

Comparison of Pulse Arrival Time and Pulse Transit Time for Continuous Blood Pressure Estimation

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High blood pressure, also known as hypertension, is one of the leading global risk factors for premature mortality, causing approximately 10.4 million premature deaths yearly. It is dangerous due to its asymptomatic nature, allowing progressive damage to occur before the disease is diagnosed. Continuous and non-invasive blood pressure measurement implemented in wearable devices could provide valuable information about blood pressure variation throughout the day and support earlier detection of elevated blood pressure levels. Technologies using photoplethysmography (PPG) and electrocardiogram (ECG) have shown promising results in continuous and non-invasive blood pressure estimation.

In this thesis, the effect of the pre-ejection period (PEP) on continuous blood pressure estimation is investigated by comparing blood pressure estimation based on pulse arrival time (PAT) and pulse transit time (PTT). A human study involving six participants was conducted. ECG, PPG, and continuous blood pressure signals were recorded simultaneously. Pulse propagation metrics were calculated from the recorded signals and analyzed using correlation-based methods.

The strongest relationship varied depending on the participant and the selected measurement approach. The findings did not provide clear evidence that excluding PEP consistently improves blood pressure estimation. The results suggest that the relationships between PTT, PAT, and blood pressure are highly dependent on measurement conditions and individual variation. Further studies with improved synchronization, improved stability in sensor placement, and larger participant groups would be necessary to better evaluate the potential of PAT and PTT methods for continuous and non-invasive blood pressure estimation.

Keywords: ECG, PPG, continuous blood pressure measurement, non-invasive blood pressure measurement, wearable devices, health monitoring

TURUN YLIOPISTO
Tietotekniikan laitos

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Korkea verenpaine eli hypertensio on maailmanlaajuisesti yksi merkittävimmistä ennenaikaisen kuolleisuuden riskitekijöistä, ja sen arvioidaan aiheuttavan vuosittain noin 10 miljoonaa kuolemaa. Hypertension vaarallisuus perustuu sen oireettomaan luonteeseen, minkä vuoksi elimistöön voi aiheutua vaurioita jo ennen sairauden diagnosointia. Puettaviin mittalaitteisiin perustuva jatkuva ja ei-invasiivinen verenpaineen mittaaminen voisi mahdollistaa verenpaineen vaihtelun seurannan ympäri vuorokauden ja näin tukea hypertension tunnistamista jo varhaisessa vaiheessa. Fotoplethysmografiaa (PPG) ja elektrokardiografiaa (EKG) hyödyntävät teknologiat ovat osoittaneet lupaavia tuloksia jatkuvassa ja ei-invasiivisessa verenpaineen arvioinnissa.

Tässä diplomityössä tutkittiin sydämen supistusta edeltävän vaiheen (pre-ejection period, PEP) vaikutusta jatkuvaan verenpaineen arviointiin vertaamalla pulse arrival time (PAT)- ja pulse transit time (PTT) -menetelmiä. Tutkimusta varten toteutettiin ihmiskoe, johon osallistui kuusi henkilöä. Osallistujilta mitattiin samanaikaisesti EKG, PPG ja jatkuva verenpaine. Kerätyistä signaaleista laskettiin pulssin etenemiseen perustuvia suureita, joiden yhteyttä verenpaineeseen analysoitiin korrelaatioanalyysillä.

Vahvin yhteys riippui osallistujasta ja valitusta mittausmenetelmästä. Tulokset eivät antaneet selkeää näyttöä siitä, että PEP:n poistaminen parantaisi johdonmukaisesti verenpaineen ja pulssin etenemiseen perustuvien suureiden välistä yhteyttä. Tulokset viittaavat siihen, että PTT:n, PAT:n ja verenpaineen välinen yhteys on voimakkaasti riippuvainen mittausolosuhteista ja yksilöllisestä vaihtelusta. Jatkotutkimuksia, joissa mittausten synkronointia parannetaan, sensoreiden sijoittelun vakautta lisätään ja osallistujamäärää kasvatetaan, tarvitaan PAT- ja PTT-menetelmien potentiaalinen arvioimiseksi jatkuvassa ja ei-invasiivisessa verenpaineen arvioinnissa.

Asiasanat: EKG, PPG, jatkuva verenpaineen mittaaminen, ei-invasiivinen verenpaineen mittaaminen, puettava teknologia, terveyden seuranta

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1 Introduction

1.1 Motivation

High arterial blood pressure, also known as hypertension, is one of the leading global risk factors for premature mortality, causing approximately 10.4 million premature deaths yearly. In Finland, close to 2 million adults suffer from hypertension, which is more than a third of the population. [1]–[3]

Hypertension is dangerous due to its asymptomatic nature, allowing progressive damage to organs such as the heart, kidneys, and blood vessels to occur before the disease is diagnosed. Prolonged high blood pressure increases cardiac workload and is associated with the development of myocardial hypertrophy over time, leading to increased myocardial stiffness and decreased cardiac function. [4], [5]

Blood pressure consists of systolic and diastolic blood pressures, where systolic represents the higher value of a blood pressure reading and diastolic the lower value. Optimal blood pressure is defined to be below 120/80 mmHg, while hypertension is diagnosed when blood pressure consistently exceeds 140/90 mmHg. Blood pressure varies between day and night and also fluctuates during the day.[1], [4], [5]

The diagnosis of hypertension is mainly based on blood pressure measurements performed by the patient at home. A regular blood pressure measurement device for consumers is an oscillometric device with an arm cuff. The measurement gives a reading of the systolic and diastolic blood pressure values at the given time. To

better measure the daily fluctuation of blood pressure, a 24 hour ambulatory blood pressure measurement can be performed. However, ambulatory blood pressure measurement is performed with the same oscillometric monitor. [1], [5]

Non-invasive and continuous blood pressure measurement techniques have been widely researched in the past several decades. Technologies using photoplethysmography (PPG) and electrocardiogram (ECG) have shown promising results, and there are already wearable devices that are using PPG to measure blood pressure. However, these devices still require periodic calibration measurements with the oscillometric device. [6]

Pulse transit time (PTT) and pulse arrival time (PAT) are technologies that have been in the interest of researchers regarding cuff-less blood pressure measurement. PTT is based on optical PPG measurement, whereas PAT uses ECG and PPG measurements together. Currently, PTT is considered to be a relatively reliable technique for continuous and non-invasive blood pressure measurement. However, PTT requires two separate PPG sensors, which can complicate its implementation in wearable devices. In contrast, PAT requires only a single PPG sensor in combination with an ECG sensor, which simplifies the implementation, as these sensors are already commonly available in wearable devices. The drawback of PAT is that it includes a component that is not directly related to blood pressure. This component is called the pre-ejection period (PEP), a period of time between electrical activation of the heart and the opening of the aortic valve, which can decrease the reliability of the blood pressure measurement. [7]–[9]

In this thesis, the effect of the PEP in continuous blood pressure measurement is evaluated by comparing the blood pressure estimation by PAT and PTT. The data used is primary quantitative data collected from 6 participants. PPG data from two peripheral sites and single-lead ECG data are collected simultaneously with the reference blood pressure measurement data. The measurement protocol consists of

three maneuvers and resting phases. PAT and PTT are calculated from the collected data and further modified to pulse wave velocity values. The relationship between PAT, PTT, PWV, and reference blood pressure data are evaluated by calculating correlation coefficient (R).

1.2 Research Questions

RQ1 Does the pre-ejection period affect the reliability of blood pressure measurement?

RQ2 Which pulse propagation method provides the most robust relationship with blood pressure?

To answer these research questions, a literature review and a human study are conducted. In the human study, the required data are collected, pre-processed, analyzed, and evaluated. The results of the experiment are then compared with the findings of previous studies.

1.3 Use of AI

In this thesis, generative artificial intelligence was used as a tool to support the coding process and to help improve the wording of the written text. The language model used was GPT-5.5.

1.4 Thesis Structure

The remainder of the thesis is organized as follows. Chapter 2 introduces the fundamental background knowledge required for understanding the study. This includes blood pressure physiology and measurement, ECG, PPG, and pulse propagation methods. Chapter 3 reviews previous research related to pulse arrival time and

pulse transit time and compares their use in non-invasive and continuous blood pressure estimation. Chapter 4 describes the measurement setup, experimental protocol, data collection process, and analysis methods applied in this study. Chapter 5 presents the collected data and the results of signal processing, pulse propagation metric calculations, and correlation analysis between pulse propagation metrics and blood pressure. Chapter 6 discusses the findings, limitations, and factors affecting the interpretation of the results. Finally, Chapter 7 concludes the thesis by summarizing the main findings and answering the research questions.

2 Background

2.1 Blood Pressure

Blood pressure is a fundamental physiological parameter that represents the arterial pressure. Blood pressure is typically expressed as systolic and diastolic blood pressure values. Systolic blood pressure (SBP) is a higher value and describes the pressure in the arteries when the heart contracts and blood is pushed from the left ventricle. Diastolic blood pressure (DBP) is a lower value, which is the arterial pressure between contractions of the heart when the heart is relaxed. SBP is dependent of the stroke volume of left ventricle and the elasticity of aorta and other big arteries. DBP is dependent of the resistance of peripheral circulation and the elasticity of the arteries and the duration of the diastole. The blood pressure below 120/80 mmHg is considered normal BP. In addition to SBP and DBP, a feature called mean arterial pressure (MAP) is the average blood pressure throughout a cardiac cycle. It is defined to be dependent of the cardiac output, which tells how much blood heart pumps in a minute, and the resistance of the peripheral circulation. [4], [5]

2.1.1 Hypertension

High blood pressure, also known as hypertension, is a condition characterized by persistently elevated arterial blood pressure above normal levels. Hypertension is defined as blood pressure values of at least 140/90 mmHg measured in a clinical

setting or 135/85 mmHg in home blood pressure monitoring. Hypertension is usually asymptomatic, but if not treated, it can cause severe structural and functional changes to the heart and blood vessels.

Vascular resistance increases in hypertension, requiring the left ventricle to work harder to maintain normal cardiac output. When this condition persists, it can lead to left ventricular hypertrophy, characterized by thickening of the ventricular myocardium. Left ventricular hypertrophy impairs cardiac function and increases myocardial workload. Over time, this condition can result in reduced vessel elasticity in the heart, brain, eyes, kidneys, and limbs. In the long term, these changes can cause complications such as coronary artery blockage, heart failure, cerebrovascular disorders, or renal failure. These changes develop slowly and often become apparent when problems begin to appear. Thus, regular blood pressure measurements enable the early detection of elevated blood pressure and facilitate early intervention, which can help prevent the development of hypertension and its associated complications. [4], [5]

2.1.2 Blood Pressure Measurement

Blood pressure measurements can be invasive or non-invasive, continuous or single measurements, performed by a healthcare professional or by the patient themselves. Blood pressure is commonly measured with an inflatable cuff from the brachial artery located in the upper arm. The measurement site is usually standardized because systolic and diastolic blood pressure vary depending on the measurement location: systolic pressure increases in the distal arteries, while diastolic pressure decreases. [5], [10]

For clinical purposes, there are three commonly used methods for measuring blood pressure: clinical measurement, 24-hour ambulatory measurement, and self-monitored home measurement. Ambulatory measurement is usually used to diagnose

hypertension, whereas home measurements are more used to follow the response to possible treatment. [4], [10], [11]

Common blood pressure measurement methods in clinical practice include auscultation, catheterization, and the oscillometric technique. The gold standard method for blood pressure measurement is intra-arterial catheterization, but in office visits, the non-invasive gold standard is the auscultatory method.

In intra-arterial catheterization, blood pressure can be measured from any arterial site by a catheter with a strain gauge. This measurement method is automatic, continuous, and invasive, and requires a healthcare professional to operate the intra-arterial catheter. Auscultation is a non-invasive method of measuring BP, in which a healthcare professional inflates a cuff and during deflation listens to the Korotkoff sounds with a stethoscope. Systolic and diastolic blood pressures are then determined from Korotkoff sounds by the operator. The oscillometric technique is the most common method in blood pressure measurement devices in ambulatory and home use. The oscillometric devices are automatic, non-invasive monitors with an inflatable cuff. Patients can adjust the cuff and operate the device on their own. However, there is no generic technique for oscillometric measurement, and the technique used varies with the device and the brand. [5], [10], [11]

An alternative method for brachial artery BP measurements is the finger cuff method, where photoplethysmography and pressure cuffs are combined. Photoplethysmography detects arterial pulsation in the finger and alters the cuff pressure according to the pulsation. This method enables the cuff to remain inflated up to 2 hours, allowing continuous blood pressure measurement non-invasively. [10]

2.2 Electrocardiogram

2.2.1 Heart and Circulatory System

The heart is a four-chambered organ that consists of the left and right atrium and the left and right ventricle. It is part of the circulatory system among the arteries, capillaries, and veins. The right ventricle pumps blood to the pulmonary circulation from where oxygen-rich blood flows to the left atrium. The left ventricle pumps blood to the systemic circulation, where oxygen and needed nutrients are transported to tissues. Carbon dioxide and other cellular waste formed in cellular metabolism are transported away from the tissue by venous circulation, and the blood circulates back to the right atrium. [4], [5] Without a functioning heart, a human body cannot survive for more than a few minutes. [4]

The heart contracts by the effect of repetitive electric activation that is spread around the heart muscle. Electrocardiogram (ECG) records the electrical activities of the heart. Figure 2.1 illustrates the ECG recorded over two cardiac cycles.

