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HOSPITAL AT HOME

A technological approach for self-measurement of blood pressure during sleep

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Resumo

O hospital em casa foi popularizado como uma forma de fornecer cuidados de saúde aos pacientes em casa. As principais vantagens prendem-se com a diminuição do tempo de internamento hospitalar, redução da lista de espera para cirurgias, alta precoce e consequente redução de custos. Apesar dos resultados obtidos por diversas pesquisas sobre a implementação desses esquemas serem discordantes e contraditórios, principalmente no que respeita à relação custo-eficiência, a satisfação dos pacientes e de suas famílias é registrado como muito positiva. Os esquemas de implementação diferem de paciente para paciente, dependendo da condição e das necessidades. Os potenciais benefícios para o paciente incluem menor exposição a atmosferas de risco, maior independência e melhoria do bem-estar.

Numa perspectiva onde o hospital para casa oferece serviços preventivos de admissão hospitalar, encontramos uma estreita relação com o conceito de envelhecimento ativo e saudável. Além disso, o desenvolvimento e a adoção de soluções hospitalares em casa podem tornar-se numa forma de alcançar os resultados propostos nas diretrizes da Organização Mundial de Saúde para um envelhecimento ativo e saudável.

Neste trabalho, foram desenvolvidos esforços para contribuir para esta realidade, através do desenvolvimento de uma solução tecnológica que permitisse a implantação do Hospital em casa. A abordagem culminou na caracterização de um dispositivo para a medição contínua da pressão arterial durante o sono.

O uso da técnica de fotopletismografia nesta abordagem é um fator diferenciador dos restantes dispositivos comerciais. Tendo sido possível obter resultados viáveis e encorajadores para a continuação do desenvolvimento desta aplicação.

Palavras-chave: Hospital em Casa, Fotopletismografia, Monitorização da Pressão Arterial

Abstract

The hospital at home has been popularized as a way of providing health care to patients at home. The main advantages typically referred point to the decreased length of hospital stay, reduced waiting list for surgeries, early discharge and sequential cost reduction. However, the results obtained by diverse researches on the implementation of these schemes are discordant and contradictory, mainly regarding to cost-effectiveness. In contrast, the satisfaction of patients and their families has been recorded as very positive, as implementation schemes differ from patient to patient, depending on condition and needs. The potential benefits for the patient include reduced exposure to risky atmospheres, increased independence, and improved patient well-being.

In a perspective where hospital to home provides hospital admission preventive services, we find a tight relation with the concept of active and healthy aging. Also, the development and adoption of hospital at home solutions can become a way to achieve the results proposed in the World Health Organization guidelines for an active and healthy aging.

In this work, efforts were made to contribute to this reality through the development of a technological solution that would allow the implementation of Hospital at Home. The approach culminated in the characterization of a device for the continuous measurement of Blood Pressure during sleep.

The use of the photoplethysmography technique in this approach proved to be a differentiating factor of the remaining commercial devices. It has been possible to obtain viable and encouraging results for the further development of this application.

Keywords: Hospital at Home, Photoplethysmography, Blood Pressure monitoring

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List of Acronyms

WHO World Health Organization

AHA Active and Healthy Ageing

PPG Photoplethysmography

PTT Pulse Transit Time

LED Light Emiting Diode

BP Blood Pressure

SP Systolic Pressure

DP Diastolic Pressure

ESH European Society of Hypertension

1

Hospital at Home as a Tool for Active and Healthy Ageing

1.1 Hospital at Home

The lack of hospital beds has been a recurring problem over the last two decades. One popular solution to this problem is the possibility of moving patients to their homes, mostly presented under the concept of Hospital at Home.

Hospital at Home is the provision of hospital admission preventive services or hospital early discharge services facilitators [23]. Since the first publications on this concept, many studies have come up with contradictory data on the cost-effectiveness of this system [24], although it is expected to reduce costs by controlling hospital admissions and reducing hospitalization time [23]. Although many significant differences in health outcomes measures have not yet been recorded, studies show an increase in the patient's quality of life as the main focus of the hospital at home concept. [25].

In general, hospital at home care is widely accepted by patients and their families. Leff *et al.* obtain consistent results with these thoughts, stating that patients and their families are more satisfied with the home care approach to general care, as well as in more specific domains such as health and personal care professionals, comfort and care attendance processes. Patients also report a high level of satisfaction with the physician's relationship compared to hospital care [26].

The hospital at home can generally be divided into two approaches, the community hospital base, associated with primary care, and the hospital base, whose responsibility lies with hospitals and their professionals [24, 23]. Nursing care, home support and services such as physiotherapy constitute the community hospital at home scheme. In the hospital based scheme, services are provided at different levels of integration with community services, according to the specific conditions of care required for each patient [23].

Several hospital at home schemes can be implemented, from schemes to specific conditions, administration of intravenous drugs, to early release post-surgery patients care [23, 27, 28, 29].

1.1.1 Advantages and Disadvantages of Hospital at Home

Corrado in [24] summarized the potential benefits of the hospital at home approach as the decreased length of hospital stay, reduced waiting list for surgeries, early discharge and sequential cost reduction. Potential benefits for the patient are reduced exposure to risky atmospheres, increased independence, and improved patient well-being. There are also, disadvantages on this approach, regarding the fact that majority of the older adults population rejects such solutions because of the complexity of surrounding equipment and increased sense of insecurity and lack of specialized support. In addition, there is still the possibility that home treatment and support may depend on informal caregivers, which may consist of increased concerns for these individuals and reduced quality of care [24].

On the other hand, regarding the criteria for implementation of this approach as effective as standard hospital care, some standards must be accomplished. The patient's outcomes (e.g., independence and mortality) and the total cost of treatment should be similar to usual care, or even more appealing. Yet, in literature, we find several evidences on low certainty that hospital at home does affect mortality, hospital readmission, or functional status [30, 31]. Apart from that, hospital at home is efficient and an accepted alternative to standard hospital care, disregarding the cost. The first time the issue of hospital at home was addressed was in 1961 [24], since then numerous approaches have been considered. Despite the advantages identified and the longevity of the concept, the hospital at home is not yet properly implemented.

The innovation and technological advances that have arisen in this area have contributed to the increasing offer of treatment options available at home for the most diverse and complex needs. So far, the difficulty of logistics and financing of implementation models has been an obstacle [30]. The figure 1.1 illustrates the complexity of the hospital to the patient's home moving process for a hospital-specific care field.

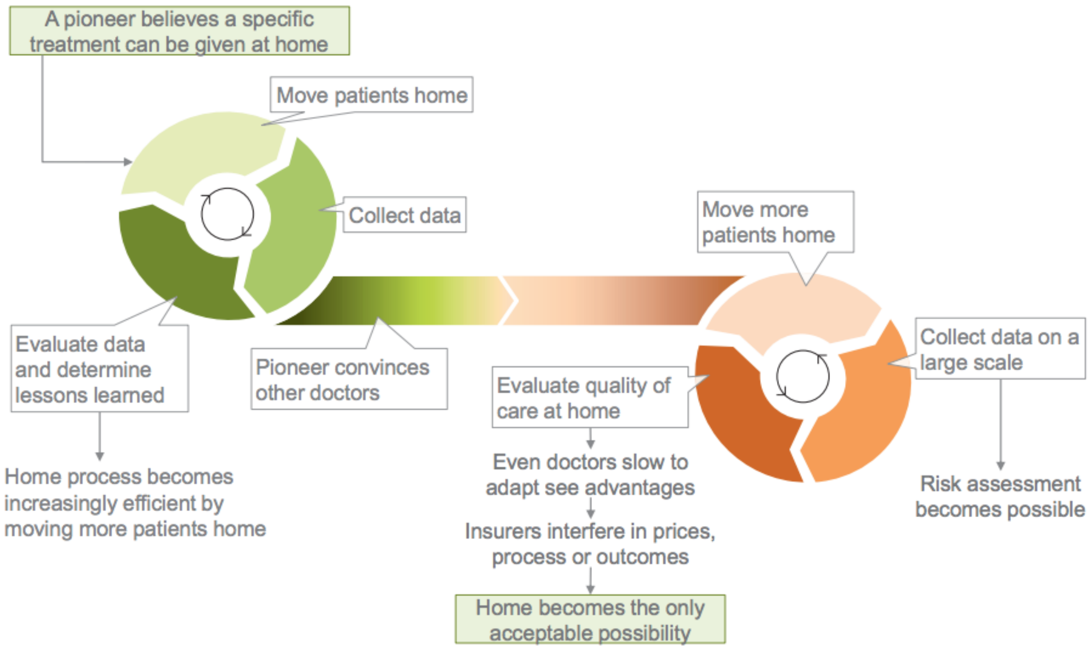


Figure 1.1: Moving from a hospital to home for a specific care field. Available in [1].

The hospital at home has generated the most diverse and contradictory opinions regarding its implementation, costs and health outcomes. However, despite these findings, in the literature there is a factor in which few studies disagree. The level of satisfaction with hospital at home care was found to be higher than the level of satisfaction obtained when compared to standard hospital care [26].

1.1.2 Hospital at Home as a concept for promoting Active and Health Ageing

The World Health Organization (WHO) has defined Active and Healthy Ageing (AHA) "...as the process of optimizing opportunities for health to enhance quality of life as people age" [32]. Health is itself a multifaceted concept, dependent on social, environmental and bio medical factors to which people are exposed throughout life [32]. The possibility of receiving health care at home can be a contributory factor for the active and healthy aging and increasing of quality of life, concepts on which countless studies have been working on [32, 33, 34].

Fernandes and Botelho in [35] note that policies must keep up with the developments and rapid evolution of health care systems resulting from the development of new technologies and means of predicting, preventing and treating diseases. Also, the authors concluded that a policy promoting active aging must be based on health, participation and safety. The need for easy access to primary and hospital care, continued or long-term care and mental health services, as well as promotion of family and social integration, should be a concern as an indispensable condition for active aging.

From the Guidelines presented by WHO[1] in order to promote a healthy aging, in the issues surrounding this work, we would like to underline the following needs [35]:

- Prevent and reduce the burden of chronic diseases;
- Provide safe and adequate environments for aging;
- Develop affordable and high-quality social and health services;
- Support informal caregivers through initiatives such as day hospital, pensions and financial subsidies and special care at home;
- Ensure access to health and social care to all, fairly and equitably;
- Provide policies, programs and services that enable people to remain at home during old age;
- Provide education and training for caregivers;

As such, means of action have to be proposed to solve the concerns regarding active and healthy aging. The implementation of hospital at home schemes can be a way of archiving the goals presented by WHO in order to promote a healthy aging. Spending less time in the hospital throughout life, allows to increase the quality of life of the person, and thus aging healthy and active. The benefits outweigh the financial motives, allowing an increase in patients' quality of life.

The hospital at home is a way of delivering health care and services closer to the patient. As previously mentioned, the cost-effectiveness of this scheme implementation is questionable, since patients recover in a similar time period compared with standard hospital and there is no comparative advantage regarding to health outcomes. However, patients report higher well-being and satisfaction compared with typical hospital care. The possibility of bringing the hospital closer to the people, taking it to their homes, optimizes health opportunities and thus contributes to their quality of life.

The concept of health is associated with the environment that surrounds the person, as such the creation of an environment conducive to the provision of hospital

[1]Active Aging. A policy framework, World Health Organization. Available in `www.who.org`

care close to the patient, with the help of new and user-friendly technologies, will contribute to promote an active and healthy aging. Hospital at home also allows for increased patient participation in their own health, having access to data and more personalized and safe support. It actively promotes the social integration of the person and the active involvement of his family, which are key concepts for healthy aging.

The Hospital at Home gives response to several needs identified by the WHO for an active aging, helping to prevent and treat diseases, developing health services closer to people, easier access to health and finally, allowing people to stay more time in their homes as they age.

1.2 Chronic diseases and healthy ageing

The effectiveness of a country's health system is not only being assessed by the number of people dying each year but also by the impact that illness and injury have on people [36].

The statistics of causes of death are a basis for analysis and action by public health authorities. As an example, if a country has a high number of deaths from heart disease or diabetes, there will be an interest in promoting programs in these areas and reversing this trend. In addition to the causes of death, another parameter to be taken into account for the evaluation of the health system and distribution of budgets is the incidence rate of chronic diseases [36].

