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Facilitating Technology-based Mental Health Interventions with Mobile Virtual Reality and Wearable Smartwatches

Use-Case Analyzing Heart Rate Variability during Slow-Breathing Relaxation Exercises

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Affirmation

I hereby affirm that this Master thesis was composed by myself, that the work contained herein is my own except where explicitly stated otherwise in the text. This work has not been submitted for any other degree or professional qualification except as specified; nor has it been published.

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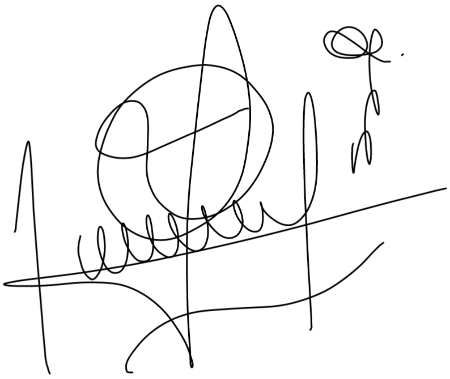

Luis Quintero

Abstract

Background: Anxiety disorders constitute a prevalent mental health disorder worldwide and there is a big gap in accessibility to mental care services between low-income and high-income communities. World Health Organization has encouraged the use of electronic and mobile health technologies to promote self-care and extend coverage of services. One psychological treatment that is suitable to be deployed using technology is the cognitive-behavioral therapy with biofeedback exercises. However, most of the existing medical and research projects related to technology-based mental health therapies use systems that are either large, expensive or require specialized personal to operate them; thus hindering a mass adoption to cover the demand of mental health solutions.

Aim: This thesis aims at validating to what extent is possible to develop a technology-based mental health intervention completely deployed over mobile systems and encouraging self-guided therapies. The work is delimited in the use-case scenario of slow-paced breathing for relaxation and anxiety management. A technical system using virtual reality and smartwatches was designed, developed and evaluated to check the system's performance.

Methods: The six activities of Design-Science research methodology were used to guide the construction and evaluation of the artifact for mental health.

Results: Three different software applications were needed to implement a physiology-driven system in the use-case scenario. Real-time signal processing algorithms to analyze user's physiology are computationally demanding in terms of packet loss, but still essential to let the system adapt and offer personalized interventions to each user. The evaluation showed that the system can function independently in real-time but some performance issues were also evident during experimentation.

Conclusion: A technology-based mental health intervention for cognitive-behavioral therapies with biofeedback exercises can be built only using mobile systems. Special endeavors are needed from the development side to integrate devices running different platforms. Real-time processing of physiological data is necessary but technicalities about latency, computational demands and communication should be taken into account. The implemented solution can be used in further research for the detection of psychophysiological states from the collected heart rate data.

Keywords: *Physiological Computing, Mental Health, e-Health, Wearable, Smartwatch, Virtual Reality, Photoplethysmography, Heart Rate Variability, PPG, HRV.*

Acknowledgments

Text for acknowledgments

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List of Abbreviations

ANS Autonomic Nervous System

CBT Cognitive-Behavioral Therapy

CV Coefficient of Variation

DSRM Design-Science Research Methodology

DWT Discrete Wavelet Transform

HCI Human-Computer Interaction

HIC High-Income Country

HMD Head-Mounted Display

HRV Heart Rate Variability

LIC Low-Income Country

PPG Photoplethysmography

RMSSD Root Mean Square of the Successive Differences

SAP Samsung Accessory Protocol

UDP User Datagram Protocol

VR Virtual Reality

WHO World Health Organization

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Chapter 1

Introduction

1.1 Motivation

The current speed of breakthroughs in digital technology comprises the called Fourth Industrial Revolution that changes how people, government and institutions interact [1]. The healthcare field is not oblivious to this disruption, particularly the mental healthcare system, which is having difficulties to meet the challenges of a growing population and more individuals suffering from mental conditions. It is estimated that, up until 2016, between 15%-20% of the world population had any type of mental health disorder, with anxiety disorders being the most common condition with an estimated prevalence of 3.8% [2]. Furthermore, the World Health Organization (WHO), in a report of 2017, demonstrated the existing large inequalities in terms of accessibility to mental health services between high-income countries (HIC) and low-income countries (LIC) [3]. Some results of these statistics show that the amount of outpatient facilities dedicated to mental health is 30 times higher in HIC than LIC; the number of mental health workers, per 100.000 inhabitants, goes from 72 in HIC to below 1 in LIC, and the number of adult outpatient mental care visits, per 100.000 inhabitants, is 7.966 in HIC and 220 in LIC.

Looking to bridge this gap, the WHO has recommended in the Mental Health Action Plan 2013-2020 [4], the "*promotion of self-care, for instance, through the use of electronic and mobile health technologies*" as one of the approaches that would provide integrated and responsive mental health care services in community-based settings.

Psychological treatments that rely less on specialized human resources are considered feasible to be implemented in scale for communities with low access to healthcare professionals, and hence with high rates of untreated cases. Compared to individualized encounters, the interventions in scale are better in terms of coverage and accessibility for the population, but still need to get more validation of effectiveness [5]. The WHO has suggested specific psychological treatments that are more suitable to evolve from expert-delivered interventions towards self-guided sessions. It includes traditional tools are such as self-help books and audiovisual material, but also suggests "*evidence-based treatments like Cognitive-Behavioral Therapy adapted to brief, basic and non-specialist-delivered versions*" [5].

Cognitive-Behavioral Therapy (CBT) is a psychotherapy that is widely used in psychology to treat anxiety disorders like phobias (e.g. fear of heights, flying, spiders, social) and post-traumatic stress disorder (PTSD) for soldiers. In general, it is applied on people that have been exposed to a traumatic event that involved threat or severe injury, and that developed an abnormal emotional response in form of fear, vulnerability or terror. The basic premise of this therapy is to encourage a personal examination of negative thoughts (cognitive part) that contribute to anxiety, and an analysis of how the body reacts (behavioral part) in situations that trigger anxiety [6]. Therefore, the high prevalence of anxiety disorders make CBT a promising target for technological therapies that could counteract the insufficient capacity of mental health services to provide face-to-face interventions [7].

The delivery of mental care has been trying to leverage from mobile technology as early as 1990s, but only the rapid advancements of the last decade have paved the way to develop low-cost, flexible, mobile solutions for tele-mental health that use smartphone as a digital lifeline that puts a therapist in every pocket [8] [9].

One CBT that has benefited from technological development is the *Exposure Therapy complemented with Biofeedback exercises* [6] [7]. Exposure therapy is a method used with people suffering anxiety disorder and consist of exercises of imaginary or real-life exposure while teaching deep relaxation and self-monitoring skills. The person is intentionally induced to the circumstances that cause distress, following a systematic plan that gradually endures the intensity of exposure until anxiousness abates [6] [10]. By augmenting it with biofeedback exercises, the users are also connected to sensors that provide immediate information about the physiological responses (e.g. heart rate, brain waves, muscular reaction) that are activated when the user is exposed to the stressor. This additional information raises awareness of what is happening inside their body, and the user can control these signals voluntarily to promote self-regulation [11] [12].

The exposure therapy with biofeedback is particularly leveraging from the technological advances in Virtual Reality (VR) and Wearable Devices. In the first place, VR is a non-invasive technology that lets users experience a 3D computer-generated scenario and interact with the artificial environment with a head-mounted display (HMD) providing first-person presence; it means, the sensation of being located in the real place [13]. This characteristic makes VR suitable to deliver exposure therapies in a safe and controlled environment; where anxiety triggers can be presented in a measured, consistent and progressive way [6]. Secondly, biofeedback implies the collection of body signals and hence the use of electronic sensors. The breakthroughs in low energy wireless communication and sensor miniaturization have produced a plethora of hardware called Wearable Devices [14], incorporating enhanced capabilities to monitor signals in an affordable, reliable, non-invasive and secure way [15]. **Ultimately, complete systems for psychological interventions might integrate VR headsets to support exposure therapy and wearable devices to collect behavioral and physiological data for biofeedback.** This technological approach integration may back up the creation of new therapeutic tools used to offer mental health assistance outside clinical or research settings, and taking advantage from the available hardware technology that has surpassed some previously existent barriers in terms of affordability and mobility [16] [17].

Emerging technologies come along with emerging research areas, and the interest to design systems capable of merging and interpreting both psychological states and physiological measures produced a research field called Physiological Computing. The term describes a technological system that incorporates psychophysiological information into its functionality, being psychophysiology the study of relations between measurements of physiology and inferences about the states of the mind [18]. Physiological Computing is considered an area potentially capable to revolutionize the field of Human-Computer Interaction (HCI) because complements the technological systems with an additional layer of awareness of the user-context, inferring the user specific emotions and cognition and feeding back this data to generate customized and tailored interactions [19].

On the one hand, Physiological Computing Systems might be considered an umbrella term for those “smart” systems with autonomy to analyze user’s psychophysiology and with adaptive capabilities. On the other hand, digital solutions to aid mental health would involve the management of both psychological and physiological components. Consequently, Physiological Computing emerges as a framework that can guide the development of systems to deliver mental health care through self-guided interventions using exposure therapy and biofeedback.

To sum up, anxiety disorders constitute a prevalent mental health disorder but there is a gap between low-income and high-income communities to access to mental care services [4] [5]. These increasingly widespread mental health conditions represent personal, social and economic burdens [7]; and is in urgent need of simple solutions that extend coverage to treat it. One of the interventions for anxiety disorders considered to offer complete psychological assistance is the use of exposure therapy with biofeedback exercises [6], which is progressively being deployed over e-health technology like smartphones, VR systems and wearable devices; making it more scalable [7]. These systems have the ability to create exposure with controlled conditions while capturing psychophysiological patterns of the user [6] [14] [16]. The latter feature makes them highly related to the area of Physiological Computing [19], which is an emerging research area that focuses on complementing technological systems with an additional layer of intelligence that is appropriate to design self-guided systems for mental health. The objective is to let computational systems process psychophysiological information from the users in real-time, so it can adapt its functionality accordingly, which can be compared to the adaptation principle used in delivering gradual exposure therapies.

This master thesis is motivated by the contextual background described above. However, it strictly falls within the area of Physiological Computing and relies on the latest research in the area in form of books [20], special book chapters in HCI [21], and PhD theses [22] [23]. Even though this master thesis is based on psychophysiology theory and use of cutting-edge technologies, the innermost rationale of this work follows a personal conviction that considers simple technology as a driving force to enhance life quality in communities with less opportunities to thrive; in this case, moving one small step forward to solve the lack of accessibility to mental health care.

1.2 Problem

Mobile technology has surpassed some previously existent barriers, becoming more relevant to be used for self-guided mental health interventions; however, there are still hindrances that need to be addressed. For instance, the rise of mobile technology was accompanied by the appearance of thousands of apps that claimed to treat all kinds of mental disorders, but the reality is that most of them have not been tested at all, as described thoroughly in [9]. In exposure therapies, the consumer-oriented VR solutions reduced the cost of the equipment and increased the performance and mobility, but there are still clinicians that are reluctant about VR efficacy [16]. The biofeedback exercises count on a market flooded with wearable sensors that might be able to replace the large and expensive used in laboratory settings, but the amount of options makes it harder to assess which devices hold strong evidence about the reliability of the measured physiological variables to allow an implementation in out-of-the-lab settings [17] [24].

Considering that technology moves faster than science and politics regarding mental health [8] [9] [25], a mobile-based approach that would allow the scalability of mental health interventions is assumed to be on early-stages in research and suffering from technological pain points.

To verify this assumption, an analysis of the state-of-the-art in physiologically adaptable systems in mental health was performed, details in section 2.3. The search resulted in a wide variety of developed applications, basic deep breathing exercises with biofeedback based on heart rate or brain signals, real-time modification of games based on arousal level, or efficacy of mobile applications connected to commercial stress management devices. Nevertheless, among the reviewed literature, only the project PhysioVR [26] was fully relying on mobile technologies, yet it did not provide all the tools to get the physiological information necessary to provide complete adaptive functionalities to the interventions. Conversely, most of the presented solutions were incongruous with the recent technological breakthroughs and incompatible to be translated into real-world, mainly because were using computer-based systems, expensive physiological sensors and setups that represent a challenge to replicate outside highly-controlled laboratory settings.

The overarching problem addressed by this research is the shortage of mobile physiological computing systems for mental health care. Nevertheless, this thesis tackles a specific intervention consisting on slow breathing exercises which aim at inducing relaxation states and maximizing cardiac responses. Therefore, the **main knowledge gap** that lays the foundation of this master thesis is the lack of physiological computing systems completely deployed over accessible mobile technology, that monitors heart data to provide real-time information about the user states, and that deliver self-guided relaxation exercises to support mental well-being.

1.3 Aim and Objectives

The project aims at bridging the knowledge gap by implementing the five-layer model of physiological computing system (defined in section 2.1.2) only using mobile-based technology to encourage easy scalability of self-guided mental health interventions.

The validation of the feasibility of construction of the solution is performed in a specific use-case scenario within the mental health therapies. The scenario consists on a guided slow-paced breathing exercise, which is an adjunct technique to traditional mental health interventions that maximizes the amplitude of Heart Rate Variability (HRV) in a person, being HRV an index associated with overall emotional and physical wellbeing. The selected use-case scenario provides enough contextual information to design, implement and evaluate the full model of physiological computing.

In one end, the designed solution utilizes a wearable smartwatch to collect photoplethysmography (PPG) signal from the user. On the other end, a mobile VR application guides the slow-breathing exercises to encourage relaxation and high amplitude of HRV signal. In the middle, several data analysis stages are built to close the loop of information flow with signal processing, psychophysiological inference and system adaptation. An early evaluation will assess the capability of the mobile system to identify in real-time the changes in HRV during a slow-paced breathing exercise.

Existing challenges in physiological computing systems [19] [21] lead to the following research objectives:

- To implement signal processing algorithms to estimate HRV in real-time from PPG time-series collected with a wearable smartwatch. (Data Science)
- To validate the detection of HRV changes in real-time under different breathing conditions guided by a mobile-VR application. (Physiological Computing)
- To conduct an early evaluation of the feasibility of construction of the system in supporting mental health interventions. (Health Informatics)

1.4 Relevance to Health Informatics

Health informatics is a field of knowledge that applies information and communication technology systems on healthcare [27]. Hence, it is strongly related to the design of socio-technical systems [28] that understand the complexity of the healthcare field and provide technology that respond to the real needs of the user. Socio-technical systems are closely tied to Human-Computer Interaction, which is the field concerned with the development of interactive computing systems that are easy to learn, effective to use and that provide enjoyable user experience [29].

The thesis belongs to the field of Physiological Computing, considered a part of of Human-Computer Interaction, and that aims at designing socio-technical systems for mental health care. Hence, the presented work is relevant to the research area of Health Informatics.

1.5 Research Questions

Based upon the knowledge gap described in the problem and the aim of the project, the research question of the thesis is:

> To what extent can a physiological computing system be deployed only using wearable smartwatches and mobile virtual reality, to support mental health interventions with slow-paced breathing relaxation exercises and heart rate variability analysis?

The work of the thesis can answer some secondary research questions such as:

- What is a feasible technical architecture of a physiological computing system fully integrated with mobile VR and wearable sensors?
- How can HRV be calculated in real-time from the heart rate signal to estimate the user performance in a self-guided slow-paced breathing exercise?
- What effects in HRV are detectable with the mobile physiological system during guided slow-paced breathing exercises?

Chapter 2

Extended Background

2.1 Physiological Computing

Since this thesis is completely demarcated within the field of Physiological Computing, it results compulsory to explain the most important elements of this research area. The following sections describe its fundamentals, the generic model of a physiological computing system, and existing issues.

Physiological Computing is a new paradigm of Human-Computer Interaction (HCI) where the systems can: 1) take physiological activity of the user as an input source, 2) analyze it in real-time, 3) estimate psychological context of the current user, and 4) adapt parts of its functioning to generate customized and tailored interactions [19]. Currently, the traditional HCI implies that technology communicates with the human users in an asymmetrical way; it means, a digital system can offer to the user a lot of information about its internal state while the computer remains essentially blind to the psychological intentions and experience of the user. Now, the new approach using physiological computing systems challenge the standard interaction, facilitating a symmetrical communication in which the system is continuously monitoring the central nervous system, being aware of the behavioral cues, psychological intentions and experience of the user [21]. This increased autonomy and adaptive capability of the systems characterizes a new generation of "smart" technology, capable to respond to a dynamic representation of the user, while moving from a master-slave to a collaborative-symbiotic relationship [19].

2.1.1 Biocybernetic Loop

The biocybernetic loop is a conceptual model developed by Pope et al. in 1995 [30] and considered the core component of all physiological computing systems. The initial experiment consisted on a system where the level of automation of a task (manual/automatic) was adapted in real-time based on the mental engagement of the user, derived from the continuous monitoring of brain electrical activity. The biocybernetic loop is derived from the cybernetic model used control theory within a closed-loop. An electronic system measures, monitors, and controls a process by taking real-time information from the output of the system; similarly, the biocybernetic loop measures physiological information, monitor changes and controls system adaptations that are timely and intuitive from the user's perspective [19] [21].

2.1.2 Generic Model

The goal and overall stages of a physiological computing system are mostly agreed; however, it does not exist yet a standard framework that assist in designing and comparing different approaches. **To facilitate the understanding of the project, this work is outlined using the "*Five-Layer Model of Physiological Computing*"**, proposed in 2018 by Kosunen on his PhD thesis [23]. The model is depicted in Figure 2.1, and builds upon the initial ideas developed by previous researchers and proposes well-defined stages that contain self-sustained problems that can be addressed separately.

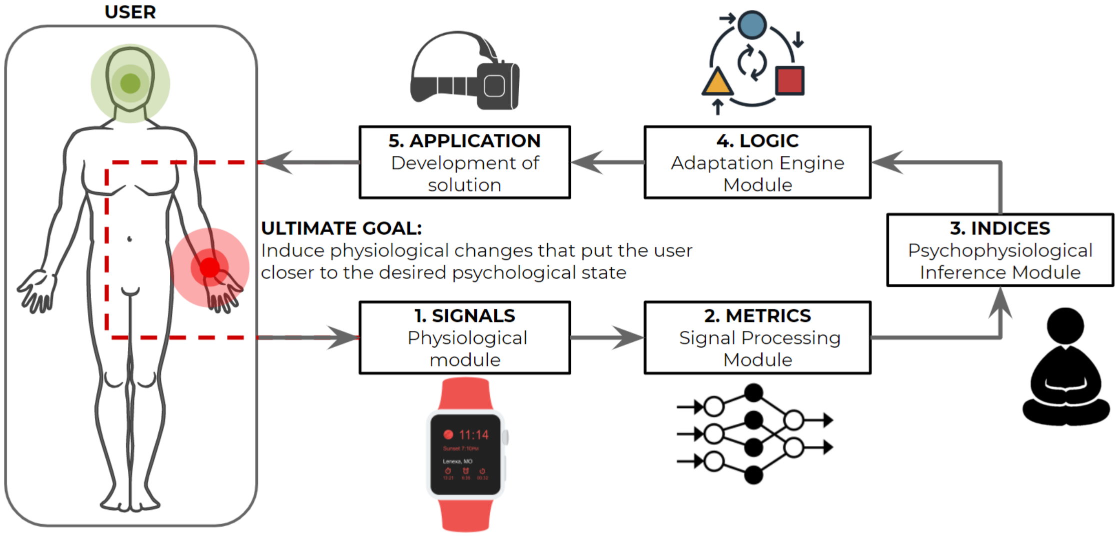

Figure 2.1: **Generic Model** - Adaptation of the "Five-Layer model of Physiological Computing" proposed by Kosunen in [23]. The original model uses stacked layers, here it was adapted in a loop that resembles the actual flow of the information.

The first block deals with the raw physiological signals that have been acquired from the sensors (such as heart, muscular, or brain activity), usually in form of time-series and including algorithms for artifact rejection such as filtering to remove interferences. Then, the next layer calculates metrics that are extracted from the raw signals to quantify features from the physiological signals. Next, the indices layer deals with the conceptual interpretation of the psychophysiology, it addresses the question of whether emotions should be interpreted categorically, as specific emotions; or dimensionally, like valence and arousal. The logic block decides how the indices are going to be used; essentially, contains the biocybernetic loop and the way how the system will change to generate the intelligent behavior. The last layer implements the actual physiological computing application, utilizing the capabilities provided by the logic layer [23].