ECG is measured by attaching electrodes to limbs and chest. The limb electrodes measure the potential difference between limbs and electrodes on chest measure the electrical field that reflects from the heart. In clinical 12-lead electrocardiogram, 10 electrodes are attached in total; six to the chest and one for each limb. [4], [5], [12] Patient needs to be still and remain silent due to distortion speaking and moving causes to ECG. [4] ECG is a useful tool for detecting arrhythmia, hypertrophic cardiomyopathy, myocardial infarction and myocardial ischemia. [4], [5]

2.2.2 Cardiac Cycle and ECG

The cardiac cycle starts when the sinoatrial node fires and the left and right atrium start to depolarize. Due to depolarization, the atria contract. Depolarization causes the P-wave in the ECG. The P-wave describes the time taken to depolarize the

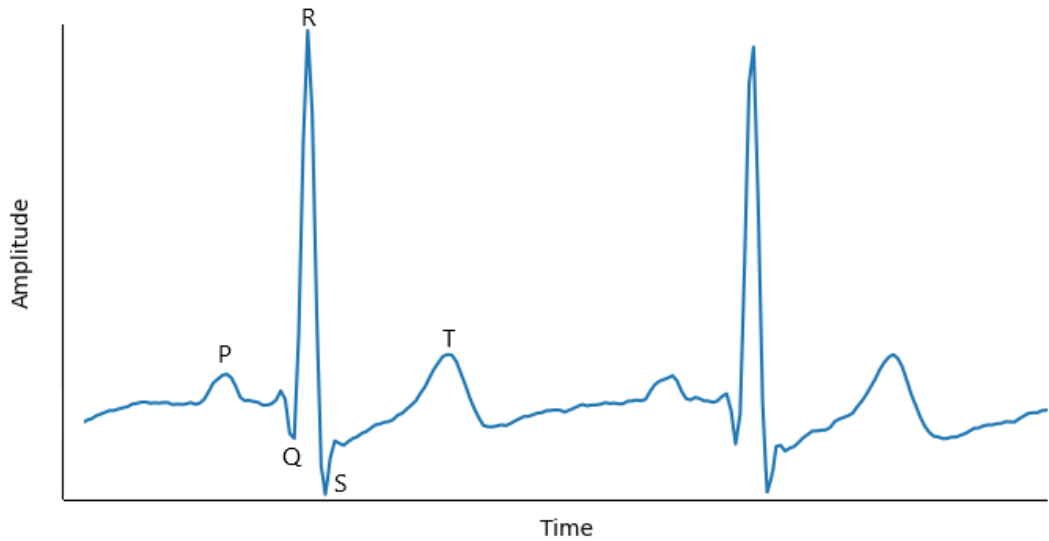


Figure 2.1: Example of an electrocardiogram (ECG) signal illustrating the characteristic P wave, QRS complex, and T wave.

atrium. The cardiac conduction system is then activated and the stimulus slowly spreads to the ventricles. During this slower spread, blood has enough time to flow from the atrium to the ventricles, before the stimulus spreads to the ventricles. This spreading phase is not shown on the ECG but when the stimulus reaches the atrioventricular node, it causes the ventricles to depolarize, creating the QRS-complex in the ECG. After the ventricles are depolarized, the ventricles contract. The pressure of the left ventricle increases without changing the ventricular volume (isovolumetric contraction). When the pressure in the left ventricle exceeds the pressure in the aorta, the aortic valve opens and blood begins to rush from the ventricle to the aorta. When blood is ejected to the aorta, a pressure pulse is generated to travel through the arteries. The time interval from the ventricular depolarization to the blood ejection and pressure pulse creation is called the pre-ejection period (PEP). It is an electro-mechanical delay and can also be defined as the period of isovolumetric contraction of the left ventricle. Repolarization of the ventricles causes the T-wave. [5], [12], [13] All the mentioned characteristics of the

normal ECG wave are demonstrated in figure 2.1.

2.3 Photoplethysmography

Photoplethysmography (PPG) is a non-invasive technique that optically measures changes in pulsatile arterial blood volume. In the measurement, the skin is illuminated with a light source and variations in the intensity of reflected or transmitted light are detected. In clinical settings, PPG is used to measure heart rate and blood oxygen saturation in the arteries, whereas non-standardized or research applications use it additionally to calculate respiratory rate, stress levels, and blood pressure. [14], [15].

A PPG sensor consists of a light source that typically is a light-emitting diode (LED) and a photodetector that converts the detected light into an electrical current. There are two different methods for measuring PPG; reflection and transmission modes. The selected mode affects the placement of the light source and the photodetector. In reflection mode, the light source and the photodetector are placed adjacently and the amount of reflected light is measured. In transmission mode, the light source and the photodetector are set on the opposite side of the measurement site, and the amount of transmitted light is measured. [15], [16]

The phase of the cardiac cycle affects the intensity of the detected light by affecting the blood volume, blood content, and arterial diameter in the measurement site. In systole, blood volume, hemoglobin concentration, and arterial diameter are maximized in the arterial site, while in the diastolic phase they are minimized. Blood absorbs light; therefore, light absorption is highest during systole, and less light reaches the photodetector. During diastole, the absorption is minimized and a higher amount of light reaches the photodetector. [15], [17]–[19]

Different wavelengths of light can be used to target different layers of the skin, depending on the measurement site and measurement mode. Typically used wave-

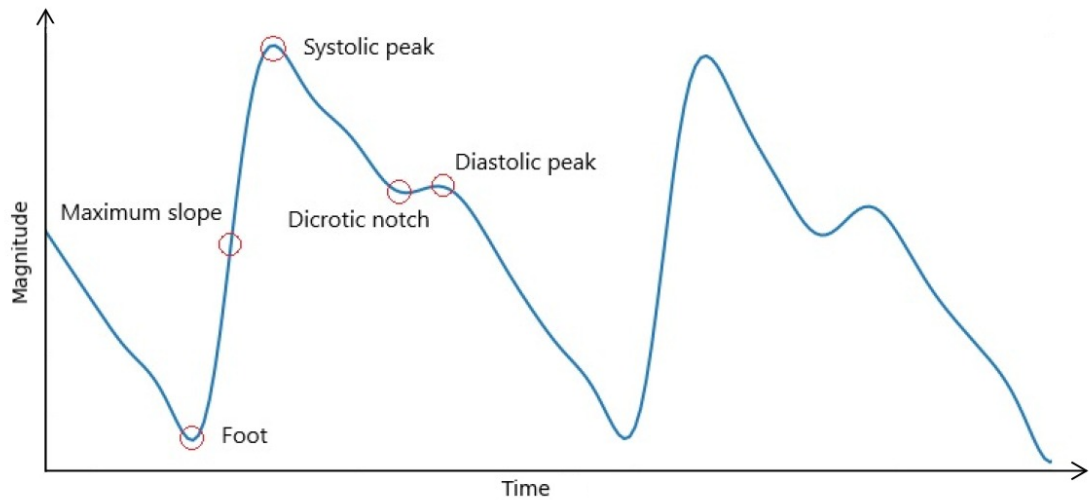


Figure 2.2: Example of a photoplethysmography (PPG) signal during two cardiac cycles illustrating the characteristic fiducial points: foot, maximum slope, systolic peak, dicrotic notch, and diastolic peak.

lengths are green, red, and infrared. The higher the wavelength, the deeper the light reaches in the tissue. The green wavelengths reach the skin's surface layers and are usually utilized in the reflection-mode measurements. Red and infrared wavelengths reach deeper in the skin and are used in transmissive-mode measurements. [16], [18], [20], [21]

The PPG signal consists of a non-pulsatile direct current (DC) component and a pulsatile alternating current (AC) component. Non-pulsatile parts, for example bloodless tissue, bones, and muscle, form the non-pulsatile and continuous DC. The DC component is not directly distinguishable in the PPG waveform, but it defines the baseline level of the signal. The AC component shows the pulsatile changes in arterial blood volume. The observed PPG waveform reflects the pulsatile variations and varies synchronously with the heart beat. [15], [22] The waveform of PPG during two heart cycles is presented in the figure 2.2. The waveform can be separated into the systole and diastole phases. The rising edge reflects the expansion of the arterial system during systole. The amplitude of the systolic peak is linked

to the stroke volume, whereas the dicrotic notch and diastolic peak are related to the wave reflections. The dicrotic notch is considered to be the dividing point of the aortic systole and diastole.[15] The amplitude of the PPG waveform is typically expressed in arbitrary units, as it depends on individual physiological properties and measurement related factors. [19]

2.4 Pulse Propagation Methods

When the left chamber of the heart contracts, it creates a pulse wave that propagates through the arteries considerably faster than blood. The propagation time of the pulse wave can be calculated, and the time can be used to estimate cardiovascular parameters such as blood pressure and arterial stiffness. Pulse transit time (PTT) and pulse arrival time (PAT) are methods that can be used to calculate the propagation time, measured in milliseconds (ms) or seconds (s). In pulse transit time, the propagation time of the pulse wave between two measurement sites is calculated. Pulse arrival time includes the pulse propagation time, but also has an additional component, the pre-ejection period, which is not directly related to pulse wave propagation. In both methods, the proximal and distal data must be acquired simultaneously to detect the pulse wave of the same heart cycle. PTT and PAT values can subsequently be used to calculate the pulse wave velocity. [5], [7]

Pulse transit time defines the time it takes for a pulse wave to propagate between proximal and distal arterial sites. The pulse wave can be detected using two separate sensors, for example two photoplethysmography sensors, or by alternative methods such as seismocardiography, ballistocardiography or strain gauge signals. Depending on the method, the measurement points can also vary. When measuring PTT using PPG signals, different fiducial points of the waveform, shown in the picture 2.2, can be used. PTT can be measured for example between two PPG systolic peaks, as illustrated in 2.3, where the PPG1 signal represents the proximal measurement

point and the PPG2 signal the distal point. [7], [19], [23]

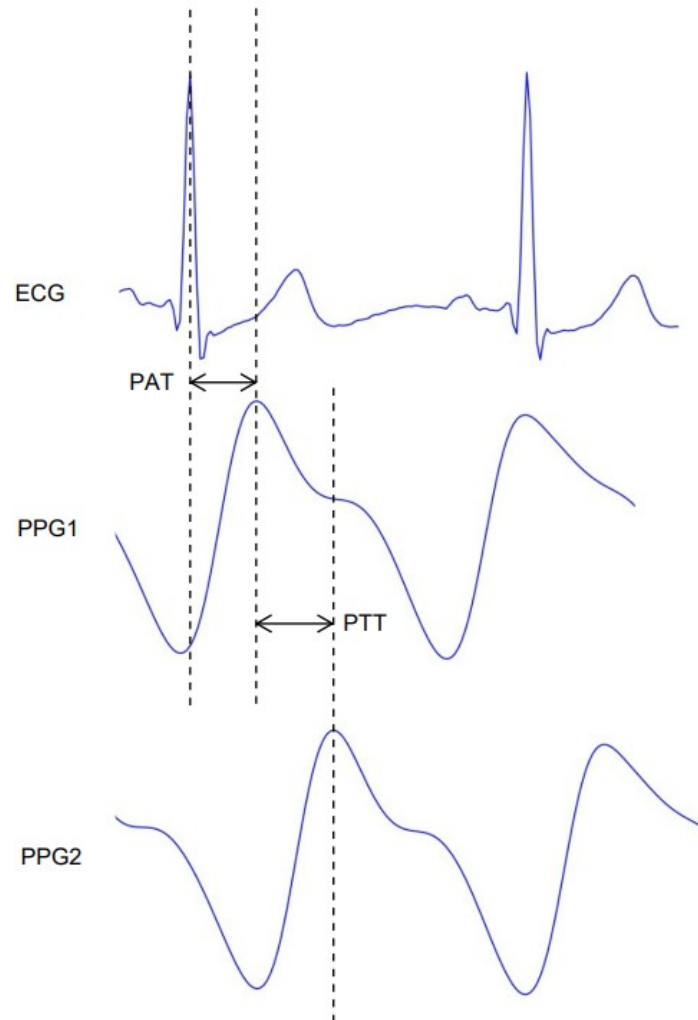


Figure 2.3: Illustration of pulse arrival time (PAT) and pulse transit time (PTT) calculated from ECG and PPG signals. PAT is measured as the time delay between the ECG reference point and the arrival of the pulse wave at the PPG signal, whereas PTT is measured between two PPG signals.