A Chronic disease is characterized by the time needed for recovery. These diseases can not be cured in a short time and are a condition whose symptoms exist continuously, and may or may not lead to the death of the person. All of them present a common factor, the fact that they lead to disruption of the quality of life and activities of the patient. Chronic diseases currently account for about 80% of the health budget in the European Union [36].

The JA-CHRODIS (Joint Action on Chronic Diseases) is a Joint European Action on Chronic Diseases and Promotion of Healthy Ageing, whose aim is to implement good practices in the prevention and management of chronic diseases [36].

According to the European Commissioner for Health and Food Safety, about half a million active-age European citizens die from chronic diseases. This represents an expenditure of about 115 billion euros in lost in productivity and expenditure on national health systems. For this reason, the political and social organisms are currently focused on addressing the issues raised by these diseases in order to contribute to more efficient and sustainable health systems [36].

Multidisciplinary intervention programs are often limited by the economic, geographic and bureaucratic means available, however remote monitoring can be a solution to support and promote the care of these patients. It is therefore crucial to identify the most relevant parameters to monitor [37].

Emphasizing the issue presented above, there is a correlation between chronic diseases and quality of life in ageing, as so being a social and economic urgency to act in this field. In this work we opted to develop efforts in this way, trying to analyze in what way we could act in the highest rate of chronic diseases. In view of the temporal characterization of this type of disease, rather than acting in the resolution of the disease, it we should act in the patient's follow-up process, so that their quality of life can improve. One of the key fields is monitoring the disease, commonly performed on daily hospital visits but that can also be done remotely. In the following points we show how the implementation of telemonitoring can and is being implemented in the main chronic diseases which affect a large amount of the world population.

1.2.1 Diabetes

Diabetes are one of the most common chronic diseases and according to WHO the number of persons suffering from this disease is increasing [38]. Results from studies involving telemonitoring patients with diabetes indicated that this patients have a better glycemic control than the others that do not [39].

The development of new therapies and clinical guidelines for the treatment of diabetes benefits from the constant capture of data on the patient's medical condition. Currently it is possible to regularly monitor the blood glucose level of a diabetic patient using a glucometer connected to a telephone network. Similarly, electronic diaries, messaging devices and cellular phones can now support timely transmission of data on a patient's diet, vital signs and symptoms. The use of diabetes telemonitoring has shown significant clinical and behavioral effects on the patient as well as the provider[38].

1.2.2 Chronic renal failure

The number of patients with chronic renal failure is also increasing, so new investments in telemonitoring are being made. Automated peritoneal dialysis, Figure 1.2, which is one of the main peritoneal dialysis is a unique candidate for support via telematic services, once the process is performed automatically by a cycler device during the night. Overall, telematic support is needed and has been well received in this area[40].

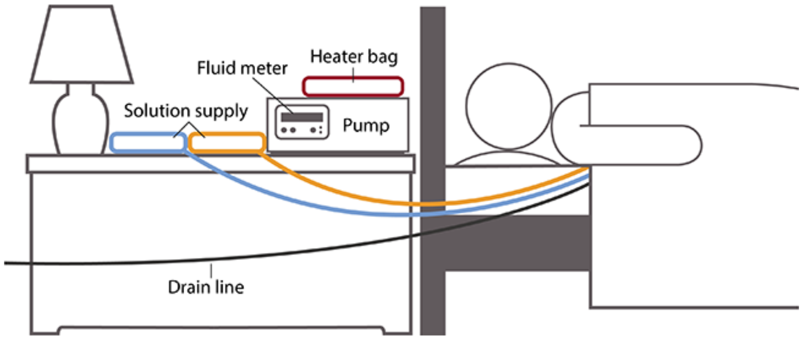


Figure 1.2: Graphical representation of automates peritoneal dialysis solution. Available in [2].

1.2.3 Heart failure

The close monitoring of patients with heart failure play a central role in avoiding hospitalization and shortening the length of hospital stay. Monitoring and support for these patients can also be provided remotely using telemedicine modules. Studies demonstrated the clinical efficacy and cost-saving potential of home telemonitoring as a means of supplementing traditional care for managing heart failure patients. The same studies advance data proving that home telemonitoring improved survival rates by 29% over usual care[41].

1.2.4 Orthopedic Disorders

In orthopedics, telemonitoring has also an important role in rehabilitation. Giansanti *et al* have designed and validated a set of devices for the measurement of finger forces in order to asses therapy after hand transplantation. These devices can be used in rehabilitation for continuous and frequent monitoring of patient function in order to assess progress and adapt the therapy needed[42]. Similar approaches can be developed for other medical diagnostics.

1.2.5 Cancer

There are also several proposals for monitoring chemotherapy at home. Chemotherapy is still administered in the hospital, except for a very small fraction of mainly palliative chemotherapy that is administered at home. However, the procedure can be performed safely at home in a way that is more patient friendly. The medication administration can be done by the patient and be monitoring by a nurse from distance[43].

The main objective of this research, here briefly summarized, was to gather some approaches in the topic "Hospital at home". It was superficially analyzed how the most representative health areas could be evaluated at home, either through the provision of medical care, disease monitoring at home or rehabilitation.

With this review it is provided evidence that confirmed the reliability and accuracy associated with home monitoring as an approach to patient self-management. Also, this studies present consistent findings related to the effects of home monitoring on patients' attitudes and behaviors. It appeared that most patients complied with telemonitoring programs where satisfied, in particular because these approaches allowed them to actively participate in the process of care, improving their feelings of security.

Most important, several studies reported evidences of positive effects on the patients' conditions promoted by home telemonitoring, especially in the cases of pulmonary conditions and heart failure. This was one of the main incentives in the moment of pondering on the area to act, thus concluding that the technological solution to be developed in this work would respond to a problem in the area of cardiology. Also, this area of medicine reports a greater number of patients and consequently is one of the most studied in the diverse fields of activities.

1.3 Purposes and Goals

Several studies support the fact that periodic monitoring of patients with heart disease is related to decreased hospital admission rates [27, 29, 24]. The economic costs associated with the systematic organization of patient follow-up encourage the development of remote monitoring systems for continuous control of clinical variables such as blood pressure, oxygen saturation and heart rate. The implementation of this type of tools allows to increase the medical management on this type of pathologies and when compared to traditional care, to gain time and resources.

This work is based on these records and proposes the development of a portable device for monitoring and continuous measurement of blood pressure during sleep.

With continuous monitoring of blood pressure, it is possible to monitor not only various cardiological health conditions as well as respiratory conditions. However, our proposal intends to respond to a specific difficulty found in the field of hypertension, since it is one of the disorders that most affects the population of developed countries and the one in which there is a greater need to intercede.

We chose the Windkessel Model combined with the Photoplethysmography technique as the scientific basis for the development of the device. This option is due to the reliability of the approach of this model to the biomechanical system of the heart as well as to the viability of the technological implementation. The Photoplethysmography technique is also a proven blood pressure measurement technique, until then used in combination with other techniques, but more recently accepted and used individually to measure a person's blood pressure.

This work began with a brief research and contextualisation of the theme and motivation of this proposal, already described in this first section.

Overall, this paper has seven global sections. Following this introductory section, we present a brief economical context about the medical technological environment.

Next, the state of the art aims to review the theoretical concepts of the circulatory system and briefly explain what the pathology of hypertension consists of. Also in this section the need to perform the self-measurement of blood pressure and the challenges that it presents, in particular challange in the nocturnal measurements, is addressed.

The methods used are presented in section 4, which explains the ideological method followed to guide the development work of a device from a basic concept and idea. It explains what consists of Photoplethysmography and how to interpret the signal obtained by this technique, as well as the explanation of the mathematical Windkessel model. It also shows how the prototype of the device was conceived and how the signal processing was done.

Following we present our proposal to continous measurement of blood pressure and then, this paper reaches the end with the presentation of the results obtained and their interpretation, together with the note of the future work to be developed.

2

Hospital at Home and the potential impact for end-users and the market

It is now estimated that half of the patients in hospitals could be sent home and assisted remotely. The current hypothesis points out that the apparent benefits surpass the financial motives, and will outcome improvements in patients' quality of life [1].

In the Hospital at Home concept, individuals may get their own medical data, and play a more active role in managing their health. Nurses will have a more active role in the patient's life, and doctors will have new insights into the health of their patients. Monitoring, data collection and storage is the key activity in the hospital-home relationship [1].

To provide certain care at home within the next 10 years, it should already be proven safe to do so or that the technology will be widely available to bring this care home in the next 10 years. However, it does not mean that all types of this care will be moved to the home since doing so might not be cost effective or might only be safe or feasible for a certain group of patients. For technology to be widely available within 10 years, it should already exist, but it might still be too expensive, large or cumbersome to use at home [1].

2.1 Technological and economical context

As a consequence of Europe's demographic trend, healthcare and the development of health decices have been main topics of discussion. In order to implement innovative technologies it is extremely important to be cost conscious and effective and to follow the guidelines in healthcare [3].

The bet on improving public health leads to an higher expectation of a healthier life and that is reflected in the increase of quality and productivity of labor.

It is therefore essential to invest in the health of working people in order to prolong their active lives and have better health. With this investment, we are reducing future costs in treating patients with preventable diseases. Currently, one in four people (23,5%) in active life suffer from a chronic limiting condition that can affect their daily activities[3]. Investment in this area becomes significant and this data may contextualize the pressure of health systems and social care structures for improving health care.

Medical devices are nowadays irreplaceable in the diagnosis, prevention, monitoring and medical treatment[3, 44]. As such, the medical device industry faces an unprecedented period of opportunity.

The increasing world population and disposable income fosters an increased demand for medical devices and medical services. The medical technology industry, mainly concentrated in the USA and Western Europe is becoming the central field of the entire healthcare sector.

In Europe it is estimated that there are around 25,000 medical technology companies, with medical technology industry being one of the main players in the European economy. It is estimated that investment in Research and Development in this industry is around 4 billion €. The medical device industry is one of the most innovative sectors with a life cycle of approximately 18 months before a product is available in the market[3, 45].

European countries spend about 10.4% of their gross domestic product on health care, of which 7.5% is spent on medical technologies[3, 45].

The annual growth of the European market is about 4% as can be seen in Figure 2.1. Being the value of this market estimated at 100 billion €.

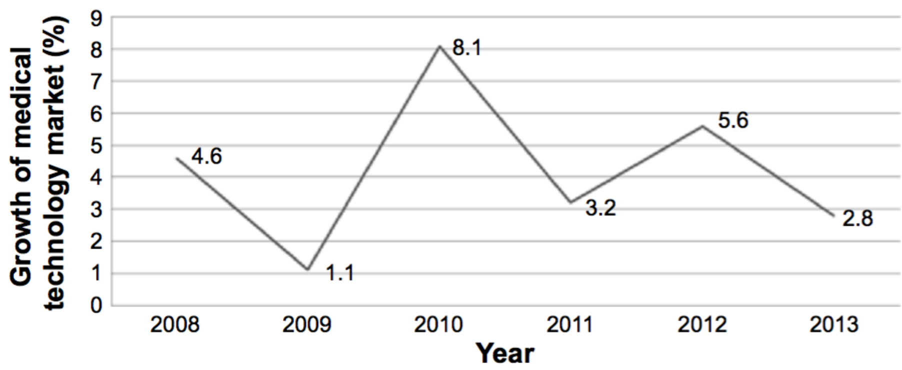


Figure 2.1: European medical technology market growth rates 2018-2013. Font [3].

Medical technologies solve problems in several areas. Overall, the main segment is the in vitro diagnostics, with the cadiology being the second and diagnostic imaging the third.

The medical device industry directly or indirectly influences the economic situation of each country by interfering with the health of the population.

2.1.1 The economy of cardiovascular diseases in Portugal

Cardiovascular diseases are one of the main causes of mortality of the Portuguese population, as such the economic impact of these diseases is considered representative for the national economy. Approximately 70% of the cardiovascular pharmacological expenses correspond to antihypertensive medications. In total, this area represents 30% of outpatient medication costs by the National Health System [46].

The Figure 2.2 represents part of a table taken from [4] where we can observe the weight of the health care costs of Cardiovascular diseases in Portugal in comparison with other European Union countries.

