify its intrinsic characteristics; including signal recording using a mobile monitor and a sphygmomanometer. Furthermore, the course of artifact detection and removal in preparation of the biomedical signals for evaluation; continues with signal analysis to obtain reliable BP related parameters. Last but not least the control in which the correlation line and correlation coefficient are constructed in pursuance of algorithm’s feasibility validation.

This project has explored the capability of wavelet analysis as an innovative method for biomedical signal processing. Furthermore, to disclosure the idea of using only PTT for blood pressure estimation, some novel parameters from the PPG’s morphology were included to the assessment. The results show a strong correlation between the estimated and reference blood pressure to be in accordance with the task objectives. This open up opportunities for the cuffless estimation of blood pressure.

Although the presented pilot study offers, a potential method for cuffless BP measurement, it should be further validated with larger sample set with corresponding standard requirement, for example, the IEEE 1708-2004 standard for wearable cuffless BP measuring devices. Moreover, there are still some challenges regarding implementation.

The achieved results provide evidence of advance estimation of SBP while compared with its respective DBP. It indicates that new parameters directly linked to DBP should be considered to improve the estimation accuracy.

Eventually, by BP monitoring in an unobtrusive mobile – based way in which a decent accuracy is achieved, allows an improved hypertension control, therefore reducing the global burden generated by cardiovascular diseases.
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