Pulse arrival time consists of the pre-ejection period and the pulse transit time from the heart to the distal measurement point. PEP depends on the electromechanical activity of the heart, which is affected by arterial and ventricular properties and therefore can vary considerably between individuals. PAT is measured from the ECG R-wave to the distal pulse wave signal, commonly measured with PPG. The same PPG fiducial points as used in PTT measurements can be applied with PAT.

As an example, the systolic peak of the PPG signal can be used with the ECG R-peak, as illustrated in the image 2.3. [11], [13], [23]

Pulse wave velocity (PWV) is a metric that describes the speed at which the pulse wave propagates between the two arterial measurement points. PWV can be defined as

$$v = \frac{d}{t} \quad (2.1)$$

where d represents the distance traveled by the pulse wave and t the pulse transit time. PWV is expressed in meters per second (m/s). Pulse wave velocity is a marker of cardiovascular risk and can be used to estimate arterial stiffness and blood pressure. [11], [23]

3 Related Work

3.1 Pulse Arrival Time

The relationship between different pulse propagation methods and blood pressure has been studied in various settings and with varying results. The use of PAT in blood pressure estimation has been under debate, as it does not purely measure the transit time of the pulse wave due to the inclusion of the pre-ejection period. No consensus has been reached regarding the effects of PEP on blood pressure estimation, but PAT continues to be studied due to its practical advantages in measurement setup and device implementation.

PAT can be calculated with different combinations of physiological signals; however, this thesis focuses on PAT derived from ECG and PPG signals. A similar signal combination was utilized in a study by Kachuee et al. [24], who developed a continuous and non-invasive blood pressure estimation method. As PEP is a feature that varies between people, the possible need for individual data calibration in PAT-based measurements has been raised. In the study, methods of PAT calculation with and without calibration were developed and compared to blood pressure. The results suggested that calibration for each individual improved estimation performance. The mean absolute error (MAE) was lower with the calibrated method: 8.21 mmHg for SBP and 4.31 mmHg for DBP. Whereas without calibration, it was 11.17 mmHg for SBP and 5.35 mmHg for DBP.

The MIMIC II database used by Kachuee et al. [24] consisted of data collected from patients in the intensive care unit (ICU). Similar to the ICU environment, where conventional cuff-based or invasive catheter-based blood pressure measurement might not always be an option, Ahlstrom et al. [25] investigated a non-invasive method suitable for use during hemodialysis. In hemodialysis, blood pressure may vary considerably, resulting in intradialytic hypotension or hypertension, creating a need for continuous and non-invasive blood pressure monitoring. In the study the relationship with PAT, PEP, vessel transit time (VTT) and systolic blood pressure were investigated. ECG, phonocardiogram (PCG) and transmissive PPG measured from ring-finger were used to determine PAT and PEP. The strongest correlation with SBP was achieved with PAT, where correlation coefficient was $= 0.80 \pm 0.06$ (mean \pm SD). PEP showed a correlation coefficient $r = 0.72 \pm 0.14$, whereas VTT achieved $r = 0.48 \pm 0.28$. Regarding hypotension and hypertension, PAT showed strong correlation with SBP in hypotension, but weak correlation in hypertension. The study suggests, that inclusion of PEP is necessary in order to achieve more reliable correlation between PAT and SBP.

Poon et al. [26] conducted a clinical study involving elderly participants with both normotensive and hypertensive blood pressure profiles. In their study, a non-invasive blood pressure measurement platform was developed. Measurements were performed by placing fingers on sensors that were integrated into the platform, simultaneously measuring both ECG and PPG. They measured the transit time of the pulse wave from ECG to PPG, which is commonly referred to as PAT in the literature, although the authors described it as PTT. Similarly, Ahlstrom et al. [25] described the transit time including PEP to be PTT. However, Poon et al. [26] neither discussed the effect of PEP nor explicitly accounted for it in their analysis. The achieved results were 0.6 ± 9.8 mmHg for SBP and 0.9 ± 5.6 mmHg for DBP, describing the mean and standard deviation (SD) of the difference between PAT and

blood pressure. The authors noted that although PAT-based estimation resulted to better estimation performance for SBP, the SD was higher with SBP than for DBP. They suggested that the effect could be explained by the generally larger changes in SBP compared to DBP.

The measurements in Ahlstrom et al. [25] study were performed in the supine position, whereas Poon et al. [26] conducted measurements in a seated position. In both settings, patient's movement was minimized. Ahlstrom et al. simulated changes in blood pressure during hemodialysis. Their results showed that the performance of blood pressure estimation dropped during hypertension. In addition to large changes in the blood pressure, measurements may also be vulnerable for motion artefacts, which can affect to the reliability of the results. Cisnal et al. [27] and Ghosh et al. [28] studied the effects of movement and posture on PAT-based blood pressure estimation.

PAT-based continuous blood pressure measurement in ambulatory settings was investigated by Cisnal et al. [27], who collected data during a 24-hour ambulatory monitoring period. ECG and reflective wrist PPG signals were recorded and used for PAT calculation. The achieved correlations between PAT and blood pressure were $r = -0.34$ for SBP and $r = -0.24$ for DBP. The estimated blood pressure values achieved a MAE of 14.24 mmHg for SBP and 9.67 mmHg for DBP. Although PAT showed a stronger correlation with SBP than DBP, the estimation performance was better for DBP. The authors suggested that SBP estimation may be more sensitive to ambulatory conditions than DBP. Similar findings were reported in Ghosh et al. [28] study, where they measured PAT under both stationary and movement conditions. PAT was calculated using ECG and PPG measured with pulse oximeter. The best performance was achieved during stationary conditions, whereas the worst during movement. The lowest root mean square error (RMSE) for SBP estimation was 5.06 mmHg in a seated position, while the lowest RMSE for DBP estimation was

5.83 mmHg in a standing position. Similarly to Cissal et al. study, SBP during movement had noticeably larger error than DBP estimation. The highest RMSE values were observed during walking, reaching RMSE 19.25 mmHg for SBP and RMSE 11.86 mmHg for DBP. [28]

Previous studies suggest that PAT may be used for non-invasive and continuous blood pressure estimation. However, challenges related to subject-specific calibration and measurement conditions, particularly regarding movement, remain.

3.2 Pulse Transit Time

PTT, defined as the time required for the pulse wave to travel between two physiological fiducial points, is often considered to provide a more direct representation of pulse wave propagation than PAT, as it excludes the potential effect of PEP. PTT can be calculated using various signal combinations and measurement locations depending on the application and sensors. However, the amount of literature on continuous and non-invasive blood pressure estimation using only PTT, and especially PTT using two PPG sensors without ECG, appears to be more limited compared to studies focusing on PAT. In addition, inconsistencies in the used terminology have been observed across the literature. Various studies have referred to their methodology as PTT even though the measured interval was determined between ECG and PPG signals and therefore included PEP. Example studies using the terminology in the described way are Ahlstrom et al., Ghosh et al. and Poon et al. [25], [26], [28] studies. These studies measured the transit time of the pulse wave from ECG to PPG, which is commonly referred to as PAT in the literature, although the authors described it as PTT in the studies. Previous study by Finnegan et al. [29] also discussed this inconsistency in terminology. Consequently, the studies included in this review have been categorized according to the measurement methodology rather than the terminology used in the original articles. Since ECG-PPG measurements

include PEP, studies using this approach may not explicitly take into account the influence of PEP in blood pressure estimation.

In this thesis, the focus of the PTT is on the approach using two PPG sensors, similarly than proposed by Byfield et al. [30]. They developed a PPG-based blood pressure measurement system that uses two reflective finger PPG sensors placed 5.5 cm apart. Systolic peaks of the PPG signals were used to calculate PTT and further derive pulse wave velocity. Across all participants, the mean pulse wave velocity was 1.61 m/s. The Spearman correlation between pulse wave velocity and blood pressure was 0.93 for SBP and 0.75 for DBP, indicating a strong positive relationship between PWV and blood pressure, particularly systolic blood pressure. PWV values were further used to develop a blood pressure estimation model using Gaussian Process Regression. Using this approach, a R^2 score of 0.88 for the systolic bp and 0.62 for the diastolic BP was achieved. The results suggest that pulse wave velocity calculated from systolic peaks may provide an effective and robust approach for cuffless and continuous blood pressure estimation. However, several potential sources of error that should be considered, were identified. First, PPG sensors were found to be highly sensitive to the pressure applied at the measurement site, as contact pressure may alter the shape of the PPG waveform and affect the detection of peaks and feet. Another challenge was light loss caused by optical scattering, which contributed to variation in PWV across participants. In addition, the placement of the PPG sensors influenced the measured values and consequently affected the calculated pulse wave velocity.

Rasool et al. [31] proposed two non-invasive and continuous blood pressure estimation techniques based on PTT using different sensor combinations. The first approach measured PTT between two PPG sensors placed on shoulder and tip of the index finger, whereas the second approach combined a piezoelectric sensor placed on the chest and the finger PPG. The piezoelectric sensor was used to detect the instant

of pulse wave generation. The results showed that the approach utilizing the piezoelectric sensor achieved better performance than the conventional PTT approach based on two PPG signals. However, both approaches relied on individual calibration, which may have improved estimation performance. The study further evaluated both techniques using leave-one-out cross-validation. The second technique reduced estimation errors particularly for systolic pressure estimation, suggesting that improved pulse onset detection may enhance the accuracy of PTT-based blood pressure estimation. Using the PPG-PPG approach, the achieved RMSE values were 8.45 mmHg for SBP and 8.32 mmHg for DBP. With the piezoelectric technique the RMSE improved to 5.72 mmHg for SBP, while DBP estimation resulted in an RMSE of 8.94 mmHg.

PTT seems to offer an alternative approach for blood pressure estimation by excluding the influence of PEP. However, factors such as the sensor pressure, light scattering, sensor placement, and movement may affect measurement performance.

3.3 Comparison of PAT and PTT

Although the relationships between PAT, PEP, PTT and blood pressure have been investigated separately, it remains unclear whether excluding PEP leads to improved blood pressure estimation. The influence of PEP may outweighed by practical challenges related to measurement conditions, such as movement and signal quality. Therefore, comparing PAT and PTT may provide further insight into the physiological and practical differences between approaches.

Wong et al. and Finnegan et al. [13], [29] investigated the effects of PEP on PAT and compared the obtained results with values obtained with PTT. In both studies, ECG, finger PPG measured using a pulse oximeter, and thoracic impedance signals were recorded. Impedance cardiography (ICG) was then derived from the thoracic impedance signal by calculating its first derivative. PAT was defined as the time

interval between ECG and a PPG fiducial point. Wong et al. [13] determined the PPG fiducial point using the first derivative of the PPG signal, whereas Finnegan et al. [29] used the foot of the PPG waveform. PEP was determined using ECG and ICG and PTT was calculated by subtracting PEP from PAT. Therefore, in both studies PTT was not obtained as an independent measurement between two peripheral measurement sites but rather derived indirectly from PAT and PEP.

Both studies reported a relationship between PEP and blood pressure; however, with differing trends. Wong et al. found an inverse correlation between PEP and SBP, whereas Finnegan et al. observed positive correlations between PEP and SBP, MAP and DBP. Wong et al. reported that SBP correlated strongly with PAT ($r = -0.81$) and moderately with PEP ($r = -0.61$), while the correlation between SBP and TT was weak ($r = -0.25$). Finnegan et al. observed that increasing SBP, MAP and DBP corresponded to decreasing PAT and PTT but increasing PEP. The largest change occurred in SBP, increasing by 21.1 mmHg (± 13.74 mmHg) relative to the baseline. At the same time, PAT decreased by 11.96 ms (± 6.57 ms) and TT by 16.84 ms (± 7.50 ms) and PEP increased by 5.46 ms (± 4.51 ms). PEP showed moderately strong positive correlations ($r > 0.62$) with SBP, MAP and DBP.