Country	CVDs		
	Cost per capita (€)	Cost per capita PPP (€)	% of total health expenditure
Austria	247	231	11.4
Belgium	199	194	8.5
Cyprus	67	74	6.7
Czech Republic	83	159	14.3
Denmark	215	162	7.0
Estonia	55	96	16.8
Finland	235	208	11.8
France	212	198	8.4
Germany	423	379	15.0
Greece	140	174	10.6
Hungary	52	96	9.3
Ireland	108	91	4.4
Italy	204	206	10.6
Latvia	24	51	11.5
Lithuania	43	90	16.2
Luxembourg	255	220	7.7
Malta	22	38	2.0
The Netherlands	260	240	10.2
Poland	46	100	15.6
Portugal	93	119	8.0
Slovakia	52	107	17.0
Slovenia	80	113	7.9
Spain	97	111	7.1
Sweden	318	261	11.6
UK	352	342	17.1
Total EU	230	230	12.0

Figure 2.2: Health care costs of Cardiovascular diseases in the EU, by country. Adapted from [4].

According to the same study, in 2003, the total costs associated with cardiovascular diseases in Portugal were 1762 million €, of which 969 million €were attributed to the total health costs. Of these, 506 million euros are due to expenses with medicines and 375 million €to hospitalizations. More, 322 million €represent costs due to loss of production as a consequence of mortality [47, 4].

It is estimated that the prevalence of arterial hypertension in Portugal is between 29.1 and 42.2 %. According to [48] the white coat phenomenon can lead to up to 13% of erroneous diagnoses of hypertension. The implementation of new measurement methods can reduce these numbers and avoid costs associated with diagnostic errors.

2.2 SWOT Analysis

The aim of this work is to develop a technological solution to facilitate and promote hospital at home. As such, we turn to SWOT analysis, Table 2.1, to identify at an early stage what strengths, weaknesses, opportunities and threats we might face in development and implementation of a new technology solution in healthcare.

Table 2.1: Swot Analysis for the implementation of a technology solution in healthcare

Strenghts	• Partnerships: HealthCare industry • Demand for innovation in health • Improved Patient well- being • Greater efficiency of operation and decision • Current Investment in Healthcare
Weaknesses	• High price in development • Concept definition • Lack of system integration • User resistance • Slow technological adoption
Opportunities	• Strong market • Hospital care is very expensive • Favorable external environment
Threats	• Lack of information • Lack of studies • Legal bureaucracy • Final user cost

2.2.1 Strengths

One of the strenghts that was immediately identified when proposing the development of a technological solution for health was the creative and scientific environment where this project was developed, that allowed to implement, test and have properly feedback about the technology we wanted to develop. Also, in recent decades there has been an increase in the demand for new technological solutions for health[49], justified by the increasing importance of the patient's well-being.

Patient well-being has been a primary objective in the healthcare industry and with more data produced by the technological solutions, healthcare providers can make better decisions about their patients care and so reduce errors in the process of decision [50]. Advances in health information technologies have occurred at an unprecedented rate and healthcare organizations have responded by increasing their investments in this area .

2.2.2 Weaknesses

Even with the increasing of investments in this area, the development of new technologies is still very expensive [51]. Also, as it has been presented in this work, the concept and implementation of hospital to home is not consensual by academics, which makes it very difficult to present a technological solution that keeps it up with the objectives of the process.

Then we face the problem of lack system integration. Since a patient's treatment involves receiving services from multiple budgetary units in a hospital, information system integration should exist between the computer-based applications within a single hospital. When healthcare organizations coordinate and integrate their internal data, they can improve operations and decision making. However, most healthcare organizations are not yet at this level of system integration [52].

In comparison with other industries, healthcare has been slow to adopt new technologies. Also user acceptance is a common problem with new technologies in healthcare area.

2.2.3 Opportunities

Ageing population is one of the biggest opportunities for the medical device development. Despite the slow adaptation of the industry to new technologies, as mentioned earlier, there has been an increased interest in the implementation of technology in common and recurring health processes.

The concept of traditional hospitalization is an expensive and dated process. As such, modifying it is a necessity identified by hospitals themselves. The implementation of the hospital at home is a new approach that may be the solution to some of the needs identified, such as improving the hospital environment and decreasing the number of admissions.

2.2.4 Threats

The lack of studies regarding this theme and the usefulness of technology implementation in traditional procedures has been a huge threat for the developers. Also, because of that, the information which is arriving to the end users is poorly and that can be one of the reasons for slow acceptance of new solutions.

Furthermore, there is a pressure from payers to develop high quality but less expensive alternatives to hospital care [53]. The rules that manage the healthcare industry are very complex, as result, some technological solutions take many years to have the permeations for been sold. Physicians, medical centers, and other healthcare providers have experienced increased paperwork and cost to incorporate the requirements of legislation into their current methods of operation [52].

3

Follow-up of cardiovascular diseases

3.1 Circulatory system

The circulatory system is responsible for the maintenance of the cells, through the distribution of nutrients and collection of metabolites, as well as the conduction of essential elements to the tissues, such as oxygen and hormones. It includes the heart, blood vessels, lymph and lymphatic vessels. The heart is responsible for the propulsion of blood, pumping oxygenated blood into the body and deoxygenated blood into the lungs.

An auricle and a ventricle compose the heart, each divided into two cavities, called left atrium, left ventricle, right atrium and right ventricle. The cardiac cycle consists in two phases, the diastole and the systole.

The ventricle diastole corresponds to the entrance of venous blood to the right atrium through the superior vena cava, passes through the tricuspid valve into the right ventricle and is pumped through the pulmonary artery into the lungs to be oxygenated. This process, Figure 3.1, is followed by systole, where the blood returns to the heart by the pulmonary veins to the left atrium, passes through the tricuspid valve to the left ventricle and finally is pumped to the various organs of the human body.

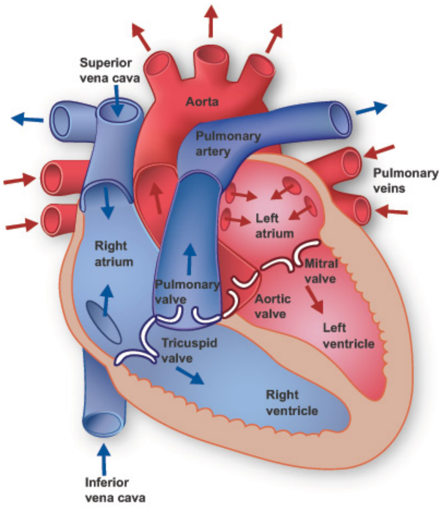


Figure 3.1: Graphical representation of the heart anatomy. Obtained from [5].

Each heart movement is accompanied by variations in aortic pressure, the minimum pressure corresponds to the diastolic pressure, when the blood enters the heart and the maximum pressure is the systolic pressure, which is the moment when the blood is bombarded to the body.

3.2 Cardiovascular diseases and Hypertension

Cardiovascular diseases are one of the main causes of mortality, with arterial hypertension being one of the most recurrent pathology, however, only one-third of the population with hypertension regularly monitors their blood pressure [54, 55].

The correct and early diagnosis, prescription of appropriate therapy and regular lifetime surveillance, accordingly with Portuguese Society of Hypertension in [56] should be the main focus when facing this pathology.The diagnosis can be reversible and it is possible to delay the injuries caused by this dysfunction and consequent mortality events, as well as to regress or even prevent the development of the disease with timely medical intervention [56, 54].

Blood pressure corresponds to the pressure exerted by blood on the walls of blood vessels. It varies between a maximum, called systolic pressure, reached at the time of contraction of the heart and a minimum, diastolic pressure, which occurs at the time of relaxation of the heart. In a healthy individual the values of systolic pressure are less than 120 mmHg and the values of the diastolic lower than 80 mmHg.

If blood pressure values exceed this norm,we have a condition of hypertension. This event is a strong indicator of potential heart attack, arterial damage or stroke. On the other hand, a very low blood pressure, hypotension, is also a concern factor as it can lead to heart damage or kidney failure. The constant monitoring of this parameter is therefore an essential factor in preventive medicine.

Blood pressure levels vary according to the sex and age of the individual. The Table 3.1 presents generally the classification of the pathology of hypertension according to the blood pressure.

Table 3.1: Blood Pressure Bin Levels (mmHg). Obtained from [22].

BP Level	**Systolic Pressure**	**Diastolic Pressure**
Hypotension	<90	<60
Desired	90-119	60-79
Prehypertension	120-139	80-89
Stage 1 hypertension	140-159	90-99
Stage 2 hypertension	160-179	100-109
Hypertensive emergency	>=180	>=110

Currently, blood pressure measurement is done through Korotkoff sounds using a sphygmomanometer and a stethoscope. As such, it requires measurement by a skilled health technician.

The measurement of blood pressure in the hospital setting does not, in general, accurately reflect the reality of the patient's Blood Pressure (BP) values. This is because BP change continuously, in particular with patients with hypertension and as such, with a single measurement it is not possible to obtain their actual value. The patient's alert reaction to the measurement procedure may itself be a source of error [56].

For this reason, it is necessary to develop alternative methods of measuring BP in order to allow the measurement of this parameter under real conditions. Self-measurement of blood pressure is thus one of the most coherent approaches respecting the identified needs and has increasing importance in the diagnosis and follow-up of hypertension [56].

Despite the interest of patients in controlling and monitoring their disease, many don't have adequate knowledge to correctly perform the measurements. However few patients are unable to perform self-measurements of blood pressure using automatic measuring devices [56].

Following in Table 3.2 are the advantages and limitations of self-measurements of BP presented by [56] according with [57]:

Table 3.2: Advantages and Limitations of self-measurements of BP

Advantages	• Possibility of frequent measurements throughout the day and for several days • Analysis of treatment effects at different times of day • Lack of alert reaction to BP measurement • Low relative cost • Easier to use • Involvement of the patient in the management of hypertension • Improved patient commitment to treatment • Improved control of hypertension rates
Limitations	• Need for patient training (reduced for automatic devices) • Ability to use inaccurate devices • Measurement errors • Potential increase in anxiety,resulting in excessive monitoring • Lack of nighttime measurements

The previous table available in the Guidelines of the European Society of Hypertension for Self-measurement of Blood Pressure, demonstrates the nonexistence of nighttime measurements as one of the limitations of BP's self-measurement process.

3.2.1 Blood Pressure Measurement

There are several approaches to noninvasive blood pressure measurement.The most commonly used and well known technique is Sphygmomanometry, Figure 3.2 which is cuff-based and so, not suitable to wear during extended period of time [54, 58].

Figure 3.2: measurement of blood pressure using the traditional sphygmomanometry method [6].

Recently new techniques have arisen to replace this method, such as Volume Clamping and Applanation tonometry, both are non-invasive and allow continuous measurement of BP. The Volume Clamping technique consists in obtain BP value by analysing pressure waves from rapidly inflating and deflating the cuff placed on the finger. However, the device used to perform the procedure is expensive and uncomfortable for continuous use. On the other hand, Applanation tonometry does not use any type of cuff, but it involves radial artery compression and as such is also an uncomfortable technique and inadequate for measurements over a long period of time. Further, due to complexity, it is difficult to perform in practice and requires constant calibration [59, 60].

Typically, BP values can be obtained by combining PPG with other techniques, Figure 3.3 such as ECG, once both ECG and PPG signals are synchronized with the human cardiac cycle. [61].

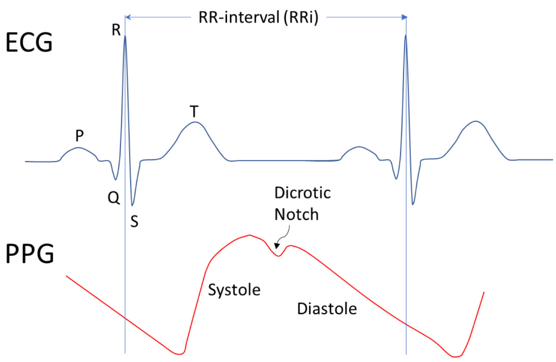


Figure 3.3: Comparison between PPG waveform with ECG [7].

One popular approach is to obtain blood pressure by studying the pulse transit time PTT, calculated from the ECG waveform. This measurement is based on the principle of pulse wave transition, measuring the elapsed time between the peaks of the ECG and comparing with the wave of PGG.

