A Wearable Device for Non-invasive Cardiac Monitoring

BY

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THESIS

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LIST OF ABBREVIATIONS

CVD	Cardiovascular diseases
UIC	University of Illinois at Chicago
RLD	Right Leg Drive
ADC	Analog to Digital Converter
HR	Heart Rate
PPG	Photoplethysmogram
PTT	Pulse Transit Time
IC	Integrated Circuit
BLE	Bluetooth Low Energy
SIG	Bluetooth Special Interest Group
SPI	Serial Peripheral Interface Bus
I2C	Inter-Integrated Circuit
MCU	Micro Controller Unit
IRB	Institutional Review Board

SUMMARY

Wearable continuous cardiovascular and physical activity monitors are becoming an integral part of comprehensive health management programs aimed at reducing hospital readmission, improving adherence to home- and tele- rehabilitation programs and increasing patients compliance and engagement in their wellness management plans. Furthermore, earlier detection of a heart disease can then lead to earlier intervention and treatment. Motivated by this observation, this thesis addresses the problem of designing a wearable device performing data acquisition and processing so that the device can be used to monitor heart failure patients not only in the hospital but also during day-to-day living activities such as walking, exercising, showering and sleeping. This device will increase cost effectiveness of tele-rehabilitation and provide objective health information to promote reimbursable clinical services. The most sought after features of this class of devices include unobtrusiveness, accuracy, ease of use and patient comfort and medical cost savings.

The Holter monitor is currently the most widely used device for outpatients, which usually records only the ECG trace and it does not typically have any real time communication; moreover, these class of devices cannot handle motion artifacts properly or the quality of recorded signal are degraded considerably in the presence of high level of exertion. The wearable device designed for this work, on the other hand, is able to record up to two leads ECG or one lead plus respiration, an embedded chest and an external finger probe photoplethysmogram(PPG). It has Bluetooth Low Energy (BLE) connectivity to send real-time data to a smartphone equipped

SUMMARY (continued)

with a graphical interface to display the readout and it is able to send the data recorded to a Cloud Server or by email. The capabilities of the designed monitoring device is complemented by Photoplethysmogram (PPG) inclusion with the purpose of measuring hemodynamic indexes and vital parameters that take into account also the peripheral circulation. In particular, a novel approach is developed to acquire the PPG from the chest which is usually associated with low dynamic range and low signal-to-noise ratio and therefore it requires more robust extraction algorithms.

Along with the device and the graphical interface, a set of digital processing techniques have been implemented to extract vital information from the raw data such as heart rate, heart rate variability and Pulse Transit Time in order to ensure the integrity and validity of the data even during activities. The proposed methods rely heavily on signal processing tools such as linear filtering and processing, adaptive filtering as well as a decisional algorithm that utilizes wavelet delineator. The proposed algorithm increase the accuracy of analysis features extraction during exertion or exercise and it achieves a high sensitivity with very low false positives observed.

CHAPTER 1

INTRODUCTION

In this chapter, the motivation of this work will be discussed including the aims along with previous work relevant to the subject matter of this thesis. To better elucidate the work, an introduction of the basics of electrocardiography and photoplethysmography will be presented.

1.1 Motivation

The annual worldwide death incidence due to cardiovascular disease (CVD) is estimated at 17 million people which is the preeminent cause of death and, unfortunately, this trend is expected to soar to 23.6 million by 2030 [1]. Furthermore, the economic burden due to health care expenses is estimate at 3 trillion dollars [2]. The same study points out that over the past few decades, high-income countries have lowered the death incidence due to heart failure, which is opposite to the trend that has been reported in low-income countries. This disparity is mainly due to the difference in the amount of investments in health care and cutting-edge equipment and devices. Cardiovascular monitoring in heart failure patients can lower the incidence of Major Adverse Cardiac Events (MACE) and improve the health related quality of life.

The World Health Organizations (WHO) summarizes the report saying: "Addressing cardiovascular diseases require concrete and sustained action in three areas which represent the key components of any global or national strategy; surveillance and monitoring, prevention and

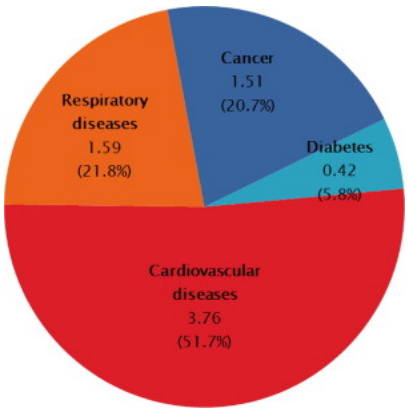

Figure 1: Economic Loss (Trillions of US$ in 2008) of Noncommunicable Disease in Low and Middle-Income Countries

reduction of risk factors, and improved management and health care through early detection and timely treatment." [1].

Monitoring can revert the aforementioned trend, conditional upon provision of health care services utilizing unobtrusive devices that patients can wear without interrupting their daily activity. Inpatient monitoring is necessary right after heart surgeries and heart failure, nevertheless, extending monitoring to outpatient is more cost-effective and yields more valuable information because it analyzes how the heart behaves during physical activity and routine activities of daily living or as a response to an emotion. In addition to monitoring disease progression, real-time physiological monitoring during activity of daily living can help establish baseline physiology and can provide objective measures for more targeted treatments and follow-up of the response of therapy and prognosis.

Nowadays there is an abundance of professional equipment for in-hospital care. These are not portable and cannot be used on a large scale for outpatient monitoring due to the high cost. Holter monitoring is the only method that is used for outpatients. It is a device that usually records three leads of ECG starting from 24 hours up to a week. The drawback is that it only records ECG for a post analysis, in fact, the majority of Holter monitors don't have connectivity for a real-time transmission.

It is true that ECG monitoring can diagnose or predict a lot of cardiovascular diseases such as tachycardia, arrhythmia, angina and myocardial infraction but it is a method that uniquely analyzes the activity of the heart. In the dedicated section 1.4 there is a complete overview of the ECG principles and techniques. Yet, the cardiovascular system is a more complex system that includes arteria, veins and microcirculation. These are susceptible to dysfunction and occlusion leading to strokes and ischemia which cannot be detected merely using the ECG.

The value of the Photoplethysmogram is that it can measure the light absorption of the blood, thus it can quantify oxygen saturation, arterial stiffness, blood pressure, Pulse Wave Velocity (PWV) and Pulse Transit Time (PTT). PWV is velocity of the blood from the heart to the recording site and PTT is the time that the blood takes to reach the peripheral recording site.

In this scenario it is warranted to design a wearable device that can be used by any health care provider to monitor heart failure patients, not only in the hospital but also during activities of daily living such as walking, running, showering and sleeping. A system that can give rich information regarding the heart and peripheral circulation conditions. Wearable continuous

cardiovascular and physical activity monitors are becoming an integral part of comprehensive health management programs aimed at reducing hospital readmission, improving adherence to home- and tele- rehabilitation programs and increasing patients compliance and engagement in their wellness management plans. These devices will increase cost effectiveness of tele-rehabilitation and promote reimbursable clinical services. The most sought after features of this class of devices include unobtrusiveness, accuracy and ease of use, patient comfort and medical cost savings.

Another motivation to design such devices comes from the academia. To our knowledge, there is not any multisensors reconfigurable wearable platform that researchers can use to collect data needed in their studies. The majority of researchers that work with biosignals use public online repositories, such as PhysioBank. Usually these are anonymized dataset from research trials and clinical records such as MIMIC II. This method can sometimes be limiting because of the restrictions associated with adhering to their protocols, selected sensors and settings. However it is still the first choice for many researchers for the following reasons:

- it is time-consuming and sometimes also hard to get approval from the Institutional Review Board (IRB) for compliance with human subject protection;
- these databases already contain annotations regarding important trace features. This allow the researches to validate their own algorithms, comparing the results with the annotations made by at least two independent experts;

If a research team needs to collect their own data, the available commercial offering will have their own set of limitations, for example: cost, obtrusiveness, proprietary formats and algorithms.

With that said, a custom device with reconfigurable biosignal acquisition is required to bridge the gap between biomedical researchers and engineering teams in order to optimize the system design and work flow.

1.2 Objective

The aim of this thesis is to design and validate a wearable biosignal acquisition and analysis platform that includes:

- a wearable device to acquire ECG, PPG and accelerometer;
- a graphical interface that displays and logs the signals in real-time.
- a set of tools and algorithms to extract vital information such as heart rate, heart rate variability and Pulse Transit Time.

Moreover, the platform should include a set of practical features such as:

- The device should be capable of recording ECG, PPG and accelerometer with a clinical grade quality. It must be a wearable device and must be as comfortable and unobtrusive as possible.
- The graphical interface must be implemented on a mobile device. It has to be able to interact with the monitor to control parameters of the acquisition chain. It must log the

raw data received from the device and send it to a Cloud server or by email at the end of the recording.

- Along with the monitor and its user interface, there should be a framework to download the data, convert into different formats, process the data and generate reports.

1.3 Previous work

This section summarizes the state of the art in terms of wearable ECG monitors. Numerous wearable ECG acquisition devices can be found in literature but most are lacking the ability to monitor the vascular component of the cardiovascular system and the modular multisensors open platform. These offerings are usually in the form of a patch which embed two electrodes or a small portable monitor. A few promising devices will be described in this section.

The first is HealthPatch MD developed by Vital Connect (Campbell, CA). It has one lead ECG, a 3-axis accelerometer and a temperature sensor. The battery lasts 3 days and it is disposable. The device is FDA cleared for marketing in the US.

The second one is Zio Patch developed by iRhythm Technologies,Inc. (San Francisco, CA). It does not have public specifications but from the number of electrodes (2/3) we can conclude that it records one lead ECG. The battery lasts 14 days and at the end of the monitoring period it has to be shipped back to the company for analysis. Both companies offer a service to analyze the data by certified cardiologists.

The most complete but less unobtrusive is the VisiMobile developed by Sotera Wireless, Inc. (San Diego, CA) which is also the closest to this work. The device consists of different modules: the device itself with a touch screen that shows the acquired data, a finger probe

for the photoplethysmogram , a cuff for the blood pressure and electrodes for the ECG. It can monitor blood oxygen saturation levels, blood pressure, heart rate, electrocardiogram readings and skin temperature. The readout from the sensor can also be accessed from a desktop computer or tablet.

Our goals is to design a multisensor and multiparameter wearable platform that includes, beside the ECG, a chest sensor and a finger probe. Usually the PPG is taken from the finger because a model to compute the oxygenation has been developed for the finger. The same principle can be applied at the chest after proper calibration and modeling.

1.4 Electrocardiography

Electrocardiography (ECG or EKG) is a diagnostic tool that measures and records signals arising from the electrical activity of the heart.

In the 19th century an Italian physicist Carlo Matteucci demonstrated that each heart contraction is due to electrical activity. It took almost 70 years to see the first clinical application with Augustus Desir Waller, at St Mary's Hospital in London in 1911. The next advancement was made by Willem Einthoven using a more precise galvanometer. He described for the first time the ECG tracing and labeled the different waves that are present in ECG, using the letter P,Q,R,S and T. This nomenclature is still used by physicians.

The heart is a muscle that is in charge of pumping blood in the circulatory system. Blood feeds all cells of our body with oxygen and nutrients and it washes away metabolic waste. The heart is composed of four chambers, two atria and two larger chambers called ventricles. The left part that include one atrium and one ventricle has arterial blood rich in oxygen content.

The right side has venous deoxygenated blood that is pumped to the lung for oxygenation. This process should be repeated at a certain rate to keep the cells nourished. A group of specialized myocardial cells make up the pacemaker which determines the rate of generation of the electric impulses that contract the myocardial muscle. These impulses are generated in the sinus node which is located in the right atrium. The electric stimulus starts in the sinus node and goes along the whole muscle across a conductive path. After the impulse is generated, it first contracts the upper section that includes the two atria and then move to the atrioventricular node, which is located between the atria and ventricles. It conducts the impulses from the atria to the ventricles. It also acts as a backup impulse generator at a lower rate of 40 bpm. The A-V node also delays the electrical impulses to give the atria enough time to eject their blood into the ventricles before the ventricles contract. After the ventricles have been depolarized and contract, the cycle starts over with another impulse from the sinoatrial(S-A) node. This process is possible because myocardial cells are different from other cell and they can transmit an electrical stimulus through conductive bundles that include Purkinje fibers and bundles of His. Current, and therefore voltage, is due to the opening of ion channels that allow an inlet and outlet flow of ions. This change in concentration causes potential difference between the inside and the outside of the cell. The process of polarization is when the voltage increases from a negative to positive. The process of repolarization is when the voltage decreases from positive to negative.

Using conductive electrodes placed on the patient's body, it is possible to analyze how the heart depolarizes and polarizes along different directions of the muscle. The external potential

of the cells is measured. This potential, in fact,can be sensed directly from the skin because the interstitial fluid is conductive.

It is necessary to use multiple electrodes placed in different parts due to the fact that the electrical activity has a well-coordinated pattern. To see if it is following the right path, the electrical impulse measured should be decomposed along different vectors. When the current flows toward the electrode this generates an upward deflection on the ECG traces and when it flows away from the electrode it produces a downward deflection, when there is no flow it stays at zero. Using multiple electrodes, the propagation of the action potential can be analyzed from different planes.

1.5 Photoplethysmography

Photoplethysmography (PPG) is a low-cost and non-invasive optical technique that measures the change in tissue optical density determined by light absorption and scattering. It is mostly used to measure the oxygen saturation but lately it has become a versatile technology and it is used in a variety of applications such as heart rate, by measuring the cyclic fluctuation in blood volume. Also, it can be used to measure blood pressure, cardiac output which is the amount of blood that is pumped in per minute, respiration, and arterial disease. All these applications require a light source to illuminate the skin and a photosensor to measure the reflected, absorbed and scattered light. Measuring the change in light intensity which depends on the blood volume, the pulse wave associated with each heart beat can be detected thus heart rate can be calculated. The accuracy of this method to determine the heart rate has been debated, nevertheless, some reports have shown it to be very accurate especially at rest.

For measuring the oxygen saturation two different light sources are needed at different wavelengths, one wavelength primarily absorbed by oxygeneted blood and the second primarily absorbed by deoxygeneted blood [3]. For this application the sensor has to be placed at the finger because the model of absorption has been developed with respect to the concentration of vessels at the finger.

The interaction of light with tissue is complex and includes optical phenomena like scattering, absorption, reflection, transmission and fluorescence. The important determinats affecting the amount of light received by the photodetector are blood volume, blood vessel wall movement [3] and light wavelength. The latter is important in light-tissue interactions and it is directly correlated with the penetration depth.

PPG is composed of an AC component and a slow changing signal (DC Component). The AC has the fundamental frequency related to the heart rate that goes from less than 1 Hz (60 bpm) to 3Hz (180bpm). The slow changing part has low frequency components related to respiration, vasomotor activity and neurogenic components.

1.6 Pulse Transit Time

Other vital parameters can be obtained merging some information from the ECG with other information from the PPG. One example is the Pulse Transit Time which is a measure of the time elapsed between the electrical activity of the heart represented by the R wave and the optically measured arrival of the pulse wave to a peripheral site. It can be measured as the difference in time between the R peak of the ECG and a reference point on the PPG (onset or peak) recorded at a peripheral site commonly at the finger. It has been shown that it has

a correlation with systolic blood pressure but it is also a function of the arterial stiffness. As a result, it cannot be used to directly measure blood pressure because it is subject dependent. However, it can detect changes in blood pressure once it has been calibrated using the standard cuff method and employing a ratiometric prediction algorithm.