Based on these findings, Wong et al. suggested that including PEP may improve systolic blood pressure estimation and that PAT may provide better predictive performance than TT. Finnegan et al. suggested that changes in PEP may influence the relationship between PAT and blood pressure. However, under the studied conditions, contribution of PEP remained relatively stable, whereas changes in PTT were larger. Therefore, the authors concluded that PAT may be sufficient for blood pressure estimation under similar conditions.

Wong et al. [13] investigated the effect of PEP under post-exercise conditions by inducing blood pressure changes through physical exercise. Similar approaches have been applied in study conducted by Esmaili et al. [8] to achieve variation in

blood pressure and evaluate how well pulse propagation metrics follow these changes. This allows investigation of whether changes in PAT or PTT reflect changes in blood pressure and how different factors, including PEP, influence the relationship. Systolic blood pressure and diastolic blood pressure has been reported to increase considerably during physical exercise.

Esmaili et al. [8] investigated the relationship between pulse propagation metrics and blood pressure under blood pressure changes due exercise. To cause variation in blood pressure, participants performed running exercises. ECG, PPG and phonocardiogram (PCG) signals were recorded after the exercise. PAT was calculated between ECG and PPG, whereas PTT was determined between PCG and PPG in order to exclude the influence of PEP. The study evaluated both PAT- and PTT-based blood pressure estimation approaches. Strong correlations with blood pressure were reported for both methods. For systolic blood pressure, PAT achieved higher correlation ($r = 0.95$) than PTT ($r = 0.89$) whereas both methods showed similar performances for diastolic blood pressure ($r = 0.84$). The authors reported that PAT achieved better performance for SBP estimation, while PTT showed advantages for DBP estimation.

In contrast to the exercise-based study designs used by Wong et al. and Esmaili et al. [8], [13], Lee et al. and Hou et al. [32], [33] utilized data collected from patients either undergoing surgery or treated in intensive care units (ICU). In these settings patient movement is generally reduced and blood pressure changes are less likely to originate from a physical activity, although physiological changes and medical interventions may still cause variations.

Lee et al. [32] utilized the open VitalDB dataset, which contains recordings collected during various surgical procedures. In the study, PAT was calculated between ECG and PPG, whereas PTT was determined between invasively measured arterial blood pressure (ABP) and PPG, combining both invasive and optical measurement

approaches. The results showed stronger correlations between PAT and blood pressure than with the ABP-PPG based PTT-approach. The correlation coefficient for PAT-based estimation were $r = -0.37$ for SBP and $r = -0.30$ for DBP, whereas the corresponding PTT-based correlations were $r = -0.12$ for SBP and $r = -0.11$ for DBP. However, this definition of PTT differs from the methods discussed previously, since the proximal timing reference derived invasively rather than from a peripheral optical signal. Therefore, direct comparison with the optical PTT approaches should be interpreted cautiously.

Similarly, Hou et al. [33] investigated PAT-based blood pressure estimation in critically ill ICU patients, mainly consisting of elderly subjects. Their findings suggest that PAT alone was insufficient for accurate blood pressure estimation, resulting in MAE values of 22.87 mmHg for SBP, 13.30 mmHg for DBP and 14.22 mmHg for MAP. The authors proposed that this reduced performance may be partly explained by the influence of PEP. They suggested that combining PAT with additional physiological and statistical features may reduce the influence of PEP and improve blood pressure estimation performance.

Previous studies suggest that pulse propagation methods have potential for continuous and non-invasive blood pressure estimation. Both PAT- and PTT-based approaches have demonstrated relationships with blood pressure. However, their performance appears to strongly depend on measurement conditions, physiological factors and methodological choices. Several studies highlighted the subject-specific nature of PAT-based blood pressure estimation. Cignal et al. and Kachuee et al. [24], [27] observed, that calibration improved estimation performance for PAT, suggesting that individually adjusted calibrations may be required. In addition, movement during the measurement was identified as an important source of error. Cignal et al. and Ghosh et al. [27], [28] showed that motion and changes in posture may reduce estimation performance, likely due to the sensitivity of ECG and PPG

signals to motion artefacts.

The influence of PEP remains inconclusive. Ahlstrom et al. [25] reported improved blood pressure estimation performance when using PAT, whereas Wong et al. and Finnegan et al. demonstrated that PEP itself may correlate with blood pressure. However, the direction and magnitude of this relationship differed between studies. Furthermore, in their studies PTT was derived from PAT and PEP rather than measured independently between two peripheral sites.

The reviewed studies suggest that experimental settings influence the relationship between pulse propagation metrics and blood pressure. Studies introducing blood pressure variation through physical exercise prior to measurement often reported stronger association than studies conducted during movement. This may indicate that controlled blood pressure variation provides more informative physiological changes for evaluating pulse propagation metrics, whereas movement during measurement introduces motion artefacts that reduce estimation performance. On the other hand, studies conducted under relatively static conditions, such as surgery or intensive care monitoring, may include smaller blood pressure variations, potentially resulting in weaker observed relationships. [27], [28], [32], [33]

A summary of the reviewed articles is presented in Table 3.1, including methodology, technology, sample size (N) and key results. Overall, the findings suggest that neither inclusion nor exclusion of PEP alone sufficiently explain differences in blood pressure estimation performance. Instead calibration, measurement conditions, physiological state, and methodological differences appear to influence the observed relationship between pulse propagation methods and blood pressure. This observation highlights the need for comparison between PAT and independently measured PTT to better understand the contribution of PEP to blood pressure estimation.

Table 3.1: Summary of related work on blood pressure estimation using PAT- and PTT-based methods. Reported results include Pearson’s correlation coefficient (r), Spearman’s correlation coefficient (ρ), root mean square error (RMSE) and mean absolute error (MAE).

Article	Methodology	Technology	N	Result
Byfield et al. [30]	PTT	PPG	26	PWV-SBP ρ 0.93 PWV-DBP ρ 0.75
Rasool et al. [31]	PTT	PPG	21	SBP RMSE 8.45 mmHg DBP RMSE 8.32 mmHg
Ahlstrom et al. [25]	PAT	ECG, PPG	8	PAT-based SBP regression $r = 0.80 \pm 0.06$
Kachuee et al. [24]	PAT	ECG, PPG	1000	SBP MAE 11.17 mmHg DBP MAE 5.35 mmHg
Cisnal et al. [27]	PAT	ECG, PPG	307	SBP MAE 14.23 mmHg DBP MAE 9.67 mmHg
Ghosh et al. [28]	PAT	ECG, PPG	14	SBP RMSE 5.06 mmHg DBP RMSE 5.83 mmHg
Poon and Zhang [26]	PAT	ECG, PPG	85	Mean diff \pm SD: SBP 0.6 ± 9.8 mmHg DBP 0.9 ± 5.6 mmHg
Hou et al. [33]	PAT	ECG, PPG	12	SBP MAE 22.87 mmHg DBP MAE 13.40 mmHg MAP MAE 14.22 mmHg
Wong et al. [13]	PAT, PTT	ECG, PPG	22	PAT-SBP $r = -0.81$ PTT-SBP $r = -0.25$
Esmaili et al [8]	PAT, PTT	ECG, PPG	32	PAT-SBP MAE 6.22 mmHg PAT-DBP MAE 3.97 mmHg PTT-SBP MAE 4.71 mmHg PTT-DBP MAE 4.44 mmHg
Lee et al. [32]	PAT, PTT	ECG, PPG	2309	PAT-SBP: $r = -0.37$ PAT-DBP: $r = -0.30$ PTT-SBP: $r = -0.12$ PTT-DBP: $r = -0.37$
Finnegan et al. [29]	PAT, PTT	ECG, PPG	27	PAT-SBP RMSE 5.48 mmHg PAT-DBP RMSE 4.49 mmHg PTT-SBP RMSE 3.91 mmHg PTT-DBP RMSE 4.01 mmHg

4 Methods

4.1 Devices

4.1.1 Measurement Device

Measurements were performed using a custom measurement device developed at the University of Turku, the Health technology research group of the department of computing. The device measures simultaneously electrocardiography and photoplethysmography. It uses a nRF52840 development kit (Nordic Semiconductor) as the main microcontroller platform, which is interfaced with ECG and PPG sensor modules. It has integrated processing and communication capabilities that enable real-time signal acquisition and system control.

The ECG module was implemented using MAX30003 integrated biopotential analog front end. This expansion board is designed for wearable ECG applications and includes filtering and analog-to-digital conversion optimized for cardiac biopotential measurements. The ECG signal measurement uses a three-electrode configuration, in which Ambu BlueSensor M ECG electrodes were used in this study. These electrodes are single-use adhesive electrodes that feature conductive wet gel, an offset connector, and a silver/silver chloride (Ag/AgCl) which all together ensure stable signal quality in acquired signals.

In addition to the ECG module, the device has a PPG module, implemented on a custom circuit board incorporating MAX30105 optical sensor. The module

includes two light-emitting diodes (LEDs) and photodetectors. The LEDs use three wavelengths; green, red, and infrared. Both PPG sensors measure reflective mode PPG. One sensor is designed for clip-on fingertip measurements, whereas the other is a standalone sensor intended for measurements at other body locations, such as the wrist.

The measurement device included software for data acquisition and recording. The device documentation was unavailable, therefore technical specifications, such as sampling frequencies and tick duration, could not be verified with certainty. The recorded timestamps consisted of raw microcontroller clock counter values.

4.1.2 Reference Device

A continuous and non-invasive blood pressure measurement device CNAP500 (CN-systems) was used as a reference device. The device consists of an upper-arm cuff, a finger cuff, a finger cuff controller, and a monitor. It measures continuous blood pressure non-invasively utilizing the vascular unloading technique, in which an inflatable finger cuff with infrared photoplethysmography sensor is used. Measurements are recorded at a sampling frequency of 100 Hz. First, the upper-arm cuff is used to calibrate the device. The blood flow in the finger is then detected with the PPG sensor. The pressure inside the inflatable cuff is modified by a pneumatic controller, which functions accordingly to the PPG readings. The cuff applies pressure to the finger so that blood flow through the finger remains constant and the blood pulsation is neutralized. The pressure applied by the cuff corresponds to the arterial pressure and can thus be used to determine the blood pressure. [34], [35]

4.2 Human Study

The experiments conducted in this thesis comprised a human study. Measurements were performed on a group of participants that were all part of a health technology research group in University of Turku. This study was conducted in accordance with the Declaration of Helsinki and the procedures followed the ethical guidelines for research involving human participants, as defined by the University of Turku. Consent was obtained from all participants before the study. The measurement protocol was introduced to the participants before the measurements, and instructions were provided to them throughout the experiment.

4.2.1 Measurement Protocol

Data were collected from a total of six participants with ages ranging from 22 years to 32 years. None of the participants had a previous diagnosis of hypertension. Participants were not instructed to avoid caffeine or nicotine prior to the measurements, and measurements were performed during the participants' normal workday.

At the beginning of the measurement protocol, pre-measurements were collected from each participant for subsequent data processing. The following distances were measured: from the suprasternal notch to the right shoulder, from the right shoulder to the right wrist, and from the right shoulder to the tip of the right middle finger. Measurements were taken with a soft tape measure. After the pre-measurements, sensors were attached to the participant.

In the measurement, photoplethysmography, electrocardiogram, and blood pressure were measured simultaneously with the measurement and reference devices. The placement of sensors is demonstrated in a figure 4.1. The CNAP blood pressure cuff was attached to the left upper arm and the CNAP finger cuff to the left middle and index fingers. Three electrodes were attached corresponding to the ECG leads for the right arm (RA), left arm (LA), and left leg (LL). The photoplethysmog-

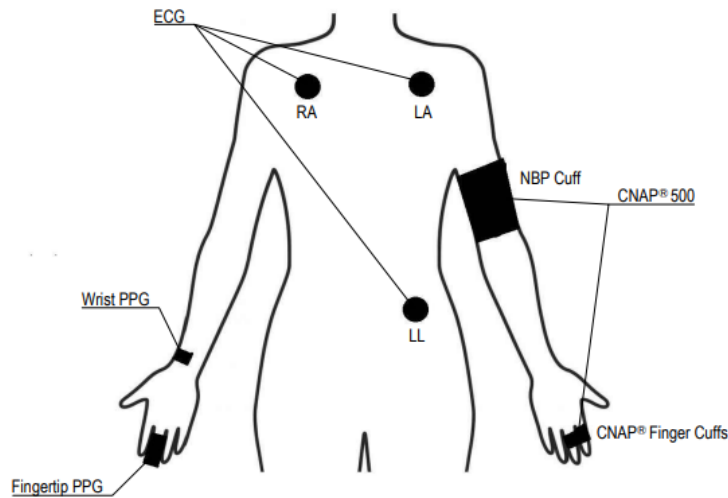


Figure 4.1: Placement of ECG, PPG, and blood pressure sensors used during the measurements.

raphy sensors were attached to the right hand. The proximal sensor was attached to the wrist over the radial artery and the distal sensor was attached to the middle finger.