Chen *et al* in [62] relate the high frequency information in the PTT with the lowest frequency information in a systolic blood pressure measurement. [63]. However, in addition to the complex model of propagation of arterial waves and the variability of the physiological parameters, the use of this method implies the comparison with measurements obtained from the Electrocardiogram or Ballistocardiography [54, 64, 65]. The following Figure 3.4 shows a commercial solution available using this method combination.

Figure 3.4: SOMNOmedics^{TM} combines the pulse transit time with ECG and SpO2 finger clip to calculate blood pressure [8].

Zheng *et al* in [66] studied the effect of the cuff pressure in PTT and concluded that the external pressure exerted by the cuff influences the results obtained in the measurements.

Chandrasekaran et. al in [67] conciliated the signal of PPG with the sonorous sound of heart beat, and through a linear regression, was able to withdraw values of BP. In its linear regression model, it was able to estimate the systolic and distal BP by the time difference between the sound wave peak and the PPG signal.

Both of these systems present a great difficulty, the coordination of both signals obtained by the two techniques.

As such, the use of optical methods for the measurement of BP using only the Photoplethysmography signal, presents unequivocal advantages when compared to those previously mentioned. The measurements are operator's independent and a PPG device has lower costs. In particular, other advantages of using PPG compared to the traditional Doppler ultrasound method is the fact that it excuses an acoustic coupling gel [63].

Hence, the single use of the PPG signal is in focus by the scientific community, and in recent years, several attempts at a single approach have been made using linear regression or neural network.

In [68], John Allen *et al* correlated the BP and PPG waveform by using linear and neural network system identification techniques. Later, S.C. Millasseau *et al* published a method that allowed the calculation of a normalised BP waveform from PPG, based on generalised transfer fuction and fast Fourier transforms [69].

Jonsson *et al* in [70] compared measurements obtained using the PGG and Doppler ultrasound techniques and verified that there were no significant differences between the two methods, thus proving the reliability of the PGG method.

However, although the results obtained in these studies are satisfactory, they can not associate the characteristics of the PPG wave with PS and PD values.

Only recently in [54] was presented a theoretical explanation of the PPG waveform and presented an algorithm for the extraction of BP from PPG Signal with high accuracy.

Lately, several medical devices that incorporate the photoplethysmography technique have started to emerge, since it is simple to implement and not evasive. Several commercial oximeters already support their measurements exclusively in this technique. However, when it comes to measuring blood pressure, this is not the case.

One of the first approaches, based on PPG, was presented by Finapres™, Figure 3.5, whose technological solution allowed the measurement of blood pressure in the finger on a continuous basis, through the pulsatile vascular discharge of the artery walls of the finger using an inflatable cuff with a built-in PGG sensor [63].

Figure 3.5: Finapres™ medical system for continuous blood pressure monitoring. Available in [9].

The Vascular Assist™ Vascular System is a commercially available device for the automatic measurement of limb pressure using the PPG technique [63].

Recently, a trend has emerged to capture the PPG signal through the use of a smart phone camera on the finger [71, 22], however, it is also possible to make a precise measurement in other regions of the body, such as the ears.

3.3 Self-measurement of blood pressure

The self-measurement of blood pressure at home has many advantages, such as the increase in the number of measurements, the absence of the white coat syndrome and the reduction of costs. It can also be decisive in monitoring antihypertensive therapies and reducing the number of doctor visits required to detect hypertension [72] .

Currently, for a patient to be able to self-measure BP in their home, they must comply with the following requirements [72, 73, 74]:

- Only use devices properly validated and accepted for the purpose.
- The use of auscultatory devices should be preceded by precise instructions to the patient on how to proceed.
- It is recommended to use upper arm devices instead of wrist and finger devices, as they are more susceptible to errors derived from the anatomy. In particular, the use of measuring devices on the finger should be analyzed, as inaccuracies may occur due to peripheral vasoconstriction and consequent alteration of blood pressure.
- The size of the cuff should be appropriate and comply with the indications of the clinical organs. The clamp should be placed device 2 to 3 cm above the arm fold.
- Before performing the measurement, the patient should rest for 5 minutes.
- BP home monitoring should always be monitored by a physician because the patient's reports can be unreliable.

The reproducibility of home BP depends on the number of measurements, with a minimum of 30 measurements being recommended for at least 3 days to obtain a stable BP[72, 75]. Following, Figure 3.6 illustrates the self-measurement of BP.

Figure 3.6: User checking blood pressure at home with an electronic sphygmomanometer. Available in [10].

The hypertension guidelines propose BP self-measurement at home as an important means of evaluation of the response to antihypertensive treatment to improve the therapy and to competing the white coat syndrome. Patients with a tendency to high BP may use this feature to monitor their condition and to identify in advance possible pathologies later validated in ambulatory[72]. Stergiou *et al.* in stated that the sensitivity of self-measured home BP may be low, but it emphasizes the importance of this method when reconciled with ambulatory monitoring [76].

Celis *et al.* conclude in their work [72] that adjusting antihypertensive treatment based on home BP contributes to a decrease in the intensity of drug treatment and a decrease in long-term medical follow-up. It is further stated that home measurement allows the discontinuation of antihypertensive drugs twice as fast.

3.4 Measurement of blood pressure during sleep

The measurement of blood pressure (BP) during sleep can provide important information for diagnosis and control of hypertension.

An individual's blood pressure may be influenced by a number of factors, such as physical activity, mental health status, medication, or cardiac system conditions. It is therefore possible that BP varies up to 10 mmHg during the 24 hours of the day [77, 73].

Currently to monitor BP's development over several hours, BP is measured at the hospital and repeated again a few times at home. However, this method does not provide sufficient information about BP dynamics. In addition, it is known that hospital measurement leads to the erroneous diagnosis of hypertension in about 25% of individuals due to the anxiety caused. For all this, it is important to measure BP over a long period of time during the person's normal activities [77, 73].

The Holter Monitor is one of the current possibilities of cardiovascular measurement and monitoring available in hospitals. It consists of a portable device, the Figure 3.7, which continuously monitors the cardiac electrical activity of patients for 24 hours.

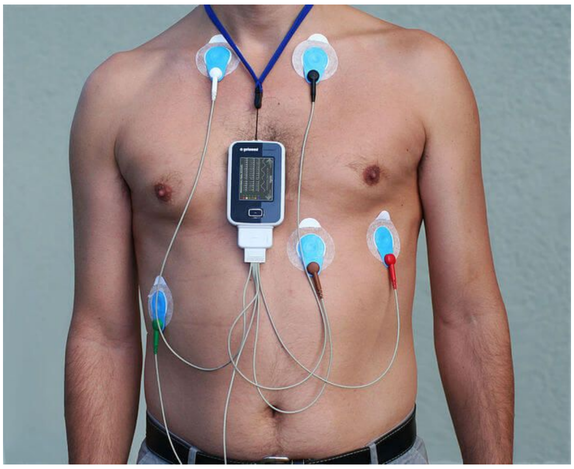


Figure 3.7: Holter Monitor Device. Image available in[11].

The clinical importance of nighttime measurement has been emphasized in several studies [78, 79] and stands out, not only for the information it can provide, but also for the challenges it entails.

For instance, the absence of a nocturnal BP pattern may be a factor indicative of cardiovascular diseases [77, 73]; as another example, a very high BP in the morning may be a warning for a stroke in the elderly [77, 80]; also, in pregnant women, hypertension during sleep is common and often associated with adversity during pregnancy [77, 81].

The BP measurement not only gives information about the state of the cardiac system, it is also a source of diverse pathological data. Dajani *et. al* in [77] concluded about several observations regarding this condition. Namely the fact that the frequency domain of the BP wave is directly associated with the nervous and respiratory system.

In a healthy individual, there is an oscillatory component of BP in the lower frequencies, which is thought to be associated with the regulation of BP. The higher frequencies are thought to be directly related to breathing. According to some studies, this pattern changes in patients with heart failure [77, 82]. During sleep, in these patients there are many oscillations in the low-frequency region of the BP that is related to their respiratory outlook. This phenomenon is known as Cheyne-Strokes breathing.

These asynchronous BP changes lead to damage to the heart and vascular system, which can consequently lead to respiratory instability and damage to the sympathetic nervous system [83].

Patients with sleep apnea are also identified as a group that experiences these variations at night. Before an episode of apnea there is an abrupt descent in the BP and at the end a rise [77, 84]. These abrupt variations favor the possibility of damage to the cardiovascular system and are often associated with the development of hypertension.

During sleep, BP is currently measured intermittently, with a period of 10-30 minutes, which makes it possible to obtain only a fraction of the BP values, so that significant variations in BP can be lost during the night, which could be relevant to understand an indication of some pathologies, such as those mentioned above.

Moreover, this methodology does not allow a detailed analysis of the wave, which in turn would allow to obtain more details of the cardiovascular condition, such as cardiac output, stroke volume and vascular stiffness [77].

The Figure 3.8 shows a Solution for measuring blood pressure for 24 hours using auscultatory or oscillometry with requirement of a cuff and measurements. This methods require at least measurements from every 20 min.

Figure 3.8: Nighttime measurement using cuff based methods[12].

As has been repeatedly pointed out, several alternatives to BP's traditional measurement method have been presented. However, opinions differ on the efficacy and veracity of these alternative solutions. One of the points of disagreement is the measurement of BP in peripheral zones, since the hydrostatic difference between the heart and these areas is more pronounced and the interference of the vasoconstriction more problematic. During sleep, these errors are minor and can easily be corrected [77, 85].

3.4.1 Challenges

Reliable information about blood pressure at night can be obtained using a device that allows the measurement of blood pressure during sleep at home over and over for a long period of time.

However, to date, there are not many attempts to develop devices to address this need. This is due to the fact that until now, with the techniques commonly used to perform the measurement, it was practically impossible to perform these measurements during sleep, since they would cause sleep disturbance [79, 86].

With the new approaches, it is now possible to continuously measure BP during sleep without awakening the person, thereby enabling a continuous uninterrupted signal to be obtained in reverse of traditional intermittent measurements that were heavily influenced by the REM and non-REM .Despite the technical challenges of measurement during sleep, this is a prime time to get BP since it is also the moment least susceptible to external and internal influences on the patient [77].

In this work we propose to respond to this limitation through the development of an automatic BP self-measuring device during sleep. This solution will also address other identified limitations such as the need for patient training and increased anxiety resulting from the number of measurements currently required.

4

Conceptualization of the technological approach for blood pressure measurement

4.1 Biodesign and Healthcare Innovation

The process of innovation allows the development of new scientific discoveries from the initial point, the idea. The Stanford Biodesign program (Figure 4.1) aims to explore this process in order to develop innovative medical solutions through the systematic evaluation and analysis of health, innovation and concept development based on needs. Although focused on the development of technology for the health area this process can be applied to any area of study [87].

Innovation requires invention and implementation to create a new idea, product, or process. In health, innovation is commonly associated with new scientific discoveries and new ideas tend to be rejected as industry sees innovation in this field too risky and academic institutions a process too commercial. Therefore, any kind of innovation in this field has to be carefully implemented [87].

To merge these two entities, Stanford has developed a program to foster their collaboration by bringing together engineers and physicians and thus unifying the world of science with clinical practice. The focus of the program is to educate future leaders in medical technology throughout the innovation process [87].

The Biodesign process, Figure 4.1, divides the design of a technological solution into key steps, the needs identification, needs filtration, concept generation, concept filtration and early stage invention and implementation [87].

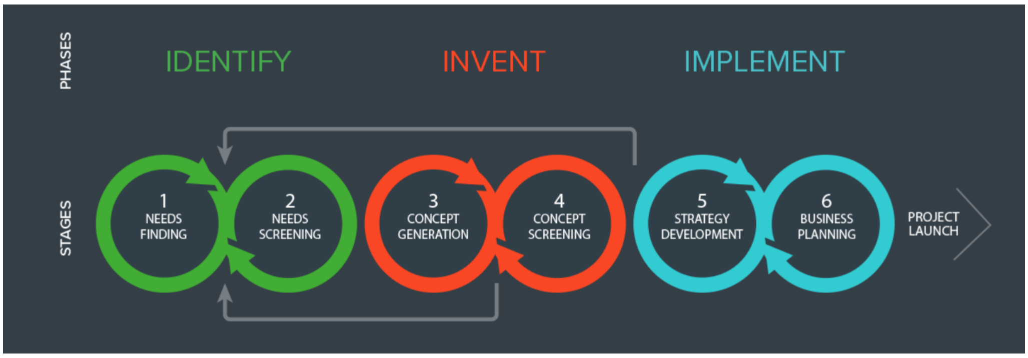


Figure 4.1: Biodesign Process Innovation. Obtained from [13].

