ABSTRACT

Title of thesis: ANALYSIS AND REFINEMENT OF
                    PULSE RATE VARIABILITY

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Heart rate variability (HRV), calculated from the cardiac intervals of electrocardiogram (ECG), is a promising marker of the cardiovascular system status and fitness. However, ECG signal is not always available and photoplethysmogram (PPG) is easier to obtain, and more widely used in clinical is running HRV analysis on pulse-to-pulse intervals of PPG signal, which is usually referred to as pulse rate variability (PRV). Thus, whether PRV can be used as a substitution of HRV is of substantial interest to researchers.

In this thesis, two issues about PRV are discussed. The first issue is the selection of characteristic point, which determines the length and location of the pulse-to-pulse interval and will affect the agreement between PRV and HRV. Six characteristic points of PPG pulse are extracted and the agreement between HRV and corresponding PRV is calculated and compared, in two situations, subjects with cardiovascular diseases (CVD) and subjects without cardiovascular diseases (non-CVD). The result indicates that pulse peak is most suitable for CVD subjects, and

50% max amplitude point and 75% max amplitude point on pulse slope are most suitable for non-CVD subjects.

The second issue studied in this thesis is the PRV refinement using arterial blood pressure (ABP) information. The relationship between systolic blood pressure extracted from ABP signal and pulse transit time (PTT) is modeled using linear kernel support vector regression (SVR) and RBF kernel SVR, respectively. Estimated PTT is used to adjust the location of PPG pulse-to-pulse intervals. PRV after adjustment is calculated, and its agreement to HRV is compared with the original PRV. For CVD subjects, the improvement to the agreement is limited, and only the agreement for variables representing long-term variability is improved. For non-CVD subjects, there is a relatively large improvement for approximately all variables after refinement and linear kernel outperforms RBF kernel in this situation.

ANALYSIS AND REFINEMENT OF PULSE RATE VARIABILITY

by

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Dedication

This thesis is dedicated to my parents, Hongyan Xu and Jiazhu Li, for their love and support.

Acknowledgments

I want to express my appreciation to all the people that helped me when I was working on this thesis research. First and foremost, I'm grateful to my advisor, Professor Min Wu, for all the advice and guidance she provided with me during the process of my pursuing the Master's degree, and also for giving me the opportunity to work in the Media And Security Team. It was an extremely precious experience for me, from which not only did I practice my technical abilities as an engineering student through various challenging and exciting projects but strengthened my analytical and critical thinking skills as well.

I appreciate our group mates, Qiang Zhu, Mingliang Chen, and Xin Tian, for their kindness and generous help whenever I encountered difficulties. I will cherish our friendship in the future and wish them the very best for their pursuing Ph.D. degree.

Finally, I want to give my sincerest gratitude to my parents. Without their unconditional support and endless love to me, I would not become who I am today, and would not be able to continue my academic overseas and graduate with this thesis successfully.

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Chapter 1:   Introduction

1.1   Motivation and Objective

Heart rate variability (HRV), which represents the pulse-to-pulse interval variation of electrocardiographic (ECG) signal that records the electrical activity of the heart from electrodes placed on the skin, is a promising tool for measuring the health status of the cardiovascular system, while also being able to reflect much information. Pulse rate variability (PRV) is a similar measurement but obtained from the photoplethysmographic (PPG) signal that is collected using a pulse oximeter and reflects light absorption changes of the skin, is also able to demonstrate the cardiovascular system status to some degree.

Papers such as [14, 20, 21, 27, 31] have mentioned the difference between PRV and HRV and discussed whether PRV is a suitable substitution to HRV, in terms of different HRV parameters and experimental conditions. However, few of them focus on the influence of different definitions of the PPG pulse cycle boundary.

In this thesis, PRV from PPG pulse-to-pulse intervals is calculated using six different characteristic points as cycle boundary, and their agreement to the gold standard, as well as HRV from ECG pulse-to-pulse intervals. The agreements using different characteristic points are then compared and the most recommended

characteristic point is selected for subjects with and without cardiovascular diseases separately. The HRV references used for comparison are calculated using two ECG pulse characteristic points in order to observe the difference between the HRV derived from ECG pulse onset point and that from ECG pulse peak point.