The experimental protocol was created in a way that allowed studying how different maneuvers might affect blood pressure. The protocol consists of a baseline measurement and three maneuver and recovery phases. Table 4.1 illustrates the different phases of the protocol and the procedures and durations of each phase.

Before data acquisition, the CNAP device performed an automatic calibration procedure. The calibration process was included in the recorded data, as the device started recording timestamps and blood pressure values immediately when the measurement session was initiated. Consequently, the beginning of the recorded CNAP data did not correspond directly to the beginning of the measurement protocol. To identify the actual start of the measurement protocol and synchronize the recordings between devices, a Custom 1 timestamp marker was inserted into the CNAP recording when the university’s measurement device and the measurement protocol was started. Similarly, the end of the measurement protocol was marked using the

Table 4.1: Measurement protocol used during data collection, including baseline, breathing maneuvers, and recovery phases with corresponding durations.

Phase	Procedure	Duration (sec)
Baseline	Rest in supine position	60
Maneuver 1	Legs raised to a 45-degree angle, normal breathing	60
Recovery	Rest in supine position	60
Maneuver 2	Deep breathing	30
Recovery	Rest in supine position	60
Maneuver 3	Rapid breathing	15
Recovery	Rest in supine position	60

same timestamp marker. However, the end marked was missing for participant 1.

During the measurement, participant was lying still on a motorized bed. In the beginning, the bed was set to a neutral position. The measurement started with a baseline phase, in which the participant was resting in a supine position for 60 seconds. In the first maneuver, participant’s legs were raised to a 45-degree angle with the motorized bed. Participant was breathing normally in this position for 60 seconds, after which the bed was returned to a neutral position, and the first recovery phase began. In the second maneuver, participant was taking deep breaths for 60 seconds. The maneuver was followed by the second recovery phase. The last maneuver was rapid breathing, in which participant was breathing quickly for 15 seconds. In the end of the measurement, a final 60 second recovery phase was taken place.

4.3 Software

The data exported from the reference device was already filtered and segmented into 5-second epochs. The ECG data recorded with the measurement device was already filtered and was ready to use. However, the acquired PPG data was raw data that required pre-processing and filtering.

Python was used as the programming language for signal processing and data

analysis, as it provides a wide variety of suitable libraries. Jupyter Notebook was used as the development environment due to its capabilities in data visualization and data analysis. The following Python libraries were utilized in the study: Matplotlib, NeuroKit2, NumPy, pandas, scikit-learn, SciPy and vitalwave.

5 Results

5.1 Collected Data

Data collection was conducted according to the measurement protocol described in Chapter 4. Figure 5.1 illustrates the raw ECG and green-wavelength PPG signals recorded from one participant over a 10-second interval. For visualization purposes, raw timestamp values were converted into seconds.

Signal quality varied between participants and measurement channels. ECG recordings from four out of six participants contained visible interference. However, the R-peaks remained clearly distinguishable, as shown in Figure 5.1, and the interference was therefore not considered to affect subsequent analysis. PPG signals collected from the wrist were generally noisier than signals collected from the fingertip.

One participant had severe noise in the wrist PPG signal, preventing reliable detection of fiducial points even after filtering. Consequently, the corresponding measurement channel was excluded from further analysis for that participant. In addition, occasional outliers were observed in red wavelength PPG recordings from both measurement sites, resulting in flattened signal segments during visualization. One participant's infrared fingertip PPG signal showed a sudden shift in the DC level approximately halfway through the measurement period; the cause of this phenomenon remained unknown. Furthermore, one ECG recording was inverted,

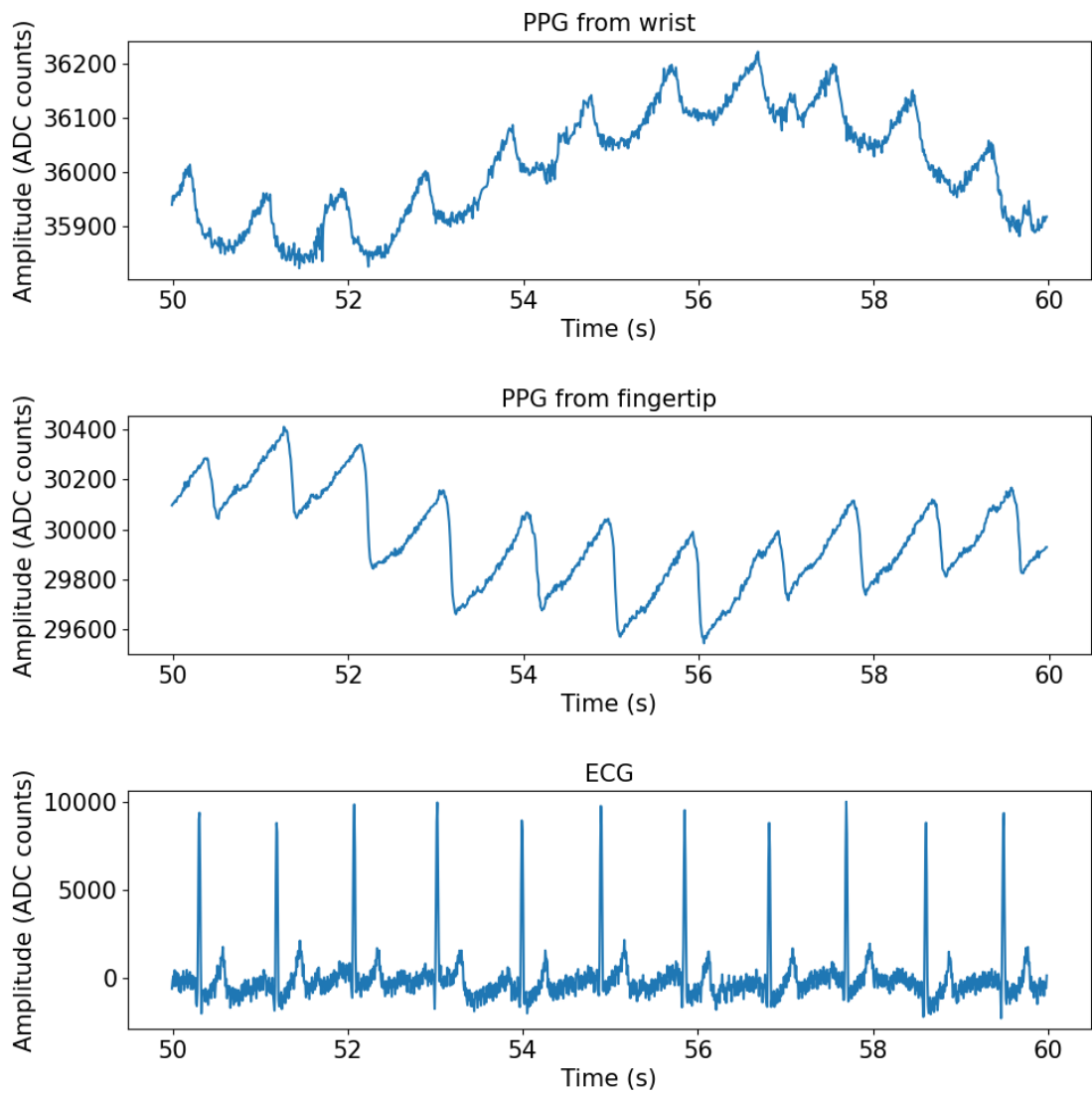


Figure 5.1: Example of raw ECG and PPG signals recorded from the wrist and fingertip over 10-second interval.

resulting in downward-oriented R-peaks. The signal polarity was corrected prior to analysis.

The CNAP device recorded blood pressure measurements, including systolic blood pressure (SBP), mean arterial pressure (MAP), diastolic blood pressure (DBP), and corresponding timestamps. The recorded blood pressure measurements for one participant are presented in Figure 5.2.

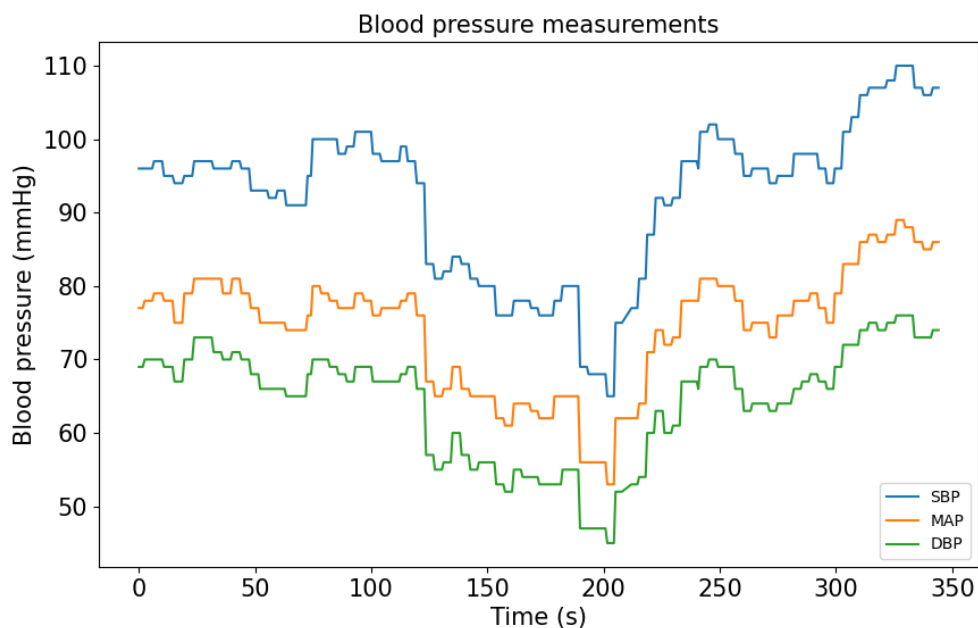


Figure 5.2: Example of recorded blood pressure measurements from one participant, including systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial pressure (MAP).

Measured blood pressure values for all participants are presented in Table 5.1 and visualized in Figure 5.3. For each participant, blood pressure values are reported as mean \pm standard deviation (SD) in mmHg.

The mean blood pressure values varied between participants and covered both lower and higher blood pressure ranges. The lowest mean values were observed for Participant 2, with SBP of 87 ± 5.7 mmHg and DBP of 67 ± 4.3 mmHg. The highest mean values were 140 ± 6.8 mmHg for SBP and 92 ± 5.9 mmHg for DBP

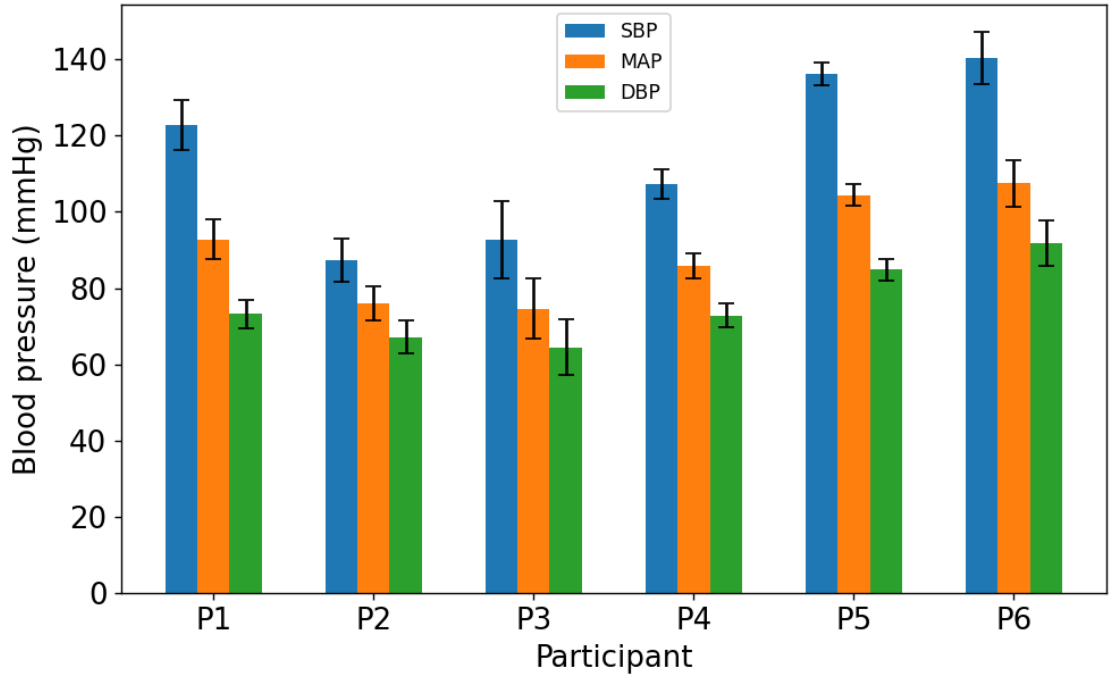


Figure 5.3: Mean systolic, mean arterial and diastolic blood pressure measured from each participant using CNAP. Error bars indicate standard deviation.