The first component of the program is defined by the choice of the central theme to be analyzed and under which all the study will be carried out. After choosing the area in question, the second phase of the program involves the consolidation of knowledge in the clinical area to be focused. The third phase corresponds to the characterization of the area, discussion of problems and brain-storming of possible solutions. This work is followed by field observations of the difficulties encountered, giving answers to questions such as which target population or possible outcomes may arise. With this, it is possible to move on to the next step, which consist in filtering the needs found and choose opportunities for action. To do this, it is necessary to collect as much information as possible and assess which opportunities will be most advantageous. Opportunities are thus classified and identified which may be more successful in the market[87].

From these various concepts and opportunities highlighted and classified then comes the final idea, thus obtaining the concept that will be implemented. It is this phase that requires deep analysis of the intellectual property of regulatory systems, repayment strategies and economic viability [87].

If the project is established as viable, it is advanced to a prototype, when engineering challenges begin to emerge. Filled with proof of concept and advancing to more advanced technological development phases [87].

For the development of the technological solution presented in this work, the stages constituting this program were respected. The work started with the idea of creating a technological solution to be implemented in the health area, however, it was not identified in which area we would act or how we could actively contribute in this field.

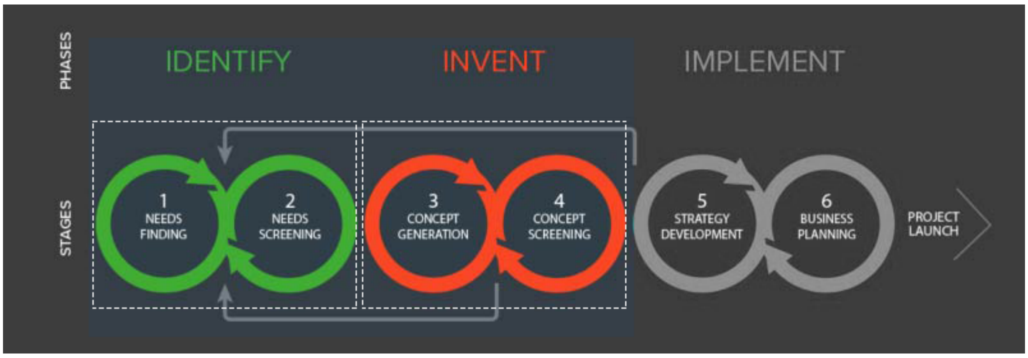


Figure 4.2: Biodesign stages considered in our work. Adapted from [13].

We have chosen to focus on the first two stages of the program, Figure 4.2. As so, we begin by identifying needs in the various fields of health and subsequently choose a field of action. This research culminated in the identification of the need to monitor patients with hypertension, in particular the challenge of creating a device that could measure blood pressure continuously during sleep. The creative and research process was also highlighted by the strong economic component that accompanied all the stages, as the program suggests.

With these observations we were then able to establish the concept that we wanted to develop and define the contribution of our work to the needs identified. The Figure 4.3 illustrates the main points of interest to which our device must respond as a differentiator from other solutions currently on the market.

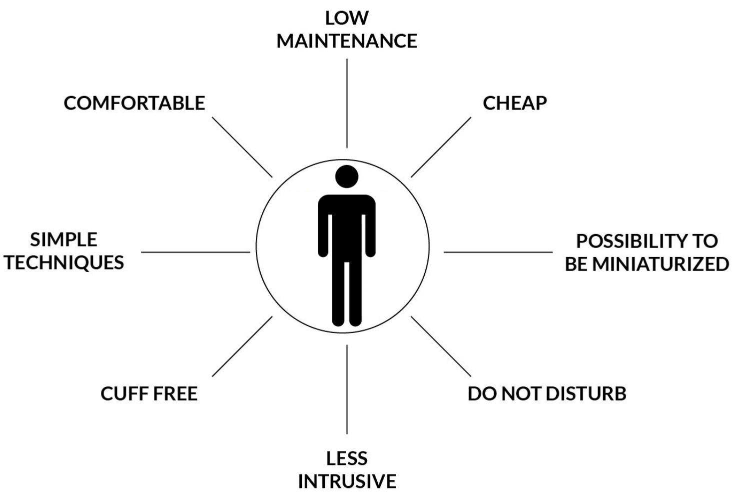


Figure 4.3: Differentiating elements of the device to be developed.

This study was essential for the choice of measurement technique to be implemented in the device. After several approaches studied, it was decided to use the technique of Photoplethysmography, because it allowed to implement a large part of the elements previously presented.

4.2 Photoplethysmography

Photoplethysmography (PPG) is a noninvasive optical technique that can be used at skin surface and detect blood volume changes in microvascular bed of tissue. This technology can be used in a wide range of medical devices, from oxygen saturation measuring to blood pressure and cardiac output [63, 88].

The PPG technology is simple, only requires a light source to illuminate the tissue and a photodetector to measure variations in light intensity according with changes in perfusion in the catchment volume, Figure 4.4. Because there is a window in the absorption spectra of water that allows visible red and near infrared light to pass more easily, it operates at a red or near infrared wavelength. [63, 89].

As light travels through the biological tissue is absorbed by the skin, bones and blood. However, it is more absorbed by the blood than by the surrounding tissues, thus allowing the detection of variation of light intensity in the boold flow by the PPG sensors. Although the voltage of the PPG signal is proportional to the amount of blood in the region where the light is incident, it is possible to detect even small variations in flow [14].

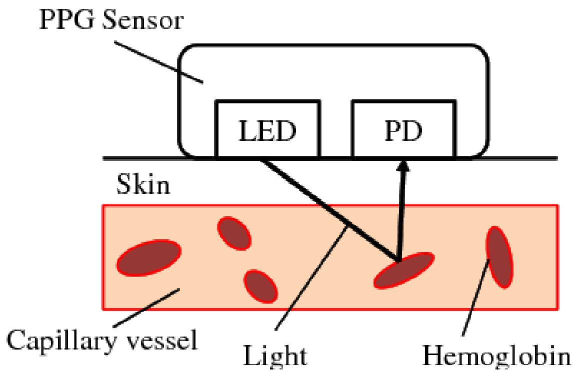


Figure 4.4: PPG signal detection process. Available in [14].

PPG waveform has two components, a pulsatile physiological waveform AC, related with cardiac synchronous changes in the blood volume with heart beat, and the DC, Figure 4.5, with lower frequency components and slower variation attributed to respiration, sympathetic nervous system activity and thermoregulation. The AC component has its fundamental frequency around 1 Hz, depending on heart rate [63].

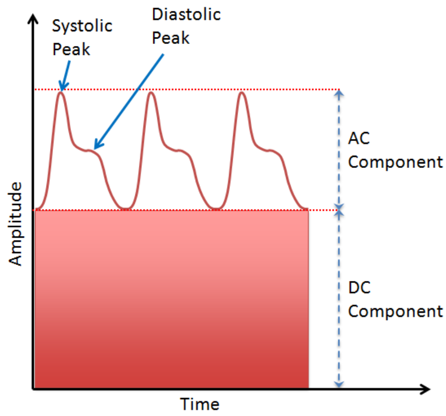


Figure 4.5: PPG wave components. Obtained from [15].

Photoplethysmography AC pulse waveform is defined by an anacrotic phase, corresponding to the rising edge of the pulse and a catacrotic phase in the falling edge of the pulse, represented in the following figure 4.6. The first phase corresponds to systole and the second to diastole. Wave reflections that can be observed correspond to periphery. The pressure pulse changes in shape and temporal characteristics as it moves towards periphery and suffers amplification due to reflection of the pulse wave and reducing of the arteries [63, 90].

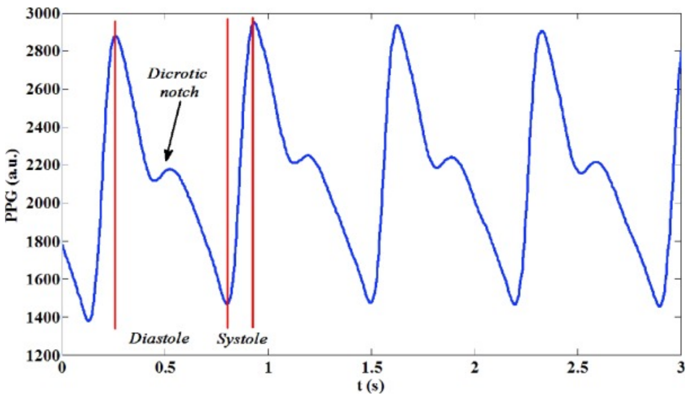


Figure 4.6: Graphical representation of PPG pulse waveform. Obtained from [16].

Although the interaction of light with biological tissue is complex and involves multiple optical processes such as scattering, absorption, reflection, transmission and fluorescence [63, 91], researches have highlighted some key factors that affect the amount of light received by the photodetector in PPG . They are blood volume, blood vessel wall movement and the red blood cells orientation [63, 88].

Also, measurements should be performed at an isosbestic wavelength, which means, close to 805 nm for near infrared range, so that changes in oxygen saturation in the blood do not interfere. Regarding the tissue penetration depth, the PPG catchment volume can be of the order of 1 cm^3 for transmission mode systems [63].

4.3 Model of Aortic Blood Flow and the 2-Element Windkessel Model

Otto Frank, a German physiologist approached the human cardiovascular bio-mechanical system to a closed hydraulic circuit. The built circuit integrated a water pump filled with water with an air region, connected to a chamber. Like the natural movement of the heart, when the system is pumped, the water compresses the air, which in turn forces the water out of the chamber [17].

This model is suitable for the illustration of blood fluid, since it takes into account the arterial compliance, that is, the elasticity and extensibility of the coronary arteries, the peripheral resistance exerted by the blood in the blood system and also the inertia of the blood throughout the cycle cardiac [17].

The Mathematical Windkessel Model assumes that the cardiac cycle starts at systole, and that this phase corresponds to $2/5^{th}$ of the total period of cardiac cycle. The arterial compliance, peripheral resistance and inertia are represented respectively by a capacitor, a resistor and an inductor. This model can be build taking into consideration two, three or four elements. Although the four element model is more accurate, with the adding of physiological factors, the computational complexity increases and the it gets harder to study the resulting curve. As so, for the approach in study, the two element model is more suitable, because this way we can have a better control of the variables and less opening to errors.

The two element model represented in Figure 4.7 takes into consideration the effect of arterial compliance and total peripheral resistance, represented in the electrical model as a capacitor (C in $cm^3/mmHg$) and as a resistor (R in $mmHg/s/cm^3$) respectively. The capacitor has the function of charge storage and the resistor as energy dissipating. The blood flow (I(t) in cm^3/s) is analogous to the current of the circuit and the blood pressure in aorta (P(t) in $mmHg$) is illustrated as the time-varying electric potential.

$$I(t) = \frac{P(t)}{R} + C\frac{dP(t)}{dt} \tag{4.1}$$

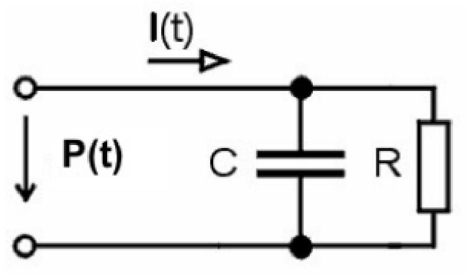


Figure 4.7: 2-Element Windkessel Model for cardiac cycle. Obtained from [17].