The main advantage of such a method is that it may provide the basis for a continuous non-invasive measurement of cardiovascular parameters unlike the standard cuff method which is not continuous because a pause of at least two minutes is required to avoid errors in the measurement. Furthermore, even if it is not invasive it is an obtrusive method that interferes with the patient's daily activities.

CHAPTER 2

DESIGN CONSIDERATIONS

In the previous chapter, motivations for a wearable cardiac monitor were presented. In the following, relevant design considerations that have to be addressed in the implementation of such a monitoring device will be discussed.

2.1 Specifications

A summary of the biosignals required for data acquisition along with the minimum specifications is presented in Table I ,Table II and Table III.

2.2 ECG

In this section the most noteworthy technical and design issues that arose during implementing and testing an ECG acquisition system will be investigated. The peculiarity of such a system is mainly the low voltage amplitude of the signals acquired. For this reason, almost all the design will be focused on improving the signal-to-noise ratio. The following are the essential system components starting from the electrodes, down through the analog and digital chain and ending eventually with various requirements of signal integrity.

Electrodes

The electrodes are necessary to pick up the action potential once it reaches the skin. The electrical activity triggered by the heart arrives at the skin thanks to interstitial fluid conductivity.

TABLE I: ECG SPECIFICATIONS

Specification	**Minimum**
Leads	1
Bandwidth	0.5-40 Hz
ADC Resolution	12bit
Input Referred Noise	25 uV peak to peak
CMRR (@60Hz)	60dB

TABLE II: PPG SPECIFICATIONS

Specification	**Minimum**
Colour Led	Red,Ir,Green
Sampling frequency	400Hz
ADC Resolution	12bit

TABLE III: ACCELEROMETER SPECIFICATIONS

Specification	**Minimum**
Bandwidth	100Hz
Sampling frequency	10Hz
Range	4g

Since this transfer of potential involves ions as charge carrier, the aim of the electrodes is to convert the potential that is transmitted trough ionic current into an electric current which can be sensed by an acquisition system. The electrode is made by an electrical conductor connected with an ionic solution. The most common adopted electrodes for biosignals measurements use silver as a metal and an electrolyte gel, as an ionic solution, where the principle anion is Cl-. Cl- is adopted because the skin interface contains an excess of chloride ions. The electrolyte gel is not essential because the body already represents the ionic media but it helps to improve the conductivity. To have an exchange of charge, a redox reaction occurs at the interface between the metal and the ionic solution. The redox reaction is between the chloride ions which are anions in the electrolyte and the silver. The result is silver chloride and free electrons that flow to the analog front-end through the electrode wire.

Amplifier

Because the signal amplitude is on the order of millivolts or less, an amplifier with high differential gain is required. The most common topology used for ECG and biopotentials is the Instrumentation Amplifier (IA). Along with the amplifier, some filters and an analog to digital converter are also needed. This is the basic analog chain but more circuit elements can be added to overcome some problems and improve the signal quality.

Other Consideration for an ECG Acquisition Design

Going into more details of design, several issues need to be considered in our design:

- Locations of the electrodes;
- Common-mode and differential-mode voltage;
- Level of Safety and Defibrillator Protection.

2.2.1 Electrodes and Locations

To obtain reliable measurement of ECG, electrodes play a major role in the measurement chain. If used incorrectly, they can introduce distortions several orders of magnitude larger than the ECG signal itself.

For a wearable monitor device one lead is sufficient (Table I) to detect abnormalities in the ECG trace. A configuration with three electrodes has been used to improve the CMRR even if one lead needs only two electrodes. In section 2.2.2 there is an expanded discussion on the use of a third electrode. Depending on the position of the electrodes, heart activity can be seen from different angles.

The ECG leads are grouped into frontal and traversal leads which can view the heart from a vertical and horizontal plane respectively. The frontal Leads and especially Leads I and II provide an unobtrusive placement and provide a diagnostic quality ECG.

2.2.2 Common-Mode Rejection Ratio

The acquired ECG signal is affected by different levels of interference. One of the most important sources of noise is the common-mode voltage which is the voltage that the body has with respect to the acquisition system. The device should sense only the differential voltage between two points, however part of the common mode voltage can be sensed as differential voltage. The aim is to minimize the effect or lower the voltage itself.

A model of interference needs to be constructed and used to reduce the effect. Coupled interference can be modeled using capacitance, for example a significant amount of electromagnetic interference is coupled to the body though the skin [4]. There are capacitances also between the body and the power lines and earth. These capacitances have been quantified to be around 300pF (between body and earth) and 3pF (between body and power lines) as reported by Huhta and Webster (1973) and by Forster (1974). The cables as well are coupled with the mains. The currents induced in the wires flow through the electrodes, it reaches the body and goes to the earth. The capacitances that the amplifier common has with the power line and the earth should also be considered. The last two can be ignored in our case because the device is battery powered. Figure 2 show the model that we have just described. All these modeled capacitors cause an unwanted current flow and therefore a noise voltage that can be differential or common mode voltages. The problem with the common mode is that it can be converted in differential voltage as a result of impedance mismatches such as electrodes impedance and cables impedance. The actual CMRR, in fact, can be lowered if the impedance of the electrodes are different by an amount proportional to the common mode voltage and the ratio between average electrode and input impedance.

There are different ways to improve the CMRR:

- Reducing the amount of common voltage that is converted in differential voltage. (reduce mismatch: precision component, cables length, increasing the input impedance, reducing the series impedance)

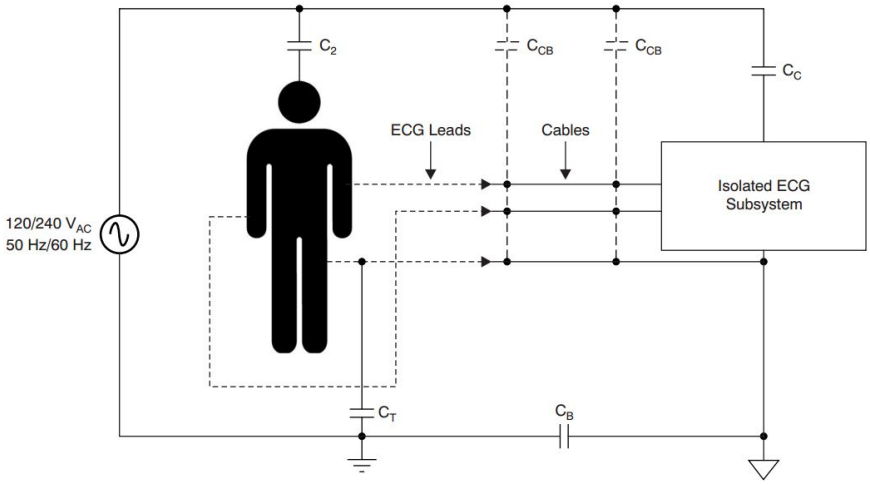

Figure 2: Model interference with capacitances.
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- Improving Isolation Capacitance: improving the isolation of the device can improve the CMR. In our case the device is battery powered, so a good isolation is already present in the circuit;
- Post Processing: if the interference is solely attributed to power interference and the frequency is determined (such as 50Hz USA, 60Hz Europe) using a digital notch filter is effective to get rid of the powerline noise.
- Faraday Shield: Covering the electronic front end with a Faraday cage can reduce the environmental interference;
- Lowering the common voltage with a Right-Leg Drive Amplifier circuit (RLD). This circuitry drives the body to the opposite voltage that it senses as common. It tries to

reduce the voltage difference between the body and the device common. This arrangement can be implemented using a closed feedback loop.

Interestingly, the last method is quite effective and it is the only technique that acts at the source of the noise, thus reducing the common-mode. The following summarizes how the Right Leg drive works. Simply connecting the device to the body though an additional electrode could reduce the common mode voltage because both the body and the device will have the same common. Looking at the model means minimize the difference between the capacitance between the body and the earth and between the device and the earth thanks to the low impedance path provided by the third electrode. Unfortunately this approach is undesirable for two reasons:

- it is not safe since it can cause current leakage thought the body;
- a poor electrode connection may be even worse because it can have up to 100 kohm resistance.

The right leg drive circuit is twofold in that it can overcome these problems. It is called this way because the third electrode is usually connected to the right leg.

The idea behind it is to add an extra amplifier that drives the patient body to the same voltage of the amplifier common since the two systems cannot be connected. To achieve this aim, the common mode can be measured and injected into the body with a reverse polarity voltage.

The mechanism explained is a closed loop system. There is a simpler implementation driving the patient using a fixed voltage but it is less effective. The RLD amplifier is configured as an

integrator that adjusts its output voltage to keep its inverting input at the same potential as the voltage applied at the non-inverting input. Figure 3 show the circuit that can implement this feature. The CMR is improved by a factor equal to (1+G) where G is the closed loop

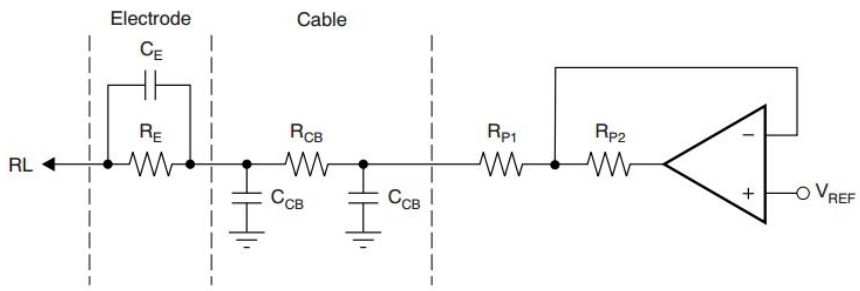

Figure 3: Right-leg drive circuit.
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gain. The value depends on the value of the feedback resistor [4]. Since the RLD amplifier is an integrator, the cutoff for the integrator time constant is determined by R and C. This RC combination establishes the dominant feedback path around the RLD to ensure stability of the overall loop. Without it, the dominant feedback path in most cases produces a loop that is not stable.

The downside of this technique is that it fails when an electrode detaches, because it causes the output from the amplifier that represents the common mode to be driven away from the reference voltage. Accordingly, to fully take advantages of this technique the effectiveness of the

electrodes' contact has to be monitored. Most of the integrated front-end provides a lead-off circuit to make sure that the electrodes are properly attached.

2.2.3 Safety and Defibrillator Protection

Designing devices that are in direct contact with the human body requires a lot of attention to meet the highest standard of safety. The two main safety requirements to satisfy are the maximum leakage current and the defibrillation protection circuit.

The maximum allowable current that may flow through the electrodes is set at 10 uA rms by the IEC 606601-1 standard. Especially AC current can be dangerous, in fact, it has been shown that 34 uA rms at 50Hz/60Hz can compromise the heart. To limit the current that may flow through the patient's body and the device, a current limiting resistor can be placed in line with the electrodes. It can be embedded in the cables or placed on the circuit board. The resistors should be matched to avoid lowering the CMRR. This issue has been addressed in more detail in the previous section.

To meet the second requirement the following points have to be satisfied. The device should be protected from high voltage generated by the possible usage of a cardiac defibrillator. At the same time it should not dissipate more than the 10 % of the defribilator's power. In addition, hospital monitors have to continue to operate within a few seconds of the discharge. However, ambulatory monitoring devices such as Holters and event recorders are not required to recover after the defibrillator discharge. The defibrillator can shock the patient with a discharge of 100 to 200 joules at 1000 Volts.

The standard tests for defibrillator compliance is by applying 5000V discharge at 360 joules across a 100 ohm resistor that simulates the body resistance. The ECG device being tested is connected in parallel across 100 ohm resistor, therefore to assure less than 10% shunt current, the resistors used in the ECG electrodes should be at least 1 kohm. Such high voltage will damage the device and it needs to be clamped down to a voltage level that does not exceed the device power supply rails. Since the voltage and the power are too high, a two steps approach is necessary to lower the voltage to manageable level. The first stage can be implemented using neon lamps but these have a large footprint or a power TVS such as SMBJ-14. The voltage reached is still too high compared to the power supply voltage. A second stage is needed to lower the voltage from 14 V to 3.3 V. For each input a dual Schottky diode after the HV clamping component is required. One Schottky diode is connected to Vss and the other to Vdd so they will conduct if the input voltage exceeds power or goes below ground. It has been implemented using RClamp3304P which is a low capacitance schottky array designed for high speed data interfaces to protect overvoltage by ESD, CDE and FET. Furthermore, a series resistor must be chosen to limit the current through the secondary stage.

2.3 PPG

The system requirements to get a photoplethysmogram include few optoelectric and electronic components:

- A light source: an integrated LED possibly with multiple wavelengths;
- An led driver to have control over the current of the LEDs;
- A photosensor to measure the reflected and scattered light;

- An analog front-end for signal conditioning and acquisition.

The photoplethysmogram takes advantage of the light interaction with biological tissue. When the light interact with a medium, in this case the skin, multiple phenomena such as scattering, absorption and reflection take place. The reflected and scattered light can be measured converting the light into voltage.The analog front-end requires an amplifier configured as transimpedance to convert the current generated by the reflected and scattered light that reach the photosensor into voltage. There are integrated circuit that includes a signal conditioning, a LED driver and an analog to digital converter along with a digital interface to communicate with a microcontroller. This solution keeps the footprint small and gives more flexibility to the system with the possibility to set some parameters such as gain, integration time and led current. Furthermore, this approach offloads the central MCU from the task to acquire the analog signal using the embedded ADC.

The considerations to improve the signal quality and dynamic range include:

- Selecting the optimal wavelength of the LED;
- Optimizing the LED current and gain;
- Optimize the wavelength and distance between light source and photosensor for a certain penetration depth;
- Selecting the best location on the chest for signal acquisition.

Selecting the optimal wavelength

The aim of this work is to have a PPG sensor with high signal-to-noise ratio. There are two ways to address this problem: increase the power of the signal and/or decrease the power of the noise. To increase the power of the signal which is the dynamic range, the wavelength should be chosen to have the highest absorption interacting with the blood. On the other hand, to reduce the noise settings, design and configurations that can lower the effect of the motion artifact need to be found.

What makes PPG works is that the blood contributes more to the pulsating component of the optical density acquisition than the surrounding tissue. Therefore, an increase in blood volume during a cardiac cycle is detected as an increase in the light absorbed and a decrease in the transmitted or reflective light. Each element, tissue and medium has a different response and it mainly depends on the wavelength used. Melanin absorb the shorter wavelengths of light. Water absorbs light in the ultraviolet and longer IR spectrum range. As a result, PPG sensors use mostly red and near-IR wavelengths as light source. However, green-wavelength PPG photosensors are widely used especially for fitness tracker or devices where it is important to reduce the motion artifacts and therefore have a high signal-to-noise ratio. A green LED has higher absorbance for both oxyhaemoglobin and deoxyhaemoglobin compared to infrared light resulting in an higher dynamic range for the green light source [5].

Optimize wavelength and distance between photosensor and LED for a certain penetration depth

Moreover, the wavelength along with the distance between the LED and photosensor determine the penetration depth of the light in the tissue. For example, green light can be absorbed by shallow tissues, while, IR or near-IR wavelengths are suitable for more deep tissue, therefore it can measure blood flow in muscles.