Blood pressure variation was intentionally caused as part of the measurement protocol through physiological maneuvers. According to the measurement protocol, blood pressure in the upper body was expected to increase during the leg elevation phase. During the slow breathing period, blood pressure was expected to decrease, whereas fast breathing was expected to increase blood pressure again. As illustrated in Figure 5.2, the measured blood pressure generally followed the expected

Table 5.1: CNAP blood pressure measurements across participants. Values are presented as mean \pm standard deviation (mmHg).

Participant	Mean SBP	Mean MAP	Mean DBP
P1	123 \pm 6.6	93 \pm 5.1	73 \pm 3.8
P2	87 \pm 5.7	76 \pm 4.5	67 \pm 4.3
P3	93 \pm 10.1	75 \pm 7.9	66 \pm 7.4
P4	107 \pm 3.9	86 \pm 3.3	73 \pm 3.2
P5	136 \pm 3.0	104 \pm 3.0	85 \pm 2.8
P6	140 \pm 6.8	106 \pm 6.1	92 \pm 5.9

trends. Leg elevation was performed between 60 and 120 seconds and deep breathing between 180 and 210 seconds, during which the blood pressure changes generally followed the expected trends. During the fast breathing phase, between 270 and 285 seconds, a slight increase in blood pressure was observed.

5.2 Data Processing and Feature Detection

The data collected were processed according to the workflow presented in Figure 5.4 similarly for each participant. First, data were preprocessed by applying outlier removal and filtering, after which fiducial points were detected. PAT and PTT were calculated using the detected fiducial points and subsequently converted into PWV values. Finally, a correlation analysis was performed against the reference blood pressure measurements.

PPG signals were inverted due to the characteristics of optical PPG measurement. The recorded PPG signal represents the amount of light that is reaching the sensor. During systole, an increase in blood volume in the measurement site changes the detected light intensity. Therefore, the signals were inverted to represent the arrival of the pulse wave as positive deflections and to enable consistent feature detection. The effect of inversion is illustrated in Figure 5.5. Additionally, the ECG signal of one participant appeared inverted and was therefore also inverted before further analysis.

Before filtering, outliers in the PPG signals were corrected by replacing the detected outliers with the average of the adjacent samples. The PPG signals contained low-frequency baseline wander and high-frequency noise. To reduce these interferences, a second-order Butterworth bandpass filter with cutoff frequencies of 0.3 Hz and 5 Hz was applied. The effect of filtering is demonstrated in Figure 5.5. As shown in the filtered signal, some residual noise still remained after filtering. However, no additional filtering was applied in order to preserve the original waveform

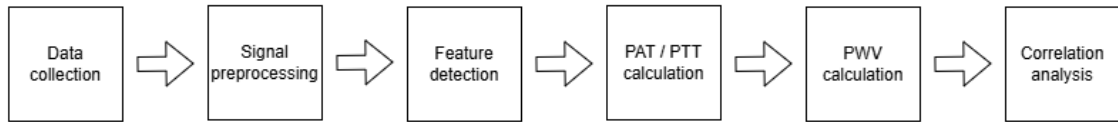


Figure 5.4: Overview of the signal processing pipeline used in this study.

morphology, as additional filtering could have distorted the waveform and affected subsequent feature detection. As discussed previously, ECG signals remained unfiltered because R-peaks were clearly distinguishable from the raw signals, and filtering could have introduced unnecessary signal distortion.

The applied feature detection algorithms required the sampling frequency as an input parameter. As the sampling frequency of the measurement device was not available, it was estimated from the recorded timestamps. Since the ECG and PPG signals were processed independently, the sampling frequency was estimated separately for each signal.

Inspection of the timestamps showed that the intervals between consecutive samples were not fully constant and had minor variation. Therefore, the most frequently occurring timestamp interval was used to estimate the effective sampling interval for each signal. First, the duration of a single timestamp unit (tick) was calculated using the total measurement duration obtained from the CNAP reference device and the total timestamp range of the recorded signal. The effective sampling interval was then estimated by multiplying the tick duration by the dominant timestamp interval, after which the sampling frequency was calculated. The resulting sampling frequencies were approximately 100 Hz for the PPG signals and 128 Hz for the ECG signals.

Feature detection was performed on the preprocessed signals to identify the fidu-

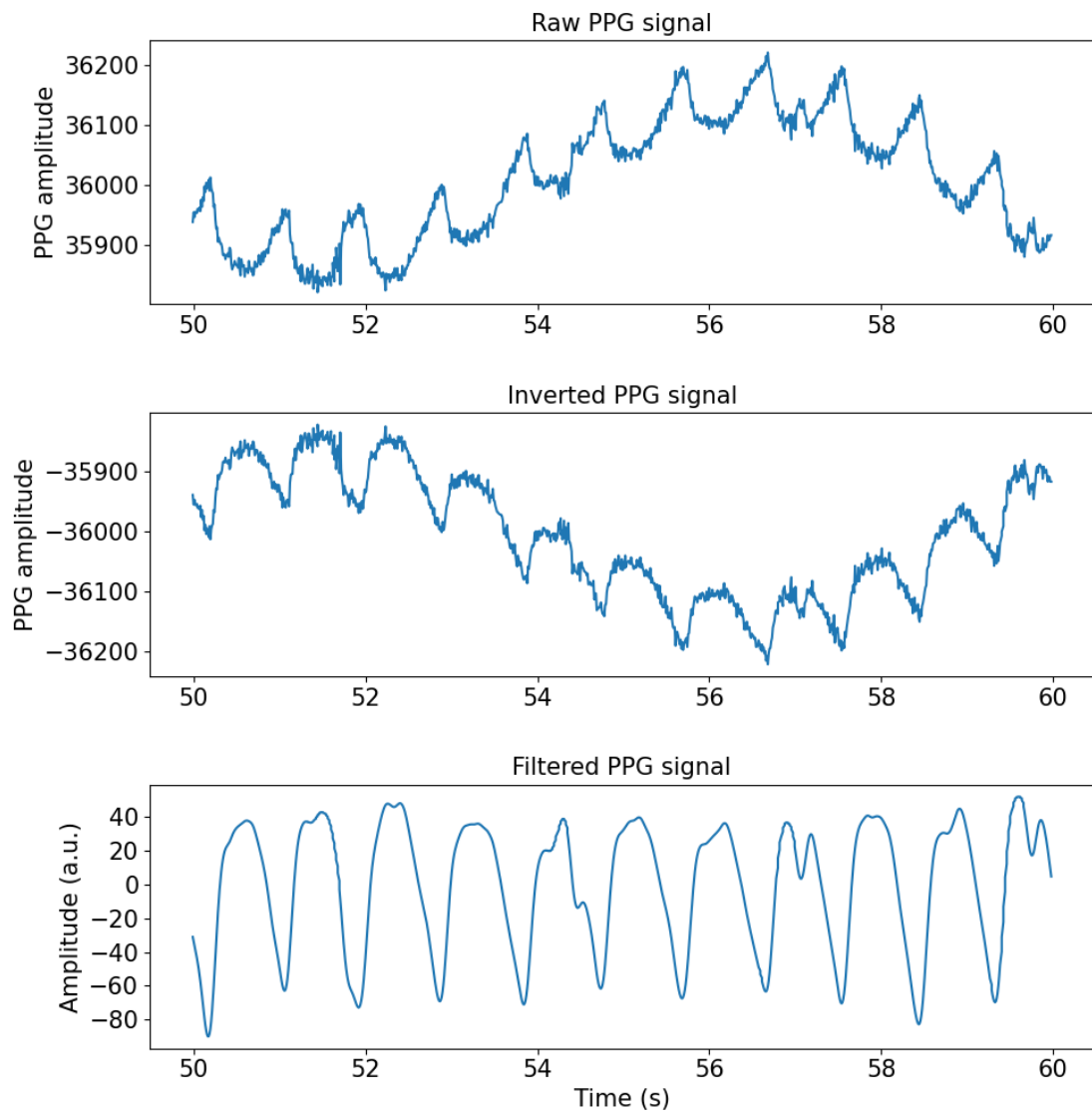


Figure 5.5: Example of preprocessing applied to the wrist PPG signal recorded at the green wavelength. The raw, inverted and filtered signals are presented for comparison.

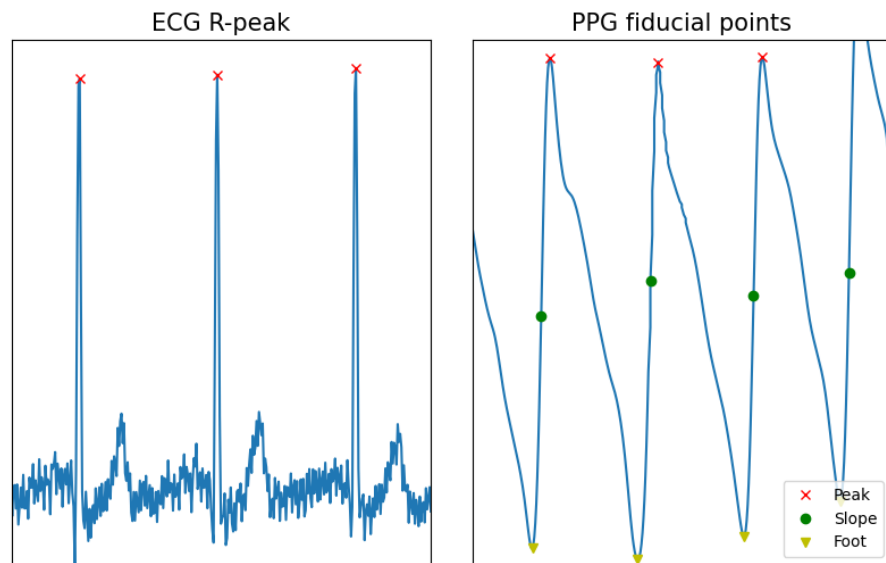


Figure 5.6: Example of detected ECG and PPG fiducial points. ECG R-peaks were extracted from the ECG signal (left). From the PPG signal (right), foot (local minimum), slope (point of maximum derivative), and systolic peak (local maximum) were identified.

cial points required for the PAT and PTT calculations. From the PPG signals, the systolic peak, foot, and maximum slope point were detected. As the systolic peak was the most distinct feature, it was detected first. The detected peaks were then used to define the search regions for slope detection by limiting the maximum derivative search to the signal segment preceding each peak. For ECG signals, R-peaks were detected and used as temporal reference points for PAT calculation. Examples of all detected features are illustrated in the Figure 5.6. The left subplot shows the detected ECG R-peaks, whereas the right subplot illustrates the detected PPG fiducial points.

5.3 Pulse Propagation Metric Calculation

PTT was calculated between the wrist and finger PPG signals. PTT was determined separately using three fiducial points: peak-to-peak, foot-to-foot, and slope-to-slope. The calculations were performed independently for each PPG wavelength channel, including green, red, and infrared. As a result, a total of nine different PTT measurements were obtained for each participant across the entire measurement period.

PAT was calculated between the ECG signal and the PPG signals. Two PAT configurations were evaluated separately: ECG to wrist PPG (PAT1) and ECG to finger PPG (PAT2). PAT was defined as the time interval between the R-peak and corresponding PPG fiducial point (peak, foot or slope).

Mean PTT, PAT1 and PAT2 values with standard deviation are presented in Table 5.4 for each feature. The reported mean values were calculated across all participants and averaged over the measured wavelengths. The pulse propagation times are reported in milliseconds (ms). When comparing the propagation times, peak-based measurement produced values were generally more consistent with the expected physiological range. In contrast, foot- and slope-based measurements resulted in considerably shorter propagation times.