2.1.3 Types of Applications

The ability to transform psychophysiological data into signals that control the behavior of digital systems can be used to develop applications in an extensive number of areas, very often the purpose is either to promote performance efficiency or maximize pleasure with the human-computer interfaces (also called hedonomics) [19]. However, within Physiological Computing, the applications mostly fall into two groups depending on the type of response that is provided by the adaption engine module of the logic block: biofeedback systems or biocybernetic adaptation [31].

Biofeedback System

The biofeedback systems rely on the principle from control theory that states that "a controller of a system can control a given variable if information about that variable is made available to it" [31]. The physiological computing system can also be used to provide biofeedback. In this case, the Logic block in the generic model does not contain a complex set of rules, but it acts just as a bridge between the Metrics and the Application blocks. Ultimately allowing the visualization of raw physiological information in a way that helps users to raise awareness of their inner processes and increase the voluntary control over them.

Biofeedback systems have been adopted to develop several applications. For instance, a biofeedback application can be utilized in rehabilitation to teach people with physical disabilities how to gain muscle control, by using as input signal the muscular information collected through EMG. Another example might detect gaze movement through special cameras to move the cursor on a screen. In videogames, let a user move an avatar through training of specific brain activity patterns collected through EEG. In psychology, biofeedback is a well-known exercise that supports the interventions to treat a wide range of anxiety disorders, for example helping users to gain control over breathing cycles.

Biocybernetic Adaptive System

A biocybernetic adaptive system use the physiological information to directly change its own functionality or appearance [31]. As opposed to biofeedback systems, the Logic block of the model is intensively used to map the physiological inference into meaningful elements in the system, comprising the most complete and "intelligent" type of physiological computing systems.

Some examples are described to contextualize where these systems can be used in simple contexts, and how they differ from the biofeedback systems. For instance, consider a camera-based system that detects fatigue through time between eye-blinks, and help users by increasing or decreasing the font size in the screen; or an application that detects frustration through blood pressure and offer timely on-screen help; or a videogame that adjusts game difficulty to maximize user's engagement [31]. In all these examples, the systems adapt to take the users to the desired states, but the users are never aware of the actual values of the physiological signals; everything is handled by the system "behind the scenes".

2.1.4 Existing Issues

The state-of-the-art has already presented the main pitfalls that need to be handled when deploying physiological computer systems [19] [21]. These hurdles were summarized and grouped according to the block that is affected from the generic model in Figure 2.1.

Signals

Use sensors that maximize comfort and minimize intrusion, while maintaining high fidelity of signal quality. Moreover, implement solutions that balance between invasiveness and stationarity of the users. For example, camera-based systems are non-invasive but require users to sit still; on the other hand, chest-straps allow mobility but are invasive requiring skin contact.

Metrics

Signal classification serves as the interface between human nervous system and a repertoire of software responses, but one physiological signal can lead to the extraction of several metrics, and some of them might differ in processing time. Hence the importance of choosing metrics that are accurate and computationally fast to facilitate real-time adaptation.

Indices

The relationship between physiological metrics and psychological meaning is complex, a one-to-one relationship is ideal but is the rarest inference in real life. It is a mistake to assume that physiology captures psychological states in a plug-and-play fashion, thus several experimental tests under representative conditions are required to establish the concurrent validity of the chosen physiological metrics.

Logic

Define the range of adaptive strategies that the system can utilize to represent the state of the user. It goes from simple if-then rules or linear equations, to complex machine learning approaches. The definition of frequency of adaptation is key. A frequent adaptation can lead to large number of false alarm or misdiagnosis of the psychological state of the user, resulting in a perceived low accuracy, low system reliability and lack of intuitiveness from the user's perspective.

Application

Define the purpose of the system, whether it is going to minimize risk, promote pleasurable human-computer interaction, promote productivity or support emotional wellbeing. The chosen display interfaces and the set of adaptive instructions equally affect the accomplishment of the system's purpose.

2.1.5 Main Research in Physiological Computing

Although detectable physiological signals have been studied since the creation of electrical devices in the beginning of the 20th century, just the rise in sensor technology presented in the last decades popularized the study of physiological computing systems.

An initial research agenda [31] was presented in 2004 by the Professor Stephen Fairclough, who has been the main evangelizer of the topic. Then, in 2009 he presented the core concepts and challenges in the seminal article "Fundamentals of Physiological Computing" [19], mentioning a clear inspiration from the Biocybernetic Loop developed by Pope et al. in 1995 [30]. In 2012, a report of the European Union about challenges in 21st century bioengineering [32], stated that physiological computing would drive the creation of intelligent technology, and claimed that "the approach of biocybernetic adaptation deserves particular attention because it is expected to become the single most widespread research topic in artificial intelligence". Later, in 2014 a full issue was dedicated to "Advances on Physiological Computing" [20] with meaningful applications that tackle the challenges of blending physiology and technology. In 2017, Stephen Fairclough published a chapter in a HCI book [21] giving an updated version of his seminal article, and identifying the needs that are still remaining in the area. Finally, the most recent projects undertaken in the field are PhD theses conducted in 2018, in Portugal based on exercise promotion over older populations [22] and in Finland based on relaxation tasks [23], proving the interdisciplinary broad range of applications that can be done within the area.

2.2 Theoretical Framework

2.2.1 Foundations on Digital Signal Processing

The architecture to implement is related with the design and development of computational systems that record physiological data, process them and provide real-time responses.

Real-Time Systems

A real-time system is defined as a "computational process that has to respond to internal or external stimuli in determined periods of time" [33]. When a real-time system is composed by several subsystems, each entity has its own local time that needs to be considered and synchronized to the other parts of the distributed systems. These systems make use of instantaneous and interval events that set the internal behavior of the system. Moreover, it is composed by inputs and outputs that compose the dynamics of the interaction between the environment and the system. A complete reference for real-time systems can be found in [33].

Discrete Wavelet Denoising (DWT)

Discrete Wavelet Transform (DWT) is one mathematical transformation used to change a signal from the time-domain to a time-frequency representation. Usually digital signals are transformed to frequency domain using Fast-Fourier Transform to analyze the extract additional features from them. However, this method gives frequency components but does not offer specificity about the moment in time when the specific frequency was detected. DWT uses a set of filters to provide information about the instant of occurrence of a particular spectral component, both increasing time-resolution and allowing frequency analysis. In this thesis, the DWT was used to build the real-time algorithm that calculates features from the heart rate time-series. An extensive and friendly explanation about DWT can be found in [34].

2.2.2 Foundations on Psychophysiology

The nervous system has two major divisions: the central nervous system which includes the brain and spinal cord, and the peripheral nervous system which is further divided into somatic and autonomic nervous system (ANS). The ANS consists on the sympathetic branch which is responsible for "fight-or-flight" responses and the parasympathetic activity that controls "rest-and-digest" behaviors [35].

Psychophysiology is the area of psychology that is concerned to the analysis of the physiological responses of the ANS. Some of the research areas are the study of emotions and response to stimuli via data collected through medical instruments that measure body events from muscles, skin, brain or cardiovascular activity [36].

Physiology of the Heart

The heart is innervated by both branches of the ANS, the sympathetic connection increases the heart rate and the parasympathetic branch decreases it. Studies have suggested that the analysis of this variation in heart beats reflects the activity of the ANS [18]. The heart rate information is usually collected in form of ECG signals, although other optical techniques could result in a PPG waveform that also allows to extract valuable information from heart functioning. The visual difference between both waveforms is shown in the Figure 2.2.

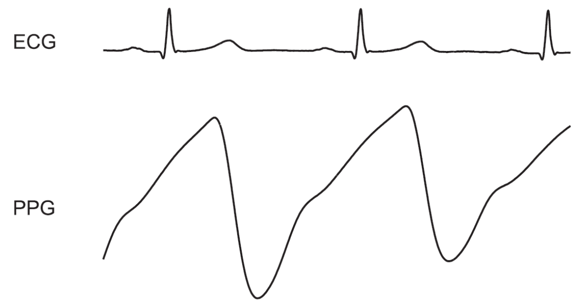

Figure 2.2: **ECG vs PPG** - Two types of heart rate signals.

Phyoplethysmography (PPG)

PPG is a simple and low-cost optical technique that can be used to detect blood volume changes in the microvascular bed of tissue. It can be measured at the skin surface with non-invasive LED sensors that are compact, sensitive and have fast response times, hence its wide usage in wearable devices. Extensive information about PPG is found in [37].

Heart Rate Variability (HRV)

One of the metrics that are widely used in psychophysiology is HRV, it is the fluctuation in the time intervals between subsequent heart beats. A healthy heart is not a metronome that pumps at the same frequency, but it follows a set of complex and non-linear behaviors that are altered by different factors which represent changes in the ANS. To calculate HRV, it is sufficient to record the peaks from the heart rate signal and get the time interval between subsequent peaks, also known as peak-to-peak interval. The Figure 2.3 depicts visually the process to calculate HRV from a set of peaks detected on a PPG signal.

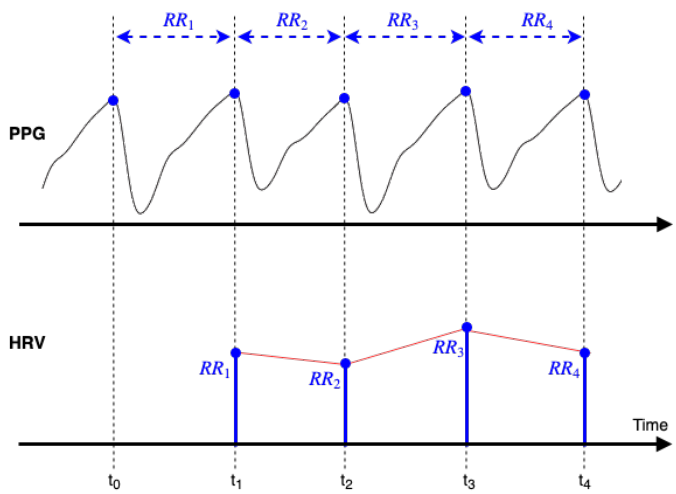

Figure 2.3: **PPG to HRV** - Visual representation of how HRV is calculated from a PPG signal.

HRV is used as an umbrella term that encompasses other metrics that describe how the rhythm of the heart varies. However, more specific metrics are extracted from HRV to examinate phenomena such as mental workload and stress response [18]. The metrics can be calculated in time-domain or frequency-domain, as described in detail in [38], but only three time-domain metrics are relevant for the thesis:

SDRR Standard deviation of all peak-to-peak intervals. Calculated in ms. SDRR measures how these intervals vary over time.

RMSSD Root mean square of successive differences between normal heart beats. RMSSD is obtained by calculating each successive time difference between heart beats in ms. Then each value is squared and the result is averaged before the square root of the total is obtained. Reflects the beat-to-beat variance in HR.

CV Coefficient of Variation. Used as an standardized measure of dispersion. CV is obtained as the ratio of the standard deviation to the mean, of the peak-to-peak intervals.

2.2.3 Mental Health Interventions

The anxiety and stress disorders are characterized by powerful responses to traumatic stressors. The most well-known are phobias, social anxiety, acute stress disorder, and post-traumatic stress disorders. Several mechanisms have been designed to counteract the increasing prevalence of mental health disorders in population. Typically, a set of options like deep diaphragmatic breathing, taking a walk or talking with supportive people are suggested for immediate stress and anxiety management. In cases with severe traumas, a pharmacological approach can be taken, but the behavioral approach is widely extended by means of Cognitive-Behavioral Therapy (CBT). These therapies involve a psychological debriefing where the individuals are exposed to the traumatic events or encouraged to share their experiences, then some generalized negative beliefs are identified and reevaluated to set more realistic contexts and expectations [6]. Although there are several types of CBT, the thesis is only associated to exposure therapy and biofeedback.

Prolonged Exposure Therapy

Exposure therapy is a technique that is used to help people overcome anxiety disorders by habituation and emotional control. It consists on making the person confront the situation that causes irrational fear, either through real-life or imaginary confrontation. The therapy follows a systematic plan of repeated exposures, each sessions gradually increases the intensity of the exposure until the person does not present mental and physical effects when facing the stressor [10].

Biofeedback

Biofeedback is a technique used in psychology to promote self-regulation of physiological responses by providing awareness of what is happening inside the body. By harnessing the power of the brain, the user can control these signals voluntarily in order to produce responses that are more helpful for physical, emotional and mental wellbeing [11]. It is considered an exercise rather than a clinical treatment because the users actively participate and reinforce the self-regulation skill through practice, similar to physical exercise [12].

To provide awareness of the physiological responses, a set of sensors are connected to the body and then transformed into meaningful visual or auditory cues that promote the changes in the user's behavior. The efficacy of this technique has been scientifically proven to treat mental conditions such as anxiety, stress, attention deficit hyperactivity disorder [12] and physical complications like chronic pain, urinary incontinence, and rehabilitation [39]; mainly using measures from brain signals (EEG), muscular activity (EMG), electrodermal activity (EDA) or face gesture analysis with cameras.

2.2.4 Emerging Technologies in Healthcare

Virtual Reality (VR)

Virtual Reality (VR) is a non-invasive technology that creates a sense of presence in a computer-generated environment. This is achieved through the use of a head-mounted display (HMD) that covers the eyes of the participant with lenses that generate the stereoscopic depth, giving a feeling of immersion in the simulated environment and allowing the interaction through head tracking [13]. VR should not be confused with Augmented-Reality (AR) or Mixed Reality (XR), which are similar technologies but utilize different visualization techniques and other interactions with the computer-generated environment.

There are three main types of VR devices: high-end, standalone and mobile-based. The high-end technology include devices that are capable to render realistic images, handle complex interactions with external controllers and let the users walk in the virtual spaces. This extended interactions imply a tethered connection to a computer with high computational capabilities and graphic processing power. Next, the standalone devices are untethered systems that contain displays and computational power similar to mobile devices. The mobile-based are systems leverage from traditional mobile-phones to generate the immersive content in an untethered fashion. This approach increases the portability of the solutions but limits the quality of the rendered scenarios and the interactions within the environments. Leading technological companies have recently released the next generation of VR devices[1], and in [25] contains a comprehensive description of existing VR systems up to 2016.

From a technological perspective VR has existed during several decades. However, only the latest advances regarding the creation of hardware with smaller size, slower latencies and more computational power allowed the rebirth and hype of VR as a visualization technology [13]. This technology has spread across different fields in academia and industry with applications for scientific and data visualization, education, exercise, design, real estate, travel, remote collaboration in industry among others [40]. In healthcare, several research projects have been conducted based on VR systems, including applications aimed at supporting surgical training for healthcare practitioners, building game-based interactive systems for physical rehabilitation, or designing virtual environments to treat phobias, anxiety or pain [41].

Clinical psychology has been trying to leverage from VR since early 1990s, especially through the design of virtual simulations that help patients to cope with mental conditions [16]. VR has now become the quintessential tool to deliver psychotherapies in form of exposure therapy [10], with proven efficacy to treat phobias (e.g. spiders, heights, flying), anxiety disorders and post-traumatic stress disorder [6].

Wearable Devices

The commercial options of technologies to monitor personal health is becoming ubiquitous with the constant release of new bands, garments, smartwatches and other types of miniaturized, portable and affordable sensors. The computing power that these devices have reached, have allowed them to collect and process physical and physiological data from the users to offer personalized and real-time feedback [24].

These type of sensors are known as wearables, and have become very popular in medical research and industry due to their capability to monitor vital signs in a reliable and secure

[1]As of May 2019, the companies that are leading the development of VR technology are Oculus and VIVE. Releasing mobile-based systems such as the Oculus Quest, standalone systems like the Oculus Go and Vive Focus, and high-end products such as Oculus Rift S and Vive Index.

way. Moreover, the nature of the utilized sensors encourages their usage among a wide variety of scenarios and make their acquisition more affordable for healthcare institutions, and more important, for patients [15]. It has been reviewed the promising effect of wearable devices as physiological monitors that help in both diagnosis and ongoing treatments with neurological, cardiovascular, pulmonary and mental conditions [14].

Smartwatches have been deemed as suitable to be used as safety monitors to detect falls in elderly population, facilitate home-based rehabilitation with interactive systems, assess treatment efficacy between outpatient visits, and for early-detection of disorders [14]. Furthermore, the vital signs collected such as HR and HRV have been used in anxiety and stress management as biomarkers to detect.

According to market statistics[2], the number of sold smartwatches is growing, being considered the largest product segment of consumer wearable devices. This gives a hint about the rapid adoption of these technologies in society, as well as its relevance as a platform that can set the foundations to advance healthcare through the delivery of scalable and customized services based on real-time acquisition of physiological data.

2.3 Related Work

As stated before in section 1.3, the main knowledge gap underlying this work is the lack of physiological computing systems completely deployed over accessible mobile technology that can assist mental health interventions. The knowledge gap was determined after conducting a scoping literature review, which is thoroughly described and analyzed in the following subsections.

2.3.1 Literature Search

Since the project intersects a variety of fields from physiology, psychology and computer sciences, several searches were performed in three different bibliographic databases: PubMed, IEEE Xplore and Springer Link. These three tools comprise an exhaustive library of peer-reviewed publications tailored to the disciplines of interest and were considered sufficient to get overall understanding of the state-of-the-art.

Research in physiological computing is relatively new, and it is not used as a standardized term for the systems that fall within the field. Conversely, most of the research projects that might be relevant to analyze are scattered within different research fields like biofeedback, intelligent interaction, affective computing, or physiologically-driven systems. As a consequence, because there are no meaning-bearing keywords which grant access to all relevant literature, the searches were not performed using specific terms but keeping in mind a question that addresses the problem to review: *What computing systems are utilized in research projects that involve physiologically controlled applications for stress/anxiety management or relaxation exercises?*

Multiple non-structured searches were used in the three databases using combination of non-controlled vocabulary like: “biofeedback”, “physiological systems”, “wearable”, “virtual reality”, “anxiety”, “relaxation”, “stress”, “mental health”. The search results were filtered by year of publication because the interest relied on analyzing the use of the latest technology. Moreover, the articles had to include in the title or abstract any hint that indicated that the project covered physiologically-controlled systems for mental health. After the exclusion of the irrelevant entries, a total of 21 publications were included for a scientometric analysis.

[2]Online smartwatch unit sales worldwide from 2014 to 2018. Link.

2.3.2 Literature Analysis

Comparison Criteria

The definition of the main research question is highly related to technical feasibility of physiological computing systems over mobile technology; therefore, the literature review was performed paying special attention to the technical architecture and devices utilized to build the physiologically-driven systems that delivered the intervention in each project.

The analysis of the literature is summarized in the Table 2.1 using four groups. If a research project has all the crosses in the columns with green background, it means that fulfills the requirements of a physiological computing system with real-time adaptation and fully mobile-based. Additionally, while analyzing the systems that were utilized in the projects, an online search of the current market price of the devices was added to facilitate an estimation of solution's scalability based on affordability.

With the intent to facilitate the comparison between publications, the related work is evaluated using the five-layer model of physiological computing explained in the section 2.1.2. Firstly, for the layer "1. Signals", the systems were examined according to the utilized devices to collect physiological data, whether they were unobtrusive accessible wearables or not, including that the sensor was able to send data directly to mobile devices. Secondly, the layers "2. Metrics & 3. Indices" were analyzed together, this choice was made because usually signal processing tasks were executed in the same hardware system that calculated psychological states, the Indices layer was always present in the projects. Thirdly, the layer "4. Logic" determined whether the intervention was displaying back to the user the raw physiological signal, like in traditional biofeedback; or the data was used to provide any kind of adaptation in the system behavior through a biocybernetic loop. Lastly, the layer "5. Application" that defines the way how the system shows information to the user, was analyzed considering three groups: a) Mobile VR, the content is shown in an immersive fashion using mobile technology; b) Desktop VR, the content uses immersive headsets with high-resolution that require computers to be executed; and c) Non-VR, use of traditional screens from mobile phones, computer or monitors.

Summary of the findings

The main finding is that, to the best of our knowledge, only one project (PhysioVR [26]) implemented a technical architecture that is close to the requirements of a portable, affordable, easily-scalable and using mobile-based technology with VR. However, the project did not incorporate sufficient tools to extract features from the physiological signals that can result meaningful for mental health projects. All the other projects were using architectures that required laboratory settings or expensive, outdated or non-mobile technology.