Location and skin coupling

Some design decisions should be taken depending on the location and to reduce motion artifact. In this work the chest has been chosen as recording site for the PPG and to acquire the PPG without much interference from the external light and to be comfortable and unobtrusive to use the device was coupled to the skin using a rubber band or strap to improve contact and keep the sensor uniformly pressed against the skin and decrease motion effect.

In the section 5 others processing methods to reduce artifacts will be described.

2.4 Bluetooth Low Energy

In this section some fundamental concepts of the Bluetooth Low Energy (BLE) and associated design consideration will be presented.

2.4.1 Background

The BLE is a wireless communication standard. It is the power-saving variant of the well known Classic Bluetooth, that emerged to serve the growing market of battery powered IoT and wearable devices such as smart watch, fitness tracker, connected car and intelligent lighting. Nowadays it is extensively adopted and supported by all mobile phone manufacturer as a defacto standard for short range connection or Personal Area Network (PAN).

It uses the 2.4GHz unlicensed radio band with a frequency hopping scheme which means that once two devices are connected they switch from one channel to the other. This technique is used to improve the immunity to interference because the 2.4GHz band is occupied by other communication protocols.

Although the maximum Bandwidth specified for BLE is 1 Mbps the effective bandwidth is lower. In the next section there is an analysis of the throughput and how to increase it to meet the requirements of this application.

Even if the BLE is the successor of Classical Bluetooth they are not compatible because the protocol is different.

Without going into the details of each layer, the communication protocol we can divide in three main blocks:

- Application
- Host
- Controller

The application interfaces with the protocol stack. Host and Controller represents respectively the upper and lower layer of the Bluetooth protocol stack. The stack can be divided in two parts because they have different requirements in terms of latency. The controller interfaces directly with radio which requires low latency.

Also, the specifications provide a standard communication protocol between the host and the controller (Host Controller Interface) to allow compatibility between hosts and controllers

of different manufacturers. Each block can be implemented in a single IC or in different ICs with three possible different architecture:

- SoC (system on chip);
- Dual IC over HCI;
- Dual IC with connectivity device.

Each of these configurations has some advantages and drawbacks. The system on chip solution uses one single IC where it runs application, host, and controller. It is the best choice in terms of footprint albeit with increased latency due to the use of one MCU for both stack and application.

The second solution adopts two ICs communicating over HCI. The controller run on an IC and communicate with the application and the host on a different IC, thus it is more modular and unblocking. It lowers the load of the application MCU but it has a larger footprint which is not optimal for a wearable device where the size is critical. The main advantage of this approach is that it allows interoperability between manufacturer because the HCI is defined by the Bluetooth specification.

The last approach has two ICs as well but it implements the host and controller on one IC and it interfaces with a second IC that has the application. The protocol used by the two ICs to communicate is proprietary because the Bluetooth specifications does not include any protocol between application and Host. This solution is not recommended unless Bluetooth connectivity is being added to a Legacy application.

2.4.2 High Throughput

Although, the Physical Layer uses a over-air data bandwidth of 1 Mbps it does not mean that the bandwidth is 1Mbps because the communication protocol define rules that limit the throughput, for example:

- Protocol overhead such as packet length, data integrity check, and general packet information;
- Connection Interval;
- Maximum numbers of packets per connection.

Master and peripheral devices communicate with one another on a given period called Connection Interval (minimum of 7.5 milliseconds up to 4secs). A communication event starts by the central (master) transmitting a packet while the peripheral device is in receive mode. If the peripheral received the packet from a central successfully, the peripheral will subsequently transmit its packet while the central is in receive mode. By default, the central and peripheral will transmit a packet even if they have nothing to send, this is often called Empty Link Layer PDU . For the cases when the central and peripheral have queued up messages, they can ask or alert the other side that they have more data to send before ending the connection event. This can result in multiple packets being exchanged during one interval. The connection event continues until a packet either fails to be received correctly, the sender is satisfied with ending the connection event, or the end of the interval has been reached. It is important to know that maximum number of packets per connection event is dependent on the BLE stack and chipsets

and is limited to 4 packets per connection event with iOS, and 6 packets per connection event in Android. In order to achieve the theoretical maximum throughput values, the system and the design of the devices must seek to use all the available time slots in a connection event to transfer data and lower the time between two connection interval.

Lower connection interval

As a peripheral/slave, one can request for the connection interval to be lowered (if applicable) using a Connection Parameters Update Request message. Some Android devices may connect at slower connection intervals initially before lowering the connection interval when requested.

Proper Methods to Transfer Data

Transferring data to and from the BLE devices can be achieved in multiple ways. In order to achieve higher throughput, the method that allows for more than one packet in a connection event needs to be selected. One should use Write Command instead of Write Request when sending data from a client to a server, and Notification instead of Indication when sending data from server to client.

CHAPTER 3

IMPLEMENTATION

The previous chapter has delineated some special aspects to be considered in the design of a wearable biosignal acquisition system. This chapter will describe how the system has been implemented. After a system overview, details of each aspect will be provided. At the end of the chapter the specifications and performance that have been achieved will be presented. Validation and data analysis in a clinical setting can be found in Chapter 4 and Chapter 5.

3.1 General Overview

The overall system that is depicted in Figure 4 includes: a wearable device, a mobile application and a set of digital signal processing techniques to extract target information from the raw data. The wearable device is the only element in the system that involve some hardware components and it performs the task of acquiring and transmitting the signals over BLE.

First, the mobile application has to pair with the device, then it sends the configuration settings input by the user for that specific recording session. Once the device is configured, it is ready to start recording and the mobile application retrieves the raw data from notification packets. The data are saved on the internal memory and displayed through the graphical interface. Furthermore, it has the functionality to send, at the end of the recording, the logged data along with the configuration by email or upload it to a Cloud server. Google Drive has been used as Cloud storage for this project.

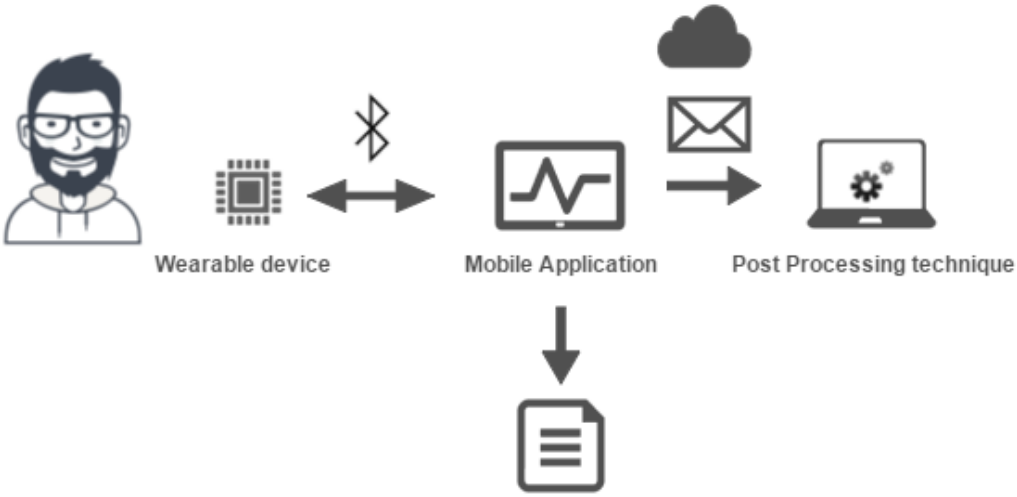

Figure 4: System overview.

At this stage the recorded data are available for post processing to extract the sought information. The data are logged on the mobile packet by packet using a Json format that includes an incrementing packet number. This solution facilitates the debugging of possible problems that can arise from the communication and it helps to identify missing packets. A python script has been implemented to download and decode each packet and create an excel file. At this point, Matlab scripting language has been used to process them.

The implementation has to meet the requirements listed in Chapter 2.

3.2 Hardware

In this section the wearable device will be analyzed from a hardware point of view. Aside from the functionalities that it has to accomplish, there are other crucial aspects to be considered in the implementation such as size, comfort level and safety standards. The wearable

perform five tasks: acquisition of three signals (ECG, PPG and accelerometer), collection and transmission of data. Figure 5 shows a complete overview of the hardware architecture. The

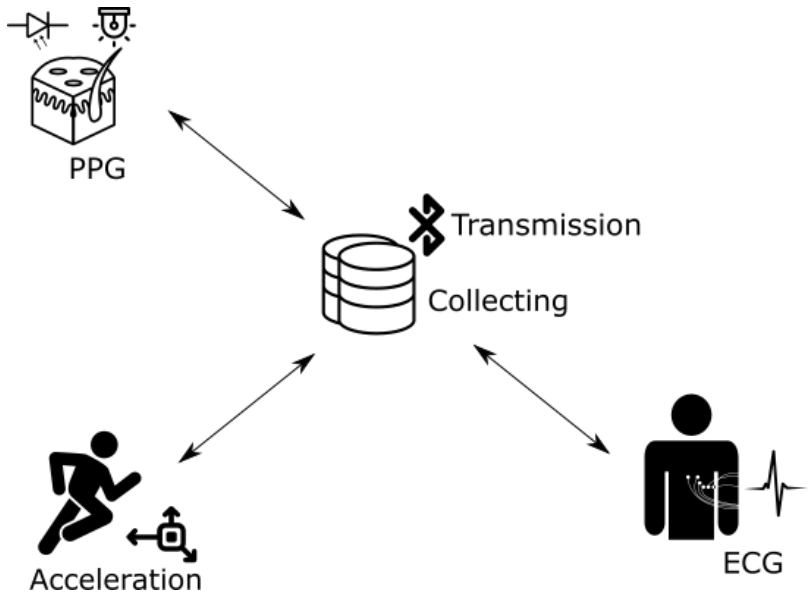

Figure 5: Hardware overview.

main MCU has to retrieve the data and send them over BLE. It interfaces the ECG subsystem using SPI protocol, to the PPG and accelerometer sub-systems using I2C protocol. To accomplish these goals a few electronic components have been chosen after a comparison analysis: a microcontroller, an ECG front-end, an integrated photosensor with led driver, a multi wavelength LED, and a tri axial accelerometer.

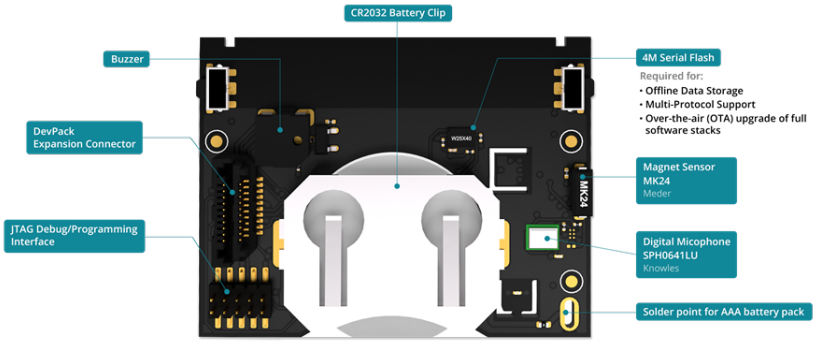

Figure 6: SensorTag back.
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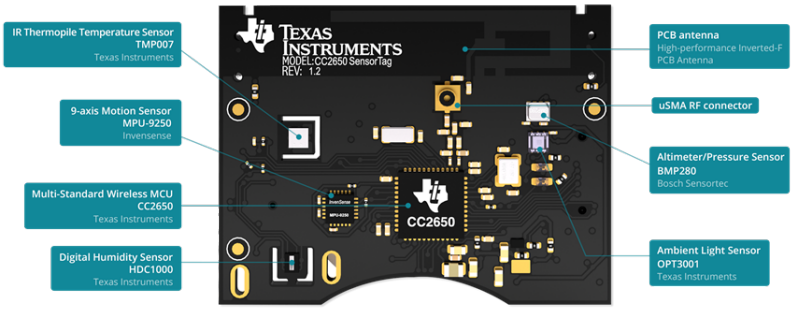

Figure 7: SensorTag front.
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The hardware has been implemented using two boards. A main board,CC2650 based Sensor Tag from Texas Instrument (Dallas, TX) and a daughter board custom designed for this application. Figure 6 and Figure 7 show the main board along with the list of available sensors on board.

This approach allows us to build our platform based on a field tested device. Only part of the resources of the Sensor Tag will be used, which are the MCU (CC2650) and the accelerometer

(MPU9250). The expansion connector has been used to connect the Sensor Tag to the daughter board. The latter will be described in details in the section 3.2.5. The programmer and debugger used is the XDS110 Debbuger DevPack from Texas Instrument and it adopts the same expansion connector. In the next sections we provide a technical description of the integrated ICs used and its rationale.

3.2.1 Controller

The microcontroller is an essential component in an embedded system. It is an integrated circuit with a processor unit, memory along with peripherals.

To make the right choice according to the requirements,a few chipsets will be compared. Nordic Semiconductor represents one of the pioneers in the Bluetooth industry. Other manufacturers to be considered are Texas Instrument that has the know-how in the RF design and other such as Cypress and Silicon Lab.

Table IV depicts a comparison between two MCU that are the most suited for this application: the CC2650 and the nRF52.

They have almost the same characteristics. The CC2650 has a bit better sensitivity and power consumption but it has less computing power since it is equipped with a Cortex M3 running at 48MHz. The nRF52832 has a Cortex M4 running at 64MHz that makes it more powerful in terms of processing capabilities. The cortex M4 architecture has a DSP module that can be used to process the data and send only the results which may lower bandwidth and power consumption.

TABLE IV: MCU COMPARISON

Features	**TI CC2650**	**Nordic nRF52832**
Processor	Cortex M3 @ 48 MHz	Cortex M4 @ 64 MHz
Flash and RAM	128 KB/ 20 KB	512 KB 128 KB
Peripherals	2 SPI, UAR, I2C, Sensor Controller Engine	SPI, I2C, UART, I2S, DMA
Receiver Sensitivity	-97 dBm	-96 dBm
Transmitter Power	+5 dBm	+4 dBm
Current RX/TX (0dBm)	5.9 mA / 6.1 mA	5.5 mA / 5.5 mA

What makes the CC2650 more suited is its unique architecture. In fact, it implements a 'dual IC' stack over one IC. It embeds a Cortex M3 core for the upper layer of the protocol stack and a Cortex M0 for the physical layer. They interface with a HCI proprietary of Texas Instrument and not the HCI defined by the SIG. Figure 8 shows the CC2650 block diagram.

This architecture approach lowers the load of the main MCU allowing less latency in the acquisition tasks that will be implemented.

Both companies have support for the firmware with an SDK. In the section 3.3.1 a few particular aspects of the firmware will be described.