According to Catanho *et al.* analysis in [17], the blood flow behaviour, *I(t)*, can be approximated to the behaviour of a sinusoidal wave with amplitude I_0. In the diastole, *I(t)=0* because the ventricles are relaxed and therefore there is no blood propulsion into the aorta. However, at systole, when the blood is expelled into the aorta, the blood flow can be modeled as sinusoidal wave as,

$$I(t) = \begin{cases} I_0 sin(\frac{\pi t}{T_s}), & (n-1)T_c < t \leq (n-1)T_c + T_s \\ 0, & (n-1)T_c + T_s < t \leq nT_c \end{cases} \tag{4.2}$$

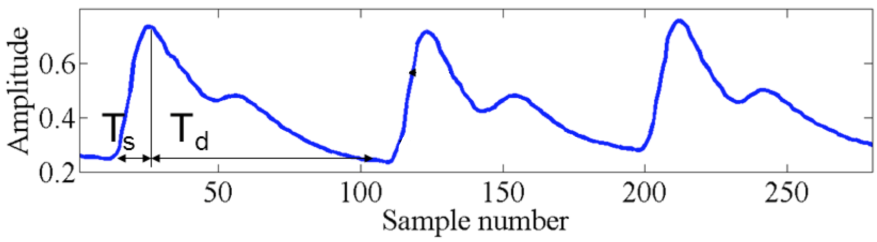


Figure 4.8: Sample photoplethysmography waveform. Adapted from [18].

and $T_c = T_s + T_d$. Where in n^{th} cardiac cycle, the t represents time, T_c the period of the cardiac cycle, T_s the systole time and T_d the diastole time, all in seconds, Figure 4.8.

Solving Equation 4.2 and considering C_0 the cardiac output, we can obtain I_0 by,

$$\frac{C_0 T_c}{60} = I_0 \int_0^{T_s} sin(\frac{\pi t}{T_s})dt \tag{4.3}$$

$$I_0 = \frac{C_0 T_c}{60 \int_0^{T_s} sin(\frac{\pi t}{T_s})dt} \tag{4.4}$$

Now, combining the Equations 4.1 and 4.2 we are able to isolate P_s and P_d as,

$$P_s = P(t|t = T_s) = P_d e^{\frac{-T_s}{RC}} + \frac{I_0 T_s C \pi R^2}{T_s^2 + C^2 \pi^2 R^2}(1 + e^{\frac{-T_s}{RC}}) \tag{4.5}$$

$$P_d = P(t|t = T_c) = P_s e^{\frac{-T_d}{RC}} \tag{4.6}$$

Equally, using the Equations 4.5 and 4.6 we can express the R and C as function of the other variables.

We can also use PPG features to estimate the value of R and C using machine learning techniques as was done in [18] by Choudhury *et. al* or artificial neural network to model the non-linearity between independent and dependent variables as presented in [20] by Banerjee *et. al.*

4.3.1 Arterial compliance

The arterial compliance (C) corresponds to the variation of arterial blood volume due to variations in blood pressure, Equation 4.7. Quantifies the elasticity of the arteries as such is one of the important cardiovascular risk factors. With aging compliance tends to decline. With decreasing arterial complacency, there is also an increase in systolic blood pressure [92].

$$C = \frac{\Delta V}{\Delta P} \tag{4.7}$$

One of the characteristics of patients with hypertension is decreased compliance as a result of endothelial dysfunction. Compliance can be measured using ultrasound techniques.

4.3.2 Peripheral resistance

Vascular resistance (R) corresponds to the relationship between blood pressure variation throughout the cardiac cycle and blood flow (Q), Equation 4.8. The resistance exerted by systemic circulation is also known by peripheral resistance.

$$R = \frac{\Delta P}{\Delta Q} \tag{4.8}$$

Vascular resistance is strongly influenced by hormones that regulate vasodilation and vasoconstriction

4.4 Photoplethysmography instrumentation

Modern PPG sensors utilise low cost semiconductor technology with Light Emiting Diode (LED) and matched photodetector devices working at red or near infrared wavelength. Emerging technologies including PPG sensors are being adopted in telemedicine and remote monitoring [63].

LEDs are used to convert electrical energy to light energy and its intensity should be constant and low in order to minimise local tissue heating. The photodetector is connected to a low noise electronic circuit and converts light energy into electrical current. Its spectral characteristics should match the LED ones. The electronic circuit includes a transimpedance amplifier and filtering circuitry, which is necessary to remove the higher frequency noise, with a high pass filter to remove the dominant DC component, enabling the AC component to be boosted to a nominal 1V peak-to-peak level [63].

There are two main PPG operational configurations, the transmission mode operation, where the tissue sample is placed between the source and detector, and the reflection mode in which the detector and LED are side-by-side, Figure 4.9. Transmission mode has more restrictions than the refection mode. According to several studies, the ear, finger and toes are the areas where pulses can easily be detected, although there are no recognised standards for clinical PGG measurement [63].

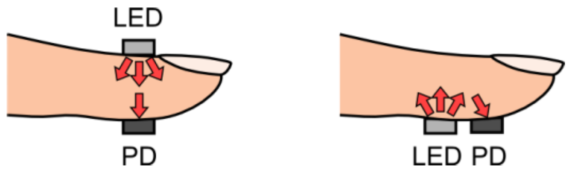


Figure 4.9: Transmission mode and Reflection mode, respectively. Available in [19].

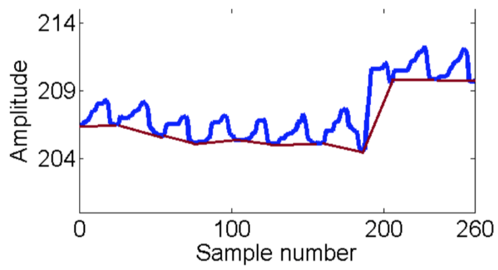
Factors such as posture, relaxation, ambient temperature and acclimatisation should be taken into account, since can influence the repeatability or reproducibility of PGG measurements [63].

4.5 Photoplethysmography signal processing

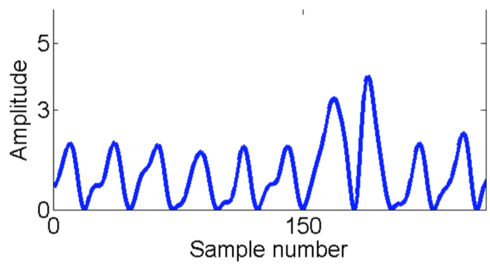
As noted above, the PPG signal is composed by a strong DC component resulting from breathing and high frequency noise and an AC component containing the wave information.

The frequency of the PPG signal, although depending on the subject, is concentrated around 1 Hz, and therefore the signal was subjected to a bandpass filter to eliminate the very high or low frequencies that were discrepant with this average.

It was also necessary to remove the DC component and fix the baseline of the signal, as this is one of the main reasons for the calculation errors of this feature. We based our methodology in the methodology presented in [20] to proceed with signal pre-processing, illustrated in the following Figure 4.10,



(a) Noisy PPG signal



(b) After pre-processing

Figure 4.10: Noise cleaning technique of PPG signal, presented in [20].

To uniform the signal, a vector F containing all n samples for one cycle of the signal was created. Subsequently, a vector F' was also created, forming a segment between the two endpoints of each cycle, with the same number of n samples and equally spaced between each value, calculated using linear interpolation.

Then subtracting F' to F, we obtain the signal in this cycle, with zero baseline, ready for more detailed analysis.

4.6 Monitoring of vital signs in the ear

Non-invasive measurements of vital signs in the ear have many advantages when compared to other body regions. This location is ideal not only physiologically but mechanically. Also, the PPG signal on the ear is as reliable as the signal obtained on the finger [21], as can be observable in Figure 4.11, where it is possible to compare two PPG signals obtained in the ear and finger respectively.

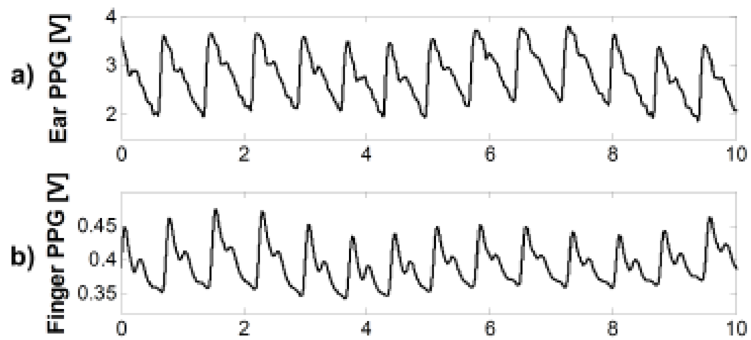


Figure 4.11: PPG signals obtained in the ear and finger respectively. Adapted from [21].

Many of the current cardiac monitoring solutions involve the use of electrodes and adhesives, which can cause skin irritation and make them unfeasible for prolonged use. The Sphygmomanometry technique involves the use of a cuff and therefore makes continuous measurements impossible. Other alternatives already presented are used on the wrist or hand and as such require constant calibration due to the variation of hydrostatic pressure relative to the heart. Placing a device at extremities makes the measurement susceptible to errors and decrease the measurement accuracy [21, 93].

The BP measurement in the ear obtained by optical methods decrease the probability of movement related errors and mechanically, the ear is in the same orientation of the heart, which decreases the need for constant calibrations [21].

5

Our proposal for continuous measurement of blood pressure during sleep

5.1 Device features

The process of implementing technology in the health area involves the adaptation of the devices so that they can be viable in a continuous use and medical accompaniment. Therefore, we briefly highlight some characteristics that the device that we propose to develop must aggregate, so that in the future it will be implemented for a medical solution.

One of the most important characteristics is the biocompatibility of the device. Since this will be in prolonged contact with the individual, the choice of materials suitable for the encapsulation is essential, avoiding allergic reactions and discomfort in its use.

Another point to take into consideration is the portability of the device. Given the environment where the solution is to be implemented, it is essential that it allows freedom of movement and that the size and weight are reduced. As well as ergonomically, it should adapt to the place of implementation, in this case, the ear.

The device to be developed must still be robust and reliable, so that there is no possible loss of information during its use. At an energy level, the device must have the lowest consumption possible, allowing its use at least 6 hours without recharging.

5.2 System architecture

Our proposal for the development of the continuous pressure measuring device is distinguished by the simplicity of the system. It is intended to develop a small device that is placed in the ear before the user falls asleep. At that moment, the signal must be acquired and the PPG signal is continuously recorded along the sleep cycles. During the acquisition hours the signal is sent via wireless communication (e.g Wi-Fi, Bluetooth) to the signal processing and analysis module. At the moment the user wakes up, the signal acquisition should be finished. The signal is then properly processed and the mean blood pressure value calculated on that night. It will then be sent to a database where the patient and the doctor can view the history of blood pressure.

At the implementation level we will then have a signal acquisition unit, the device, a signal processing and analysis unit and a control center where the database will be available. In this phase of the project will only be studied how to implement the acquisition unit and process the signal. In the figure 5.1 we can see schematized the architecture of the system.

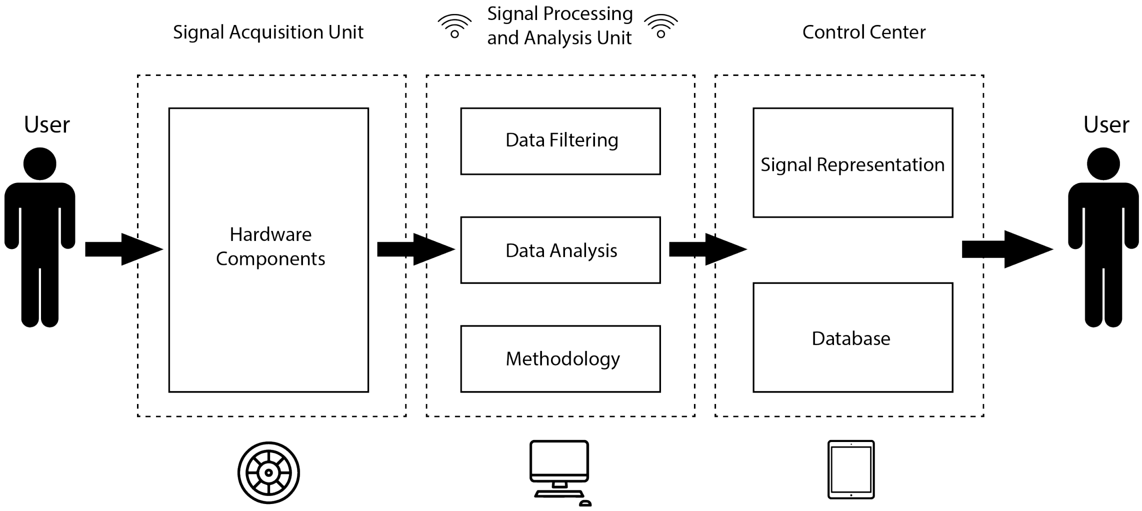


Figure 5.1: Architecture of the system.