The second problem examined in this thesis is on PRV refinement with blood pressure information. The motivation is that the difference between pulse-to-pulse intervals of the ECG signal and that of the PPG signal corresponds to changes in pulse transit time (PTT) and is related to blood pressure. Utilizing the synchronized arterial blood pressure (ABP) signal, the relationship between PTT and systolic BP calculated from ABP is modeled and PTT is estimated using the model. The estimated PTT is then applied for pulse-to-pulse interval adjustment of the PPG signal. For situations that subjects with and without cardiovascular diseases, the agreement between the original PRV and HRV and the agreement between the adjusted PRV and HRV are calculated and compared to observe and analyze the influence of refinement respectively.

1.2   Outline of Thesis

After introducing the background and motivation of this thesis in Chapter 1, Chapter 2 presents an overview of the background and the technical issues involved in the thesis. In Chapter 3, different PPG characteristic points are extracted. Then the corresponding pulse rate variability is calculated and evaluated according to its agreement to ECG derived heart rate variability for subjects with and with-

out cardiovascular diseases. The results for different characteristic points are then compared. Chapter 4 focuses on estimating pulse transit time using blood pressure information and using the estimated result to refine the PPG signal in order to increase its pulse rate variability agreement to heart rate variability. Conclusion and future research plans are presented in Chapter 5.

Chapter 2: Related Researches

2.1 Background

2.1.1 Heart Rate Variability

Heart rate variability, which is a reflection of the oscillation of the cardiovascular system parameters, can be used to evaluate the regulation between cardiovascular system and the autonomic nervous system, due to the relationship between them, while also to predict and prevent cardiovascular disease [1].

Reduced HRV is an indicator of mortality after myocardial infarction [2, 3]. Congestive heart failure, diabetic neuropathy, or post-cardiac-transplant depression may also relate to varied HRV, usually lower. In the psychophysiology field, HRV has been discovered to connect with emotional stimulation, while high-frequency activity decreases when there is acute time pressure, emotional strain [4] and elevated state anxiety that may due to focused attention and movement suppression [5]. [6] has revealed that people who worry more tend to have reduced HRV.

In summary, HRV is a promising tool to be used as a marker of cardiovascular and autonomic system health, and an indicator of physical and mental status.

HRV is usually measured using ECG signal, wave collected through the elec-

trodes placed on the skin and used for the detection of the electrical changes during cardiac activity.

Figure 2.1 shows a plot of the ECG signal.
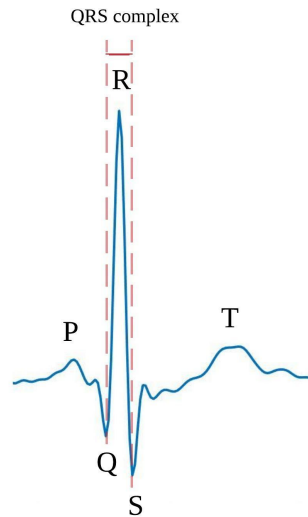
Figure 2.1: Electrocardiographic (ECG) Signal

There are three main components in ECG wave: P wave that indicates the atria depolarization, QRS complex that represents the depolarization of ventricles, and T wave that represents the repolarization of ventricles [7].

ECG is considered as the gold standard of heart rate variability measurement due to its clear waveform, and thus the heartbeats that are not originating from the sinus node can be excluded.

Heart rate variability can be measured by specific parameters, which is called HRV analysis. The work in [1] has clarified and standardized different kinds of HRV measurements or HRV variables. They can be divided into time domain and

frequency domain. Time domain variables measure the instantaneous heart rate and the intervals between adjacent QRS complexes or RR intervals as they are usually defined as the intervals between successive R peaks. The specific intervals used here, which usually means the intervals generated from sinus node depolarization, are referred to as normal-to-normal (NN) intervals.

Table 2.1 indicates the commonly used statistical time domain measurements that could be derived from instantaneous heart rates or NN intervals for HRV analysis.

Table 2.1: Commonly used time domain parameters of HRV

Variable	Units	Description
mean	ms	Mean value of NN interval length
SDNN	ms	Standard deviation of NN interval length
RMSSD	ms	The square root of the mean of the sum of the squares of differences between adjacent NN intervals
pNN50	%	Percentage of intervals the length of which differing from their adjacent intervals by more than 50ms

Frequency domain measurements focus on the power distribution within NN intervals, which is derived from power spectral density analysis. Major spectrum components in short time recordings (generally 2 to 5 min) [8, 9] are very low frequency (VLF), low frequency (LF), and high frequency (HF) components. For long term recordings (usually last for 24 h), there is an ultra low frequency component in addition to the other four spectrum components. These frequency domain measurements are shown in Table 2.2.