3.2.2 Analog Front-End ECG

The real challenge designing an ECG front-end is the high amplification and high CMRR required because the ECG signals are in the order of few millivolts peak to peak and are

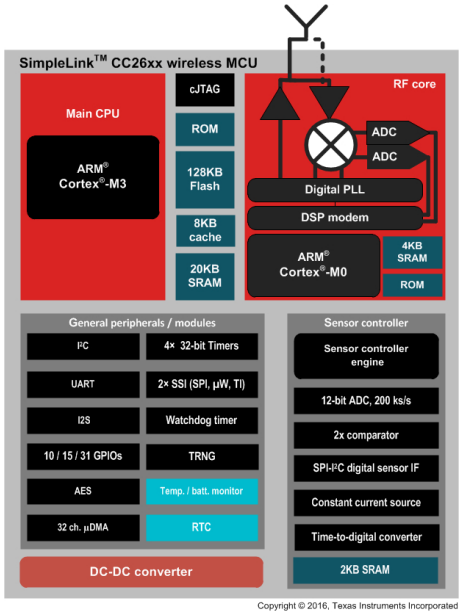

Figure 8: CC2650 Block Diagram.
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contaminated with different kind of noise. One of the most important source of noise is our body that acts as an antenna capturing electromagnetic interference.

There are two approaches for the acquisition chain of signals with low signal to noise ratio and low amplitude:

- A discrete analog acquisition chain;
- A module that integrates all the elements required for the acquisition chain including a digital communication interface.

The first solution can be implemented with a discrete instrumental amplifier which fulfills the requirements of high amplification and high CMRR. One example extensively used in biomedical

application is the INA family from Texas Instrument. Along with the amplifier, the acquisition chain needs other elements such as filters and an ADC. Most MCUs have general purpose ADCs that do not satisfy the requirements to acquire a clinical grade ECG trace. It is clear that the discrete solution is not recommended due to the large footprint and the inflexibility due to the inability to change parameters once the passive elements have been chosen.

An application-specific IC that implements an ECG Analog-Front End (AFE) is more feasible for its smaller size, lower power consumption and the possibility to configure parameters of the analog chain setting the value of configuration registers through a digital communication interface. Furthermore, the integrated approach has added other features that can be used to improve the signal to noise ratio such as an integrated RLD and shield drive circuits.

Table V makes a comparison between available integrated circuits that implement a complete front end for biosignals acquisition. The HM301D from STMicroelectronic is promising in terms of power consumption but it is still in evaluation and it does not have a RLD drive circuit which it is a crucial element to improve the CMRR. The ADAS100 has some useful features such as the shield drive circuit and pace detection but it has the highest power consumption and larger footprint compare to the other available options. The ADS1292 from Texas Instrument represent the best trade off between functionality and power consumption. The ADS129x series which integrates two channels analog front end and SPI digital communication interface. Each acquisition channel includes a programmable gain amplifier (PGA) and a delta sigma 24-bit data converter and electromagnetic interference (EMI) filter. Also, the module provides also other functionalities such as a right leg drive (RLD) amplifier, lead off detection circuit and a

TABLE V: ECG FRONT-END COMPARISON

Features	**ADS1292**	**HM301D**	**ADAS1000**
Manufacturer	Texas Instrument	ST	Analog Devices
Channels	2 channels or, 1 channel+respiration	3 channels	3 channels+respiration
Communication	SPI	SPI	SPI
Power Consumption	335 uW/channel	1mA/channel, (3.3 mW/channel)	15mW (3 leads)
RLD	Yes	No	Yes
Respiration			
Resolution	24bits	16bits	19 bits
Others features	None	Body impedance	Shield Drive
Lead-off detection	Yes	Yes	Yes
Pace detection	No	Yes	Yes
Maximum sampling rate	8 kSPS	10 kSPS	8 kSPS
Price	10$	(12$) in Evaluation	20$

respiration module. The central MCU has to initialize the IC configuring sampling frequency and gain for each channel, then enable the interrupt mode and when it is ready send a start command. An interrupt will be triggered at the end of every acquisition alerting the MCU that a new sample is ready to be retrieved. This decentralized architecture offloads the MCU and therefore lowers the system latency.

Each channel has an EMI filter with bandwidth of 3MHz at -3dB and the input signal can be chosen between different sources that are: direct signal from the electrodes or after the respiration module, the internal temperature sensor and the internal signal generator for debug purpose. The conditioning circuit has a PGA with programmable gain from 4 up to 12. Following the PGA there is a filtering stage that has an internal resistor of 2 kohm that with an the external capacitor set the cutoff frequency of the filter to remove the glitch from the PGA output and acts as a antialiasing filter. A 4.7nF external capacitor that has been used to set the cutoff frequency at 8.4kHz at -3dB.

To improve the CMRR the integrated right leg drive amplifier has been used. The average of two electrodes signals has been chosen as reference signal. Few passives are needed to have the system stable. To have a approximately bandwidth of 106Hz, a capacitor of 1.5nF and a 1 Mohm resistor for the feedback loop and a 100 kohm for the limiting current resistor have been used [4].

Since the IC allow us to have a respiration measure as well, the design of the external circuit has been implemented in a way that depending on the passive that are populated it is possible to select between two configurations: two channels differential ECG to use to record 2 different leads or one channel ECG and use the second channel to feed the respiration module. For the first approach four electrodes are needed, for the second, instead, three electrodes are needed considering always a configuration with the drive leg drive circuit.

To connect the electrodes cable to the board a 2.5mm jack with four contacts has been adopted which represent the smallest solutions for an easy plug in solution without the need of screws.

3.2.3 PPG

The photoplethysmogram portion of design has been implemented using the SI1147 Light sensor from Silicon Labs (Austin, TX) which comprises all required elements including three photodiodes (a large IR, a small IR and visible), preamplifier, analog to digital conversion on chip and a led driver acting as current sink which can drive up to three LED from 5mA to 300mA. The microcontroller interfaces with the PPG sensor over I2C communication protocol in an interrupt activated mode rather than a polling mode. Photoplethysmogram acquisition parameters, including the forward current and pulse widths of the attached LED are controlled by setting the internal configuration registers which give more control over the data acquisition and its dynamic range by controlling the LED driving current and the time that the LED have to be on. The chosen RGB LED was the LE RTDUW S2W from OSRAM (Munich, Germany).

3.2.4 Accelerometer

The requirements for the accelerometer are not very strict. The accelerometer onboard of the SensorTag was used which is the MPU9250 from Invensense (San Jose, CA) and configured for a sampling rate of 60hz with 180Hz of bandwidth and 8g of range.

3.2.5 PCB

The application-specific PCB layout has been carried out in Altium Designer Software (v16). The board has to be connected on top of the main board through the expansion connector. For

this reason the size of the board should be the same a that of the main board or smaller. We have designed a dual sided board because the photosensor and the LED has to be on the side in contact with the skin while the rest of the components should be on the other side.

Following the PCB layout guidelines [6] provided by Texas Instrument, a few issues need to be considered in the PCB layout regarding the ECG front end. The ADS1292 has two power supplies: one for the analog front end and a second one for the digital circuit. Both should be bypassed with 10-uF and a 0.1-uF solid capacitor. The supply for the analog section should be low noise and possibly shielded and connected directly to the supply. The return current from digital circuit such as the microcontroller should not cross the ADS1292 and the analog supply. The capacitor that determine the cutoff frequency after the PGA should be placed as close as possible to the ADS1292.

Regarding the design of the LEDs and the photosensor since they drain more power compared with the rest of the system, they have been placed in a section that don't cross the analog biosignals acquisition. For the external finger probe a small board from Silicon Lab has been used which provides the SI1147 along with the capacitors needed. It connect to the application specific board through a flat flex connector. The board has been manufactured by a company along with the stencil. Assembly and re-flow using the T962A SMD Reflow Oven was done manually. To guarantee isolation between the wearable and the patient body a layer of conformal coating has been added. The device in fact should be isolated from the body to improve the CMRR and for safety reason addressed in section 2.2.3.

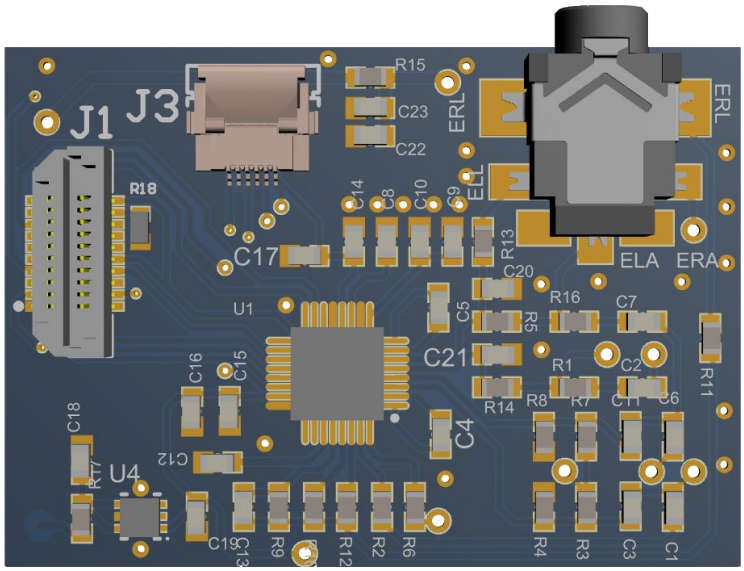

Figure 9: Top layer of the designed PCB.

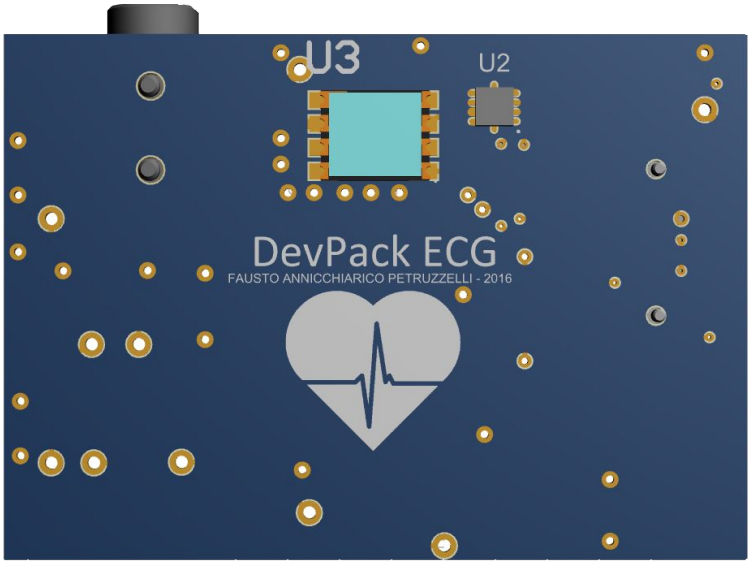

Figure 10: Bottom layer of the designed PCB.

3.3 Software

This section aims to describe the software necessary to have the complete system working. The software part will include either the firmware that will run on the embedded device and the android mobile application.

3.3.1 Firmware

The firmware plays an important role in the system and represents the semi-permanent software that will run on the microcontroller which is in our case the CC2650. In terms of firmware we will focus mainly on an architecture that can ensure a real-time acquisition needed to guarantee synchronized signal acquisition with equispaced samples. It has to acquire the data from the sensors and send it over BLE. Both acquisition and sending data have strict requirements in terms of latency because the system should react to each interrupt triggered by the sensors to retrieve data and be able to catch all the asynchronous connection event of the BLE to be able to send all the acquired data.

It is crucial to design a software architecture that satisfy these requirements and the choice was to take advantage of a Real-Time Operating System (RTOS) which is an operating system with a deterministic execution pattern. Usually every application has multiple tasks that need to run at the same time but each processor can have only one thread that means only one task running at time. The difference between a general purpose OS and a RTOS is in the scheduler which is the module that decides which task has to run based on some rules. In a RTOS the unique rule is the priority resulting in a deterministic pattern.

TI provides a Software Development Kit (SDK) for the Bluetooth microcontroller CC2650 that includes a RTOS and a Bluetooth Stack. The TI-RTOS is a royalty-free OS based on the SYS/BIOS kernel and operates as real-time, pre-emptive, multithreaded operating system with tools for synchronization and scheduling.

The Bluetooth Stack is designed to take advantage of the hardware architecture of the CC2650. The CC2650 it is a multi-standard MCU that supports different wireless protocols such as BLE. It is more than a MCU, in fact, it embeds three MCU which are: a cortex M0 (CM0), a cortex M3(CM3) and a low power sensor controller.

The CM0 (radio core) is in charge of the physical layer. The radio firmware has been designed from TI and the developer should not modify it. This allow to frees up the CM3 (system core) that is responsible for all the other layers from the physical to the application. The application is the application-specific firmware designed to satisfy the requirements. It interacts with the stack through a set of APIs called Indirect Call Framework (ICall) which provide communication between the application and the Bluetooth Low Energy protocol stack. Furthermore it provide methods to abstract some operating system functions such as messaging, thread synchronization and heap allocation and management. Due to shared resources and to maintain interprocess communication, the application must use ICall.

The following describes how the software architecture has been implemented. Each sensor has its own task which is essentially always asleep to minimize the power consumption. Only when an interrupt hardware triggered by a sensor, it wakes up through a semaphore post. The Interrupt Service Routine (ISR) associated with the hardware interrupt only posts a semaphore

allowing the system to be ready to catch other higher priority hardware interrupts coming from other sensors. Once the task wakes up it retrieves the data from the sensor that has triggered it then return to sleep mode again. Figure 11 depicts a flowchart of the firmware architecture.

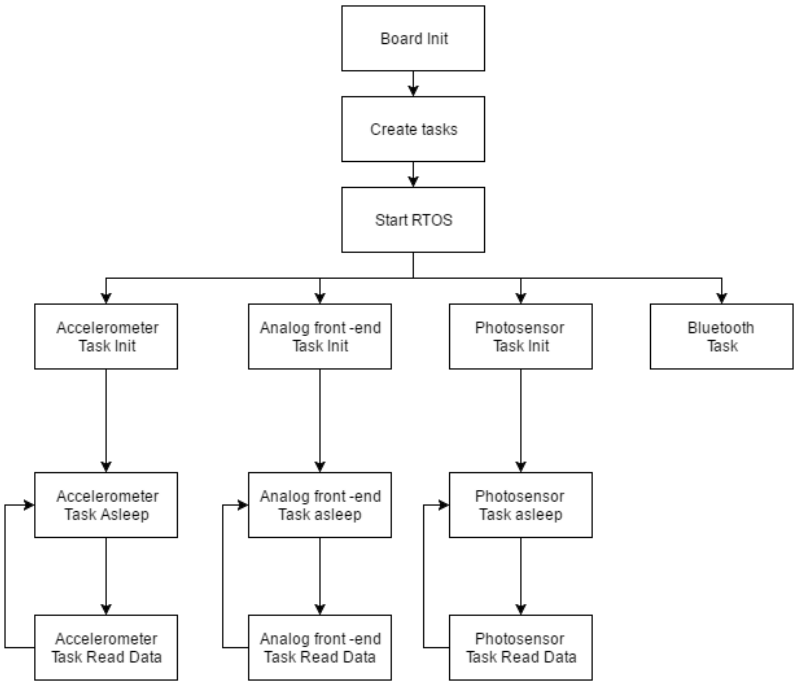

Figure 11: Firmware architecture scheme.

3.3.2 Mobile Application

A mobile app rather than a desktop application has been developed to satisfy the requirement of mobility and to allow also an outpatient monitor. First a list of requirements:

3.3.2.1 Functional Requirements

The functionalities that it should have are:

- graphical user interface to display the readout;
- data logging on the internal memory;
- simultaneous storage of configuration parameters and acquired data;
- transmitting records to a Cloud storage or by email;
- interact with the monitor to change some parameters of the acquisition chain.