The two groups used to classify the projects according to the Signals layer were enough to get a glance about the portability of the physical setup to which the participants were subjected. Those systems that included brain signals required more complicated technical architectures, the cause is that their receiver applications are mostly adapted to desktop computers and not to mobile phones. Related to the Metrics layer, several projects used cardiovascular signal as a data source to provide biofeedback. The increased interest in using this type of data might be explained because heart signals have the best relationship between reliability of the signal and easiness to collect data. For instance, when the user of a VR system moves, the heart signal is not strongly affected by noise components that might modify the original data, being opposite to brain or muscular data which are highly sensitive to the position of the electrodes, or to facial expression measurements that would require the users to sit still during the interventions. From the Application block, the literature review shows that the VR devices used ten years ago presented much lower technical specifications, for example the headsets had ten times lower field-of-view and one quarter of the resolution of current devices. It reveals the early interest in unveiling the potential of VR technology in psychology even when the hype was not started, and supports the timeliness of the project to incorporate existing cutting-edge technologies in the area.

About the individual findings, one study exposed the problem of lack of inherent engagement in the normal relaxation therapies [42]; this is a pain point that can be counteracted by using VR technology. Moreover, a short study stated that "the integration of smartphone and mobile biofeedback in physiological and psychological markers of stress illustrates the potential scalability of these types of interventions" [43] and two other studies claimed as future work the inclusion of more advanced stress monitoring features based on HRV indexes [44] [45]. These statements support the idea that the proposed mobile-based physiological computing system might set the ground to develop efficient, low-cost, and complete interventions; as well as encouraging future research to be conducted outside the laboratory settings, during longer periods of time and using clinical population in their real-life context. Finally, some research entities to highlight due to their relevance in the reviewed topic are the journal "Applied Psychology and Biofeedback", and the researchers in the field of biocybernetic adaptation Parnandi and Gutierrez-Osuna.

Novelty of the thesis

Therefore, the novelty of this thesis is manifold. Based on the analysis of the table, there are not many research projects that focus on the implementation of physiological computing systems for mental health, and only one of them was found to have a similar scope than the presented thesis. Hence the novelty of the thesis relies on the implementation of a mobile-based system that collects heart rate information and calculates metrics that are more complex than current provided physiological metrics, providing a framework for more complete interventions under research settings and future in-situ deployment in population needing accessible mental health treatments.

Additionally, the use of mobile-VR and smartwatches in this study is relevant because these two technologies are new and affordable, with an increasing adoption by final users, which facilitates the scalability of psychological procedures involving exposure therapies and biofeedback.

Furthermore, the validation of a mobile-based architecture has the potential to drive the change in the way how mental health services are delivered nowadays, integrating additional source of information to conduct preventive or therapeutic interventions in a self-guided manner for a population that is more tech-savvy, health conscious, receptive to mobile, and willing to use these systems beyond office-based settings [8] [17].

Table 2.1: Analysis of related work based on generic model of physiological computing.

		Building Block from Generic Model	1.		2. & 3.		4.		5.		
Ref	**Year**	**DESCRIPTION**	*Wearable Sensors*	*Non-wearable sensors*	*Mobile Phone*	*Computer*	*Biocybern. Adaptation*	*Traditional Biofeedback*	*Mobile VR*	*Desktop VR*	*Non-VR*
[46]	2017	Virtual Sophrologist: The aim was to develop a VR neurofeedback relaxation training system. A relaxing environment changed depending on the estimated meditation score. Measuring EEG through Emotiv EPOC headset (U$800) and mobile-VR headset to visualize.		X	X		X		X		
[44]	2014	Positive Technology App: Aims at testing the efficacy of an application that uses wearables for the self-management of psychological stress. Measuring HR from any commercial sensor compatible with Bluetooth Smart protocol. iOS application for smartphone/tablet.	X		X			X			X
[45]	2014	Chill-Out: An adaptive biofeedback game that teaches relaxation skills by monitoring breathing rate of the user. Measuring HR and breathing rate with Zephyr BioHarness BT (U$700) and EDA with FlexComp Infinity (U$6500). Mobile application running on Android 2.3.		X	X		X				X
[47]	2017	Deep Breaths: Tool that allows users to experiment various respiratory pacing signals in order to maximize relaxation. Measures PPG from a wristband Empatica E4 (U$1700) and runs on iPod Touch.	X		X			X			X
[48]	2008	Aims at integrating a portable biofeedack device into clinical practice, measuring the effectiveness of RSA biofeedback devices as an adjunct to CBT. Used a commercial device that estimated stress, and relaxation levels.		X	X			X			X
[43]	2016	Aims at evaluating the efficacy of biofeedback stress management intervention with mobile smartphone and gaming apps. Measuring EDA with Pip device (U$150) and HR with iHealth pulseoximeter (U$80). The mobile games ran in an iPhone 4S.	X		X			X			X
[49]	2005	Goal of the study is to document the efficacy of VR exposure therapy on cardiac response and automatic processing of stimuli against arachnophobia. Measuring HRV with a CardioPro. Visualization with I-Glass SVGA VR Headset (no longer available). The adaptation was performed graduating the level difficulty, not automatically but adjusted by the therapist.		X		X	X			X	
[50]	2018	Examined the effectiveness of respiratory biofeedback in lowering arousal after stress. It measured EEG through B-Alert X10 system and task runs on desktop-based Oculus Rift VR headset.	X			X		X		X	

Table 2.1 continued from previous page

		Building Block from Generic Model	1.		2. & 3.		4.		5.		
Ref	**Year**	**DESCRIPTION**	*Wearable Sensors*	*Non-wearable sensors*	*Mobile Phone*	*Computer*	*Biocybern. Adaptation*	*Traditional Biofeedback*	*Mobile VR*	*Desktop VR*	*Non-VR*
[51]	2018	Emotional Labyrinth: Design and preliminary evaluation of a general-purpose architecture for affective-driven VR applications in mental health. Measures ECG, EMG, respiration and EDA through BiosignalsPlux (U$1000) and runs on desktop-based HTC Vive headset.	X			X	X			X	
[52]	2009	INTREPID: Proposes an improvement of existing treatments for generalized anxiety disorder using biofeedback-enhanced VR system for relaxation and controlled-exposure. Measures EDA and HR through NONiPOD integrated pulseoximeter (no longer available).	X			X		X		X	
[53]	2016	Proposes a system for Home-Based VR exposure therapy for patients with social phobia through virtual health agents. Adapts phobic stressors automatically depending on patients' anxiety levels. Measuring HR through Zephyr HxM device (U$700) and desktop VR system.	X			X	X			X	
[54]	2016	RelaWorld: Neuroadaptive VR meditation system. Measures EEG signals through QuickAmp system and running the environment in desktop-based Oculus Rift VR headset.		X		X	X			X	
[55]	2016	VR-enhanced respiratory biofeedback system for patients suffering from physical symptoms related to clinical conditions marked out by anxiety disorders. Measuring breathing through Zephyr Bioharness 3 (U$700) and running a NeuroVR scenario in a laptop.	X			X		X		X	
[56]	2014	Interreality: Develop a technological protocol for management of psychological stress and comparing it with a non-technological protocol for CBT. At-office measures include HR, HRV, breathing rate with a custom system (U$2500) and desktop-based VR system VUZIX Wrap 1200VR (U$2200), and at-home therapy measures with Empatica E3 (U$1000) with smartphone.	X			X		X		X	
[57]	2018	BioPad: Framework to use off-the-shelf video games for stress management through slow-paced breathing. Measures HRV and EDA through chest strap sensor Zephyr Bioharness 3 (U$700) and game consoles with controllers to show the applications.	X			X	X				X
[58]	2011	Aims at examining HRV biofeedback as a stand-alone intervention for reducing anxiety in college students. Compares the biofeedback system HeartMath Freeze-Framer 2 (available in 2005) and emWave (available in 2007). The guided respiration was performed through videos in computer.	X			X		X			X

Table 2.1 continued from previous page

		Building Block from Generic Model	1.		2. & 3.		4.		5.		
Ref	**Year**	**DESCRIPTION**	*Wearable Sensors*	*Non-wearable sensors*	*Mobile Phone*	*Computer*	*Biocybern. Adaptation*	*Traditional Biofeedback*	*Mobile VR*	*Desktop VR*	*Non-VR*
[59]	2014	Aims at maintaining player's arousal by modifying racing game difficulty in weather, steering and speed. Measuring EDA through the wired system FlexComp Infinity (U$6500). Game showed in an LCD monitor, and interaction with racing wheel.		X		X	X				X
[42]	2018	Gaming away stress: Design, implementation and evaluation of three respiratory biofeedback games. The sensor was the chest strap Zephyr BioHarness 3.0 (U$700) to monitor breathing rate, connected via Bluetooth to an LG Nexus 4 Phone running Android OS 5.1, which ran the three apps.	X		X		X				X
[60]	2017	AmbuRun: Interaction with a VR ambulance game that adapted speed and difficulty based on real-time assessment of frustration and excitement in the user, through neurofeedback. Used Emotiv EPOC headset (U$800) to capture EEG, and FOVE VR headset (U$600) to visualize the game.	X			X	X			X	
[61]	2017	Aims at comparing the effectiveness of two biofeedback mechanisms to promote acquisition of deep breathing skills using a casual game. Compares explicit biofeedback with a version that alters the internal parameters of the game. Measuring BR, HR through Zephyr BioHarness BT (U$700), EDA through FlexComp Infinity (U$6500). The app was displayed in a Google Nexus 5 phone.		X	X		X				X
[26]	2016	PhysioVR: Open-source software to facilitate the integration of physiological signals measured through wearable devices in mobile-VR applications. Implements an early evaluation with a system that captures HR using a smartwatch and low-cost mobile VR headset.	X		X		X		X		

Chapter 3

Research Methodology

This chapter describes the research methodology and methods that frame the thesis. For the sake of clarity, research methodology refers to the general theory of how research should be undertaken; and research methods refer to the specific techniques and procedures used to obtain and analyze data, such as questionnaires, observation, interviews, quantitative and qualitative analysis techniques [62].

3.1 Selection of Research Methodology

The research question of the thesis is highly focused on technological systems and lean more towards applied research than theoretical research. Therefore, it demands a research methodology suitable to guide this type of work in a systematic way, with clear strategies that frame the creation of knowledge around the discussed problem.

The considered quantitative research methodologies for the project were: Experimental, Requirements Engineering, and Design Science. The experimental methodology in computer science is highly based on the collection of data, but a part of the thesis involves the construction of the system that performs data collection, and this part is not considered on the methodology. On the other hand, requirements engineering is solely based on the elicitation of needs that would dictate the functioning of the prototype, leaving aside the scientific evaluation. Finally, design science was chosen as the research methodology to follow because it comprises both stages, construction of the system and its evaluation.

3.2 Design Science Research Methodology (DSRM)

Design science is a paradigm that seeks to create innovations to define new ideas, practices, and products through the analysis, design, implementation, and use of information technologies artifacts with high relevance in real-world problems [63]. In the methodology, **the term "*artifact*" is a general word used to refer to a bundle of elements packaged in a form of hardware or software, usually technology-based solutions, aiming at producing results that are of real interest in practice and not only theory-based**.

According to the guidelines for design-science research [63], the artifacts are rarely matured systems used in practice. On the contrary, these artifacts allow to acquire knowledge to demonstrate feasibility of the design process, giving information about whether the construction of a system could be effectively and efficiently accomplished. Once feasibility is demonstrated, the arise of new artifacts can be performed by delivering subsequent significant improvements in the product, process, or methods under construction.

In the article describing the Design-Science Research Methodology (DSRM) [64], all the conceptual principles and practice rules from the former publications were incorporated into a process model, shown in the Table 3.1, that standardized the design-science process with steps that make the solutions valid and valuable to be incorporated in research.

Table 3.1: Process Model of the Design-Science Research Methodology (DSRM)

Activity	Name	Description
1	Problem and Motivation	Specification of the research problem and justification of the value of the solution. To capture the complexity of a problem, an atomization in subproblems might be useful.
2	Objectives of the Solution	Analysis of how the new artifact would tackle the problem better than existing ones, and list of system's requirements.
3	Design and Development	Definition of desired functionality, architecture to be used and creation of the artifact, which can be any designed object in which a research contribution is embedded in the design.
4	Demonstration	Proof that the artifact solves one or more instances of the problem, it can be through experimentation, simulation, case study, proof, among others.
5	Evaluation	Analysis about how the artifact supports the solution of the problem based on the objectives from activity 2, by using quantifiable measures, observations or satisfaction surveys.
6	Communication	Transfer the knowledge to researchers and relevant professionals about the problem, its importance, artifact's utility, novelty, rigor of the design, and effectiveness.

3.3 Application of DSRM to the Research Problem

The aim of the research project describes the development of technology-based systems with clear practicality in a well-defined real-life problem, characteristics that highly relate to the definition of "artifact" presented in DSRM and makes it a suitable methodology to follow in this thesis.

In general, the artifact that the thesis plan to design, implement, and evaluate is a physiological computing system completely deployed over mobile-based technologies, looking to provide easiness of scalability to support the design of further self-guided mental health interventions. However, this description of the artifact is still abstract because the spectrum of mobile-based devices is very wide and there are numerous different mental health interventions. Thus, the description of the artifact to be built is narrowed down to a more specific real-life context that proofs the feasibility of construction of the envisioned system in one instance of the overall problem.

Consequently, the application of DSRM consists on the design of an artifact for a specific scenario mental health intervention and uses a specific set of devices. Namely, **the artifact to build is a physiological computing system that stimulates slow-paced breathing at a frequency of 0.1Hz guided by a mobile-VR application and calculates HRV in real-time using heart rate data from a smartwatch.** The way how the first three activities of DSRM are utilized to develop the artifact are described in the section 3.4, and the details of the last three activities of the DSRM are explained in the section 3.5.

3.4 Artifact Construction: Development of Mobile-Based Physiological Computing System

This section describes how the first three activities of the DSRM led to the construction of the artifact that is intended to solve the main research question.

3.4.1 Problem and Motivation of the Use-Case Scenario

The simplified reasoning behind the selection of the use-case scenario is that slow-paced breathing exercises with monitoring of Heart Rate Variability Biofeedback (HRVB) are deemed as a suitable technique to aid traditional psychotherapies in a mobile-based approach. Moreover, it provides enough contextual information to test the feasibility of construction of the five-layer model of a physiological computing system considering the available resources of the project.

The following paragraphs explain how a slow-breathing exercise constitutes a first step to solve the main knowledge gap of the thesis, as well as the motivation behind the selection of this specific scenario.

Controlled Breathing in Mental Health

Controlled breathing is an ancient common practice among Eastern cultures originated with spiritual purposes, but was popularized in the West in the 1960s due to an increasing interest to be used as a complementary therapy for respiratory and circulatory diseases [65]. Controlled breathing is linked to mental functions and hence is an essential element in meditative practices like yoga or pranayama. The technique consists on exerting a direct and conscious regulation of the parameters in respiration, such as frequency, deepness or inspiration/respiration ratio [66].

The average breathing frequency for most of the people is between 0.15Hz and 0.4Hz, which means that a person executes between 9 and 24 breaths per minute. Nevertheless, research has suggested some benefits existing by slow paced breathing, especially at a frequency of 0.1Hz, or 6 breaths per minute [65] [66] [67].

The documented effects of slow-paced breathing in healthy humans include benefits in respiratory system such as increase in tidal volume, and efficiency in gas exchange; the cardiovascular system is affected by an increase in the stroke volume, and sometimes a decrease in mean blood pressure [65]. However, the most consistent discovery in slow-paced breathing compared to spontaneous breathing is the cardiorespiratory coupling; where the respiration rate, heart rate, and blood pressure are synchronized and cause a maximization in the amplitude of the Heart Rate Variability (HRV) signal [68].

HRV, defined in detail in section 2.2.2, is a measure calculated as the time between two subsequent heart beats. It is known that the heart does not beat in a periodic way like a metronome even when the person is still, and HRV allows to analyze this variation in heart speed. HRV tends to be in synchrony with the respiration cycle in a phenomenon known as Respiratory Sinus Arrhythmia (RSA) [69], where heart rate increases during inhalation and decreases during exhalation.

From the physiological standpoint, it is suggested that the HRV is controlled by the baroreceptor reflex (baroreflex). The baroreflex is a mechanism that includes blood pressure receptors in the aorta and carotid artery, responsible of monitoring blood pressure fluctuations and respond to acute changes [65]. The receptors in the baroreflex are mediated through the vagus nerve directed by the nucleus tractus solitarius in the brainstem, which increases the heart rate through sympathetic activation, or decreases it through parasympathetic activation. Thus, HRV is often seen as a measure of the body's ability to change between parasympathetic and sympathetic autonomic control. Finally, since the nucleus tractus solitarius that mediates HRV is also directly communicated with the amygdala, which is the brain's emotion controller. Several studies have been conducted to show the effects of HRV for treating mental health conditions [68].

HRV is mainly related to mental health through exercises of HRV Biofeedback (HRVB); also referred as respiratory biofeedback, heart coherence biofeedback, baroreflex biofeedback or resonance frequency feedback. Traditional biofeedback, explained in section 2.1.3, consists on displaying body information to the user to encourage voluntary control over these signals. In one specific case of HRVB, the person is promoted to control HRV through slow-paced breathing, creating a sinusoidal curve that reaches maximum amplitude when the respiration frequency is 0.1Hz. Ultimately, HRV is often considered a measure of physical and emotional resilience, and HRVB is regarded as a suitable technique to promote self-regulation and treat anxiety, stress and depression [65] [66] [67]; but more rigorous clinical trials are needed to determine its true size effect [68] [70].

As all the biofeedback modalities, HRVB seems a promising exercise to complement validated treatments for mental health such as CBT, but it is not yet a commonly-used practice due to the high cost and restricted mobility of the devices needed to setup the system [70]. Some research projects have tried to aim this pitfall by developing physical prototypes to provide HRVB. Among the found system architectures, the projects in [71] and [72] designed shirts with special electrodes that measured heart and respiration signals, but these setups were intrusive for the users and used computers to collect and process the physiological data. The studies in [73] and [74] built wearable-based platforms, and were using mobile phones instead of computers to process the data, but still used an elastic belt to hold the sensors around the thorax or abdomen, resulting uncomfortable for the users. The research in [75] performed a usability study in a completely mobile-based system that used chest-strap to collect signals, and a videogame to guide the controlled-breathing exercise. It highlighted the potential of game-based systems to motivating the users in the task. Furthermore, none of the found prototypes for HRVB included mobile-VR technology to guide the exercise, or smartwatches to collect heart rate signals, or a real-time adaptation module that provides customized guidance, just as in the proposed artifact that follows the five-layer generic model of physiological computing in Figure 2.1.

Finally, the main knowledge gap of the thesis is related with the lack of physiological computing systems deployed over mobile technologies, but according to the described context, this issue also encompasses the existing problems to spread out the use of HRVB with slow-paced breathing exercises for mental health. Hence, considering the available resources with heart rate sensor and mobile VR, this specific scenario becomes a suitable option to benefit from the increasing improvements and affordability of wearable technologies, through the artifact proposed in this work.

3.4.2 Objective of the Artifact

The solution was designed with the main purpose of validating whether a mobile-based architecture can detect changes in HRV under two conditions, when the user is breathing at normal pace and when the user is induced to slow-paced breathing at 0.1Hz. The results of this initial validation can lead to subsequent experiments that assess effects of HRVB and real-time adaptation from a medical perspective using mobile-based systems.

Table 3.2: Available resources for the development of the artifact.

Hardware	
Samsung Gear S9 [1]	Mobile phone used to run the applications, algorithms and communication between entities in the physiological computing system. Associated with the blocks METRICS and INDICES in the generic model.
Samsung Gear VR [2]	Device used to transform the smartphone into a mobile Virtual Reality headset, serving as a visualization platform for the virtual environment CalmPlace.
Samsung Gear Sport[3]	Smartwatch with a built-in heart rate monitor that records PPG signals from the wrist of the user. Associated with the block SIGNALS in the generic model.
Software	
CalmPlace[4]	Application developed for the mobile-VR headset. The relaxation experience includes some meditation and respiration exercises intended to support mental health but does not include any physiological sensor in the original version. Associated with the block APPLICATION in the generic model.
PhysioVR [26]	Early-stage open-source research project that facilitates the flow of information along the five-layer model of physiological computing. Mainly associated with the LOGIC block and utilized as the linker between captured physiological signals and a mobile-VR application.