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Table 2.2: Commonly used frequency domain parameters of HRV

Variable	Units	Description	Frequency Range
ULF	ms^2	Power in ultra low frequency range	$\leq$0.003Hz
VLF	ms^2	Power in very low frequency range	0.003 - 0.04Hz
LF	ms^2	Power in low frequency range	0.04 - 0.15Hz
HF	ms^2	Power in high frequency range	0.15 - 0.4Hz
LF/HF		Ratio LF$[ms^2]$/HF$[ms^2]$	

The variation of the power spectrum distribution over these frequency ranges may reflect the autonomic modulation changes of the heart period [10–12].

The non-invasive characteristic of HRV analysis promotes its extensive usage as a long-term health tracking and monitoring tool.

2.1.2 Photoplethysmogram

Comparing to the ECG signal, the PPG signal is also collected in a non-invasive way but has the advantage to be less expensive and easier to use. PPG wave is usually optically obtained by a pulse oximeter, which illuminates the skin and collects the light absorption changes, at the fingertip or other places, and can detect variations in blood volume in the tissue of microvascular bed [13].

PPG signal reflects cardiac cycle to some extent due to the AC component in it generated because of arterial pulses, the source of which is from the heartbeat pumping [14]. The variation of the pulsatile component in the PPG signal arises from arterial blood pulsation, the comparatively static component of which is due to venous volume changes, vasomotor activity, and thermoregulation [18], and the
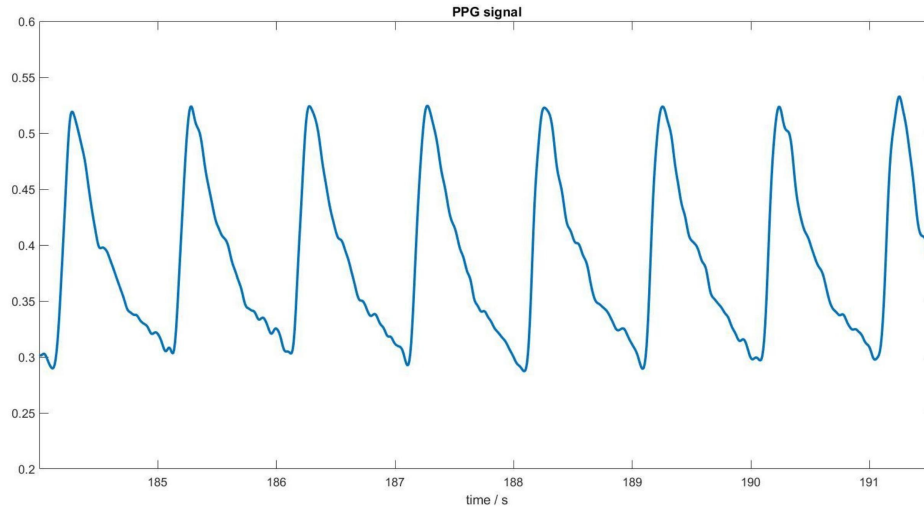
Figure 2.2: Photoplethysmographic (PPG) Signal

fluctuation part resembles instantaneous cardiac activity.

Moreover, it is also known that PPG can reflect autonomic influences [15–17].

Therefore, it is worth to conduct HRV analysis on the PPG signal and to study whether PPG derived PRV can be used as a surrogate of HRV.

PPG signal collection does not need electrodes placed on the body, which is more convenient and avoids awkwardness. Besides, since other physiological parameters, such as blood oxygenation and ventilatory rate, can also be obtained from PPG signal, apply PRV for cardiovascular system monitoring is more suitable for situations that need multiple parameters derived simultaneously, for example, sleep disorder studies. Furthermore, there are morphological variations in the ECG signal that will make it difficult for detection algorithms to distinguish QRS complexes with abnormal P waves and T waves [19].