In the Figure 5.2 we can observe the intended design for the measuring device. The electronics consist only in a lilyad to allow communication via wi-fi, a sensor to get the signal and a small battery.

The encapsulation would be carried out in a flexible bio-polymer to adapt the position of the user and decrease the discomfort in its use.

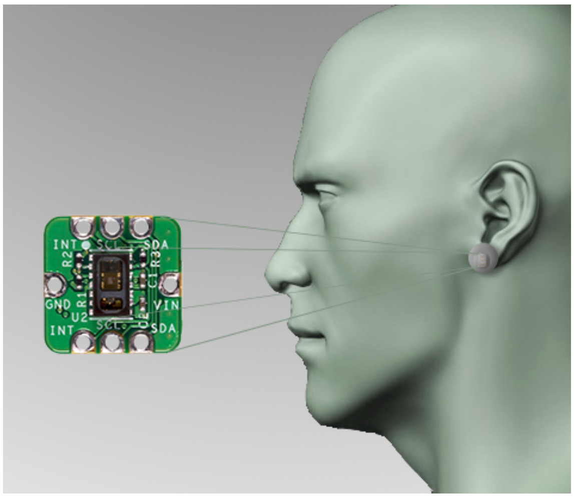


Figure 5.2: Graphical representation of the device.

5.3 Signal acquisition

The work began with a proof of concept and the first order of work consisted in obtaining a basic signal of PPG in the finger and its processing, in order to verify the possibility of obtaining the values of diastolic and systolic pressure.

It was then necessary to schematize what electronic components would be required to perform the PPG technique. After a deep research of the solutions that were available in the market, it was concluded that it would not be advantageous to build a LEDs and photodetetor circuit from scratch, since it is possible to find boards with integrated circuits that responded to our first needs.

It was thus chosen for this first approach and signal obtaining, the MAX30102 Evaluation Kit from Maxim Integrated. The kit consists of two boards, a USBOSMB motherboard, a daughter board that includes the MAX30102 and an accelerometer. The power of the kit is supplied by USB, being +1.8V to the sensor and +4.5V to the internal LEDs of the MAX30102 [94].

The MAX30102 sensor included in this kit was useful for a first study of signal acquisition, since it already included internal LEDs and respective photodetectors that enabled the performance of the PPG technique. Furthermore, it already incorporated the optical and electronic elements of low noise that allowed the rejection of ambient light. It has been specially developed to incorporate mobile and portable devices such as wearable devices and fitness assistant devices and also, the communication protocol used is compatible with the I2C interface [94]. The layout of the sensor PCB board is shown in figure 5.3

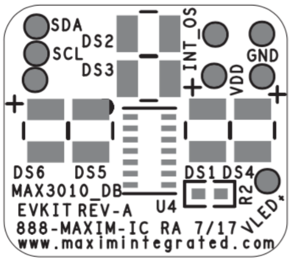
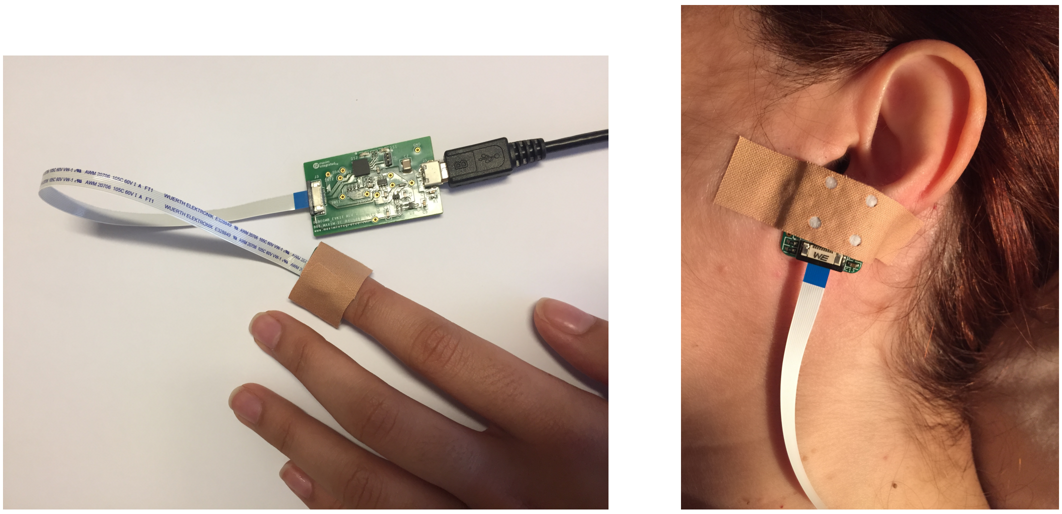


Figure 5.3: MAX30102 daughter Board PCB Layout [21].

We used the kit software to get raw data from the LEDs. We then calculated the blood pressure according to the methods described in the previous section.

As already mentioned, firstly the signal was obtained on the finger and processed. After, the process was repeated with ear signal acquisition. Both signal acquisition are illustrated in Figure 5.4.



(a) Acquisition of the sign on the finger

(b) Acquisition of the signal in the ear

Figure 5.4: Acquisition of the signal using the sensor MAX30102.

At a later stage, it was decided to evaluate the interference of the kit in the acquisition of the signal. As such, it was decided to test the acquisition of the signal with a new architecture, Figure 5.4, this time using an Arduino and MAX30100 Heart-Rate Oximeter Pulse Sensor also from Maxim Integrated.

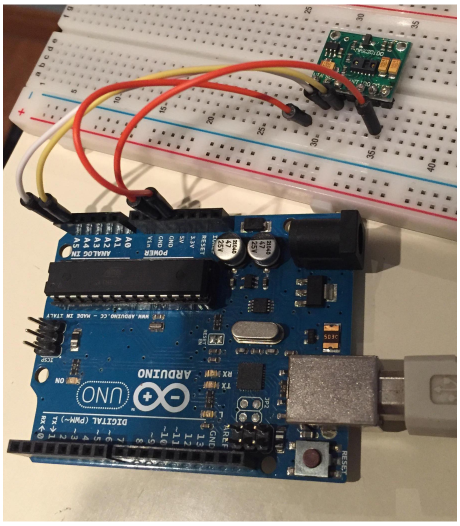


Figure 5.5: Alternative architecture to the Maxim Integrated Kit.

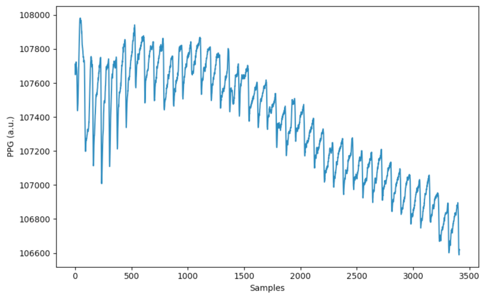
At a later stage, we worked with the MAXREFDES117#, Figure 5.2, sensor also from the same provider. This sensor is smaller than the two sensors mentioned above and as such is more suitable for the intended application, because the tiny board allows it to be placed in the ear more comfortably. It has also integrated the red and infrared LEDs and the power supply.

5.4 Signal processing

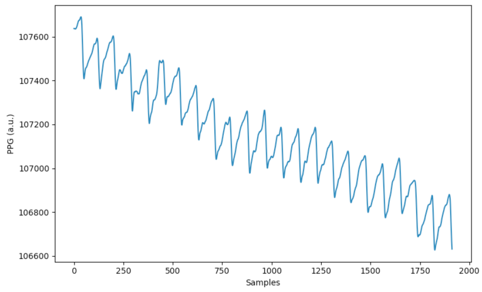
As explained in the previous section, initially the PPG signal was acquired using the Maxim Integrated kit using the software provided with the kit.

After data collection, the signal was segmented according to its temporal acquisition and discrepancies were removed, which could be sources of error. The first and final data, whose values were most likely to have been obtained with interferences created by performing anomalous movements, were eliminated. Only the signal corresponding to the moment of stabilization of the user and the assembled system was then considered.

The processing of this signal was performed using *python* tools and libraries. The *scipy.signal.lfilter* was used to filter the data along one dimension with an IIR filter, the result of which can be seen in the following Figure 5.6.



(a) PPG signal before applying the IIR filter



(b) PPG signal after applying the IIR filter

Figure 5.6: Noise cleaning for for the obtained PPG signal

The next processing step consisted of the removal of the DC component and baseline. The maximum and minimum values of the signal were identified and the baseline of the signal was calculated using the linear interpolation method. The Figure 5.7 shows the signal maximum values identification process.

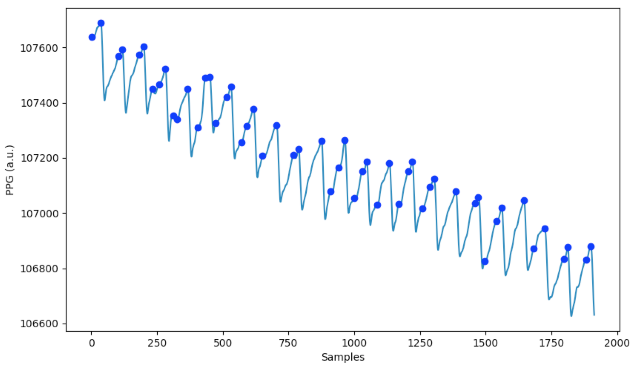
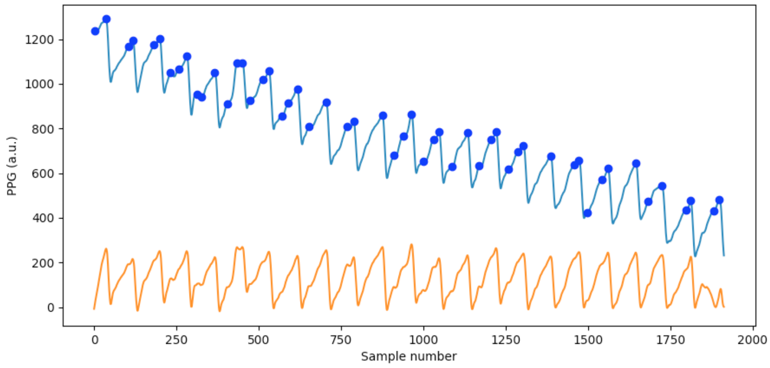
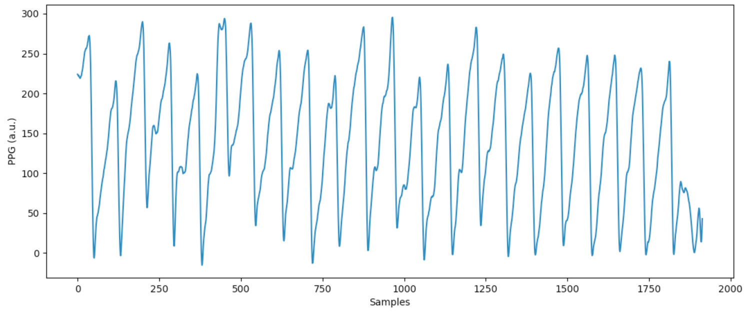


Figure 5.7: Identification of the maximum values in the obtained PPG signal.

The identification of the peak signal peaks was important for the identification of cardiac cycles, as well as the physiological study of the signal. It was also useful for calculating the baseline. The baseline was then removed from the signal. The following Figure 5.7 shows the comparison of the signal obtained after acquisition and the final signal ready for analysis.



(a) Comparison of the signal before and after removal of baseline.



(b) PPG signal after processing

Figure 5.8: PPG signal processing

From this final signal it was then possible to withdraw the user's systole and diastole time value and proceed to the final stage of blood pressure value calculation.

6

Proof of concept and discussion

6.1 Blood Pressure Calculation

6.1.1 Inputs and assumptions

Respecting the method presented in [20] and [18] it was considered as initial conditions that the cardiac cycle started at systole with a pressure of 80 mmHg. The diastolic pressure following this phase was calculated according to 4.6 and so on.