3.4.3 Design Requirements

The main aim of the thesis of analyzing feasibility of construction of the artifact; however, it was necessary to define a set of technical requirements that enhance the system's practicality and take into account the available resources in terms of technological tools and time.

The first source of requirements was the list of existing challenges in each layer of the generic model of physiological computing, discussed in section 2.1.4. An analysis was performed to determine which of these caveats could be addressed with the available hardware and software resources. The second source of requirements was the literature review about the existing slow breathing projects that incorporated HRV biofeedback techniques. Thus, the main requirements that comprise the functionalities of the artifact were defined as follows:

- The artifact must implement each of the five layers of the generic model.
- The physiological sensor shall be comfortable allowing mobility of the user, minimizing the intrusion of the sensors.
- The acquired heart rate signal must maintain high fidelity and quality.
- The processing of heart rate signal shall be computationally fast to facilitate a real-time approach.
- The Logic block shall be evaluated only when the concurrent validity of the metrics is demonstrated. It implies that the HRV metric needs to be proven as a predictor of the two respiration states and their corresponding psychological meanings.
- The application has a specific goal and the adaptive instructions affect the accomplishment of the system purpose.

3.4.4 Available Resources

The available resources for included hardware and software tools, described in the Table 3.2, which are associated with the blocks of the generic model in Figure 2.1.

[1]Product website: Link
[2]Product website: Link
[3]Product website: Link
[4]Application website: Link. Mimerse is a Swedish startup that supported this thesis providing access to the smartwatch, VR devices, and source code of the application CalmPlace.

3.5 Artifact Evaluation: Research Study Design

This section outlines the elements that comprise the activities "Demonstration", "Evaluation" and "Communication" of the DSRM, leading to the overall validation of the artifact.

It is very important to highlight that, although the six building blocks of the physiological computing system are developed in the artifact, the evaluation scenario omitted the Logic block. According to the physiological computing foundations [19], the adaptation engine has to be designed only when the validity of the physiological metrics are evaluated. Hence, the artifact evaluation measured the ability to collect reliable data to detect a psychophysiological variable without adaptation. The results of this study might lead to a proper evaluation of the full biocybernetics loop, including the Logic block.

3.5.1 Motivation of the Evaluation Approach

According to the seminal paper about design-science research [63], an artifact can be evaluated in terms of functionality, completeness, consistency, accuracy, usability, performance or other attributes that might include mathematical evaluation. Moreover, the artifact should be considered complete only when well-executed evaluation methods proof that it fulfills the requirements and constraints of the problem that was meant to solve [64].

Among the proposed design evaluation methods presented by Hevner et al. in [63], the artifact was decided to be evaluated following the descriptive method in form of scenario, which consist on "constructing detailed scenarios around the artifact to demonstrate its utility" and is suitable to be used for "especially innovative artifacts for which other forms of evaluation may not be feasible".

It turns out important to recall that the main research question revolves around the technical feasibility of implementation of the mobile-based architecture, hence the use-case scenario that was specified to build the artifact is sufficient to demonstrate the practical utility of the framework. Additionally, since the aim of the thesis is not to assess clinical validation of the physiological system, the comparison with other systems that promote slow-breathing exercises or induce relaxation is irrelevant.

Ultimately, the use-case scenario is also aimed at providing data to respond the secondary research questions contemplated in the thesis, therefore the evaluation of the artifact addresses the statistical significance test for specific sub-hypothesis described in the data analysis.

3.5.2 Participants and Recruitment

The number of recruited participants for the study were 11 healthy volunteers, students in Stockholm, and between 23-33 years old. The only exclusion criterion was whether the volunteer presented any visual impairment that could not allow them to use the VR system. For recruitment, it was chosen a non-probabilistic convenient sampling [62], which is applicable for the research project because of the easiness of access to participants. The collection of exploratory data was chosen due to time constraints to conduct the study, but still able to gather enough data to answer the defined research questions.

3.5.3 Data Collection Tools

The intervention useD the smartwatch device and mobile phone running the virtual environment to record three main variables: 1) Raw PPG signal measured from the user with the smartwatch, 2) HRV signal calculated in real-time by the system, and 3) a log

Table 3.3: Sequence of tasks in the study protocol.

N	Task	Description	Duration
1	Informed Consent	Ask for written informed consent from the participant and explain the purpose of the study.	∼3min
2	Connection of Devices	Connect the smartwatch and the VR headset to the participant.	∼3min
3	PART 1: Experiment Baseline	The user is immersed in the CalmPlace application, the person is breathing in a normal pace. Record of PPG signal and real-time HRV calculation.	∼3min
4	PART 2: Experiment Intervention	In the middle of the relaxation session, the application CalmPlace shows a blue object in the middle of the virtual scene that guides the breathing exercise at a pace of 0.1Hz. Record of PPG signal and real-time HRV calculation.	270 sec
5	Questionnaire	Self-administered questionnaire asking for demographic information, perceived level of engagement, and perceived level of relaxation.	∼3min
6	Debriefing	Removal of devices, explanation of the objective of the study at each stage, and finalization.	∼2min

of events reported by the signal processing module. The CalmPlace application recorded timestamps that allowed the synchronization of data between the intervention sequence and the smartwatch sensor. Additionally, a self-administered questionnaire at the end of the intervention was used to retrieve basic demographic information, ask for previous experience of the participant with VR, any previous cardiovascular complication, perceived level of engagement, and perceived level of relaxation. All the study was conducted by the author of the thesis who had direct interaction with every participant.

3.5.4 Intervention Description

The protocol followed a within-subject study design, meaning that there was only one group where every participant was exposed to several stages of interventions [62]. The procedure involved the measurement of physiological data during a predefined session in CalmPlace divided into **baseline** and **intervention**. The complete protocol followed the sequence described in the Table 3.3. The template of the informed consent is attached in the Appendix A and the post-experiment questionnaire in Appendix B.

Initially the participant was placed in a quiet room without external noises that could distract them from the virtual reality environment CalmPlace. The informed consent was filled in, and the two parts of the experiment were explained, describing the changes that were going to happen in the scenario and as shown in Figure 3.1. During the 540 seconds of the experiment, the scenario displayed different visual and auditory cues that tried to induce a relaxation state in the user, going from dusk with northern lights to vivid noon. When the middle of the session was reached in the second 270, the blue object (rounded in the orange box in the right side of the Figure 3.1) appeared to guide the breathing exercise at 0.1Hz. The verbal instruction to the participant before the experiment was: "When the blue object appears, try to follow the pattern breathing-in when the object is inflating, and breathing-out when deflating". The perceived difficulty to follow the pattern was assessed in the questionnaire.

Figure 3.1: **Experiment Protocol** - Two parts of the experiment in CalmPlace relaxation experience. Left: Baseline with free breathing. Right: Intervention with slow-paced breathing (guided by the blue object). Both images show the climante sequence going from dusk to noon.

3.5.5 Data Processing and Analysis

The data processing and analysis to evaluate the artifact under the specific use-case scenario was performed offline by the experimenter using the software R-project [76].

As described in section 4.1, each application of the architecture stores independent event log files, making important to perform a **data synchronization** step. It is likely that the three different systems in the architecture use different internal clocks, thus complicating the identification of data segments that correspond to the two parts of the experiment. The red lines of the timing diagram in the Figure 3.2, visually depicts the temporal offset that needed to be corrected to do an adequate analysis of the data. The application 1 which runs on the smartwatch that collects the data samples, is started at point t_0, then the application 2 starts processing the data in the phone only when the log is created at t_1, and the application 3 that executes the intervention in VR starts when the session is configured by the experimenter at t_2. Hence, it was required to know the last sample that was read at t_2, t_3 and t_4 in order to find the subset of samples that belongs to the baseline (yellow highlighted box) and intervention (blue highlighted box) of the experiment. For this reason, the monotonic timestamp calculated from the application 1 in the smartwatch was also propagated along the data workflow to be used as time reference, and the application 3 used it to write in an event log file the monotonic timestamp respective to the experiment start, change between experiment stages, and experiment end.

The Figure 3.2 also shows the different **performance variables to evaluate the artifact**; the dashed blue arrows represent the time window in which each variable was calculated. First, the total number of recorded samples (N_T) in each application was stored to validate the need of time synchronization,. The number of samples recorded during each part of the experiment, baseline (N_B) and intervention (N_I), were used to calculate packet losses along the architecture workflow.

Using the data collected in the application 2, the performance of the algorithm for real-time HRV calculation was measured based on the proportion (p) of signal segments in which PPG peaks could be detected, respecting to the total number of signal segments that were processed. Moreover, the peak-to-peak time was calculated to create the array with the final HRV waves during both experiment baseline with normal breathing (HRV_B) and during experiment intervention with guided breathing at 0.1Hz (HRV_I).

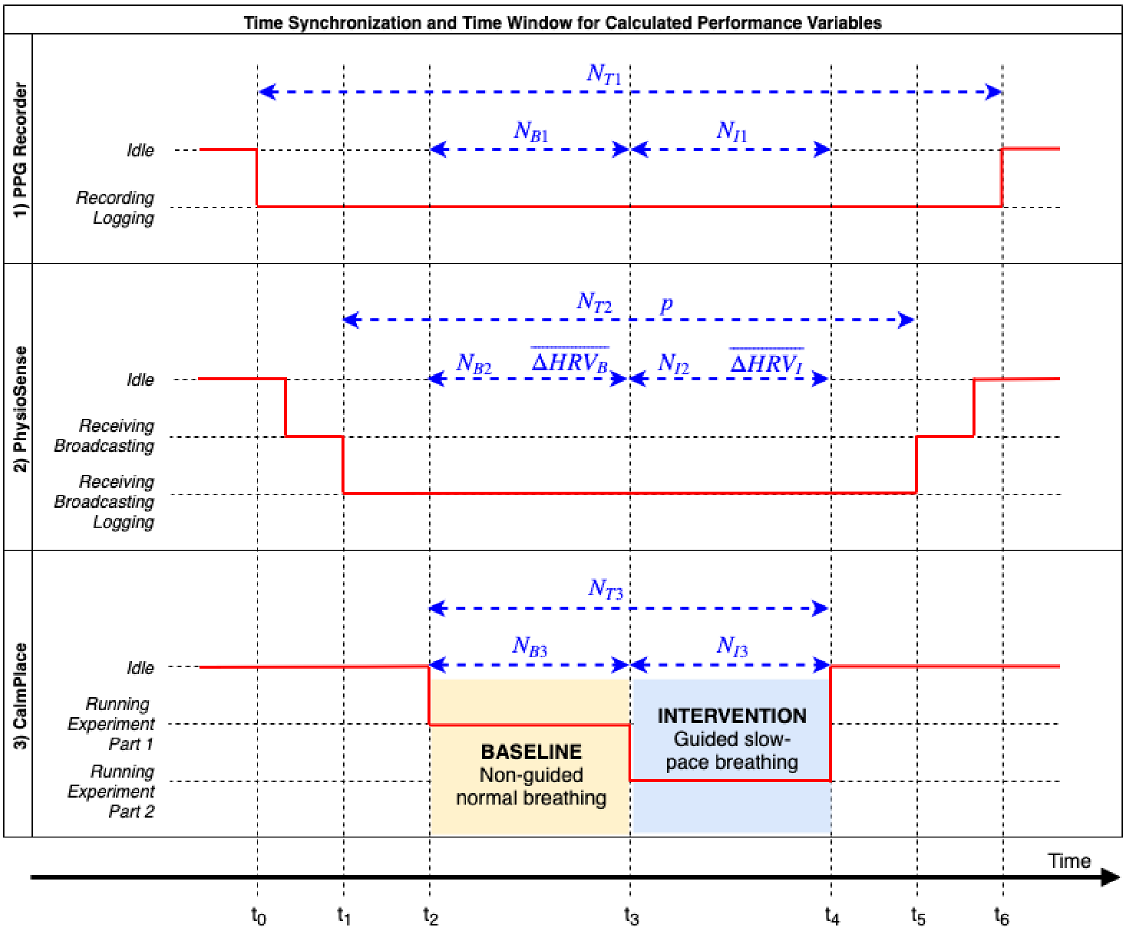

Figure 3.2: **Data Processing and Analysis** - Timing Diagram showing the time offset between systems in the architecture, and time windows for each calculated variable. The left axis represents the possible state of each system.

At the end, the brief qualitative analysis contained **comments about detected issues in the system functioning** during the intervention to check if all the requirements were fulfilled, and to point out any technical limitations that need to be reviewed for future experiments that intend to use the artifact.

Statistical Analysis

As described in the motivation of the use-case in section 3.4.1, the changes in HRV during normal breathing (baseline) are presumed to be lower than the changes in HRV during slow-paced controlled breathing (intervention). For this reason, the differences of standard deviation of HRV (SD), RMSSD and coefficient of variation (CV) between baseline (μ_B) and intervention (μ_I) were calculated for each subject. Consequently, the null and alternative hypotheses are defined as follows:

$$H_0 : \mu_B \geq \mu_I \qquad H_1 : \mu_B < \mu_I$$

The data analysis requires the use of a non-parametric statistics because the sample size is small. The **Wilcoxon signed-rank test** was chosen besides other non-parametric tests because the data are collected from the same participant, thus generating dependent samples [62].

The statistic of the Wilcoxon signed-rank test (W) is computed as the smallest sum of ranks. Then, it is compared to the critical value ($W_{critical}$) corresponding to the one-tailed test, with level of significance $\alpha = 5\%$ and according to the sample size. The null hypothesis is rejected if the $|W| \leq W_{critical}$.

3.5.6 Ethical Considerations

The research project addresses the ethical issues related to conduct the experiment, data collection and reporting. The recorded data are handled under strict confidentiality to present the results and does not allow identification of the participants. The smartwatch utilized in the intervention does not produce physical harm to the user. The VR technology can produce side effects such as motion sickness, headaches or dizziness; these consequences only happen to some users, and the effects will be minimized through constant supervision from the experimenter and will be warned at the beginning of the experiment. The virtual environment used to guide the intervention is a relaxation experiences and does not contain elements that may induce negative emotions like fear, stress or anxiety. All the participants sign off a written informed consent before the study, it contains the aim of the project, description of the protocol, health considerations, and the possibility to withdraw at any time during the study.

3.5.7 Communication Plan

The results and the design of the system are communicated in the present thesis and are intended to be published as a scientific article in a conference related with health informatics, physiological computing, or data science during the second semester of 2019.

Chapter 4

Results

The results are divided in two subsections corresponding to the steps described in the research methodology. The first one describes the artifact construction, considering the elements in section 3.4, and the second part responds to the evaluation methodology in section 3.5.

4.1 Artifact Construction: Development of Mobile-Based Physiological Computing System

The overall goal of the artifact is to allow real-time use of physiological signals in virtual reality applications for mental health. In this initial use-case, aiming at detecting changes in HRV during slow-breathing at a frequency of 0.1Hz. The system architecture was designed based on the use of the available resources and technical feasibility to transmit the physiological data throughout the whole pipeline.

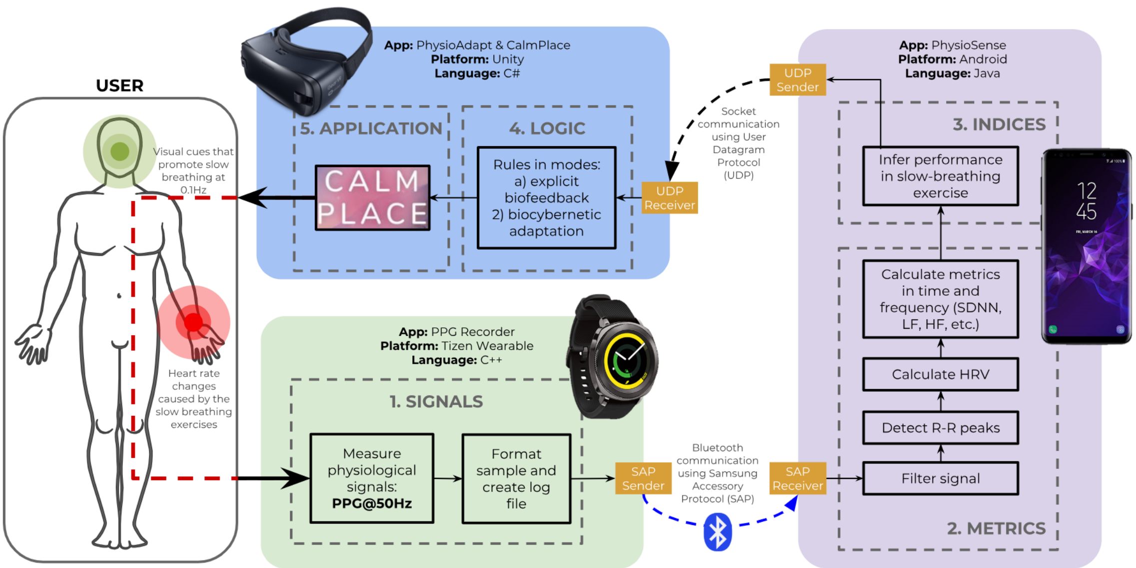

Figure 4.1: **Implemented Architecture** - Artifact Architecture of the Physiological Computing System using the smartwatch sensor, PhysioVR and CalmPlace to promote physiologically adaptable exercises for slow breathing.

The Figure 4.1 shows the technical aspects of the implemented physiological computing system, which is an extension of the conceptual five-layer model depicted in Figure 2.1.

These five-layers are developed in the architecture using three software applications that exchange information between themselves in real-time. Each of them is represented in the diagram as a colored block that contains the specific tasks running on each of them.

4.1.1 App 1: PPG Recorder

The first application is responsible for acquiring the physiological signals from the users and send it to the mobile phone, corresponding to the SIGNALS block of the five-layers model in the Figure 2.1. The utilized device is the smartwatch Samsung Gear Sport which contains a heart rate monitor that records photoplethysmography signal (PPG), described in section 2.2.2. Since the manufacturer does not provide a native application to collect the raw PPG signal, which is needed to execute real-time signal processing; then a customized program was developed using C language and the IDE Tizen Studio [77]. The result of the application is shown in the image Figure 4.2. Note that the designed application can collect either PPG or HR by tapping the checkbox in the interface, but for the scope of the thesis only the former is relevant to calculate HRV.

Figure 4.2: **App 1. PPG Recorder** - User interface of the smartwatch application that records either PPG data or HR data, and sends it to the mobile phone.

The main functions of the smartwatch application are recording data from the sensor and broadcast the measure value to the application running in the mobile phone. However, two engineering problems related to these functions were encountered and solved using scientific articles and software development tools.

The first challenge to be addressed was the definition of the sampling frequency that would guarantee the reliability of the time series representing the PPG signal. On the one hand, if the sampling frequency was very low, it could omit valuable information needed to calculate the HRV from the user. On the other hand, if the sampling frequency was too high, it would affect the duration of the device's battery without providing additional information. After researching in the area, the work of Choi and Shin [78] validated that the minimum sampling frequency to extract reliable HRV from wearable devices was 20Hz. However, after initial tests that did not show significant battery drains, the chosen sampling frequency for the application was 50Hz to increase time resolution of the peak detector.

The second challenge was related with the communication between the wearable and the mobile phone, the chosen workaround was to use the proprietary Samsung Accessory Protocol (SAP) which allows send data over Bluetooth between Android mobile devices and Samsung wearables. Besides been sent through Bluetooth, each sample was also formatted, timestamped and recorded in local log files in the smartwatch to facilitate data synchronization between the acquisition module and the processing module, as well as making easier offline processing of the data.

4.1.2 App 2: PhysioSense

The second application is responsible of receiving the physiological data sent via Bluetooth by the smartphone and estimate the psychophysiological inference to be used in the adaptation engine, these tasks correspond to the METRICS and INDICES blocks of the five-layers model in the Figure 2.1.

The mobile phone utilized was the Samsung Galaxy S9 running Android operating system. PhysioSense is part of the PhysioVR framework developed by Muñoz et al. [26]. The original application was augmented with two main features: 1) compatibility with Samsung smartwatches, and 2) more important, the addition of a module that processes physiological signals in real-time to extract more features from the signals, which could provide more meaningful information for applications aiming at using physiological adaptation. The application was developed using Java language and the IDE Android Studio [79]. The result of the application is shown in the image Figure 4.3, the left side shows the original user interface, and the right side displays the extended version with compatibility to new set of devices, acquisition control, and real-time information of the received data.