3.3.2.2 Software Architecture

The Bluetooth communication task is running as a service using BLE API of Android OS to communicate and receive data from the wearable device to the user interface.

3.3.2.3 User Interface

The application is composed of four screens. The first screen allows the user to start the scanning process to find the BLE cardiac monitor device. A filter has been adopted to show only the devices that have the right feature based on manufacturer Id. Once the user select the devices the setting screen appear. The setting screen allows the user, most probably a researcher to input configuration parameters before the device start the acquisition. Figure 12 and Figure 13 show the parameters that the user can set. In the upper part of the screen there are application related parameters such as the duration (in seconds) of the chunk of data that the user want to show in GUI. Follows the device parameters which are divided per each sensor.

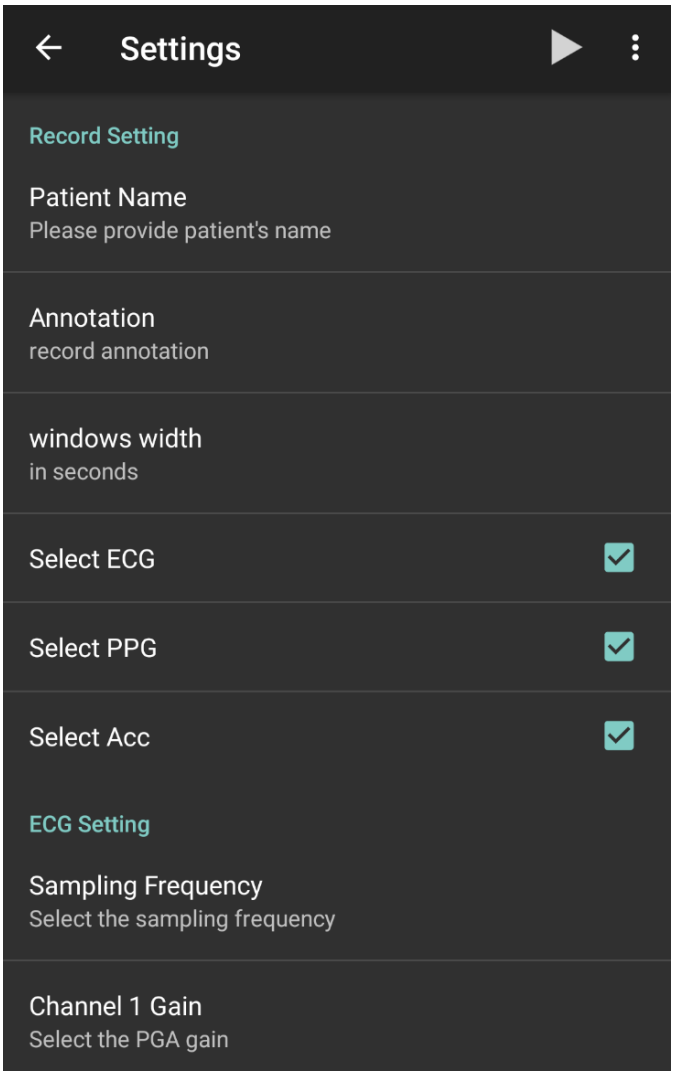

Figure 12: GUI panel displaying application settings.

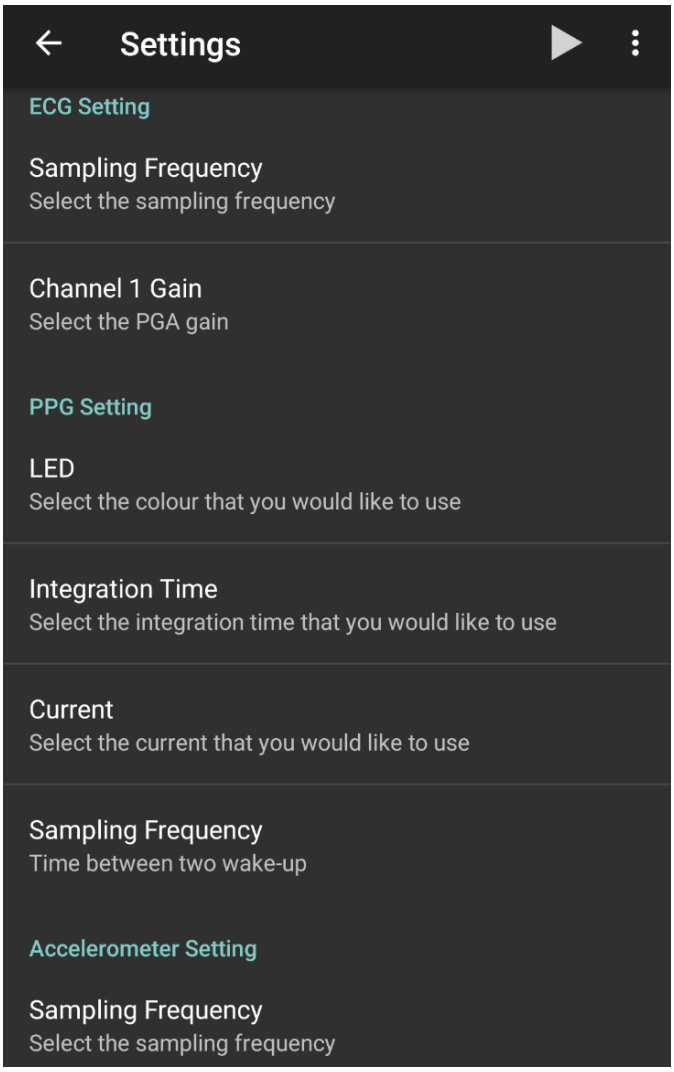

Figure 13: GUI panel displaying device settings.

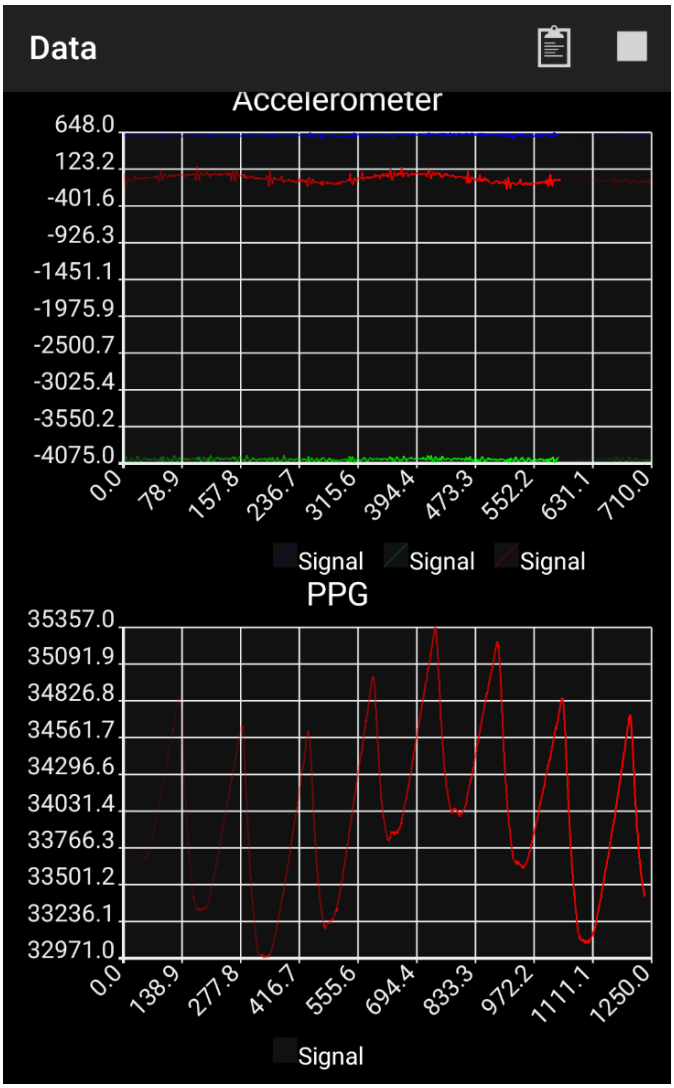

Figure 14: GUI panel display accelerometer and PPG data.

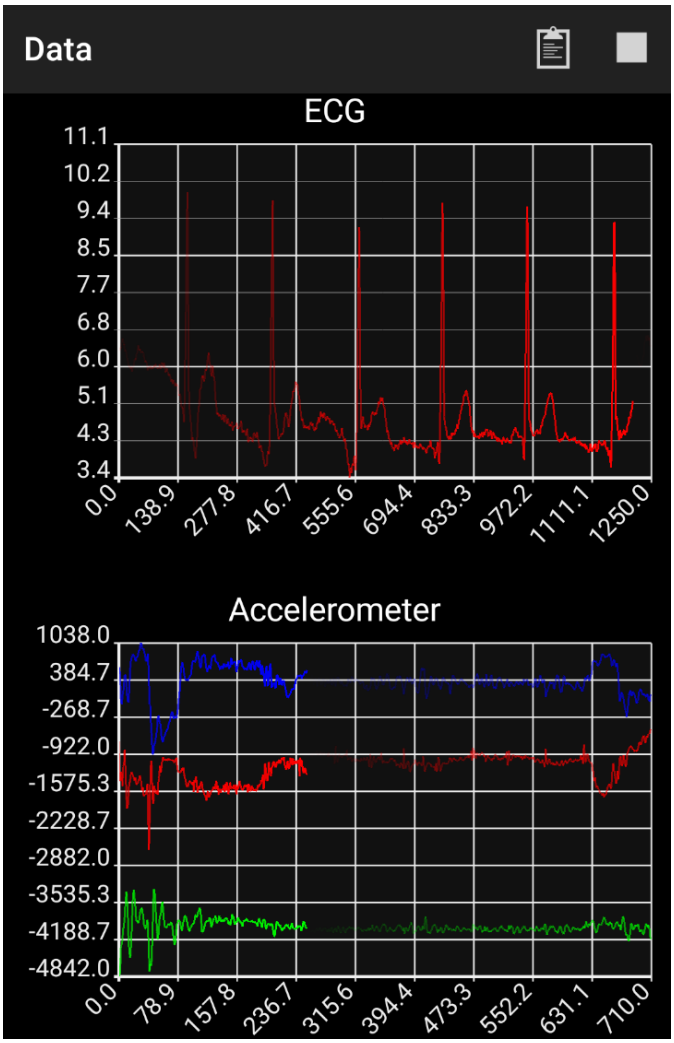

Figure 15: GUI panel display ECG and accelerometer data.

For the ECG acquisition it is possible to set the gain and the sampling frequency. Regarding the PPG, the user has the ability to select the following parameters:

- integration time, which is the time that the LED is kept on for each measurement;
- LED forward current;
- sampling frequency;
- LED wavelength (colour).

In terms of accelerometer data it is possible to select the sampling frequency, the bandwidth and the range.

Once the user has selected all the parameters, the acquisition can start. The next screen shows the data real time over three graphs and allows the user to start the logging.

3.4 CardioMonitor Specifications

TABLE VI: SENSOR OVERVIEW

Biometric data measured	ECG, PPG, Activity, Respiration Rate
Communication	Bluetooth Low Energy
Photosensors specifications	Maximum sampling: 400Hz Wavelength: RGB
ECG specifications	Maximum Sampling Frequency: 500Hz ENOB: 18bits
Weight:	50 gr
Dimensions:	2.8 cm x 4 cm
Power source	Lithium battery
Capacity	250mAh
Power consumption	80mAh in continuous acquisition

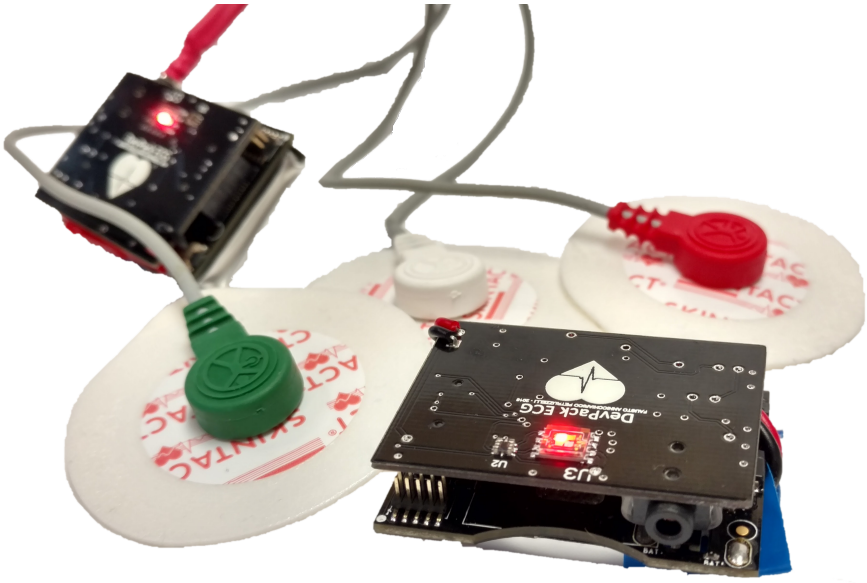

Figure 16: Wearable device with cables and electrodes.

CHAPTER 4

CLINICAL TEST

After extensive testing that has been carried out to ensure electrical safety and functionalities the device is ready for a small clinical trial. Its aim is to evaluate the usability of the platform and collect data to develop a novel algorithm for heart rate detection and Pulse Transit Time even during activity. This chapter will present the clinical testing conducted at Integrated Physiology Lab at College of Applied Health Science of the UIC.

4.1 Motivation

Besides evaluating the usability there are other motivations that have driven this small clinical trial:

- Evaluate the quality of the signals
- Test the reliability and comfort of the device on the chest
- Find locations where the device can pick up a signal with higher signal to noise ratio
- Try different wavelength for the LED and different distance between the photodiode and photosensor
- Collect data during activity to develop an algorithm to extract feature to compute cardiovascular indexes such as HR and PTT estimation

4.2 Eligibility

Inclusion Criteria:

- Male and female > 18 years old
- BMI 18.5-40.0 kg/m

Exclusion Criteria:

- Uncontrolled hypertension ($\geq$ 160/95)
- Pacemaker
- Other electronic assistive medical devices, such as neurostimulators
- Stage III and Stage IV CHD and Heart Failure
- Arrhythmias or dysrhythmias
- Pregnancy
- Non-English speaking

4.3 Protocol

Six eligible participants were recruited. They performed the test protocol twice. First they wore the device with the chest PPG and that was followed by wearing the device with the finger strap.

The protocol was pretty simple. First, they had to record the base line for 1 minute. After that they walked on the treadmill at speeds from 1 mph to 6 mph . They had to step off the treadmill for recovery.

Before the test, vital demographic information and blood pressure were recorded. After the test, participants rated the comfort of the device. The participant is given 2 minutes to rest after stepping down from the treadmill.

4.4 Analysis

Figure 17 shows a participant with the wearable device attached. The participants found the setup unobtrusive. Figure 19 thru Figure 21 show a series of plot of acquired ECG, PPG and accelerometer at different activity levels. The first three rows are the accelerometer components along the three axis, the third row shows the PPG signal and the fourth displays the ECG trace. It is clear that as the level of exertion increases there is an additive noise component in the ECG and PPG traces. This additive noise progressively increases at higher walking and running speed.

Next chapter will analyze different methods to clear the data and extract vital indexes.