The pulse oximeter has been widely used in clinical nowadays, and an ECG device is not applicable in some specific situations, such as during magnetic resonance imaging (MRI). Therefore, apply PRV parameters as a substitution of HRV parameters is a topic worth researching and would benefit the field of cardiac signal measurement.

2.1.3 Comparison of Heart Rate Variability and Pulse Rate Variability

Many studies are talking about the issue of whether PRV can be used instead of HRV. In summary, PPG mean pulse rate can be used as a substitution of the mean heart rate derived from ECG with sufficient high agreement [20]. When focusing on whether PPG can be used in HRV analysis, most researches compared the HRV variables generated from RR intervals (RRI) of ECG signal and PRV variables derived from pulse-to-pulse intervals (PPI) of PPG signal.

According to different studies for PRV and HRV agreement, sampling rate [21], location of pulse sensor [22–24], statistical evaluation methods, experimental condition [25], etc. all will influence the comparison result.

For specific HRV variables, there is good agreement between PPG-derived mean interval length and ECG-derived mean interval length, especially for subjects at rest. The result matches the conclusion we have before about the mean heart rate calculated from the two signals. Although there are deviations of PPI from RRI, they will not affect the mean value for these deviations tend to cancel each

other out. With different experimental conditions, there is also research found that mean HR was consistently underestimated by mean PR at an average of 1.8 - 3.9 bpm [27].

For other HRV variables, there are not consistent results for all researches. Generally, for subjects at rest [23, 28] or during night sleep [29], there is relatively high agreement on all HRV variables, and the agreement decreases for subjects during upright position or exercise [14, 30]. Relevant studies also show that variables that are determined by short-term variability, such as RMSSD, pNN50, HF components, LF/HF, are more likely to have a low agreement between HRV and PRV than variables that are determined by long-term or overall variability [31, 32]. [21] points out that PRV tends to overestimate HF components to a more substantial degree and overestimate LF component to a smaller degree. Thus it will underestimate the LF/HF ratio. [14] compared HRV and PRV for subjects on a tilt table and found PRV estimation usually has positive deviation, especially for measurements related to high-frequency activities. They thus concluded that the difference between HRV and PRV is a result of PTT variation, rather than random detection errors during pulse cycle boundary locating. They also suggested that PTT variability is specifically relevant in the HF domain, probably due to respiratory activity.

Besides, PPG signal is more sensitive to motion artifacts [33]. Researchers in [34] found that for standing up situation after walking, a moderate or exhaustive exercise in the supine position, the HRV variables did not have a general agreement that variables like RMSSD, LF, HF, etc. had a minimal agreement. The motion compensation also could not improve the agreement.

Result in [14] indicated that the difference between PRV and HRV does not result from only artifacts, noises, or random oscillations during peak detection. The delay between ECG R peak and its corresponding PPG characteristic point (PPG pulse peak, pulse onset, etc.), which is usually referred to pulse transit time (PTT), is related to pulse wave velocity and the length of vascular path from heart to the location where PPG signal is collected, and is negatively correlated with blood pressure, arterial stiffness and age [35]. The difference between PPI and RRI may due to physiological processes [21, 36], for resting subjects mainly arising from the variability in PTT. This conclusion has been demonstrated to show in some studies [37–39] and is induced by respiratory activity, which may lead to the result that PRV and HRV has a relatively high disagreement for variables that represent short term characteristics, as respiratory activity usually has a high frequency.

Moreover, the method to detect pulse cycles as well as the detected point location also impacts PRV accuracy. PRV is generated from PPI extracted from the PPG signal, and it has been discussed in [16] that the exact location of PPI depends on the definition of its boundaries and the algorithm used to detect them. The differences in PPI locations will, in turn, cause a further distinction between PRV and HRV. There are some comparative studies in [26, 58].

In [58], researchers compared the PRV and HRV agreement for PPG onset, 20% amplitude point, local maxima of PPG pulse's first derivative, 50% of total amplitude point, 80% of total amplitude point and peak point as PPI characteristic point, and got the conclusion that the most suitable location for healthy subject at rest is local maxima of pulse's first derivative, the best position for healthy subjects

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after exercise is 20% peak point, and for subjects with cardiovascular diseases (CVD) is PPG onset point.