Table 5.2: Measured pulse propagation times for each method. Values are reported in milliseconds (ms) as median \pm standard deviation.

Method	Peaks (ms)	Foot (ms)	Slopes (ms)
PTT	100 \pm 40	40 \pm 10	30 \pm 10
PAT1	190 \pm 90	70 \pm 90	80 \pm 50
PAT2	280 \pm 20	20 \pm 10	100 \pm 10

The reason for these observations is illustrated in Figure 5.7, where the ECG signal and filtered PPG signals are shown using their original raw timestamps. The same behavior was also observed in the raw PPG signals, indicating that the filtering process itself did not introduce the effect. Neither was the issue caused by time

conversion, as the signals were still represented in their original timestamps.

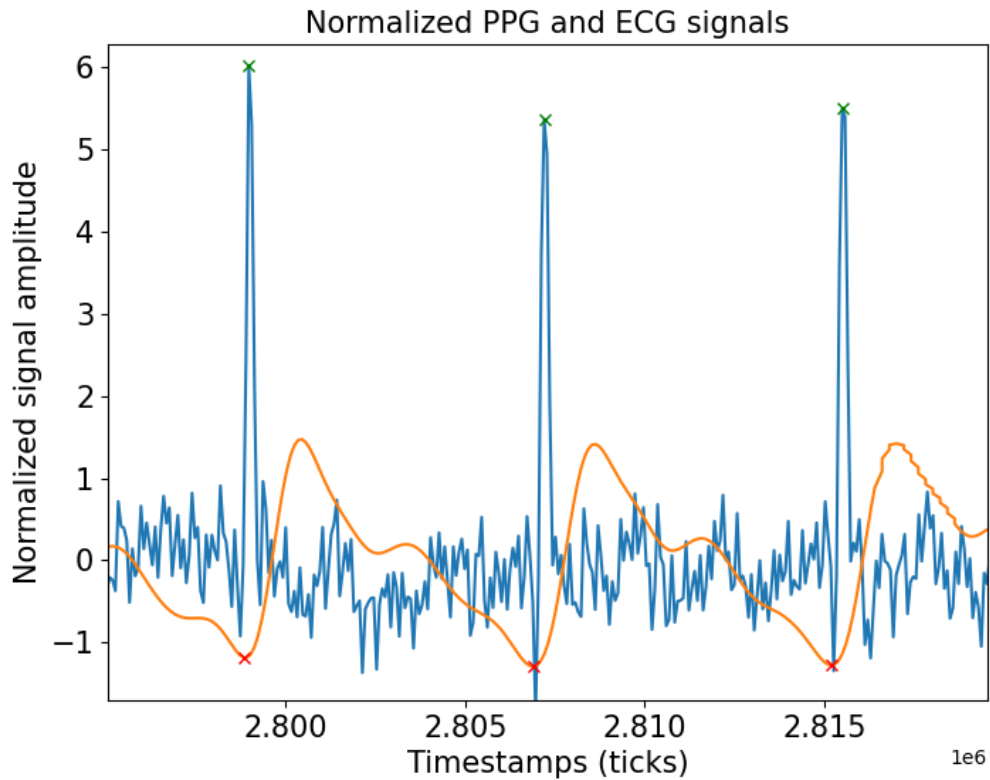


Figure 5.7: Normalized ECG and PPG signals demonstrating the temporal alignment between ECG R-peaks and PPG fiducial points. The delay between the signals appears shorter than physiologically expected.

From visual inspection of the measured signals, the temporal relationship between ECG and PPG appeared physiologically inconsistent in some parts of the recording. Physiologically, the pulse wave detected in the PPG signal should follow the ECG R-peak. However, in some cases the detected PPG foot appeared before the corresponding ECG R-peak, while the following pulse wave occurred to be too late to represent the same cardiac cycle. This created situations, where the calculated pulse arrival times became negative or unrealistically short. Similar behavior was observed for slope-base features, whereas peak-based features generally produced more plausible timing relationships. One possible approach would have been

to apply an offset correction to align the PPG signal with the ECG signal. However, determining the correct offset without introducing bias into the final results was considered challenging. To avoid artificially improving the observed relationships, no manual alignment correction was applied. As a consequence, the calculated propagation times may have been shorter than their true physiological values.

PWV values were calculated using Equation 2.1 by dividing the propagation distance by the measured pulse propagation time. Described timing effect further influenced the pulse wave velocity estimates, as shorter propagation times result in higher PWV values. Consequently, unrealistically small pulse propagation times produced unrealistically high PWV estimates. The results of the PWV calculations are presented in Table 5.5

Table 5.3: Measured PWV values for each method. Values are presented as median \pm standard deviation (m/s). Foot-based PAT1 and PAT2 PWV estimates were excluded due to physiologically unrealistic values.

Method	Peaks (m/s)	Foot (m/s)	Slopes (m/s)
PTT	3.80 ± 2.22	6.11 ± 2.38	6.44 ± 2.45
PAT1	5.49 ± 21.01	–	12.88 ± 9.58
PAT2	4.32 ± 0.79	–	9.79 ± 1.67

5.4 Data Analysis

Correlation analysis was performed for all calculated pulse propagation metrics against the reference blood pressure measurements. As the blood pressure data were originally segmented into 5-second epochs, the pulse propagation metrics were processed using the same epoch length to ensure temporal consistency between datasets. To calculate correlations, the compared data and the reference data were required to have equal lengths. Therefore, the blood pressure values were resampled to match the pulse propagation data.

Pearson correlation coefficient was used to evaluate the linear association between pulse propagation data and blood pressure data, whereas Spearman correlation coefficient was used to evaluate monotonic relationships that were not restricted to linear associations. All reported correlations were statistically significant, with p-values below 0.005.

Figure 5.8 illustrates the calculated PTT values before and after epoching. The relationship of epoched PTT and systolic blood pressure is illustrated. As PTT and blood pressure are generally expected to have an inverse relationship, the PTT signal was inverted for visualization purposes to ease comparison of signal trends.

Overall, the calculated correlation values were low, indicating weak or non-existent associations between pulse propagation metrics and blood pressure. However, when the pulse propagation signals were visually compared with blood pressure, similar overall patterns could be observed, although differences in signal timing were present. The described phenomenon is illustrated in Figure 5.8.

No consistent lag was identified across participants or signal types that could explain the observed timing differences between pulse propagation metrics and blood pressure. Nevertheless, an exploratory lag analysis was performed to investigate whether temporal alignment could improve the observed correlations. Figure 5.9 demonstrates the effect of lag adjustment on the correlation values. In one participant's PTT signal, introducing a relatively large lag increased the Pearson correlation coefficient from $r = 0.14$ to $r = 0.49$.

However, it should be noted that the expected physiological relationship between PTT and blood pressure is inverse. Therefore, although lag adjustment increased the positive correlation coefficient, such results should be interpreted with caution, as an improved correlation does not necessarily reflect a true physiological relationship between the signals.

Although clear temporal lags were observed in some cases and individual correla-

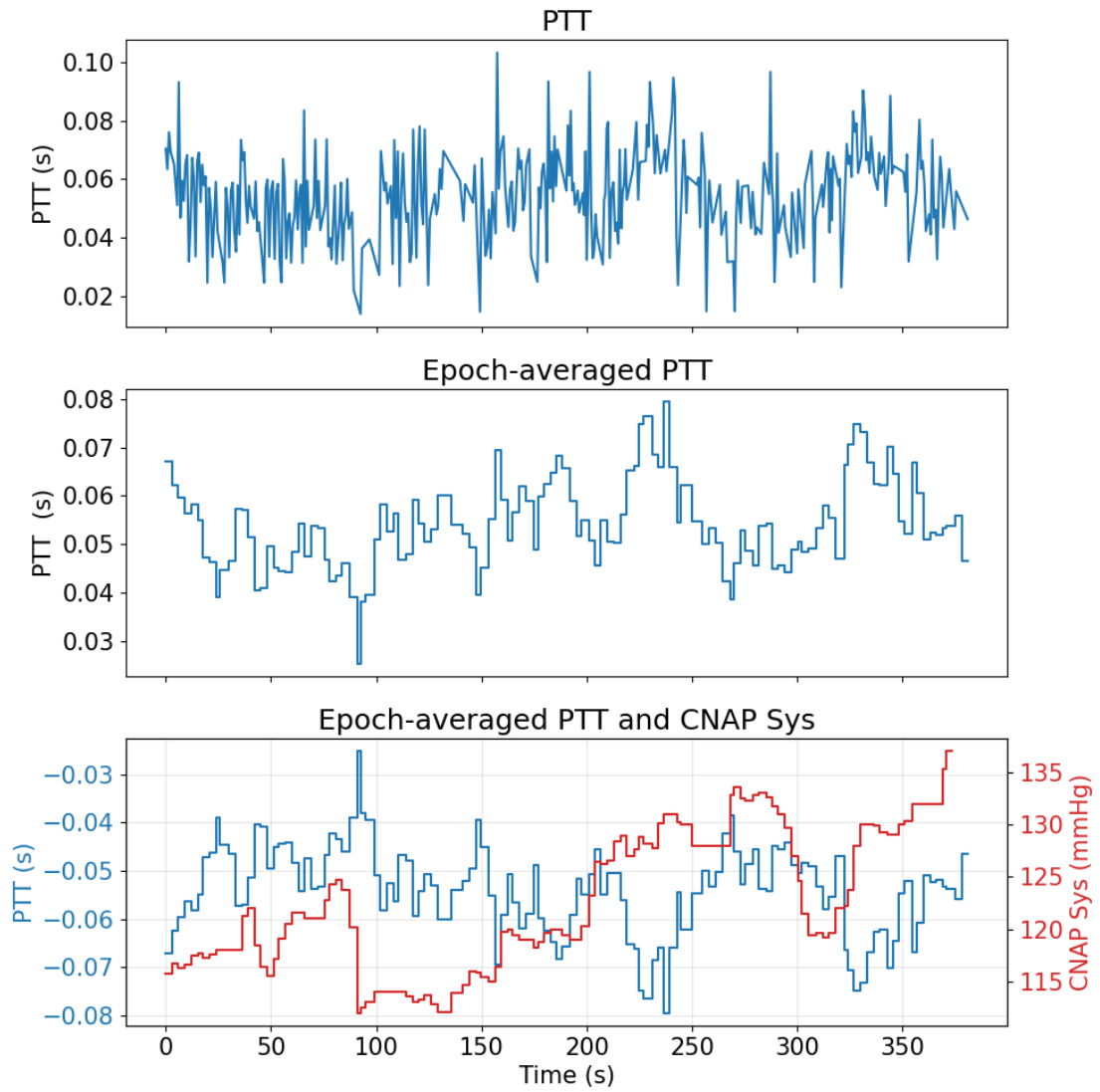


Figure 5.8: PTT, epoch-averaged PTT, and inverted epoch-averaged PTT plotted against systolic blood pressure.

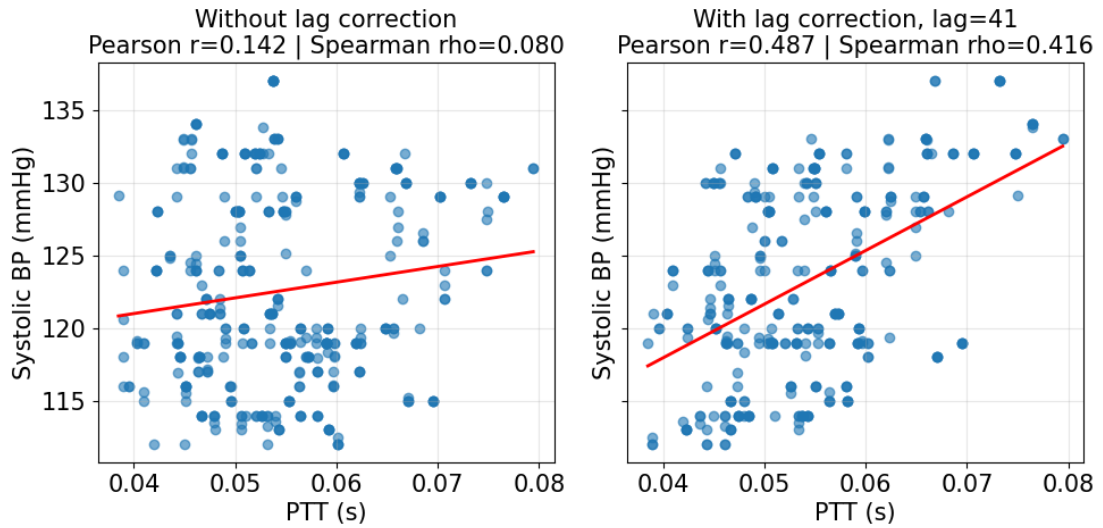


Figure 5.9: Relationship between PTT and systolic blood pressure before and after lag correction. Pearson and Spearman correlation coefficients are shown for comparison.

tions could be improved by applying lag correction, no consistent lag was identified that would apply across all participants for a given signal. Therefore, no lag correction was applied in the final analysis.