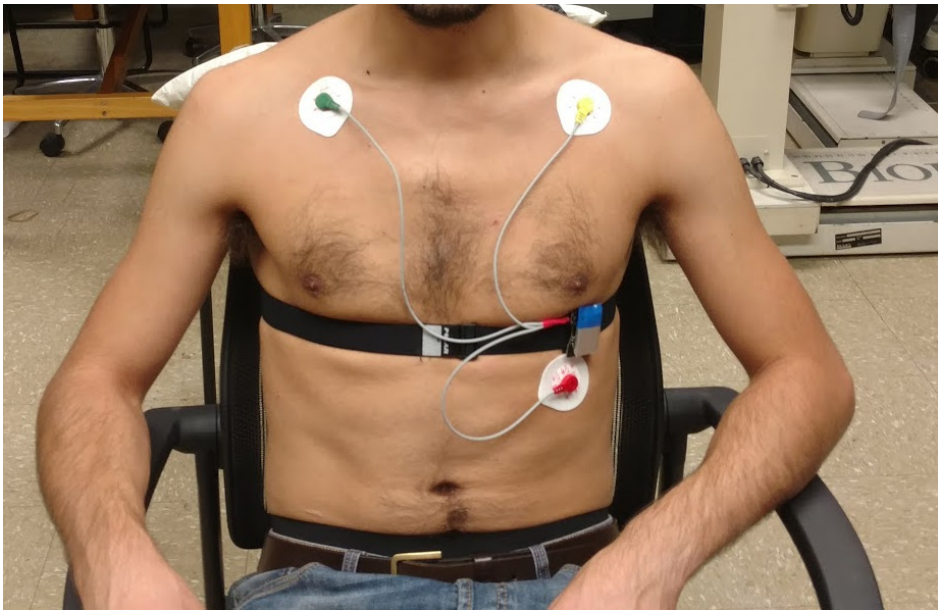

Figure 17: Participant with the wearable device attached.

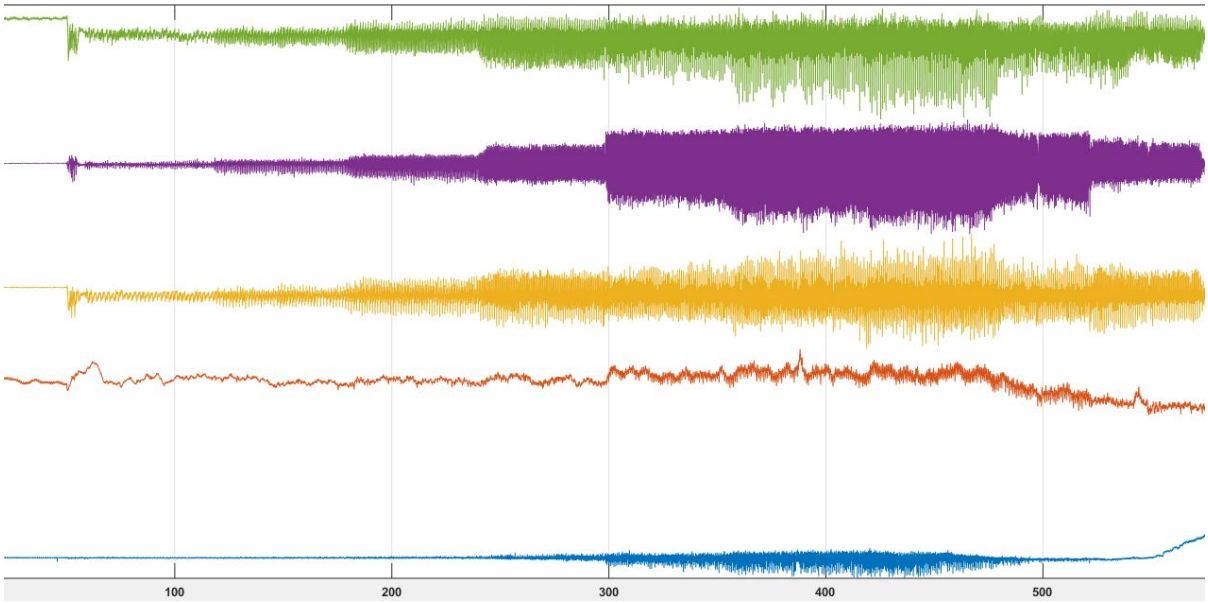

Figure 18: Snapshot of the entire acquisition session.

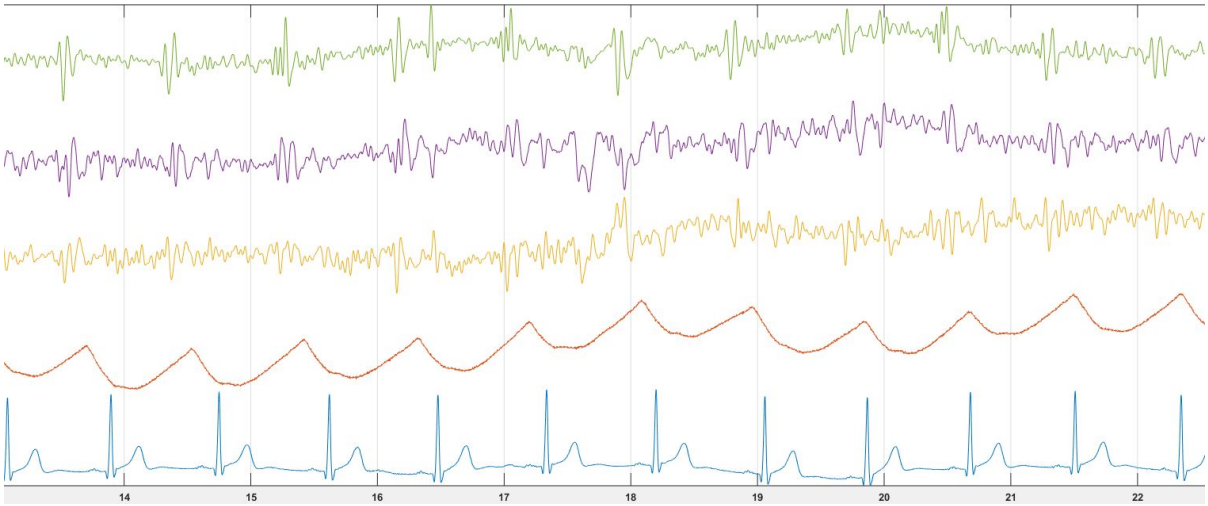

Figure 19: Data acquired from a participant while at rest. The ECG trace shows all the ECG wave (P,QRS,T)

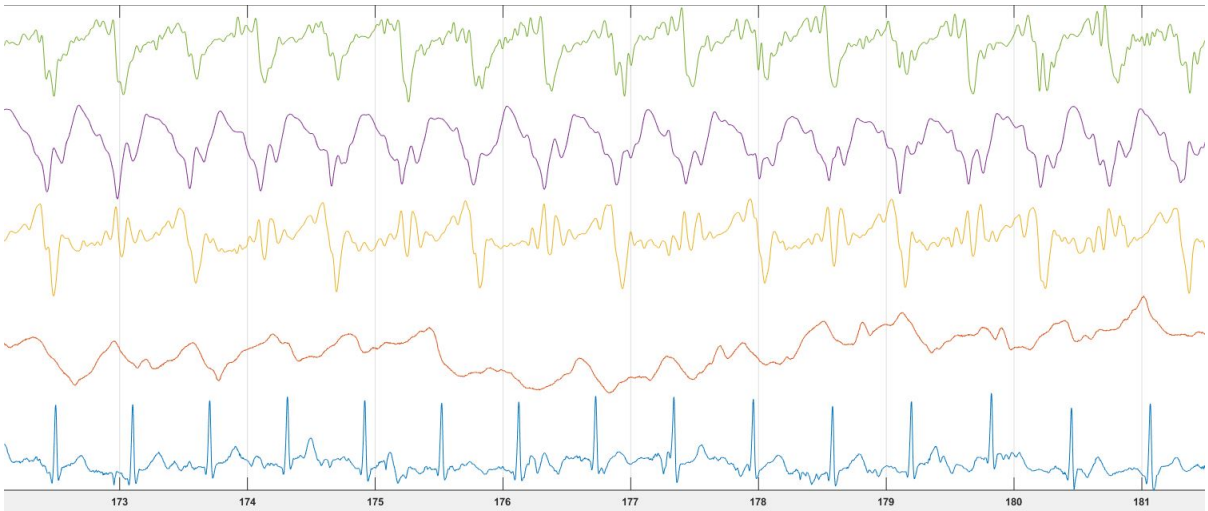

Figure 20: Data acquired from a participant while walking at 3 mph. Additive noise start to appear.

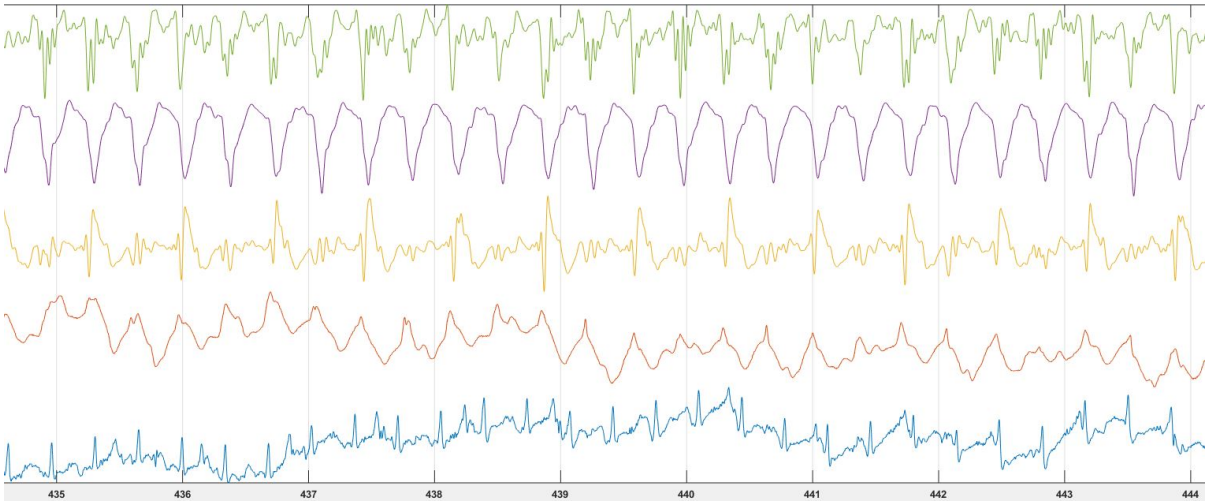

Figure 21: Data acquired from a participant while running at 7 mph. Additive noise with hogher amplitude and lower visibility of the true signal.

CHAPTER 5

POST PROCESSING

At this point, we have a platform that is able to acquire, display and store biosignals. The next step will be processing the data to make inference and summarize the information encoded using few coefficients. This section will discuss the sources of noise that degrade the signals along with some possible approaches that can be used to enhance the signal quality.

The most common approach can be broken down in three parts: first, a noise suppression stage that is followed by a feature extraction and lastly a decision algorithm to evaluate the reliability of the extracted features according to a set of constraints.

The first stage includes the challenging task of minimizing the noise effect and it comprises different approaches according to the type of noise. These may be:

- a linear filter with fixed coefficients;
- an adaptive filter that changes the coefficients in a way that minimizes a certain cost function;
- representing the signal in another functions space such as frequency domain or multiresolution analysis using wavelets transform.

The next stage of data abstraction and summarization is carried out through enhancing the information content of the acquired signal with the purpose of extracting the following

cardiovascular indexes such as heart rate, heart rate variability and Pulse Transit Time using a multimodal algorithm.

The last step is to validate the indexes obtained in the previous stage by feeding the parameters to a supervisory algorithm that will validate the outcome based on a set of physiological constraints and historical data. One example is that the HR cannot change abruptly from one time point to the next. The next sections will discuss in more detail each stage with respect to digital signal processing techniques applied.

5.1 Signal Quality and Noise Analysis

Since the data are degraded by a level of noise especially during motion, a noise suppression stage is needed. The sources of the noise in the signal will be analyzed to model the main causative factor and related effects, following which, the most effective methods to minimize it will be investigated.

The most common noise sources that affects any biosignal are:

- Baseline wander;
- Power line interference;
- Muscle noise;
- Motion artifacts.

The baseline wander and other low-frequency components can be caused by the respiration and body movements. These can cause problems if the aim is to analyze the low frequency ST-T segment and if there is a decisional statement in the algorithm that depends on time domain

thresholding because it has to keep track of the bias and consequently adapt the threshold. One approach is using a linear high pass filtering with 0.5Hz as cutoff frequency and polynomial fitting which can be implemented with a decimation or low pass filter to estimate the baseline and afterward remove it from the input signal.

Power line interference are caused by the electromagnetic field from the power line which can cause 60Hz (50Hz in Europe) and related harmonics sinusoidal interference. Power line noise is an important issue that affects every kind of signal acquired from a device powered by a DC switching or AC power supply. DC switching power supplies are not a real issue because the switching frequency usually is far beyond the signals bandwidth. In our case it is a minor problem because the wearable is battery powered and there is only a small amount of noise due to the body and electrodes that act as an antenna and pick up the power line frequency from the surrounding devices powered from the line. The simplest and most effective is a notch filter at the power line frequency. This technique is effective to remove only the power line interference and some instrumentation noise because the precise frequency of the power supply is known. Removing interference due to baseline wander and powerline is mainly filtering out narrow bands within the signals bandwidth or frequencies outside the acquired biosignals spectrum that might carry information.

Muscle noise and motion artifacts on the other hand are more difficult to filter out because they overlap with the actual acquired biosignals spectrum. Therefore, a fixed filter is not adequate for the removal of the EMG noise. These sort of issues are commonly solved with

other techniques such as adaptive filters or representing the signal in another domain where the noise does not overlap the biosignals information.

Adaptive filters do not need the precise location of the noise in frequency domain and the bandwidth of the noise can be superimposed on the signal. These kind of filters need only a reference signal that can be a signal correlated with noise interfering with the signal (or a model of the noise) or a signal correlated with the signal itself.

A promising technique that is extensively used to delineate features is wavelet transform which is a multiresolution time frequency analysis. Wavelet transform overcomes the limitations of Short Fourier Transform related to the trade off between the time domain resolution and frequency domain resolution facilitating a more comprehensive way to extract information bypassing the impact of the noise.

In all these signal processing techniques and in any biomedical signal processing, it is necessary to avoid altering the information that the signals might have. For example distortion may be introduced by digital filters in the form of phase shifting and selective frequencies attenuation. Possible distortion caused by the filter should be carefully quantified and corrected.

After an overview of the most often used methods, we provide a description of the processing steps that have been used in this work.

In the PPG waveforms it is noticeable that there is a DC component which is mainly related to the light absorption of other tissues and media rather than blood. Furthermore, there is low frequency content due to respiration and body movement.

A high pass filter with a stop band at 0.2Hz and a pass band at 0.4Hz has been applied to attenuate that frequencies content. The cutoff frequency has been chosen following the fact that the fundamental frequency in a clear PPG signal represents the heart rate and the heart rate should not be lower than 40 bpm which corresponds to a frequency of 0.67 Hz.