Figure 4.3: **App 2. PhysioSense** - User interface of the application PhysioSense. Left: Original version from paper in [26]. Right: Extended version with the thesis' work.

The application was provided with a receiver of the SAP protocol to collect the incoming data via Bluetooth from the connected smartwatch. Then, the data are buffered in a time series of the PPG signal to detect peaks on it and to calculate time interval between peaks to build the HRV signal.

The signal processing workflow is based on the pseudo-algorithm proposed by Bhowmik et al.[80], which contains the mathematical steps necessary to estimate HRV from PPG signal collected through the smartwatch. The original paper evaluated the performance of the algorithm in an offline setting, meaning that the parameters were fine-tuned after the acquisition to maximize the peak detection in their dataset. However, this represented a new challenge for the designed physiological system because it was meant to work in real-time. The original pseudo-algorithm was re-implemented in Java and included in the PhysioSense Android application, enabling real-time HRV calculation. The evaluation of the system is mostly based on the assessment of the performance of this algorithm.

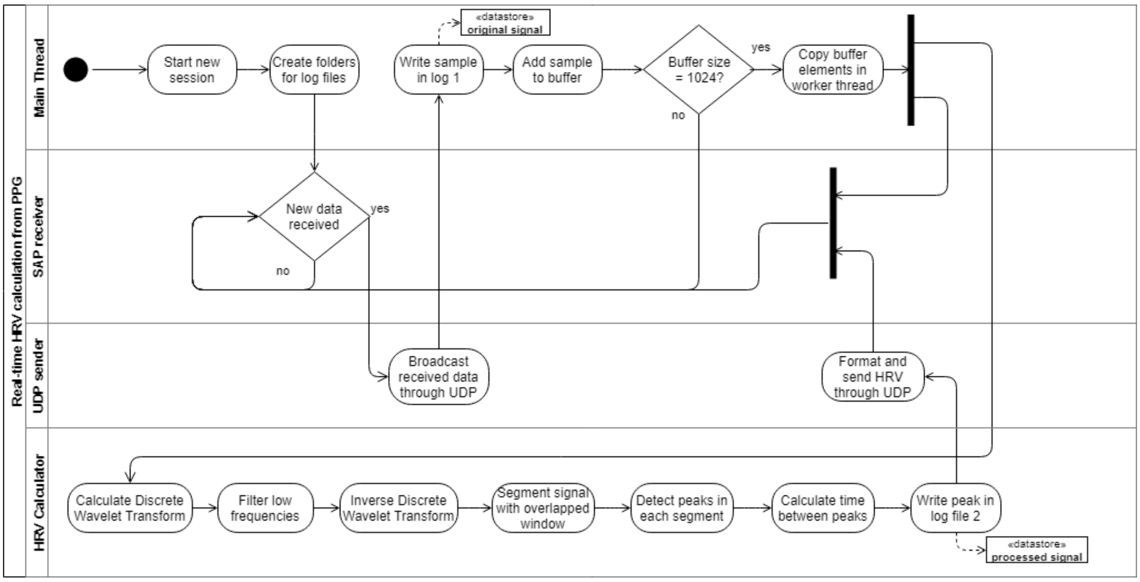

Figure 4.4: **HRV Calculation** - Activity diagram of the algorithm to calculate HRV in real-time from PPG data. Based on algorithm described in[80].

The activity diagram of the Figure 4.4 depicts the implemented algorithm. PhysioSense serves as a bridge by taking every message read via the SAP receiver and forwarding it through UDP to reach the visualization environment in VR. Additionally, it controls the creation of log files between different recording sessions. When a user starts a new session, the corresponding folders are setup to log all the incoming data and the results of the real-time HRV calculator.

The decisions that were taken to transform the pseudo-algorithm that calculates HRV into real-time processing affect several stages in the signal processing workflow. The original pseudo-algorithm[80] proposed five stages: 1)Signal denoising with Discrete Wavelet Transform (DWT), 2) trend removal with average filtering, 3) signal split in segments, 4) peak search with autocorrelation function, and 5) interpolation of peaks. However, the last stage was not included in the implementation utilized in PhysioSense. The reasoning behind this decision was that a set of interpolated peaks in the invalid segments would create fake peaks that alter the HRV that is intended to be measured, the final choice was to omit the segments where no peaks were found during the real-time processing to avoid false positives.

The output of the four stages used to calculate HRV in real-time in Java was evaluated offline using an R-script that visualized the peak detection algorithm. The input for the validation was a 20 seconds test signal that was recorded with the smartwatch on the author of the thesis. This time series was used to fine-tune the parameters that could lead to a better peak detection, and ultimately a better HRV in real-time. The Figure 4.5 shows the original recorded signal (left), the result after the four stages (center), and the mapping of the detected peaks back into the original recorded signal. The parameters used to detect the peaks in this sample signal were set via trial-and-error and finally deployed on the PhysioSense Android application.

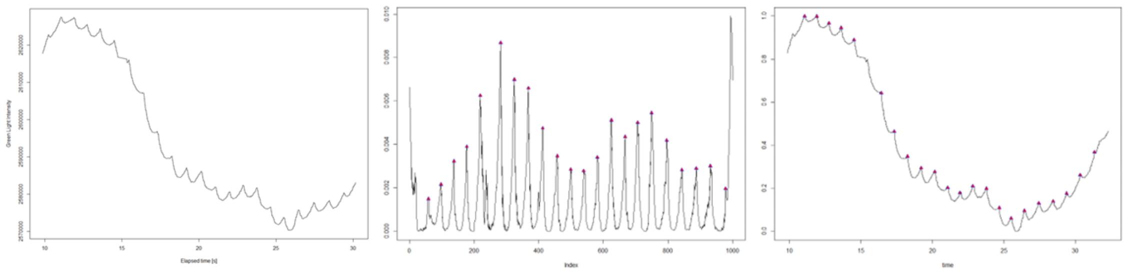

Figure 4.5: **Example Peak Detector** - Result of real-time peak detector in a test signal to fine-tune processing parameters. Left: Original signal. Center: Processed signal and peak detector. Right: Mapping of peaks in original signal.

Most of the parameters suggested by the original pseudo-algorithm were used in the final version of the HRV detector. However, there were some changes in the DWT and the addition of some parameters concerning the real-time processing. These values were set as follows:

- Signal buffer = 1024 samples
- Number of DWT decompositions = 5
- Window overlap = 224 samples

The signal buffer is the amount of data that is going to be collected by the system before running the HRV calculation, starting from the DWT. As described in the section 2.2.1, the DWT facilitates time-frequency analysis through consecutive decomposition of the signal. The mathematical procedure to decompose the signal in frequency components implies that after each decomposition the signal is subsampled by 2 to increase resolution in time. Thus, the algorithm is meant to be computationally faster when the number of samples is a power of 2. As a result, the chosen buffer size was 1024 samples.

The size of the signal buffer could have allowed up to 10 decompositions, but according to the conditions specified in the original article, the necessary number of decompositions to denoise the PPG signal were 7 to filter frequencies lower than 0.3Hz. However, when applied on the test signal the low frequency components were not filtered adequately, and after some validations the final chosen number of decompositions was 5. The breakdown of the decomposition process is presented in the Figure 4.6, it shows how the 32 samples corresponding to the Coefficients of Approximation L5 represent the frequency information from 0Hz to 0.78125Hz. Then, these 32 samples were set to zero to filter the signal and the inverse DWT was applied to reconstruct the original signal without the baseline component. After this reconstruction and the trend removal, the peaks could be successfully detected as shown in the Figure 4.7.

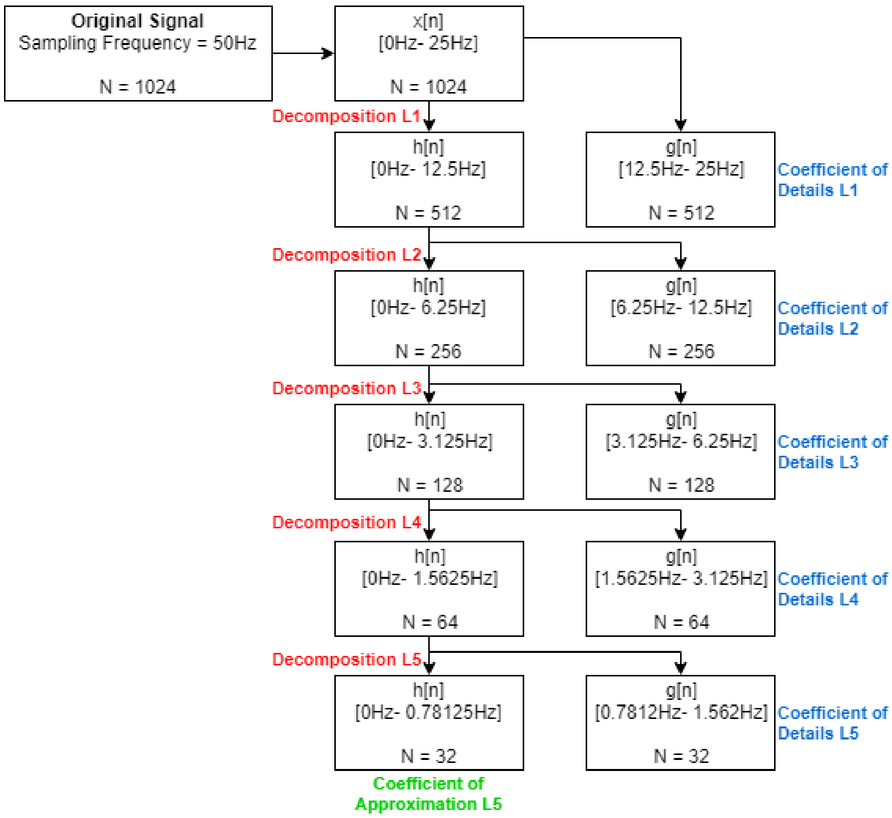

Figure 4.6: **DWT** - Breakdown of the Sub-band Coding Algorithm used signal decomposition performed by the Discrete Wavelet Transform during HRV calculation

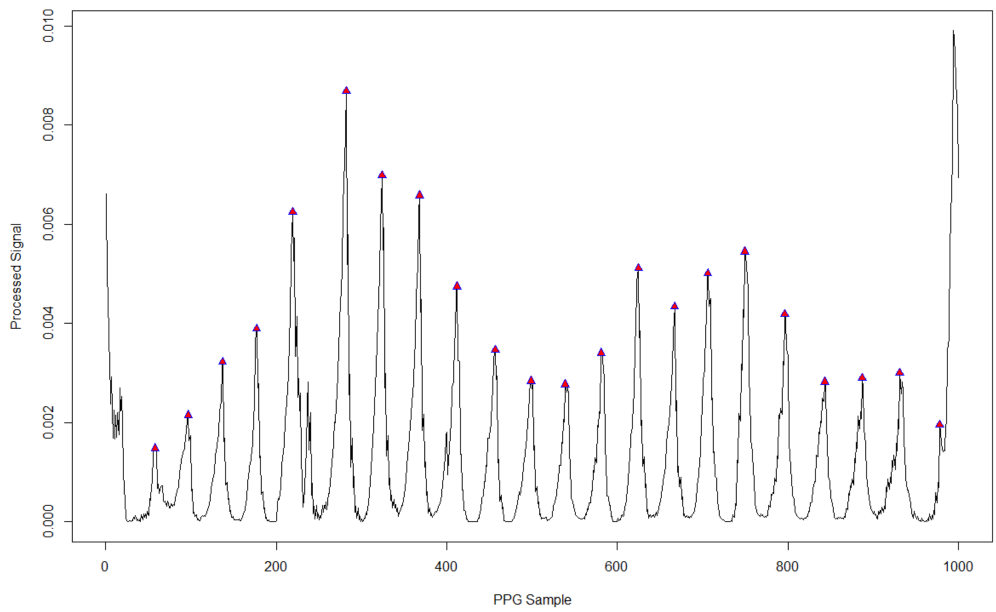

Figure 4.7: **Peak Detector** - Result of the peak detector algorithm for HRV calculation, applied on a test signal.

The real-time nature of the algorithm implies that a set of consecutive signal blocks are defined to process the acquisition of new data. Given that the size of the buffer was set to 1024 samples, the sampling frequency is 50Hz, and supposing that the buffer is completely emptied after each HRV calculation; then the algorithm would be activated approximately every 20.5 seconds. However, in the Figure 4.7 can be visualized that the borders of the reconstructed signal contained high values that might be part of a peak but that cannot be determined due to the signal split. To counteract this effect, the real-time processing of the signal is performed using overlapping windows, causing the first calculation around 20.5 seconds from the start of the session, and the subsequent calculations approximately every 16 seconds. With this approach, a segment of data is used to preprocess the signal, but the peaks are only detected in a subset of the segment, keeping some samples in the buffer to be used in the next calculation.

Considering that the original pseudo-algorithm recommended the split of the signal in segments of 4 seconds, meaning 200 samples, it was decided that the 1024 samples were used to execute the four stages of signal processing, but only the middle 800 samples were going to be used for peak detection and HRV calculation. It resulted in data buffers that contained four segments to detect peaks and kept a subset of the last 224 samples to be used in the next HRV calculation.

As an example, the output of the peak detection for HRV in two subsequent segments is shown in the Figure 4.8. The blue line represents the original signal, the green line is the processed signal, and the two vertical dashed black lines delimitate the sections where the peak detection was performed. Note that in the first segment the first 112 samples the peak calculation is not done, and this chunk is never processed. In the second segment, the first 112 samples already contain the peaks that were detected from the previous execution, but this is still included in the signal processing to avoid the problem in the edges that was previously described. This same process is executed every time the buffer is full and until the application is stopped or a new session is started.

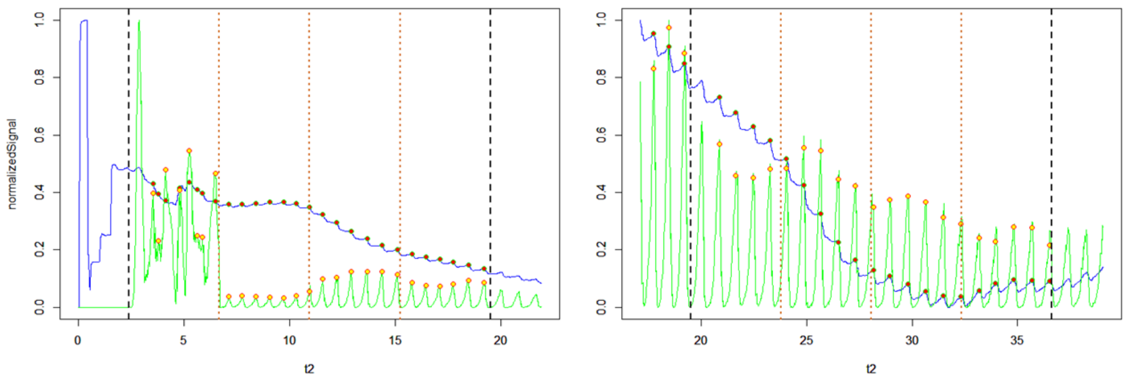

Figure 4.8: **Peak Detector with Overlapped Windows** - Result of peak detector in two subsequent segments with overlapping windows.

The last part of the algorithm is related with communication and data logging. A local file that is created per session stores the result of the processed signal and the calculated HRV. The latter value is also sent through the UDP port 1111 to be read by another application running on the same Android device, in this case, the VR application CalmPlace that would react to HRV changes.

4.1.3 App 3: CalmPlace

The third application that is part of the architecture is the virtual reality environment for relaxation CalmPlace, this software oversees the reception of physiological information to set the events and behaviors that are going to respond to specific conditions of the signal, and it is part of the LOGIC and APPLICATION blocks of the five-layers model in the Figure 2.1.

The application runs on the same mobile phone than the application PhysioSense, and they communicate via UDP. The module that handle the physiological signals in the virtual environment was developed using C# and the Unity game engine[81]. Unity is a game development framework that has increasingly been used in the field of serious games to design interactive applications for physical and mental health interventions[82][83], thus the compatibility of the artifact with this tool is key to facilitate the scale the use of physiological signals in future interactive solutions for health.

In the virtual environment, the module that controls the reaction towards physiological data has the appearance shown in the Figure 4.9. There are certain parameters that can be set regarding the execution of the adaptation rules. First, before any adaptation is done in the CalmPlace scenario, a baseline is calculated during a time that is easily set by the user at the beginning of the therapy, with the options of 5, 15, 30, 60 and 120 seconds, by default is 30 seconds. Then, the calculation interval is the period in which the adaptation rule is going to be triggered after the baseline, configurable in 5, 10, 15 or 20 seconds, by default is 15 seconds. Two types of adaptation are available depending on which physiological variable is desired to be used as a controller, either increase HR or maximize HRV. When the adaptation goal is to minimize HR, the average HR information is collected in the baseline and every calculation interval; otherwise is the amplitude of the HRV signal which is collected. At the end, when the timeout for a new adaptation is set, the physiological variable collected during the calculation interval is compared to the value in the baseline and clamped in a linear model from 0 to 1; where 0 means very far from the goal, and 1 that the adaptation goal has been reached. As an example, in the virtual reality experience the adaptation rule controlled the time of the day, going from dusk to noon.

Nevertheless, it is important to recall that, even though both HR and HRV signals were made available, the current work is primarily interested in adaptation using HRV due to its significance in mental health therapies. **Moreover, although the adaptation rules were implemented, the evaluation of the artifact was not using the adaptation system during the intervention**. This decision responds to the design requirements and recommended steps in the development of physiological computing systems, where the first step is to assess the reliability of the physiological metrics before assessing the effects of the whole biocybernetics adaptation in helping the user to reach the goal[19].

4.2 Artifact Evaluation: HRV during Slow-Paced Breathing Exercise

According to the research study design, the evaluation is performed to identify whether the artifact can properly measure, transmit and analyze PPG data to identify changes in the HRV amplitude between normal breathing exercises and breathing at resonance frequency of 0.1Hz guided through VR.

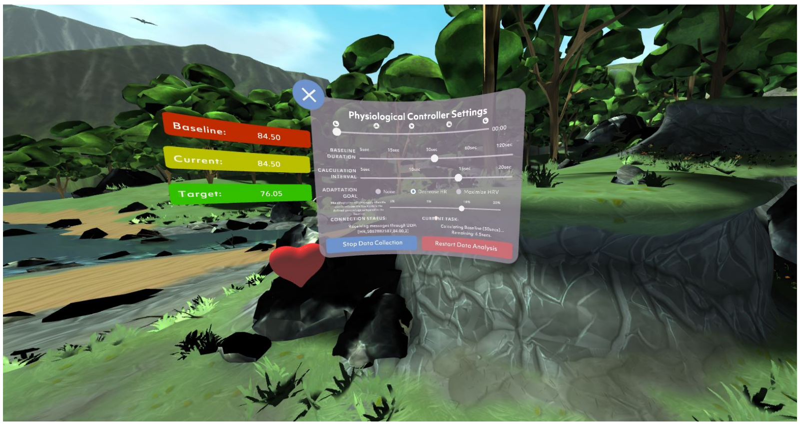

Figure 4.9: **App 3. CalmPlace** - User interface of the panel included in CalmPlace to control the responses to the physiological signals received from PhysioSense.

4.2.1 Demographic Results

A total of 11 volunteers were part of the experiment, age between 23 and 32 years old (27 ± 3.24), and five male and six female participants. 10 participants reported previous experience with VR systems and nobody reported any previous cardiovascular problems during the past 5 years that could affect results in heart data.

4.2.2 Questionnaire Results

The customized questionnaire (Appendix B) used a 5-point Likert scale to assess understanding of the instructions, perceived level of engagement with the virtual reality environment, and perceived most relaxing intervention during the experiment. The distribution of the answers is presented in the Figure 4.10.

All participants reported a clear understanding of the given instructions for both parts of the experiment. The second question intended to measure perceived level of engagement with the virtual environment, all the participants reported positive level of engagement and mental blockade of external sounds or triggers. No negative answers were reported regarding difficulties to follow the pattern object that guided the respiration at 0.1Hz. The comparison about perceived relaxation level between two parts reported a level of relaxation of 3.45 ± 1.04 during normal breathing and 3.27 ± 1.19 during slow-breathing. Finally, one participant reported "little dizziness comparable to motion sickness" but completed the whole experiment.