The PPG signal is periodic and synchronized with the cardiac cycle [95, 96]. After some cycles the wave stabilizes and we are then able to calculate the blood pressure values.

Due to the impossibility of obtaining real parameters based on the study of an individual, the values for the parameters R and C were calculated using mathematical modeling by Catanho *et. al* and are available in [17].

As so, it was considered that the systemic resistance was $R = 0.95000\ mmHg/s/cm^3$ and systemic arterial compliance was $C = 1.0666\ cm^-3/mmHg$.

Knowing that the blood flow in a cardiac cycle is close to $C_0 = 90\ cm^3$ and assuming that T_s=2/5T_c, Catanho *et al.* concluded that the constant I_0= 424.1 mL, which is the maximum amplitude of the blood flow in systole [17] and the value considered in this approach.

All this inputs were introduced in the equations 4.6 and 4.5 and the T_s and T_d obtained from the PPG wave as shown in Figure 4.8. Following this method, we were able to calculate the values os BP registered in the PPG signal.

6.1.2 Blood Pressure Value

The photoplethysmography method combined with the Windkessel Model is a simple approach to calculate blood pressure. This methodology also makes it possible to use basic electronics for signal acquisition.

After carrying out all the work orders already described throughout the previous sections, we were able to obtain several viable blood pressure values. To evaluate the response of the combination of these two methods, several signals were acquired in individuals of different gender and ages, during different periods of time. With this acquisition, we intended to do a proof of concept and conclude if this methodology was able to provide a plausible blood pressure value.

The experimental values were acquired continuously and the values with the commercial monitor were acquired the moment before the continuous acquisition begin.

Although we were able to calculate viable BP values, when comparing the values of blood pressure calculated by our system with values obtained using a commercial blood pressure monitor, we can observe differences in the final results.

In table 6.1 the values obtained experimentally and the comparative values are recorded.

Table 6.1: Comparison between experimental blood pressure values (Systolic Pressure (SPe) and Diastolic Pressure (DPe)) and values obtained with a commercial blood pressure monitor (Systolic Pressure (SPc) and Diastolic Pressure (DPc))

	Age (years)	**Time (min)**	**SPe (mmHg)**	**DPe (mmHg)**	**SPc (mmHg)**	**DPc (mmHg)**	**Error SP (%)**	**Error DP (%)**
Woman	22	5	120	80	116	71	3,45	12,68
	31	120	121	81	125	80	3,20	1,25
	51	180	124	80	144	84	13,89	4,76
Men	26	5	120	82	124	76	3,23	7,89
	55	10	124	80	140	83	11,43	3,61
	22	5	122	81	123	76	0,81	6,58
						Error mean	6,00	9,19

As we can observe the mean error in the calculation of the diastolic pressure (DP) is around 6% and the calculation of systolic pressure (SP) 9%.

One of the above measurements was repeated, now for a period of 60 min, in which blood pressure was measured using the commercial BP monitor every 20 min, table 6.2. This verification allowed us to consider the accuracy of our measurement over this period.

Table 6.2: Measurement over a 60 min period compared with repeated measurements from the BP commercial monitor.

	Age (years)	**Time** (min)	**SPe** (mmHg)	**DPe** (mmHg)	**SPc** (mmHg)	**DPc** (mmHg)	**Error SP** (%)	**Error DP** (%)
Woman	51	60	124	80	144	84	13,89	4,76
					145	84	14,58	4,76
					144	84	13,89	4,76
						Error mean	14,12	4,76

Given the tables 6.1 e 6.2 it is possible to observe an incidence of the experimental measurements around the value of Distolic Pressure of 120 mmHg and systolic Pressure of 80 mmHg. This was suspected due to the maintenance of the R and C parameters for all measurements. A brief analysis was then made of how the variation of these parameters were influencing the measurements, Figure 6.1. For this, the value of T_s and T_d were kept constant and the R and C values varied.

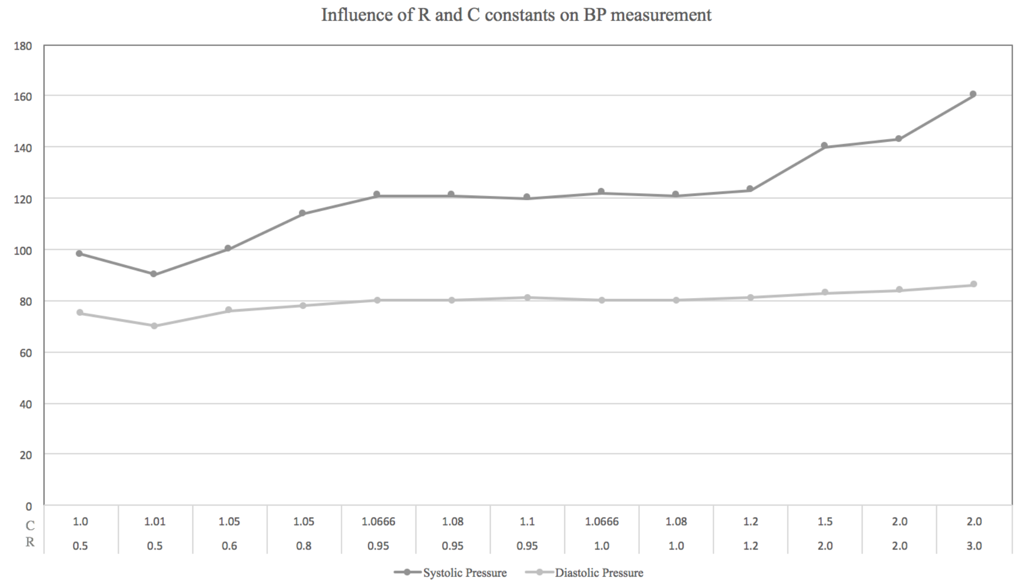
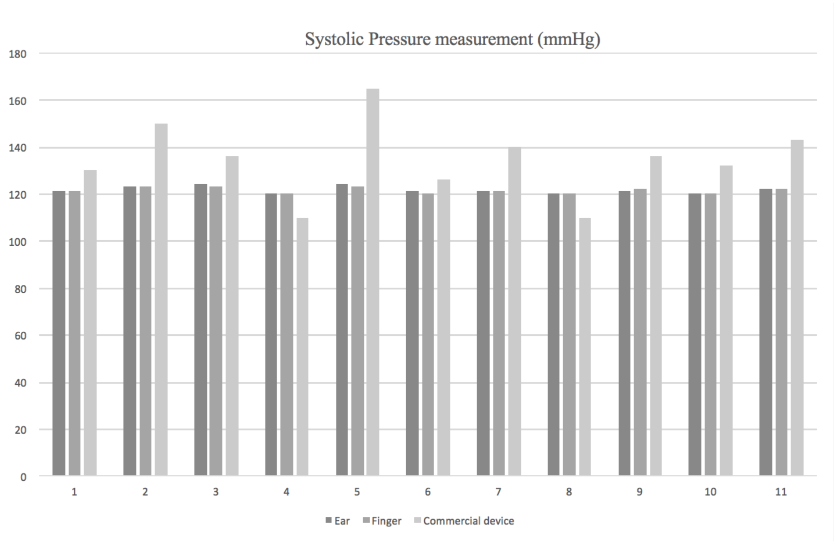
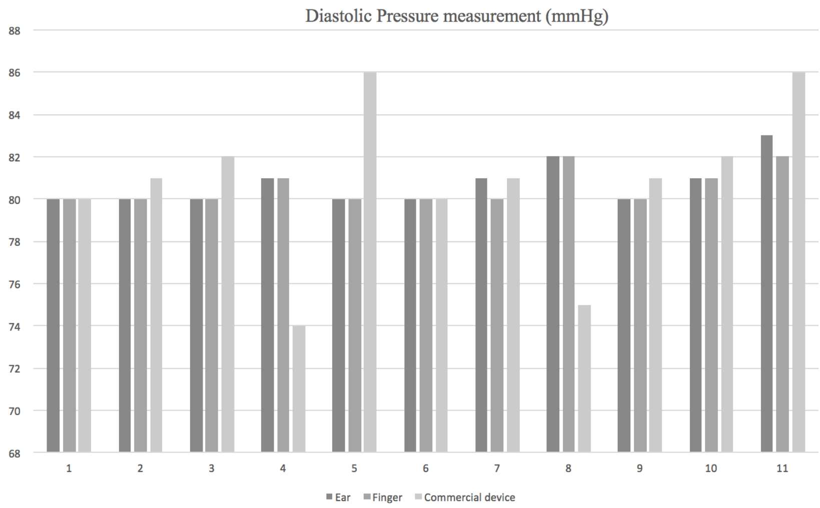


Figure 6.1: Graph of the influence of of R and C constants on the Blood Pressure measurement.

In general, it is possible to conclude that with the increase of both arterial compliance (C) and peripheral resistance (R) at same time, the systolic and diastolic blood pressures increase. However, the individual influence of each parameter on the method under study could not be proven, since the sample number is not significant. However these results demonstrate that the influence of both parameters on the measurement is significant.



(a) Systolic pressure measurement in ear, finger and arm.



(b) Diastolic pressure measurement in ear, finger and arm.

Figure 6.2: Blood pressure measurements using PPG technique on ear and finger and using a commercial electronic device.

Shown in the figure 6.2 are a sample of eleven measurements of blood pressure, systolic and diastolic using the method under study in the ear and the finger and comparing with blood pressure values using a commercial electronic device. The PPG signals were all obtained during the same time, 3 min, and the comparative values measured before the start of this acquisition.

As we can see, it was found that the values obtained for systolic and diastolic pressure are similar both measured in the finger and in the ear, as we expected.

In these acquisitions there is also the divergent trend already mentioned of the measurements using the experimental set-up and the values that are considered real through the measurement with the commercial device.

6.2 Considerations on blood pressure results

This differences between experimental BP values and the ones obtain with the commercial BP monitor are easily justified by all the estimations made to implement the method above mentioned. Firstly, the reduction of the cardiovascular bio mechanical system to a model with only two elements, although valid, lacks some anatomical and physiological considerations.

Further, for all study subjects, the same values for the R and C parameters were considered. This was done because we did not have the value of these parameters for each individual, or even the average value according to age and gender. It would therefore be imperative that an individual study be carried out for each person to obtain these parameters. Only then could we ensure the accuracy of the measurement. The remaining estimations and considerations referred in the section 6.1.1 also influence the result, in particular with regard to constants.

From the PPG signal the time of each cycle is obtained and as such the processing of this signal is also a source of error.

Despite these divergences, these results were able to proof the concept and thus we registered the legitimacy of this approach for the continuous measurement of blood pressure.

7

Conclusion and future ambitions for self-measurement of blood pressure during sleep

This work was developed within the framework of EIT Health projects in collaboration with the Instituto Pedro Nunes. We were challenged to contribute with research and technology development to a theme in which both institutions actively work, active ageing. The concept of hospital at home is largely associated with active ageing, for which I set out to work in this area.

The objective of this work was to get through the various stages of development of a viable product to medical devices market. It was decided to go through the research phase, needs analysis, economic feasibility of the area and start of the study of implementation.

We concluded the research phase with the interest and ambition to develop a device that continuously measures blood pressure during sleep as a way of responding to an identified need in hypertension disorders.

The final results of this study allowed us to concluded that although the approach chosen allows us to calculate the blood pressure using a continuous signal, we are still far from being able to correctly estimate the blood pressure.

Some of the reasons identified relate to the fact that in this work, we chose to use the 2-Element WK model to estimate the value of BP, however this method does not take into account several parameters that intervene in the system. As so, the results would have to be validated using the 3 and 4 Element WK model.

The chosen methodology should also be tested with a greater variety of signals. In the future, the noise cleaning algorithms must be improved and it would be important to individually study a person and obtain their specific values for C and

R.

In general, the basis for choosing this methodology to implement the device is due to the need for proof of concept and feasibility of the initial idea to develop a device for the continuous measurement of blood pressure.

Later, to implement such a medical device we would still face the need for standardization of data to facilitate interpretation by clinicians.

Moreover, we would like not only to review the above points, but also to continue for the study of device encapsulation, taking into account the study of design and the materials to be incorporated.

This project also produced a scientific contribution that was approved as an article in the eTELEMED conference 2018 under the title "Hospital at Home: Contribution to active and healthy aging".

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