If the sampling frequency is 250Hz the corresponding minimum order of such filter is around 3000 to have 80dB of attenuation. To optimize the performance we have designed a filter using 6 Hz as sampling frequency with 64 taps to get a 80dB of attenuation. The filter is upsampled by a factor of 40 that is approximately the signal sampling frequency (250 Hz) divided by 6. We will end up having the same number of taps but using this approach only 64 of the coefficients are relevant to compute the output and the rest are zero. This can be implemented easily on an embedded microcontroller even without a Digital Signal Processor (DSP) module. The drawback of this design is that the frequency response will have equispaced gaps in frequency which can be ignored in our application because the bandwidth of the PPG goes from 0.5 to 4Hz or 12 Hz taking into account the content of the first two harmonics. The only reason why the data are sampled at high frequency is to identify the peaks and the onset as precise as possible in time domain.

Also the ECG has a DC component which can cause problems if we are planning to detect the QRS complex using a time domain amplitude thresholding. Since the QRS detection algorithm used is intolerant to baseline wander, this step can be skipped to minimize any distortion that may be introduced by filtering.

In the following figures the ECG DC component has been removed for visualization purpose only.

5.1.1 Spectral Analysis

The first analysis that has been carried out is a Short Time Fourier Transform with 8 seconds window and 2 seconds overlap. This decision represents a reasonable choice because the heart rates cannot change abruptly. Two type of activities have been analyzed: walking on the treadmill and jumping.

Figure 25 depicts the result of the STFT for the PPG signal. The highest content in the PPG signals coincides with the heart rate. It starts at around 1.2Hz which corresponds to 72bpm and increases linearly with the walking speed. It is clear that the accelerometer frequencies which represent the noise affects the PPG data. The lower highlighted area is similar to the fundamental frequency of the accelerometer.

A STFT is less appropriate for the ECG because the bandwidth is larger (0.5 to 60Hz) and the information is more spread out over the whole bandwidth. From Figure 24 is possible to highlight the accelerometer fundamental frequencies with related harmonics which are less prominent compared with the PPG.

The STFT of the signal acquired during jumping showed interesting results in which the region that represent the fundamental frequency in the accelerometer is also very prominent in the ECG spectrogram. To prove that the noise is confined within that region, a QRS detection has been carried out before and after attenuation of those frequencies. Figure 22 shows the result of the heart rate computed as difference between R to R.

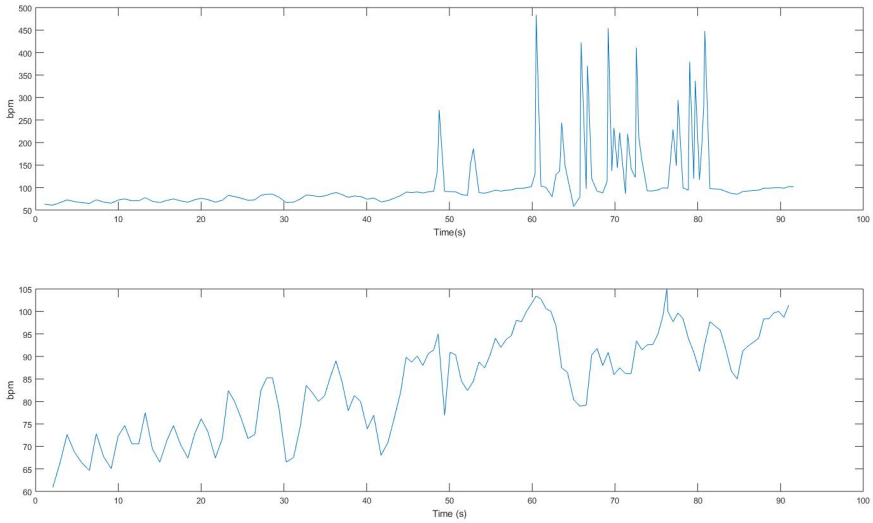

Figure 22: Heart rate computed before and after removing noise.

5.2 Feature Extraction

This research work mainly focused on feature extraction aspects from a noisy signal rather than denoising the signal. The ultimate goal is to perform morphological analysis for the purpose of deriving cardiovascular indexes including heart rate, heart rate variability and pulse transit time. To compute these parameters we have to extract the R wave of the ECG in addition to the onset and the peak of the PPG. The heart rate is coded also in the frequency content of the PPG.

5.2.1 ECG features

There are different algorithms and methods developed over the past years to identify the QRS complex or R wave in a ECG trace such as:

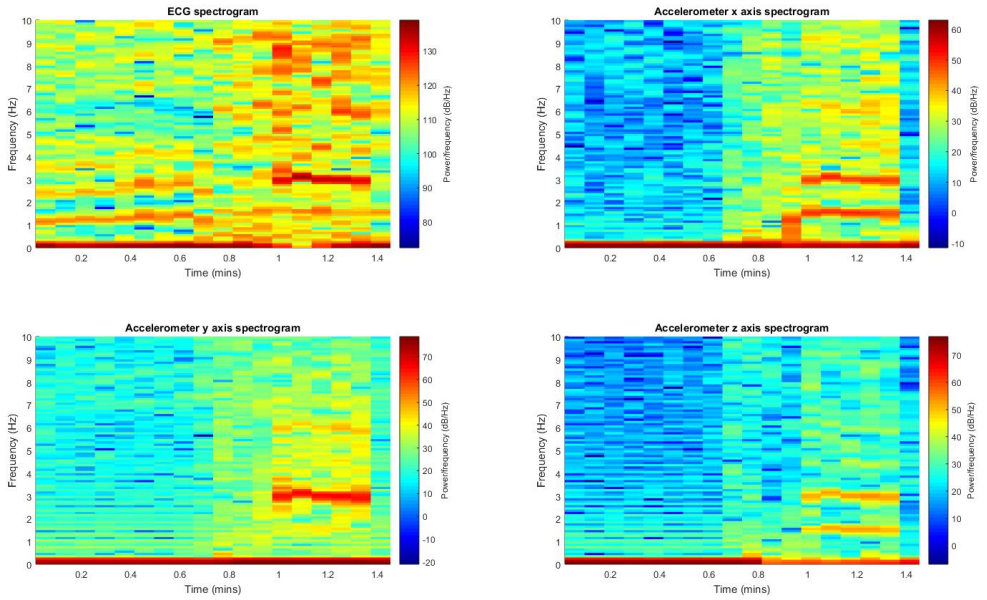

Figure 23: Spectrogram of ECG and accelerometer components acquired during jumping at a fixed time interval.

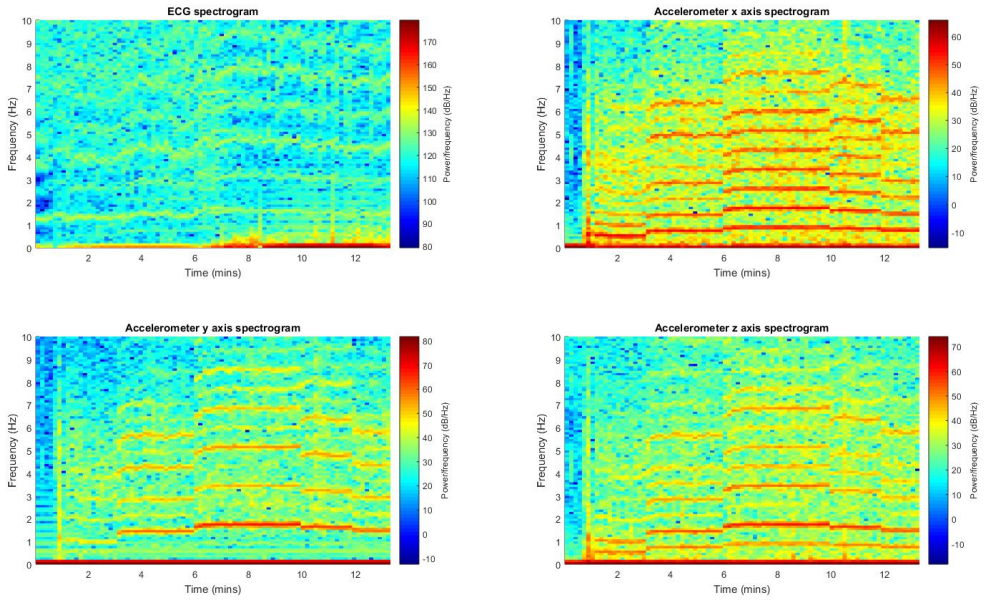

Figure 24: Spectrogram of ECG and accelerometer components acquired following the clinical protocol.

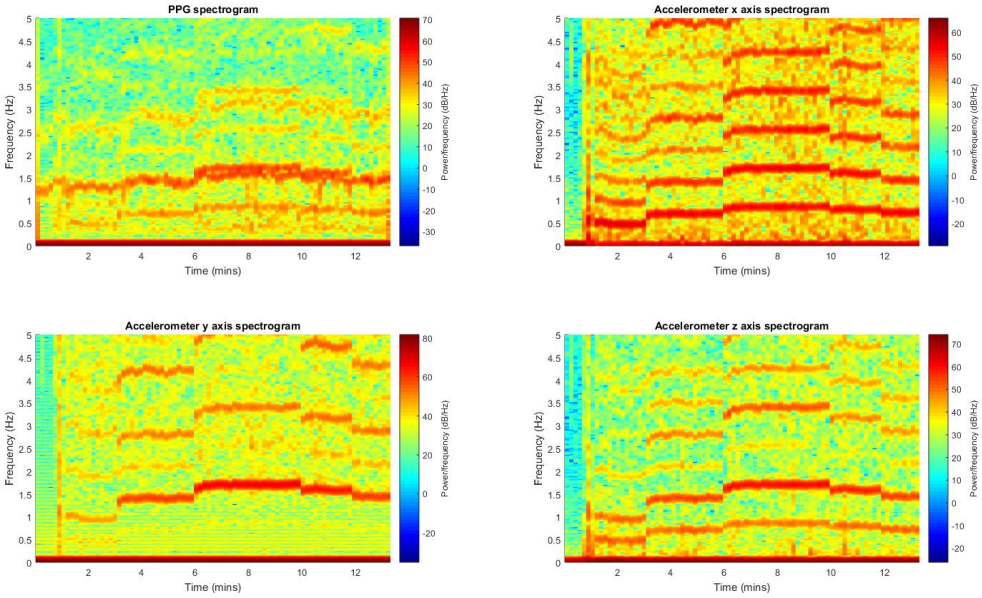

Figure 25: Spectrogram of PPG and accelerometer components acquired following the clinical protocol.

- Amplitude thresholding;
- Pan Tompkins algorithm;
- Wavelet thresholding.

The simplest method is a time domain amplitude thresholding which takes advantage of the higher amplitude of R wave. The only requirement is to remove the DC component from the input signal. This approach only works with signal at rest or with low level of activity.

The second solutions is the Pan Tompkins algorithm which is one of the most used method to detect the QRS wave and it can adapt to the signal bias changes. The efficacy of this algorithm is attributed to the fact that the analysis takes into account both the slope and the width of the QRS complex.

The previous discussed technique works best at rest or low level of motion, while the wavelet transform maintain a high level of information even at higher level of exertion. Wavelet transform overcomes the problems of the STFT in terms of frequency and time resolution. It decomposes the signals using a function by means of dilation and translation and if the mother wavelet is chosen with certain criteria it can emphasize some properties of the signal.

To extract the R wave a Continuous Wavelet Transform (CWT) has been carried out using Complex Morlet (cmor1-1.5) as mother wavelet over a range of scales from 2 to 400. The mother wavelet has been chosen minimizing the difference between one ECG pulse and the chosen wavelet in time domain which can be computed through the energy. Even if the continuous wavelet transform contain redundant coefficients, it is an effective visualization tool to localize and accentuate specific signal properties. Once the problem has been modeled, a Discrete

Wavelet Transform (DWT) can be used to optimize the detection and to develop an embedded algorithm that can run on a microcontroller.

Figure 26 show the CWT on a data recorded at rest. The R waves are well delineated even during high level of exertion (Figure 27).

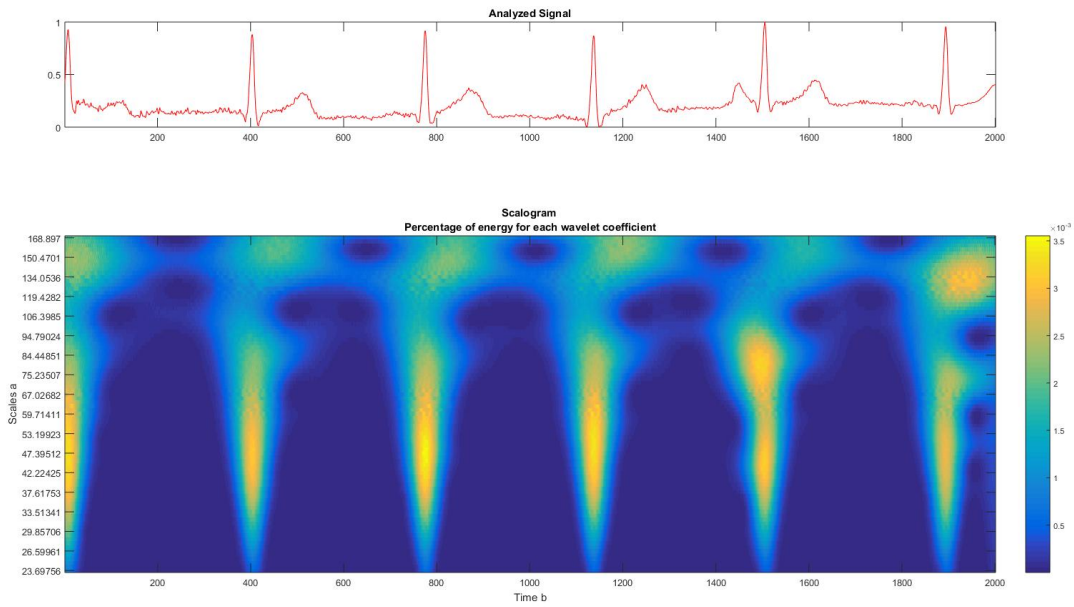

Figure 26: Continuous wavelet transform (scale 2 to 200) at rest.

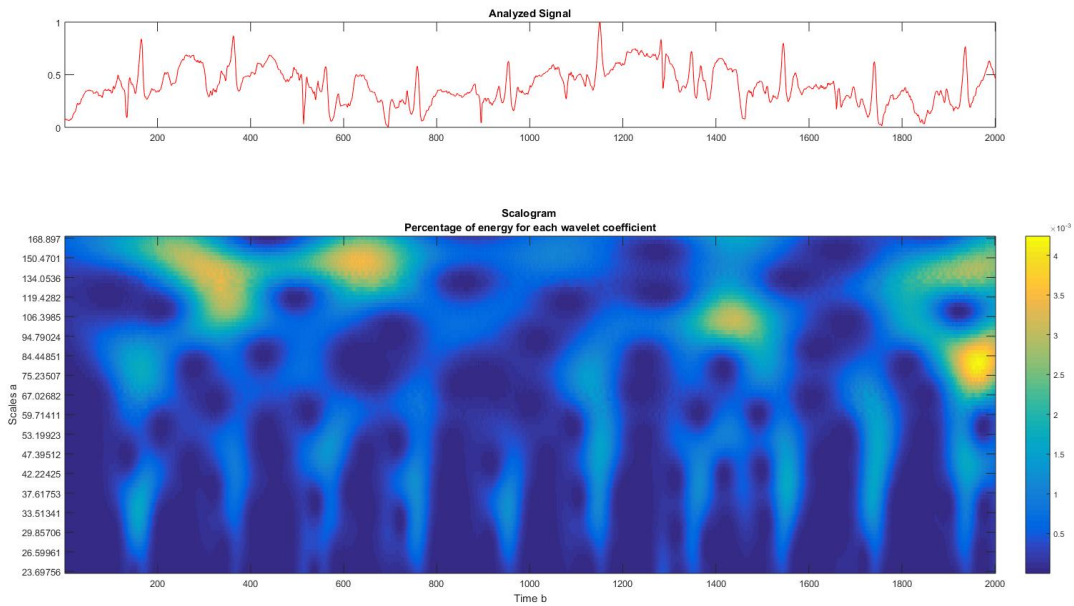

Figure 27: Continuous wavelet at 6mph.