4.2.3 Artifact Functioning

This subsection contains the technical evaluation of the system as described in the methodology to process and analyze the data in section 3.5.5.

From the telecommunication standpoint, the objective to measure the number of packets per stage was threefold: 1) Validate need of time synchronization, 2) Evaluate the effectiveness of the SAP protocol and UDP protocol in transmitting the physiological data in real-time, from the smartwatch to the virtual environment; and 3) Detecting performance and stability issues from the proposed architecture. The Table 4.1 summarizes the values of these variables per participant and per application.

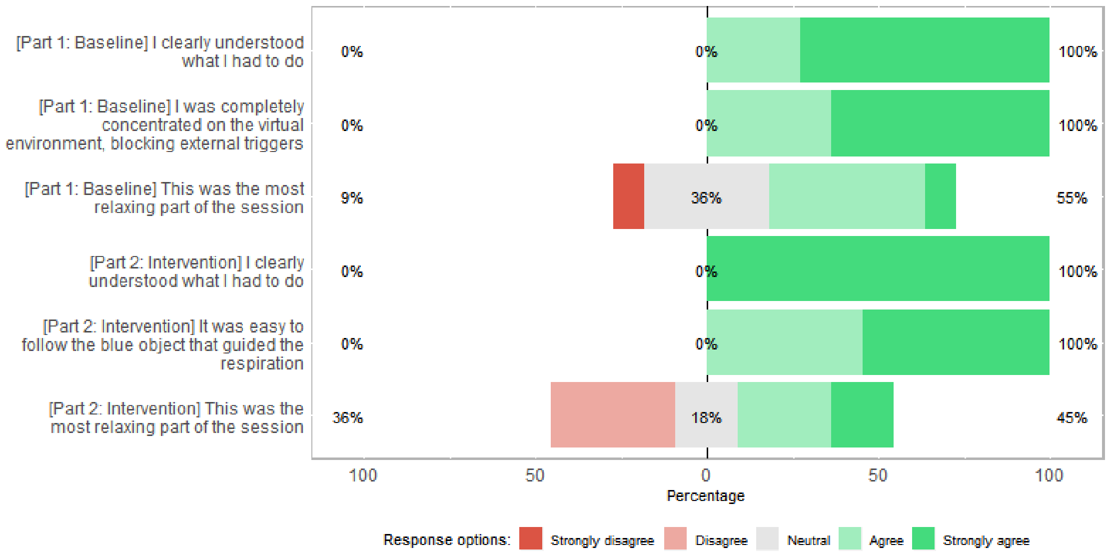

Figure 4.10: **Questionnaire Answers** - Diverging stacked bar chart summarizing the results from the questionnaire administered post-experiment.

Table 4.1: Summary of the data collected during the experiment, grouped per participant and per application.

	App 1: PPG Recorder			**App 2: PhysioSense**			**App3: CalmPlace**		
ID	N_{T1}	N_{B1}	N_{I1}	N_{T2}	N_{B2}	N_{I2}	N_{T3}	N_{B2}	N_{I3}
1	230941	10289	6552	21245	10289	5284	8325	5427	2895
2	28042	12599	10543	26457	12599	9399	11764	6844	4920
3	32348	12601	12601	32348	12601	12601	14010	6744	6947
4	30424	10745	12562	14486	6392	7669	14486	6392	7669
5	20173	10760	3414	17600	10760	2196	6978	5800	1176
6	24487	12599	5869	22251	12599	4725	9140	6746	2394
7	31389	12600	12600	30296	12600	12085	13182	6783	6399
8	23880	10750	8098	22233	10750	6963	9428	5712	3714
9	17883	10732	2823	16551	10732	1636	6392	5518	872
10	14677	9773	1	14677	9773	1	93	92	1
11	26725	10622	10471	25476	10622	9325	10391	5501	4887

Time Synchronization

The comparison of the total number of recorded samples showed that, for all the sessions: $N_{T1} > N_{T2} > N_{T3}$; validating the necessity to make time synchronization of the different datasets because the length of the log files was different in each system.

The application 3 contained an event log system with timestamps that were intended to facilitate time synchronization for post-analysis. However, due to an undetected software bug, this file was not created in 5 out of the 11 experimental sessions. In these cases, a workaround was used to calculate the timestamps that would allow to split the signal into the two corresponding parts of the experiment. However, the log file that with physiological data was created successfully in all cases, and contained the data received in the experiment's duration. Thus, the start of the experiment baseline (Part 1) was set to the timestamp of the first logged data sample (t_b), the start of the experiment intervention (Part 2) was set to the timestamp corresponding to $t_b + 270$ seconds, and the end of the session was set to the timestamp $t_b + 540$ seconds. The validation of the workaround in sessions without correputed data resulted in a difference of about 60ms, considered an acceptable error to continue with the analysis.

Packet Loss throughout Data Workflow

Given the different transmitters and receivers used in the architecture, the analysis of packet loss provided insights about the performance of the system in handling real-time information at the specified sampling frequencies and computational demands from the algorithms and visualization techniques. Later, the three sources of data in the systems were synchronized to consider only the time window corresponding to the experimental session; meaning that the total packet loss was comparing the sum of $N_B + N_I$ per participant and per application, as shown in Figure 4.11.

Analyzing the data from the 11 participants, the packet loss in the Bluetooth link between the PPG recorder in the smartwatch and PhysioSense in the mobile phone was $8.1\% \pm 10.9\%$; between PhysioSense and the VR environment CalmPlace was $47.3\% \pm 22.2\%$, and the total packet loss in the physiological computing system from end-to-end was $53.3\% \pm 15.6\%$. However, as can be seen in the Figure 4.11, **the two observations that are drawn in red lines had a clearly differentiable behavior. These two observations were considered outliers from the calculation and only the remaining 9 observations were finally processed**, reducing the dispersion in packet losses with $5.5\% \pm 2.9\%$ between PPG recorder and PhysioSense, $46.9 \pm 0.8\%$ between PhysioSense and CalmPlace, and $49.7\% \pm 2\%$ from end-to-end.

System Stability Issues

The two outlier observations drawn with red color in the Figure 4.11 match with the experimental sessions that presented special conditions.

First, the uppermost red line corresponds to a session in which PhysioSense was not properly setup by the experimenter, causing the physiological data to be stored but not processed in real-time with the HRV calculation. This observation was the only observation that did not present packet loss between PhysioSense and CalmPlace, providing insights about the impact of the algorithm execution had in the data throughput.

On the other hand, the lowermost red line corresponds to a session in which the PPG Recorder in the smartwatch stopped recording data before the baseline, resulting in small number of total recorded samples and incomplete HRV data to compare algorithm performance.

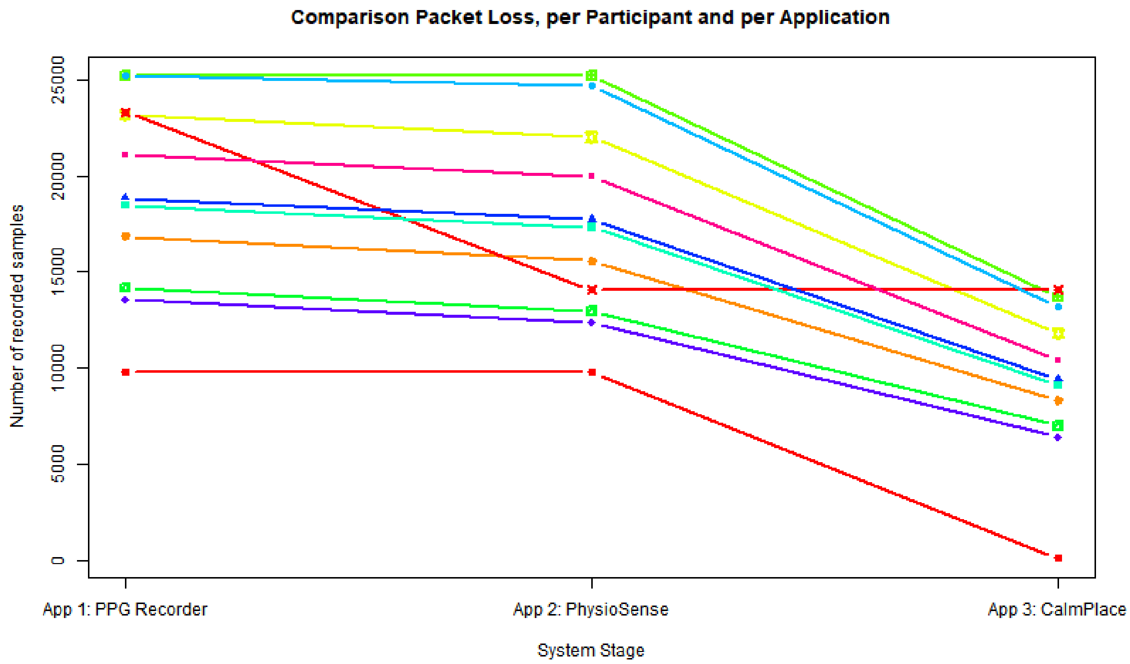

Figure 4.11: **Packet Loss** - Parallel plot with number of received messages along physiological system stages per participant.

In addition, the **main technical issue of the whole physiological system was the stability of the application PhysioSense**, which was always running as an background application in Android. It was stopped in the middle of the experiment in 9 out of the 11 sessions, affecting the data collection and calculation of HRV. According to the messages of the mobile phone, the operating system detected that the battery was being drained by a background application and forced the end of this process while the virtual environment was in execution. The Figure 4.12 depicts the time when PhysioSense was active for each experimental session; the first dashed line indicates the change in the experiment between baseline and intervention, and the second line shows the expected end of the experiment. The bar plot indicates that only two participants could complete the whole experiment with PhysioSense running in the background, but one of these corresponds to the session in which the algorithm for HRV calculation was not properly setup; resulting in only one session that was finished without inconveniences.

4.2.4 Algorithm for Real-Time HRV Calculation

From the 11 participants, the analysis of performance of the algorithm for real-time HRV calculation only considered 9 observations, the two outliers that were dismissed from this analysis held the anonymous identification codes 4 and 10.

The Table 4.2 summarizes the results related with the algorithm for real-time HRV processing. The first subheading shows the results of the implemented peak detector described in the section 4.1.2, applied over the whole array of data captured by PhysioSense for each user. The second subheading describes the analysis of the originally captured HRV signal split into the baseline and the intervention durations. The rest of the table shows the signal percentage that was affected by post-processing of HRV signal and the features extracted from it.

Table 4.2: Performance of the algorithm for real-time HRV calculation in the application PhysioSense. Excluding outliers with indexes 4 and 10.

	Peak Detection			**Features from Originally Calculated HRV**				**Processed Proportion**		**Features from Processed HRV**							
ID	S_P	S_V	$S[\%]$	$\mu(HRV_B)$	$\sigma(HRV_B)$	$\mu(HRV_I)$	$\sigma(HRV_I)$	$P_B[\%]$	$P_I[\%]$	$\mu(HRV_B)$	$\mu(HRV_I)$	$\sigma(HRV_B)$	$\sigma(HRV_I)$	$RMSSD_B$	$RMSSD_I$	CV_B	CV_I
1	105	83	79.0	1028.0	1632.8	1004.0	1749.6	8.29	5.17	731.2	0.106	127.8	749.40	150.23	2.141	0.175	0.200
2	131	113	86.3	975.5	1178.3	866.8	1440.9	4.69	3.74	824.3	9.015	191.1	680.94	192.65	4.463	0.232	0.283
3	161	142	88.2	947.8	1282.0	831.5	795.3	7.02	6.77	764.9	6.837	169.0	793.91	145.89	22.836	0.221	0.184
5	87	80	92.0	758.7	602.3	687.0	101.5	6.58	0.00	708.8	0.000	126.3	686.99	101.48	6.323	0.178	0.148
6	110	91	82.7	850.5	1322.0	697.6	153.7	5.97	3.91	644.9	4.842	162.1	675.18	111.64	3.771	0.251	0.165
7	150	122	81.3	1089.4	1629.7	831.1	1017.9	5.24	3.72	838.7	16.413	164.8	730.89	204.12	0.388	0.197	0.279
8	110	104	94.5	876.5	548.2	774.4	229.7	6.46	7.87	798.4	1.325	94.0	752.51	141.18	16.021	0.118	0.188
9	82	66	80.5	920.1	1365.2	1289.1	2137.7	5.42	0.00	709.2	4.207	167.8	792.43	302.30	26.284	0.237	0.381
11	126	103	81.7	539.2	1135.4	637.6	257.9	6.58	5.21	475.4	48.437	157.6	613.99	184.88	11.495	0.331	0.301
Avg	**118**	**100**	**85.14**	**887.3**	**1188.4**	**846.6**	**876.0**	**6.25**	**4.04**	**721.8**	**10.131**	**151.2**	**719.58**	**170.49**	**10.414**	**0.216**	**0.237**

μ: Mean. σ: Standard Deviation - S_P: Number of processed segments in PPG signal during the experiment. S_V: Number of processed segments with valid peaks to calculate HRV. $S[\%]$: Proportion of signal segments where PPG peaks were detected. $HRV[msec]$: Heart rate variability, time between two successive peaks, calculated separately during baseline (HRV_B) and intervention (HRV_I). $P[\%]$: Proportion of samples from original HRV that were affected after the post-processing of the signal of the baseline (P_B) and intervention (P_I). $\mu(HRV)$ and $\sigma(HRV)$: Mean and Standard Deviation of HRV during experiment baseline (HRV_B) and intervention (HRV_I). $RMSSD$: Root mean square of the mean of the squared differences in time between successive peaks. CV: Coefficient of Variation.

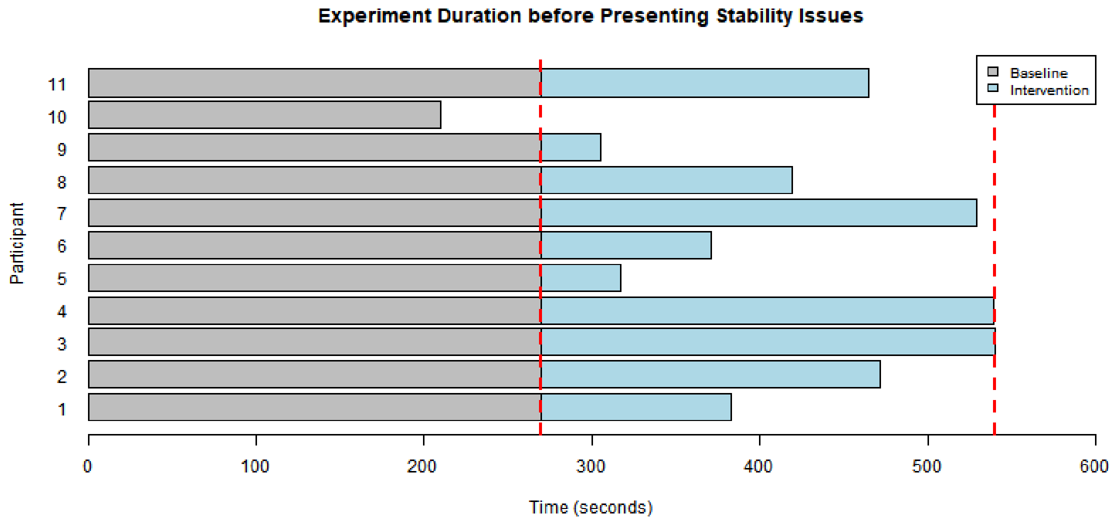

Figure 4.12: **PhysioSense Time** - Duration of the experiment, per participant, before PhysioSense was closed by the operating system.

The normal heart rate range is 40-150BPM, even under slow-breathing exercises, therefore the valid time range between consecutive peaks should be between 1500-400ms. However, the calculated HRV signal was presenting values exceeding this range and had to be post-processed.

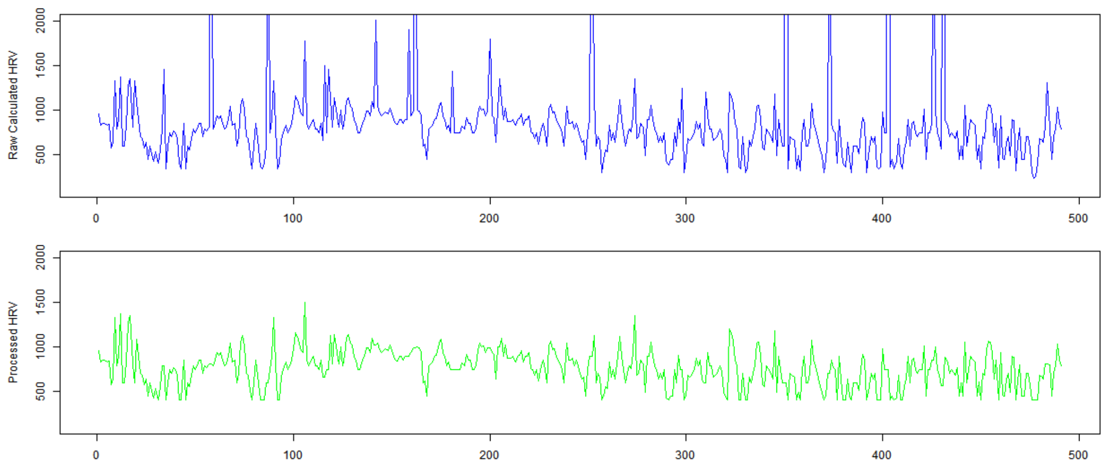

Figure 4.13: **Post-Processing HRV** - Example of one HRV signal before (top) and after (bottom) processing the outlier values.

Two reasons were detected as the causes of big peak-to-peak times. First, the algorithm for real-time HRV peak detection splits the signal in data chunks of four seconds but some segments were not returning valid peaks, causing the time difference between two consecutive peaks being in the order of several seconds. This was a flaw in the design of the system's architecture, caused by the decision of skip the step of peak interpolation in the PhysioSense implementation, such as described in 4.1.2. Second, when the algorithm collected the 1024 samples in the buffer to execute the HRV calculation, the system could not read samples at 50Hz because the working thread was busy during the data analysis, causing that some PPG signal peaks were omitted.

The issue with HRV outliers is depicted in the Figure 4.13 with the example of one participant's data, the blue line (top) represents the original recorded data with samples that cross the valid range. The post-processing algorithm consisted on three stages: 1) Clamping the window in the range 400-1500ms, 2) Using moving windows of 10% of the signal length with 50% overlap to detect the values that were outside 2.5 standard deviations, and 3) assign to these positions the previous valid value to generate a difference between peaks of 0ms. Result of the post-processing is shown in the green line (bottom) in Figure 4.13.

It was necessary to filter out the outliers that could have affected the calculation of dispersion metrics and get a signal that represented better the real behavior of HRV during the experiment. As an example to show the dispersion before and after the processing of HRV, the coefficient of variation (CV) was calculated per participant and the results are displayed in the Figure 4.14. The coefficient of variation shows the relationship between the standard deviation and the mean value of the signal. The bars show that the variability of the HRV signal was considerably reduced, just after processing between 3%-8% of the data that were outliers, according to P_B and P_I in the Table 4.2, and increasing the resolution to detect changes for the final statistical test.

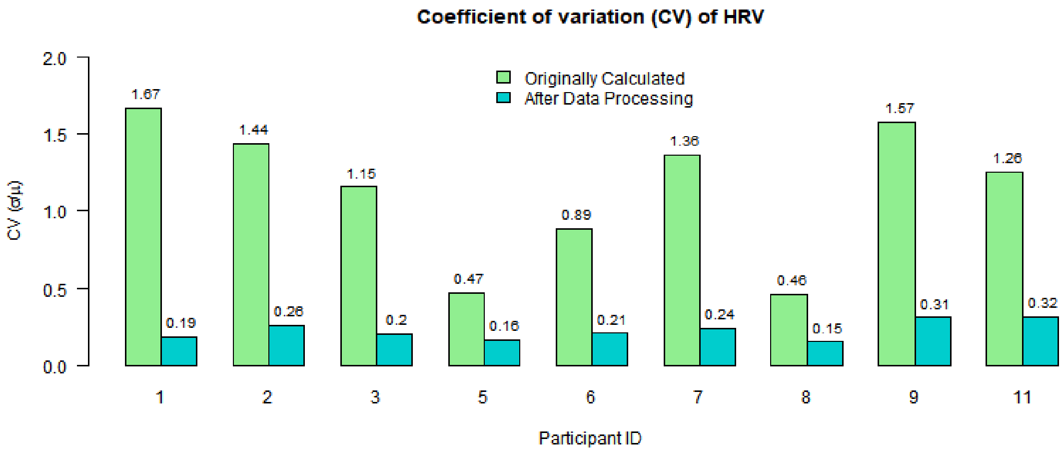

Figure 4.14: **Post-processing results** - Change in variability before and after processing outliers in HRV signal, per participant.