The correlations calculated for PAT1, PAT2, and PTT using the complete dataset are illustrated as scatter plots in Figure 5.10, where each participant is represented by a different color. Participant 4 (green) was excluded from the PTT analysis, due to unrealistic values.

Among evaluated pulse propagation metrics, PAT1 was the only method that demonstrated the expected inverse relationship with blood pressure. The scatter plots highlight the inconsistent behavior observed across the calculated pulse propagation metrics and participants.

The pulse propagation times are represented in seconds for visualization purposes, however, the actual values are in the millisecond range. PTT represents the propagation time between the wrist and finger measurement sites and is therefore considerably shorter than PAT values, where the propagation time is measured from

the heart to either wrist or finger.

Table 5.4: Correlation between PAT methods and blood pressure using the fiducial points that produced the strongest correlation.

Participant	PAT1 slopes - MAP		PAT2 peaks - SBP	
	Pearson r	Spearman ρ	Pearson r	Spearman ρ
P1	-0.16	0.28	-0.14	-0.12
P2	0.11	0.08	0.03	0.05
P3	-0.02	0.03	0.01	0.06
P4	-0.17	0.21	-0.17	-0.32
P5	0.03	-	0.20	0.26
P6	-0.13	-0.21	0.11	0.10

The high pooled correlations should be interpreted with caution, as the pooled correlation appeared stronger than the participant-specific correlation. This stronger pooled correlation is likely explained by aggregation bias. When data from all participants are combined, differences in baseline PAT/PTT values and blood pressure between participants may create an overall trend, even though the within-participant correlations remain weak or inconsistent. This phenomenon can be observed in Table 5.4, where the correlations calculated separately for each participant remained weaker than the pooled correlations.

Table 5.5: Best performing pulse propagation method and fiducial point for each participant and blood pressure measure. Measured values are presented in Pearson (r) and Spearman (ρ) correlation coefficients.

Participant	SBP		MAP		DBP	
	Method	r / ρ	Method	r / ρ	Method	r / ρ
P1	PAT1 Slope	0.65 / 0.67	PAT2 Foot	0.60 / 0.66	PAT2 Foot	0.42 / 0.48
P2	PTT Foot	0.36 / 0.35	PAT1 Foot	0.42 / 0.35	PAT2 Foot	0.38 / 0.33
P3	PTT Foot	0.66 / 0.66	PTT Slope	0.46 / 0.44	PTT Slope	0.53 / 0.57
P4	PAT2 Peak	0.40 / 0.46	PAT1 Slope	0.61 / 0.49	PAT1 Slope	0.65 / 0.51
P5	PAT2 Foot	0.32 / 0.30	PAT1 Slope	0.13 / 0.16	-	-
P6	PTT Peak	0.49 / 0.34	PTT Peak	0.49 / 0.31	PTT Peak	0.53 / 0.35

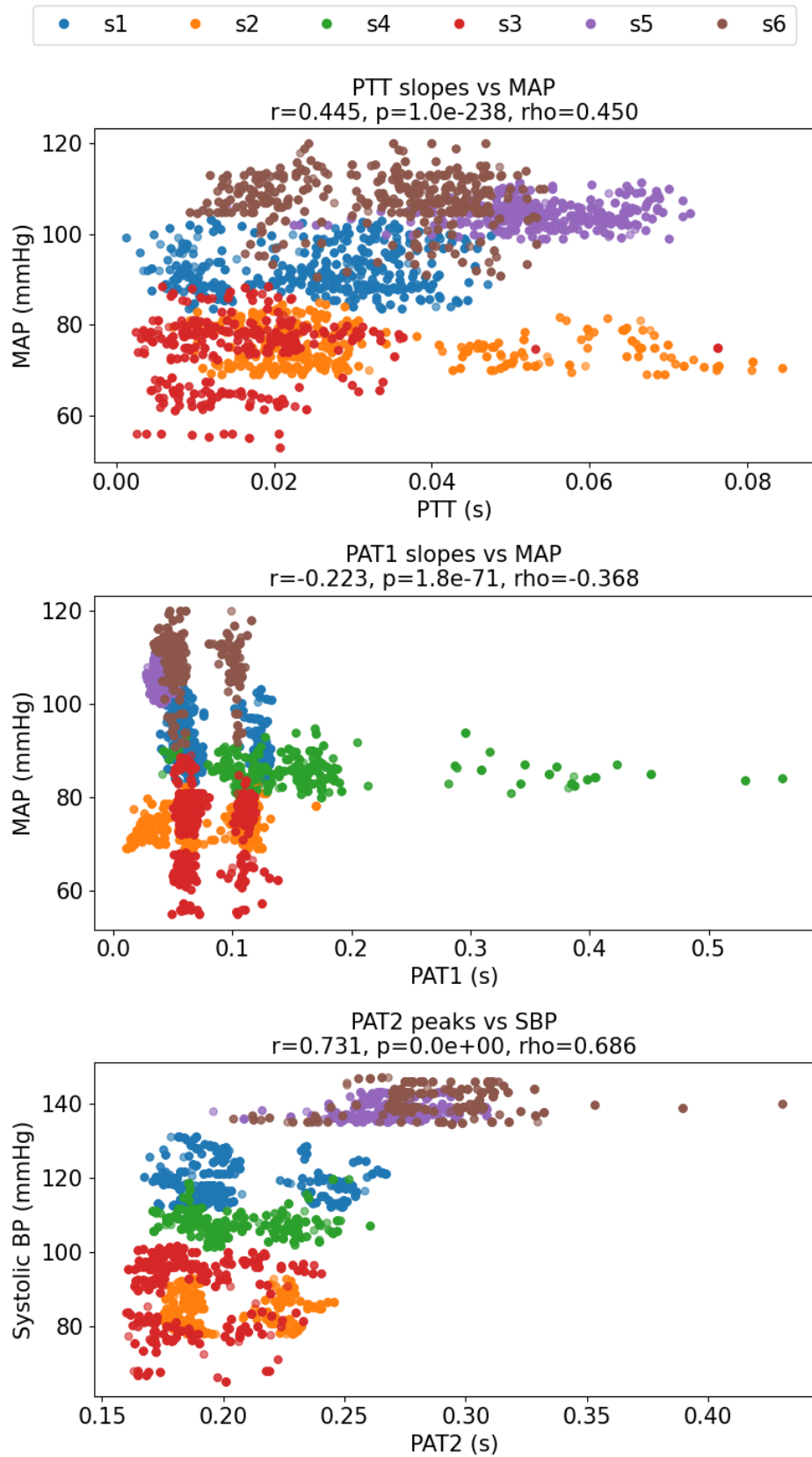


Figure 5.10: Correlation calculated for PAT and PTT using complete datasets. Each participant is represented by a different color. Participant 4 (green) was excluded from the PTT analysis.

Finally, the correlations between pulse wave velocity and blood pressure were calculated. As already observed in PAT1, PAT2 and PTT analyses, combining all features and wavelengths into a single correlation value did not produce strong or consistent results. The resulting correlations remained low, and both the magnitude and direction of the associations varied between methods and participants. Therefore, calculating one overall correlation was not considered meaningful.

Instead, the best-performing method for each participant and each blood pressure measure (systolic, diastolic, and mean arterial pressure) was collected and summarized in Table 5.5. No clear wavelength-specific pattern was observed in the results, and therefore all wavelengths were evaluated together.

The results show that the selected methods varied between participants and blood pressure measured. No single pulse propagation method consistently produced the strongest correlations. PAT1, PAT2, and PTT each appeared as the best performing method in different cases. Overall, moderate correlations were observed, but the optimal method differed across participants and blood pressure measures, suggesting that the performance of pulse propagation metrics may depend on the individual rather than one generally applicable method.

6 Discussion

The results of the conducted human study showed considerable variation between participants. Although some participant-specific combinations of pulse propagation methods and fiducial points produced moderate correlations with blood pressure, no single method consistently outperformed the others. Generally, one fiducial point produced the strongest association across systolic, diastolic, and mean arterial pressure for each participant, but the optimal method varied. These findings indicate that the relationship between pulse propagation metrics and blood pressure is participant-specific and may depend more on physiological and measurement-related factors than on the choice of PAT or PTT.

The findings are partly consistent with previous studies. Several studies have reported strong associations between PAT and systolic blood pressure. Ahlstrom et al. suggested that including PEP is essential for systolic blood pressure estimation [25], whereas Poon and Zhang similarly reported stronger results for systolic than diastolic blood pressure when using PAT [26]. Esmaili et al. also found that PAT showed the strongest relationship with systolic blood pressure, whereas PTT performed better for diastolic blood pressure [8]. In contrast, the present study did not demonstrate a clear advantage of either PAT or PTT for systolic blood pressure estimation. Instead, the strongest correlations varied between participants.

The participant-specific variability observed in this study suggests that measurement-related factors may have had a greater influence on the findings than the choice be-

tween PAT and PTT itself. Although previous studies reported stronger associations between pulse propagation metrics and blood pressure, differences in measurement protocols, sensor configurations, and experimental conditions may partly explain why the findings differed from those reported in previous studies.

One important source of uncertainty was the PPG measurement process itself. Previous studies have shown that pulse propagation metrics are sensitive to sensor placement, contact pressure, and optical scattering [27], [28], [30]. Similar challenges were encountered during wrist measurements, where the reflective sensor had to be manually positioned over the radial artery. Although the sensor was secured using tape after optimal placement had been identified, maintaining consistent positioning and contact pressure throughout the protocol remained difficult and likely contributed to the observed variability between participants.

Another important limitation was uncertainty related to signal timing and synchronization. Because documentation of the university's measurement device was unavailable, technical specifications such as sampling frequencies and timestamp resolution could not be verified. Sampling frequencies were therefore estimated from timestamp intervals and the total duration of the CNAP recordings. In addition, some detected signal features appeared earlier than physiologically expected, suggesting imperfect synchronization between the recorded signals. Since both PAT and PTT rely on precise temporal relationships, these uncertainties may have affected the calculated pulse propagation metrics and their associations with blood pressure. Although lag correction was investigated, no consistent correction applicable to all participants was identified.

Finally, the study included six healthy participants representing a relatively narrow age range. Consequently, the findings cannot be generalized to broader populations, particularly individuals with hypertension or other cardiovascular conditions. These limitations should be considered when interpreting the study findings.

7 Conclusion

In this thesis, two pulse propagation methods and their relationships with blood pressure were investigated. PAT and PTT were evaluated as potential methods for continuous and non-invasive blood pressure estimation. While PAT is easier to measure in practice, it includes PEP, which is not directly related to pulse propagation and may therefore affect the relationship with blood pressure in comparison to PTT, which measures only the propagation time of the pulse wave. Therefore, this thesis examined whether excluding PEP results in a more robust relationship with blood pressure.

Two research questions were addressed. The first research question investigated whether the pre-ejection period influences the relationship between PAT and blood pressure. Based on the results of the conducted human study, no clear conclusion could be drawn regarding the effect of PEP. The observed relationships varied considerably between participants, and no consistent pattern was identified indicating that the inclusion of PEP either improved or reduced the performance. However, PTT did not consistently outperform PAT, suggesting that PAT may still remain a possible method for blood pressure assessment.

The second research question examined, which pulse propagation method provides the most robust relationship with blood pressure. Based on the results of this study, no single method outperformed the others. Although PTT excludes PEP and has been previously suggested to provide a more robust method for blood pressure

estimation, in this study it did not perform considerably better than PAT. Therefore, both methods remain relevant alternatives for continuous non-invasive blood pressure estimation.

Limitations should be considered when interpreting the results. In particular, uncertainties related to device specifications, temporal signal alignment, synchronization accuracy, and PPG sensor placement may have affected the calculated pulse propagation metrics and the resulting correlations. Additionally, the small sample size limits the generalization of the findings.

Future work should focus on improving signal synchronization and sensor fixation, especially for the wrist PPG measurements, where maintaining stable pressure and sensor positioning proved challenging. Improving measurement reliability may enable a more accurate comparison between PAT and PTT and further clarify their suitability for continuous blood pressure measurement.

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