5.2.2 PPG features

Other sought features to extract from PPG are the onset and the peak by running a local search for local maxima and minima taking advantage of the fact that the first derivative is equal to zero.

The first derivative has been implemented with a differentiator filter up to 15Hz. Furthermore, a low pass filter with pass band at 15Hz and stop band at 20Hz has been designed to limit the effect of higher frequency component that can be interpreted as local maximum or minimum.

This approach works at rest and low level of exertion but can lead to misclassification with higher level of activity. To increase the robustness of the algorithm, a wavelet based delineator has been designed to identify regions with higher probability for finding onsets and peaks. Energy maximization as described earlier suggest sym3 or db3 as mother wavelet.

From the transform coefficients the 60th scale was chosen and the resulting coefficients have been rectified with a threshold value of 0.3. Figure 28 shows the CWT that has been carried out using the PPG signal.

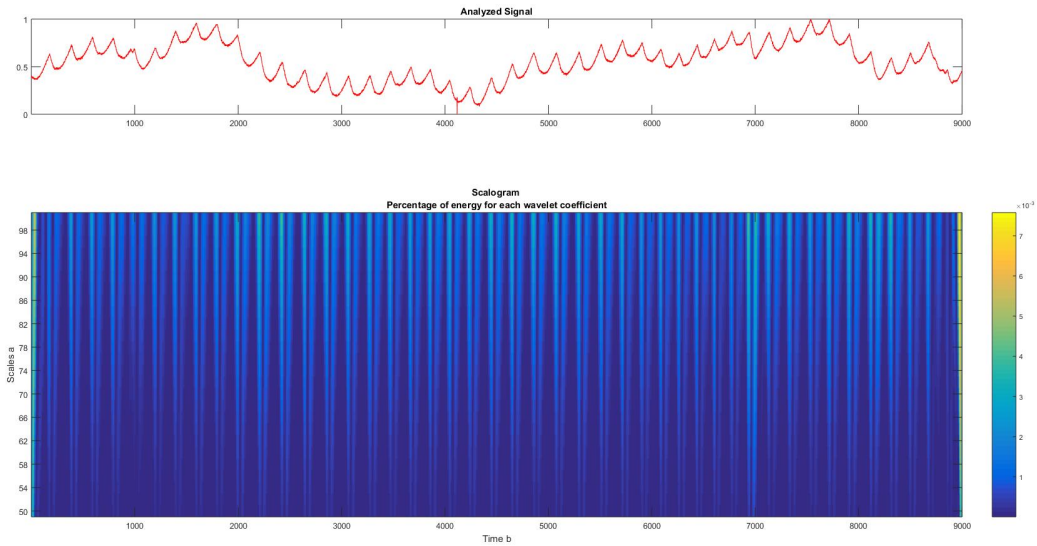

Figure 28: Continuous wavelet photoplethysmogram at rest

5.3 Decisional algorithm

The noise suppression and feature extraction stages identify regions with highest probably of finding onsets or peaks of the PPG signal. This information is fed to a decisional algorithm that goes back in the raw data to find the precise location through a local maximum or minimum search. The last decision establish the reliability of the features just identified based on the difference with the past values and if they are within specified range. For example the HR cannot go lower that 40bpm or higher that 250bpm.

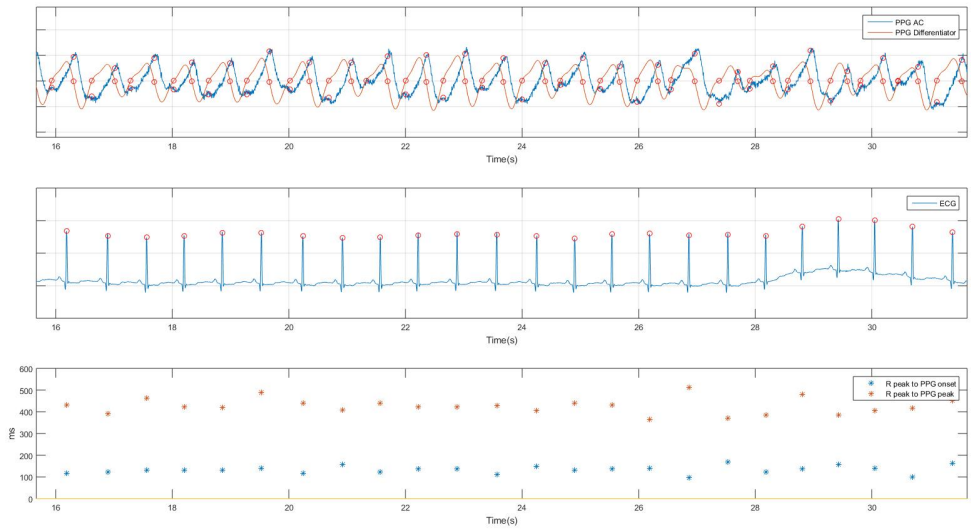

Figure 29: PTT at rest.

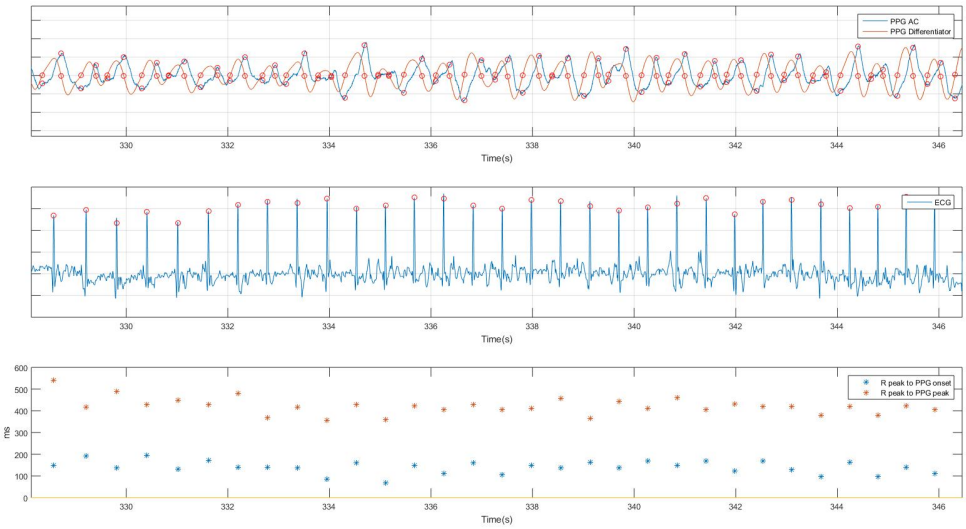

Figure 30: PTT at 3mph.

5.4 Cardio Framework

All the processing techniques used for this work has been integrated in a Matlab program with a Graphical User Interface which is shown in Figure 31. This facilitated performing manual annotations of signal features such as the onset and peak of PPG signal waveforms and the R Wave of the ECG waveforms. This can be followed by comparing the results with automated recognition regarding these same fiducial points in the acquired data. The manual annotation represent the only way to evaluate the performance of the algorithm previously discussed.

First, the user selects the record to analyze, zoom in to expand the segment of interest, apply manual annotations and save it for future analysis or retrieve previously saved annotations. A this point, the user can decide to run the complete detection algorithm or analyze the signals

using one of the techniques discussed before by selecting from the adjacent menus. Furthermore, the user can input the parameters needed such as cutoff frequency for the linear filtering or selecting the mother wavelet or the scale for a wavelet analysis.

The features extracted by the algorithm are displayed and evaluated in comparison to the manual annotations. The indexes computed to quantify the performance of the algorithm are sensitivity and positive prediction. The sensitivity is computed as number of true positive divided by the sum of true positive and false negative. In our case the true positives are the number of features recognized and the false negatives are the features that the algorithm did not recognize albeit manually annotated as positive. The positive prediction index is computed as number of true positive over the sum of true positive and false positive. False positive points are the features falsely recognized by the algorithm that do not have a corresponding manual annotation.

Furthermore, there is the facility to plot the points detected by the automated algorithm against the manual annotation. This facilitates evaluating the algorithm with respect to time precision, systematic error, and quality of fit.

5.5 Validation and Results

This algorithm has been validated comparing the results of the automated algorithm with the manual annotations performed by two independent observers using the software discussed in the previous section. The annotations usually are performed by independent experts and this method is accepted in research projects to validate the effectiveness of automated algorithm for the analysis of biosignals datasets.

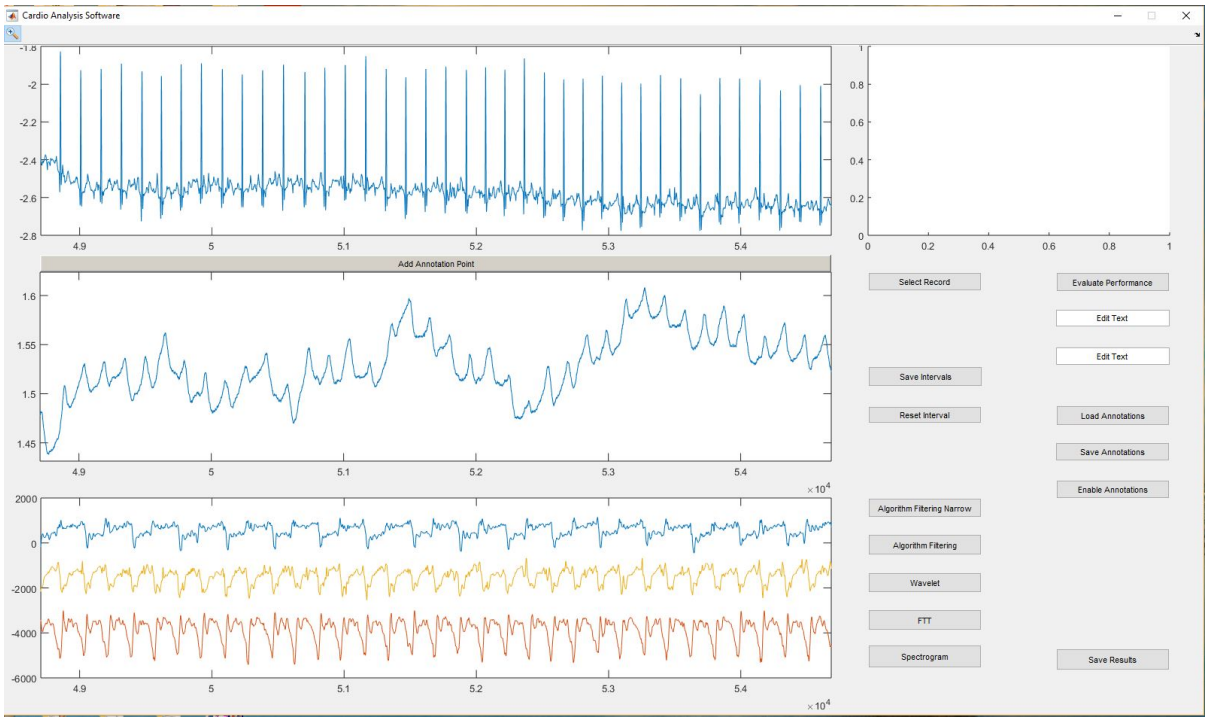

Figure 31: Cardio Software GUI.

Using the data collected during the clinical trial that enrolled 5 subjects and included exercise data corresponding to 5 treadmill speeds for each subject, a sensitivity of 96 % and a positive predictive value of 97% has been achieved. These results agree with previously reported data from other research groups (Faroog et.al.,2010) that reported the algorithm achieved sensitivity of 96.89% and positive predictivity of 94.55% within an acceptance level of 12 ms.

CHAPTER 6

CONCLUSION AND FUTURE WORK

A wearable device has been designed to acquired biosignals along with a mobile application and an algorithm to extract some cardiovascular indexes. The algorithm devised demonstrates the possibility of acquiring high quality signal and extraction of features from peripheral site other than the finger including the chest which opend the door for a class of wearable that are unobtrusive and precise.

The future work will be mainly to optimize the platform at different levels, for example:

- Design a final board that can fit on top of an adhesive path with the electrodes embedded
- Improving the comfort level optimizing the shape of the patch and the site considering the quality of the signal as well
- Embed the processing on board which may require a microcontroller with more processing power(for example a core Cortex M4) and a DSP module
- Add a memory to store the data if the connection with a smartphone is dropped

APPENDIX

Fausto Annicchiarico Petruzzelli <fannic2@uic.edu>
to copyrightcouns.

Hello TI,
I am a student of University of Chicago at Illinois. I am working on my master thesis.
I designed a wearable BLE cardiac monitor that include an ECG monitor. I used hardware from Texas Instrument such as CC2650 for the BLE, ADS1292 for the ECG acquisition, SensorTag.

I' d like to use some of your diagrams and photos in my manuscript.

Below there is the list of resources that I would like to use:

http://www.ti.com/lit/an/sbaa188/sbaa188.pdf, figure 1,(page 2) ,figure 4 (page5)

http://www.ti.com/lit/ds/symlink/cc2650.pdf, figure 1.1 (page 3)

https://e2e.ti.com/blogs_/b/connecting_wirelessly/archive/2015/06/03/create-develop-prototype-3d-print-your-iot-idea-with-simplelink-sensortag , The second figure.

The thesis will be published on https://indigo.uic.edu . It will be completely free. If you have any other question don't hesitate to contact me.

Sincerely,

Fausto Annicchiarico Petruzzelli <fannic2@uic.edu>
to copyrightcouns.

Hello TI,
I am a student of University of Illinois at Chicago. I am working on my master thesis.

Bassuk, Larry <l-bassuk@ti.com>
to me

Dear Fausto,

Thank you for your interest in Texas Instruments. We grant the permission you request in your email below.

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Regards,

Larry Bassuk
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From: Fausto Annicchiarico Petruzzelli [mailto:fannic2@uic.edu]
Sent: Thursday, November 03, 2016 11:54 AM
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Subject: [Requests & questions from ti.com] Request permission use diagram

CITED LITERATURE

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8. http://reactivex.io/. Technical report.

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English	Full working proficiency
Chinese	Basic
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Fall 2015	RA position with full tuition waiver plus monthly stipend
Fall 2015	Italian scholarship for TOP-UIC students
TECHNICAL SKILLS	
Programming	C, C++,VHDL
Software	LabVIEW, Eagle CAD, Vision, Code Composer, MATLAB, Simulink, ModelSim-Altera, Quartus
Hardware	NI DAQ, NI CompactRIO, CANbus Analyzer, Spectrum analyzer, Digital and Analog Oscilloscope