4.2.5 Comparison of HRV between Normal and Slow-Paced Breathing

The goal is to compare the experiment's baseline during normal breathing and the experiment's intervention during slow-paced breathing. The evaluation checks whether the PPG data collected with the smartwatch and the HRV calculation algorithm allow to find a statistically significant difference among the two conditions. For this purpose, the metrics Coefficient of Variation (CV), RMSSD and Standard Deviation (SD) were used, based on the Table 4.2 and summarized in the boxplot of the Figure 4.15.

The critical value for one-tailed Wilcoxon signed-ranked test, level of significance $\alpha = 5\%$, and sample size $N = 9$ is $W_{critical} = 8$. The calculated W statistics for each variable were: 15 for CV, 20 for RMSSD and 17 for SD. Since all of them are higher than the $W_{critical}$, then there is not enough evidence to reject the null hypothesis that HRV features during normal breathing are lower or equal than HRV features during slow-paced breathing, using the data recorded with the developed artifact.

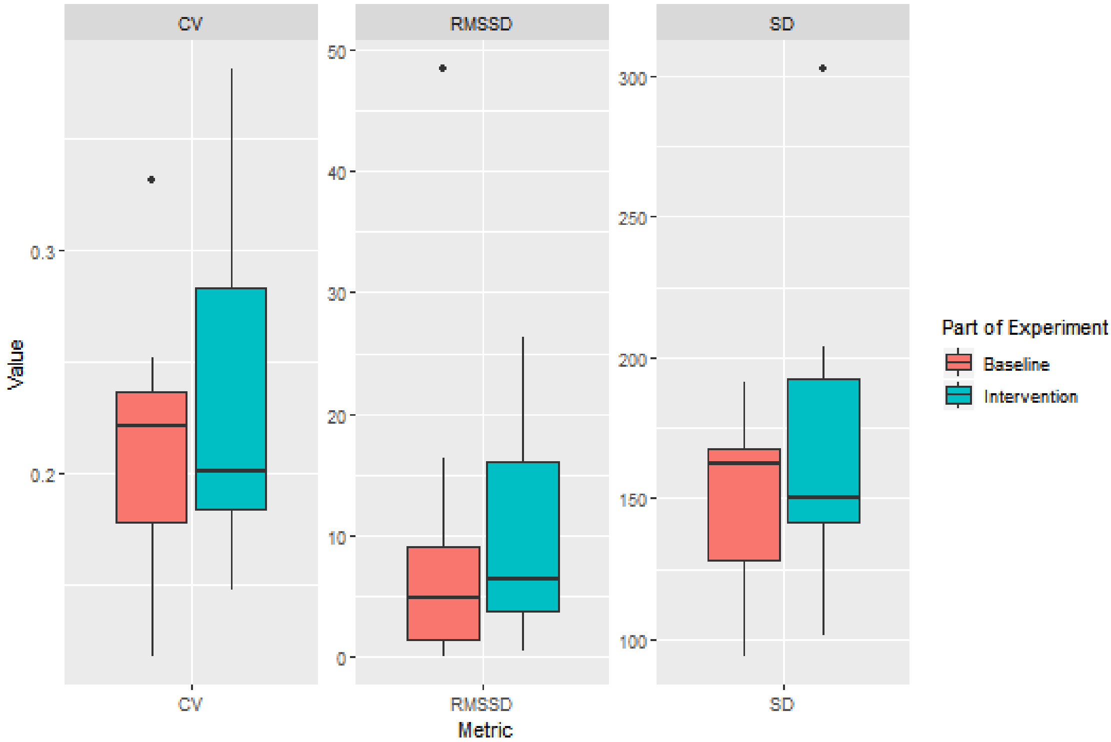

Figure 4.15: **Statistical Test** - Box plots showing the difference in the HRV features between baseline and intervention. Slight HRV increase is perceived in during slow-breathing intervention, but the difference is not statistically significant.

Chapter 5

Discussion and Conclusion

5.1 Main Findings

The aim of the thesis was to implement the Five-Layer model of physiological computing systems using a mobile-based approach to facilitate the development of technology-based therapies in research and medical settings. The knowledge gap that was addressed is the lack of computing systems that make easier the scalability of mental health interventions without requiring wired setups or bulky devices to collect physiological data.

The major finding of this thesis is related with the proven technical feasibility of construction of the proposed system based on available wearable health monitors and mobile devices. The Five-Layer model of Physiological Computing [23], showed in the Figure 2.1, was set as the reference for the architecture. The first part of the results presented the design and development of the architecture with three software applications that comprise the five blocks of the model. The second part was an early evaluation, which analyzed the performance of the system in terms of packet loss during data transmission, real-time processing of physiological data, and possible adaptation strategies. In general, the results showed an acceptable performance, indicating that the implemented system might be considered as a technical example in the use of interactive and cutting-edge technologies to support mental health interventions in a mass scale. Nevertheless, additional research from the technical and medical perspective is required.

The significance of the thesis compared to the previous studies in the field is mainly the use of real-time metrics from physiological signals in computational systems, specifically the capability to use HRV features from smartwatch signals. These data extend the spectrum of metrics that can be used by a system to understand the users' psychophysiology. Due to its relationship with parasympathetic and sympathetic activity in the brain, HRV also turns out to be a relevant metric to be associated with specific aspects of mental health and be further studied by using the proposed architecture. Additionally, according to the analysis of technologies described in the section 2.3, similar research projects on mental health were using either wired sensors, computers to process the data in real-time, or were not using mobile VR to deliver the interventions. Conversely, the presented architecture leverages from the use of wearable devices to collect physiological data, mobile phones to perform real-time processing, and use of mobile VR; thus enhancing the portability and scalability of these setup for projects aiming at conducting further research with HRV over mental health interventnions.

5.2 Considerations from Artifact Construction

The technical implementation is heavily based on the previous study PhysioVR [26]. However, compatibility with a new type of smartwatches was added, associated with the SIGNALS block of the generic model; and a module that performs additional analysis from the PPG signal by calculating HRV features, linked to the block METRICS. HRV features are more associated to biofeedback techniques and mental health interventions than normal heart rate values, such as it was provided by the first version of PhysioVR. Finally, the new spectrum of metrics benefits the psychophysiological inference, linked to the block INDICES, that could be estimated from the user.

Even though the construction of the physiological computing system was seen as feasible, some technical elements need to be addressed. Initially, the interoperability for data transmission between peer technologies is still a challenge. When trying to scale up the PhysioVR (running Android OS) with compatibility for new type of smartwatches (running Tizen OS), the different operating systems between the wearables and PhysioVR implied different programming languages and development environments, demanding extra workload from the development side. This burden will exist for every new device that is intended to be incorporated as a source of physiological data, but this initial effort is counteracted afterwards by the increase in system's portability. A standard that defines for transmission of physiological data in real-time over Bluetooth networks could solve this hindrance.

Concerning ethical and legal issues, the solutions that promote use of technology to bridge the existing gaps in healthcare face different challenges regarding privacy, accessibility and free informed consent [84]. The artifact that was built is not exempted from these issues because the collection of the physiological data using digital health sensors is sensitive to be transferred to other devices and be accessed by more people, hence the importance of anonymity when collecting the data. From the ethical standpoint, the nature of the project aims at increasing scalability of the technology, which is socially positive because it seeks to grant access to technology-based health services to those communities that cannot have them. But, simultaneously, it might foster reduction of human contact between medical users and patients, eventually leading to patient's isolation and risks of psychological complications caused by technology flaws or misuse.

5.3 Considerations from Artifact Evaluation

The evaluation did not include the adaptation because, as recommended by physiological computing seminal articles, it is required a validation of the metrics in inferring psychological states in the user before enabling the automatic biocybernetic adaptation mode [19].

The administered questionnaire resulted in positive acceptance in terms of engagement. The perceived relaxation was reported higher during the baseline in spontaneous breathing than during the slow-breathing. The reason might be associated with the required sustained attention to follow the breathing pattern, whereas the first part did not have a specific mental task but just enjoying the environment. In order to measure the perceived relaxation level in a more homogeneous way with the artifact, it is recommended to conduct the new protocol showing the breathing object at two different respiration frequencies. In this way, since both scenarios would require similar mental workload, the bias that was induced by the guiding breathing pattern might be reduced.

The log files recorded in the three different applications were fundamental to perform a reliable analysis post-intervention, without these data the time synchronization could not have been executed, demonstrating the importance of this stage in its functioning as a real-time system. However, although a workaround was found for the error in which log data was not properly stored in CalmPlace for some sessions, it proved vulnerabilities in terms of stability that need to be addressed from the technical perspective.

The degree of packet loss along the architecture provides insights about the computational intensity required to handle the data acquisition, signal processing and rendering of virtual reality environment. The biggest contribution for packet loss was the algorithm for HRV calculation that was running in PhysioSense, which was corroborated with the data of the participant in which the algorithm was not activated and did not report packet loss.

The algorithm for real-time HRV calculation is the major bottleneck in the data workflow. Actions from the development standpoint are required to reduce its impact in the overall performance of the application, aiming at alleviating CPU usage to avoid that the operating system closes PhysioSense from running in the background. First, one of the recommendations is to reduce the acquisition sampling frequency from 50Hz to 20Hz, which still follows the valid ranges found by Choi et al. [78]. The choice of using a high sampling frequency because a battery drain was not detected was proven as premature, since it did not anticipate possible performance issues. Consequently, changing the sampling frequency would require fine-tuning the parameters of HRV calculation. The use of spectral analysis led to an initial choice of 1024 samples for the buffer size, but according to the DWT algorithm, the number of frequency decompositions and window overlapping can be reevaluated to reduce processing time per segment of PPG data. Secondly, other recommendation is to use multithreading in the Android application to parallelize the tasks of acquisition, processing and communication among different cores of the computing unit. Lastly, regarding the errors induced in the HRV calculation, not having implemented the interpolation algorithm of the peak detector from Bhowmik et al. [80] was a main cause of having long peak-to-peak times. Although the offline post-processing algorithms could counteract the effects caused by the system instabilities, the inclusion of these algorithms in the real-time algorithm is necessary to increase the quality and reliability of the calculated HRV values.

After the post-processing, the calculated HRV data were within reasonable values for all the participants, demonstrating that the system is suitable to calculate this type of signals under the defined conditions. The validation can be done in new studies that seek to compare peak detector accuracy between the designed solution and a gold standard, which could be taken from other wearable systems with proprietary built-in peak-to-peak interval calculation (such as in Garmin or Polar smartwatches). Recalling that these options are proprietary that do not allow other applications to use these data in external applications, which make them inconvenient for physiological computing systems.

The metrics chosen to compare the HRV between baseline and intervention produced data that were aligned with the hypothesis of the use-case scenario of the artifact. The initial assumption that slow-breathing maximizes changes in HRV could be seen in the boxplots in the Figure 4.15. However, the differences were not sufficient to be considered statistically significant. One of the reasons could have been the insufficient collected data, both from the number of participants and the instability issues that caused the system to crash. Further studies with more observations would allow to draw more definitive conclusions.

5.4 Considerations about Wearables and Virtual Reality for Mental Health

The wearable devices with physiological measurements use proprietary software, which impedes the access to raw data and hence it cannot be used to transmit information to external applications. For this reason, the artifact presents important contribution in democratizing the use of this data on broader type of solutions, such as in the case of mental health. This restriction to the data makes it more difficult to validate the effectiveness of these solutions in measuring physiological metrics, and some studies have reported the existing concerns with wearable manufacturers that do not invest enough on research to provide reliable technology [24].

VR technology has become more likely to assist the therapies for mental health treatments because it is more portable and affordable for consumers than never before. The fact that VR elicits higher engagement, user acceptance and uses realistic environments allow safe assessment of dangerous situations. For instance, exposure therapy for treating fear of heights is now possible without putting the user at a life-threatening risk. The use of CalmPlace in the artifact was just one example of the type of interventions for anxiety management, but the whole physiological computing system can be adaptable to practically any VR application that is developed in the Unity game engine. It implies that physiological data can be used in the increasing number of technological solutions for health that are being developed in research and industry. In spite of the diversity of types of VR devices, mobile VR has been giving universal access to the people to immersive technology, encouraging the development of more digital solutions to provide global, cost-effective and evidence-based services aimed at improving mental health.

Furthermore, the design of biofeedback systems for mental health should rely more on existing hardware, testing its feasibility on medical settings instead of designing new physiological sensors that will have to pass through safety approvals. The frequent release of electronic devices for VR and wearable health monitors are considered a likely path to make easier the acquisition of physiological signals for VR-based biofeedback tools.

Finally, in the same way this thesis involves the work from a local company that uses VR for health, it is recommended that future related projects strive for the creation of alliances between healthcare, research, and commercial sectors. When this condition is fulfilled, a big gap in the field of technology-based medical applications might be reduced, because the digital solutions resulting from this partnerships would be designed for use in real-life settings, evidence-based, and adapted to socio-cultural aspects of the target populations who urge to receive cost-effective solutions for mental health [7].

5.5 Limitations of the Study

From the research protocol there are some details to highlight. First, when explaining the experiment intervention, the participants were told to follow the specific frequency of the guiding object, but they did not receive instructions about the deepness of breath. Through observation, it was detected that only some participants were taking deep breaths, whereas others were breathing with the deepness of a spontaneous respiration cycle. This might have affected the homogeneity of the HRV data that was collected under both conditions and needs to be considered in further research. In addition, the process to put the wearable device worn on the participant's wrist differed among participants, generating different signal-to-noise ratio of the heart rate signal. The effect was evident especially due to inclusion of components in low-frequency band, which could be caused by movements of the sensor on the wrist. Thirdly, a protocol to define an ideal baseline state should be planned, for instance, letting the user rest for a specific amount of time before the data collection starts.

The HRV calculation was dependent on the respiration but an adequate respiratory-sinus arrhythmia analysis could not be calculated during the experiment because the real respiratory signal could not be measured from the participants. The second part of the experiment supposed that the user was following the breathing pattern correctly, and since any volunteer reported difficulties in the post-experiment questionnaire, this assumption was used during the inferential data analysis.

Despite the mentioned restrictions, the internal validity of the project was not affected because the main research question was intended to validate technical feasibility of construction and was not framed as an evaluation from the psychophysiological point of view, thus permitting certain level of flexibility to make assumptions that facilitated the experiment. Conversely, the external validity which explains to what extent the study can be generalized outside the study sample [85], is affected because the sample size was very small to draw definitive conclusions about the changes between normal and slow-paced breathing.

5.6 Future Work

The current work aimed at designing and conducting an evaluation of the physiological computing architecture as a whole entity, yet more research is encouraged from the technical and medical standpoints. From the technical side, further evaluations could be aimed at evaluating individual stages of the deployed architecture to enhance its robustness and stability. For instance, assessing accuracy of the peak detector, impact of the real-time HRV calculation in packet loss, validation of HRV features able to properly discriminate slow-paced breathing, visual cues in the virtual environment that could elicit higher perceived relaxation states in the users; and response of the adaptation logic which was already implemented, but not assessed, in the current artifact. From the medical perspective, as stated in the fundamentals of physiological computing, the final goal is to use psychophysiological inference to provide computational systems with awareness of the user. Therefore, the future work should be also aimed at validating the whole biocybernetic loop under clinical conditions. In order to prevent ethical and legal consequences, the future studies that use this system for medical validation should seek for approval from a regional ethical committee, while providing adequate informed consent that follow the data protection rules.

A short-term study might replicate the use case of slow-breathing exercises at 0.1Hz solving the aforementioned methodological limitations. Considering a more representative sample of volunteers, and calculating other temporal and frequency features from the HRV signal such as described by Shaffer et al. [38], which could lead to statistically significant results. In addition, these features could be used to develop machine learning algorithms to build a model that detect the two states normal breathing and slow-breathing from data captured with wearable smartwatches.

5.7 Conclusion

The main research question explored in the thesis was:

To what extent can a physiological computing system be deployed only using wearable smartwatches and mobile virtual reality, to support mental health interventions with slow-paced breathing relaxation exercises and heart rate variability analysis?

The results obtained from the project confirm the feasibility of construction of a physiological computing system only using mobile devices. However, the early evaluation also unveiled some technical and methodological elements to be considered before further implementation on mental health projects.

Positive aspects from the construction of the physiological computing system are that it proved that wearable and immersive technology is ready to provide customized solutions for different areas. In this case, such as recommended by the World Health Organization, mental health could leverage from the technology to support scalability of mental health interventions in communities that lack these services. In order to accomplish this goal, projects that put together research, healthcare and industry fields are needed to tackle the problem from all the perspectives. This type of alliances encourages the design of systems that consider the feasibility of the self-guided therapies keeping in mind effectiveness assessment, medical pertinence, user-experience, and a way in which the technology can be easily spread out throughout targeted populations. Moreover, these digital solutions resulting of these partnerships should evaluate and rely on existing VR and wearable devices to speed up the process of medical validation, instead of focusing on the design of more electronic devices for this purpose.

Some elements of the physiological computing system still require improvement. The main pitfall was related with technical instabilities, mainly due to a high computational demand caused by the real-time HRV calculation. Moreover, the chosen use-case scenario was sufficient to build the technical architecture from end-to-end, but future evaluation needs to overcome the described methodological limitations to try to achieve statistically significant results analyzing HRV in normal and slow-paced breathing.

The answers for secondary research questions are summarized as follows:

1. *What is a feasible technical architecture of a physiological computing system fully integrated with mobile VR and wearable sensors?*

The feasible technical architecture was designed and implemented based on the set of requirements and specific use-case described in the section 3.4. Leading to three interconnected software applications that contained the five-layer generic model of physiological computing, and thoroughly described in the section 4.1.

2. *How can HRV be calculated in real-time from the heart rate signal to estimate the user performance in a self-guided slow-paced breathing exercise?*

A peak detector was implemented in the architecture based on previous technical papers, described in the section 4.1.2. It permitted the real-time estimation of features from the HRV signal, enriching the amount of information that can be put into the computational systems to cause an automatic adaptation, according to the biocybernetic loop of physiological computing. Ultimately aligned with the goal of offering systems for self-guided mental health interventions.

3. *What effects in HRV are detectable with the mobile physiological system during guided slow-paced breathing exercises?*

Although the physiological computing system could detect changes in HRV between normal and slow-paced breathing, this difference was not statistically significant for three different metrics of dispersion analyzed (standard deviation, RMSSD, and coefficient of variation). Improvements in the experiment protocol and overcoming the technical instabilities are suggested before collecting more data to validate this assumption. These statistical results did not affect the design and development of the final technical architecture.

References

[1] World Economic Forum. The Fourth Industrial Revolution: what it means, how to respond, 2016.

[2] Hannah Ritchie and Max Roser. Mental Health, 2019.

[3] WHO. *Mental Health Atlas.* World Health Organization, 2017.

[4] WHO. *Mental Health Action Plan 2013-2020.* 2013.

[5] WHO. Scalable psychological interventions for people in communities affected by adversity. Technical report, World Health Organization, 2017.

[6] MAJ Melba C Stetz, Richard I Ries, and Raymond A Folen. Virtual Reality Supporting Psychological Health*. In S. Braham and L.C. Jain, editors, *Advanced Computational Intelligence Paradigms in Healthcare 6. Virtual Reality in Psychotherapy, Rehabilitation, and Assessment*, chapter 2, pages 13–29. Springer Berlin Heidelberg, 2011.

[7] Joseph Firth, John Torous, Rebekah Carney, Jill Newby, Theodore D Cosco, Helen Christensen, and Jerome Sarris. Digital Technologies in the Treatment of Anxiety: Recent Innovations and Future Directions. *Current Psychiatry Reports*, 20(44):1–8, 2018.

[8] David D Luxton, Russell A Mccann, Nigel E Bush, Matthew C Mishkind, and Greg M Reger. mHealth for Mental Health : Integrating Smartphone Technology in mHealth for Mental Health : Integrating Smartphone Technology in Behavioral Healthcare. *Professional Psychology: Research and Practice*, 42(6):505–512, 2011.

[9] Emily Anthes. Mental Heath: There's an app for that. *Nature*, 532:20–23, 2016.

[10] E. Etchemendy, R. M. Baños, and C Botella. Virtual and Augmented Reality as Useful and Efficacious Tools for the Psychological Treatment of Emotional Disorders. In Pietro Cipresso and Silvia Serino, editors, *Virtual Reality: Technologies, Medical Applications and Challenges*, chapter 2, pages 31–54. 2015.

[11] Krista West. *Biofeedback*, volume 91. Chelsea House, 2007.

[12] Dana L Frank, Lamees Khorshid, Jerome F Kiffer, Christine S Moravec, and Michael G McKee. Biofeedback in medicine: who, when, why and how? *Mental Health in Family Medicine*, (7):85–91, 2010.

[13] William Sherman and Alan Craig. Introduction to Virtual Reality. In William Sherman and Alan Craig, editors, *Understanding Virtual Reality Interface, Application and Design*, chapter 1, pages 6–13. Morgan Kaufmann, 2003.

[14] Weidong Huang, Jane Li, and Leila Alem. Towards Preventative Healthcare : A Review of Wearable and Mobile Applications. *Data, Informatics and Technology: An Inspiration for Improved Healthcare*, pages 11–14, 2018.

[15] Mostafa Haghi, Kerstin Thurow, and Regina Stoll. Wearable devices in medical internet of things: Scientific research and commercially available devices. *Healthcare Informatics Research*, 23(1):4–15, 2017.

[16] Brenda Kay Wiederhold, Virtual Reality, and Giuseppe Riva. Virtual Reality Therapy : Emerging Topics and Future Challenges. *Cyberpsychology, Behavior, and Social Networking*, 22(1):3–6, 2019.

[17] Nele A J De Witte, Inez Buyck, and Tom Van Daele. Combining Biofeedback with Stress Management Interventions: A Systematic Review of Physiological and Psychological Effects. *Applied Psychophysiology and Biofeedback*, 2019.

[18] Benjamin Cowley, Marco Filetti, Kristian Lukander, Jari Torniainen, Andreas Henelius, Lauri Ahonen, Oswald Barral, Ilkka Kosunen, Teppo Valtonen, Minna Huotilainen, Niklas Ravaja, and Giulio Jacucci. The Psychophysiology Primer : A Guide to Methods and a Broad Review with a Focus on Human – Computer Interaction. *Foundations and Trends® in Human-Computer Interaction*, 9(3):151–308, 2015.

[19] Stephen H. Fairclough. Fundamentals of physiological computing. *Interacting with Computers*, 21(1-2):133–145, 2009.

[20] Stephen H. Fairclough and Kiel Gilleade. Advances in Physiological Computing. In Stephen H. Fairclough and Kiel Gilleade, editors, *Advances in Physiological Computing*, Human–Computer Interaction Series, London, 2014. Springer London.

[21] Stephen H Fairclough. Physiological Computing and Intelligent Adaptation. In Myounghoon Jeon, editor, *Emotions and Affect in Human Factors and Human-Computer Interaction*, chapter 20, pages 539–556. 2017.

[22] J.E. Muñoz. *Supporting Physical Training in Healthy Older Adults Through Biocybernetic Adaptation and Exergaming.* PhD thesis, University of Madeira, 2018.

[23] Ilkka Kosunen. *Exploring the Dynamics of the Biocybernetic Loop in Physiological Computing.* PhD thesis, University of Finland, 2018.

[24] Jonathan M Peake, Graham Kerr, and John P Sullivan. A Critical Review of Consumer Wearables , Mobile Applications , and Equipment for Providing Biofeedback , Monitoring Stress , and Sleep in Physically Active Populations. *Frontiers in Physiology*, 9(June):1–19, 2018.

[25] Christoph Anthes, Rubén Jesús García-Hernandez, Markus Wiedemann, and Dieter Kranzlmüller. State of the Art of Virtual Reality Technology. *2016 IEEE Aerospace Conference, At Big Sky, Montana, United States*, (10):1–19, 2016.

[26] John Edison Muñoz, Teresa Paulino, Harry Vasanth, and Karolina Baras. PhysioVR : A Novel Mobile Virtual Reality Framework for Physiological Computing. In *International Conferences on e-Health Networking, Applications and Services (Healthcom)*. IEEE, 2016.

[27] Enrico Coiera. Introduction to health informatics – the systems science of healthcare. In *Guide to Health Informatics*, chapter 1, page xix. CRC Press, Sydney, 2015.

[28] Gordon Baxter. Health and Social Care, 2011.

[29] Jennifer Preece, Helen Sharp, and Yvonne Rogers. The process of interaction design. In *Interaction Design beyond human-computer interaction*, chapter 9. Wiley, 4 edition, 2015.

[30] Alan T Pope, Edward H Bogartb, and Debbie S Bartolomeb. Biocybernetic system evaluates indices of operator engagement in automated task. *Biological Psychology*, 40:187–195, 1995.

[31] Jennifer Allanson and Stephen H. Fairclough. A research agenda for physiological computing. *Interacting with Computers*, 16(5):857–878, 2004.

[32] Knud Böhle, Christopher Coenen, Michael Decker, and Michael Rader. Biocybernetic Adaptation and Human Computer Interfaces: Applications and Concerns. In *Making Perfect Life, European Governance Challenges in 21st Century Bio-engineering*, chapter 5, pages 136–157. STOA, Brussels, 2012.

[33] Dan Ionescu and Aurel Cornell. *Real-Time Systems Modeling, Design and Applications.* World Scientific Publishing, 2007.

[34] Robi Polikar. The Wavelet Tutorial. Technical report, Rowan University, 2001.

[35] Sylvia S Mader. The Nervous System. In *Understanding Human Anatomy and Physiology*, chapter 10, pages 140–162. 5 edition, 2004.

[36] John Cacioppo, Louis G Tassinary, and Gary G Berntson. *The Handbook of Psychophysiology*, volume 44. Cambridge University Press, 2007.

[37] John Allen. Photoplethysmography and its application in clinical physiological measurement. *Physiological Measurement*, 28(3):1–39, 2007.

[38] Fred Shaffer and J. P. Ginsberg. An Overview of Heart Rate Variability Metrics and Norms. *Frontiers in Public Health*, 5(September):1–17, 2017.

[39] Oonagh M Giggins, Ulrik Mccarthy Persson, and Brian Caulfield. Biofeedback in rehabilitation. *Journal of NeuroEngineering and Rehabilitation*, 10:1–11, 2013.

[40] Mel Slater and Maria V. Sanchez-Vives. Enhancing Our Lives with Immersive Virtual Reality. *Frontiers in Robotics and AI*, 3(December):1–47, 2016.

[41] Robert Riener and Matthias Harders. *Introduction to Virtual Reality in Medicine.* 2012.

[42] M. Abdullah Zafar, Beena Ahmed, Rami Al-Rihawi, and Ricardo Gutierrez-Osuna. Gaming away stress: Using biofeedback games to learn paced breathing. *IEEE Transactions on Affective Computing*, pages 1–14, 2018.

[43] Alison Dillon, Mark Kelly, Ian H. Robertson, and Deirdre A. Robertson. Smartphone applications utilizing biofeedback can aid stress reduction. *Frontiers in Psychology*, 7(JUN):1–7, 2016.

[44] Silvia Serino, Pietro Cipresso, Andrea Gaggioli, Federica Pallavicini, Sergio Cipresso, Danilo Campanaro, and Giuseppe Riva. Smartphone for Self-Management of Psychological Stress: A Preliminary Evaluation of Positive Technology App. *Revista de Psicopatología y Psicología Clinica*, 19(3):253–260, 2014.

[45] Avinash Parnandi, Beena Ahmed, Eva Shipp, and Ricardo Gutierrez-Osuna. Chill-Out: Relaxation Training through Respiratory Biofeedback in a Mobile Casual Game. In *Lecture Notes of the Institute for Computer Sciences, Social Informatics and Telecommunications Engineering*, pages 252–260. Springer, 2014.

[46] Guoxin Gu and Claude Frasson. Virtual Sophrologist : A Virtual Reality Neurofeedback Relaxation Training System. In Claude Frasson and G Kostopoulos, editors, *Lecture Notes in Computer Science*, pages 176–185. Springer, 2017.

[47] Adam Hair and Ricardo Gutierrez-Osuna. Deep breaths: An internally- and externally-paced deep breathing guide. In *International Conference on Affective Computing and Intelligent Interaction*, volume 1, pages 85–87. IEEE, 2018.

[48] Robert Reiner. Integrating a Portable Biofeedback Device into Clinical Practice for Patients with Anxiety Disorders: Results of a Pilot Study. *Applied Psychophysiology and Biofeedback*, 33(1):55–61, mar 2008.

[49] Sophie Côté and Stéphane Bouchard. Documenting the Efficacy of Virtual Reality Exposure with Psychophysiological and Information Processing Measures. *Applied Psychophysiology and Biofeedback*, 30(3):217–232, 2005.

[50] Angelica M. Tinga, Ivan Nyklíček, Michel P. Jansen, Tycho T. de Back, and Max M. Louwerse. Respiratory Biofeedback Does Not Facilitate Lowering Arousal in Meditation Through Virtual Reality. *Applied Psychophysiology Biofeedback*, 44(1):51–59, 2019.

[51] Sergi Bermudez i Badia, Luis Velez Quintero, Monica S. Cameirao, Alice Chirico, Stefano Triberti, Pietro Cipresso, and Andrea Gaggioli. Towards Emotionally-Adaptive Virtual Reality for Mental Health Applications. *IEEE Journal of Biomedical and Health Informatics*, 2194, 2018.

[52] Federica Pallavicini, Davide Algeri, Claudia Repetto, Alessandra Gorini, and Giusseppe Riva. Biofeedback, virtual reality and mobile phones in the treatment of generalized anxiety disorder (GAD): A phase-2 controlled clinical trial. *Journal of Cyber Therapy and Rehabilitation*, 2(4):315–327, 2009.

[53] Dwi Hartanto, Willem-Paul Brinkman, Isabel L. Kampmann, Nexhmedin Morina, Paul G.M. Emmelkamp, and Mark A. Neerincx. Home-Based Virtual Reality Exposure Therapy with Virtual Health Agent Support. In *Pervasive Computing Paradigms for Mental Health, MindCare*, pages 85–98, 2015.

[54] Ilkka Kosunen, Mikko Salminen, Simo Järvelä, Antti Ruonala, Niklas Ravaja, and Giulio Jacucci. RelaWorld: Neuroadaptive and Immersive Virtual Reality Meditation System. *International Conference on Intelligent User Interfaces - IUI*, (March):208–217, 2016.

[55] Luca Morganti and Michele Cucchi. Virtual Reality Enhanced Biofeedback: Preliminary Results of a Short Protocol. In *Pervasive Computing Paradigms for Mental Health, MindCare*, pages 120–127, 2015.

[56] Andrea Gaggioli, Federica Pallavicini, Luca Morganti, Silvia Serino, Chiara Scaratti, Marilena Briguglio, Giulia Crifaci, Annunziata Giulinato, Giuseppe Bernava, Genaro Tartarisco, Giovanni Pioggia, Simona Raspelli, Pietro Cipresso, Cinzia Vigna, Alessandra Grassi, Margherita Baruffi, Brenda K Wiederhold, and Giuseppe Riva.

Experiential Virtual Scenarios With Real-Time Monitoring (Interreality) for the Management of Psychological Stress: A Block Randomized Controlled Trial. *Journal of Medical Internet Research*, 16, 2014.

[57] Zelun Wang, Avinash Parnandi, Ricardo Gutierrez-osuna, and Senior Member. BioPad : Leveraging Off - the - Shelf Video Games for Stress Self - Regulation. 2194(c):47–55, 2017.

[58] Gregg Henriques, Steven Keffer, Craig Abrahamson, and S. Jeanne Horst. Exploring the effectiveness of a computer-based heart rate variability biofeedback program in reducing anxiety in college students. *Applied Psychophysiology Biofeedback*, 36(2):101–112, 2011.

[59] Avinash Parnandi and Ricardo Gutierrez-Osuna. A comparative study of game mechanics and control laws for an adaptive physiological game. *Journal on Multimodal User Interfaces*, 9(1):31–42, 2015.

[60] Hamdi Ben Abdessalem and Claude Frasson. Real-time Brain Assessment for Adaptive Virtual Reality Game : A Neurofeedback Approach. In *Brain Function Assessment in Learning*, pages 133–143, 2017.

[61] Avinash Parnandi and Ricardo Gutierrez-Osuna. Visual Biofeedback and Game Adaptation in Relaxation Skill Transfer. *IEEE Transactions on Affective Computing*, pages 1–14, 2017.

[62] M.N.K Saunders, A. Thornhill, and P. Lewis. *Research Methods for Business Students*. Pearson, 6 edition, 2012.

[63] Alan R Hevner, Salvatore T March, Jinsoo Park, and Sudha Ram. Design Science in Information Systems Research. *MIS Quarterly*, 28(1):75–105, 2004.

[64] Ken Peffers, Tuure Tuunanen, Marcus A. Rothenberger, and Samir Chatterjee. A Design Science Research Methodology for Information Systems Research. *Journal of Management Information Systems*, 24(3):45–77, 2007.

[65] Marc A. Russo, Danielle M. Santarelli, and Dean O'Rourke. The physiological effects of slow breathing in the healthy human. *Breathe*, 13(4):298–309, 2017.

[66] Andrea Zaccaro, Andrea Piarulli, Marco Laurino, Erika Garbella, Danilo Menicucci, Bruno Neri, and Angelo Gemignani. How Breath-Control Can Change Your Life: A Systematic Review on Psycho-Physiological Correlates of Slow Breathing. *Frontiers in Human Neuroscience*, 12(September):1–16, 2018.

[67] Mikołaj Tytus Szulczewski and Andrzej Rynkiewicz. The effects of breathing at a frequency of 0.1 Hz on affective state, the cardiovascular system, and adequacy of ventilation. *Psychophysiology*, (5):1–13, 2018.

[68] Paul M. Lehrer and Richard Gevirtz. Heart rate variability biofeedback: How and why does it work? *Frontiers in Psychology*, 5(JUL):1–9, 2014.

[69] Fumihiko Yasuma and Jun-ichiro Hayano. Respiratory Sinus Arrhythmia* Why Does the Heartbeat Synchronize With Respiratory Rhythm? *Chest*, 125(2):683–690, feb 2004.

[70] V. C. Goessl, J. E. Curtiss, and S. G. Hofmann. The effect of heart rate variability biofeedback training on stress and anxiety: A meta-analysis. *Psychological Medicine*, 47(15):2578–2586, 2017.

[71] Zhengbo Zhang, Weidong Wang, Buqing Wang, Hao Wu, Hongyun Liu, and Yukai Zhang. A prototype of wearable respiration biofeedback platform and its preliminary evaluation on cardiovascular variability. In *International Conference on Bioinformatics and Biomedical Engineering, iCBBE*, pages 1–4. IEEE, 2009.

[72] F. Abtahi, G. Ji, K. Lu, K. Rodby, and F. Seoane. A knitted garment using intarsia technique for Heart Rate Variability biofeedback: Evaluation of initial prototype. In *Proceedings of the Annual International Conference of the IEEE Engineering in Medicine and Biology Society, EMBS*, pages 3121–3124. IEEE, 2015.

[73] Wanqing Wu, Heye Zhang, Sandeep Pirbhulal, Subhas Chandra Mukhopadhyay, and Yuan-ting Zhang. Assessment of Biofeedback Training for Emotion Management Through Wearable Textile Physiological Monitoring System. *IEEE Sensors Journal*, 15(12):7087–7095, 2015.

[74] F. Abtahi, A. Berndtsson, S. Abtahi, F. Seoane, and K. Lindecrantz. Development and preliminary evaluation of an Android based heart rate variability biofeedback system. In *36th Annual International Conference of the IEEE Engineering in Medicine and Biology Society, EMBC*, pages 3382–3385. IEEE, 2014.

[75] Thomas Wollmann, Farhad Abtahi, Aboozar Eghdam, Fernando Seoane, Kaj Lindecrantz, Martin Haag, and Sabine Kock. User-centred design and usability evaluation of a heart rate variability biofeedback game. *IEEE Access*, 4:5531–5539, 2016.

[76] The R Foundation. R project.

[77] Tizen Project. Tizen Studio.

[78] Ahyoung Choi and Hangsik Shin. Photoplethysmography sampling frequency: Pilot assessment of how low can we go to analyze pulse rate variability with reliability? *Physiological Measurement*, 38(12):2252–2256, 2017.

[79] Google. Android Studio.

[80] Tanmoy Bhowmik, Jishnu Dey, and Vijay Narayan Tiwari. A novel method for accurate estimation of HRV from smartwatch PPG signals. In *Proceedings of the Annual International Conference of the IEEE Engineering in Medicine and Biology Society, EMBS*, pages 109–112. IEEE, 2017.

[81] Unity Technologies. Unity.

[82] Bruno Bonnechère. *Serious Games in Physical Rehabilitation.* Springer International Publishing, 2018.

[83] Maria R Dekker and Alishia D Williams. The Use of User-Centered Participatory Design in Serious Games for Anxiety and Depression. *Games for Health Journal*, 6(6):327–333, 2017.

[84] Kush Wadhwa and David Wright. eHealth: Frameworks for Assessing Ethical Impacts. In Carlisle George, Diane Whitehouse, and Penny Duquenoy, editors, *eHealth: Legal, Ethical and Governance Challenges*, pages 183–210. Springer Berlin Heidelberg, Berlin, Heidelberg, 2013.

[85] Kenneth S. Bordens and Abbott Bruce B. *Research design and methods: A process approach.* McGraw-Hill, 8th edition, 2002.

Appendix A

Template for Informed Consent

Name of the student: Luis Eduardo Vélez Quintero
Supervisor: Panagiotis Papapetrou, PhD, Professor, DSV, Stockholm University

Participant Number: _

Informed Consent

The study you are requested to participate is part of a master's thesis in Health Informatics. The purpose is to identify whether smartwatches can identify changes in heart functioning caused by different breathing exercises guided in virtual reality. The participation in the study is entirely voluntary. If you choose to participate, you will be asked to use a relaxation application in a virtual reality headset while a smartwatch collects heart rate information from your wrist. In the second part of the experiment, you will be asked to synch your breathing frequency with a visual cue that will appears in the virtual environment. At the end, you are asked to fill out a form about the experience. The total duration of the experiment is maximum 20 minutes. The study is completely anonymous, and the aggregated data will be only used for academic purposes.

There are no known risks for you participating in the study. However, some people might experience side effects such as dizziness while using the virtual reality system. In any case, remember that you have the right to withdraw completely from the study at any time.

Your signature below indicates that you have decided to participate in this study and you have read and understood all the information provided above.

Name:

Signature:

Date:

Appendix B

Post-Experiment Questionnaire

Questionnaire originally administered using a digital version in Google Forms.

Name of the student: Luis Eduardo Vélez Quintero
Supervisor: Panagiotis Papapetrou, PhD, Professor, DSV, Stockholm University
Email: luva3178@student.su.se

Questionnaire Experiment Virtual Reality – Smartwatch

Please respond the following questions regarding the relaxation experiment using Virtual Reality and Smartwatches. Thank you for your participation.

Participant Number: *[Used for internal match of datasets]*
Age:
Gender: *Male. Female. Prefer not to say.*

Before the experiment, did you have previous experience using virtual reality?
Yes. No. Not sure.

During the past five years, have you suffered from any cardiovascular disease?
Yes. No. Not sure.

Questions with Likert Scale: [Strongly disagree, disagree, neutral, agree, strongly agree]

In the FIRST part of the session (before synchronizing the respiration with the blue object):

I clearly understood what I had to do.
I was completely concentrated on the virtual environment, blocking external triggers.
This was the most relaxing part of the session.

In the SECOND part of the session (while you were synchronizing the respiration with the blue object):

I clearly understood what I had to do.
It was easy to follow the blue object that guided the respiration.
This was the most relaxing part of the session.

If you had any inconvenience during the experiment (dizziness, uncomfortable devices, etc.). Please describe it here: *[Open answer]*