Paper [26] compared the PRV agreement to HRV when pulses were detected using a different method. They studied the slope detection (extract the maximum slope point), peak detection and correlation detection (with a pattern representing a cardiac pulse, detect the location that the real signal has the highest correlation coefficient with the pattern) and found that slope detection has comparable results with correlation detection and both methods are better than peak detection. However, the gold standard chosen in this paper is derived by slope detection of ECG signal and may be affected by the shape of QRS complex. Furthermore, it didn't connect the discrepancies between HRV and PRV with the location information.

2.1.4 The Relationship between Pulse Transit Time and Blood Pressure

The relationship between PTT and BP has been studied by many researchers, and many models have been come up with to describe it. Paper [59] presented an arterial wall model to constitute the relationship between BP and arterial elasticity and an arterial wave propagation model to represent the relationship between arterial elasticity and PTT, with physiological conditions needed for them. They are especially suitable for measuring the relationship between PTT and diastolic BP [60, 61]. Paper [62] neglected or approximated unknown parameters, for example, the arterial wall elasticity in the previous model, and built a model that

measures the relationship between PTT and BP using the following equations:

$$BP = \frac{A}{PTT^2} + B \tag{2.1}$$

where A and B are subject-dependent parameters. Paper [63] estimated BP from PTT using the equation below:

$$\Delta BP = -\frac{2}{\gamma PTT} \cdot \Delta PTT \tag{2.2}$$

under the circumstances that if arterial wall thickness and diameter variations that correspond to BP changes can be omitted, where γ is the coefficient. Paper [64] proposed a linear approximation of the model:

$$BP = a \cdot PTT + b \tag{2.3}$$

And [65] presented a non-linear model:

$$BP = a \cdot \ln PTT + b \tag{2.4}$$

[66] provided a model that estimates BP from PTT and heart rate (HR):

$$BP = a \cdot PTT + b \cdot HR + c \tag{2.5}$$

Although involving physiological elements, estimating blood pressure from pulse transit time is feasible.

2.2 Technical Background

Heart rate variability variables are measured from ECG RR intervals (RRI) or PPG pulse-to-pulse intervals (PPI). Therefore, before running the analysis, ECG characteristic points (R peak, onset) and PPG characteristic points (pulse peak, pulse onset, and other characteristic points used for comparison) need to be extracted.
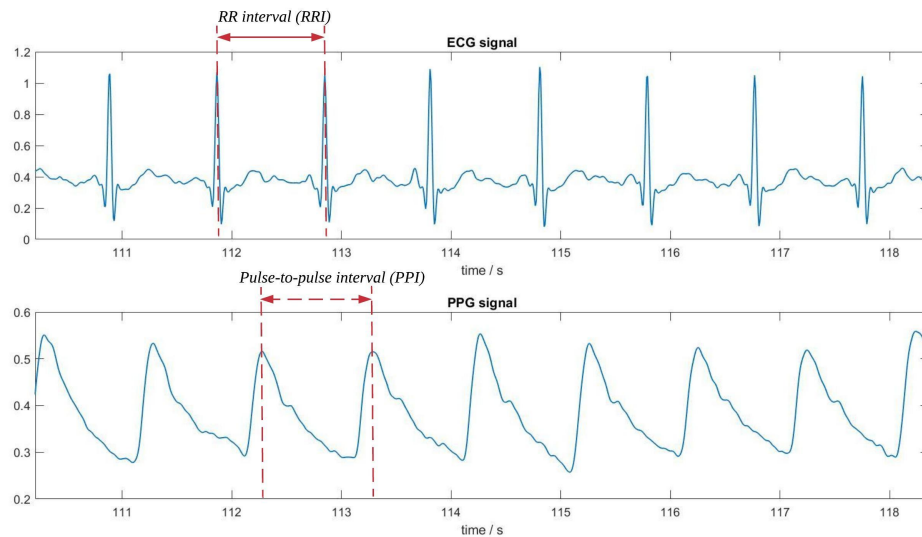
Figure 2.3: ECG RR interval and PPG pulse-to-pulse interval

A lot of detailed processes are involved in the extraction and further processing for HRV analysis. The PhysioNet Cardiovascular Signal Toolbox [44, 45] provides a variety of tools used for cardiovascular signal processing that can be used for signal preprocessing, RR interval / pulse-to-pulse interval extraction, and HRV analysis implementation.

Figure 2.4 shows the block diagram of preprocessing cardiovascular signals and calculating corresponding HRV parameters.
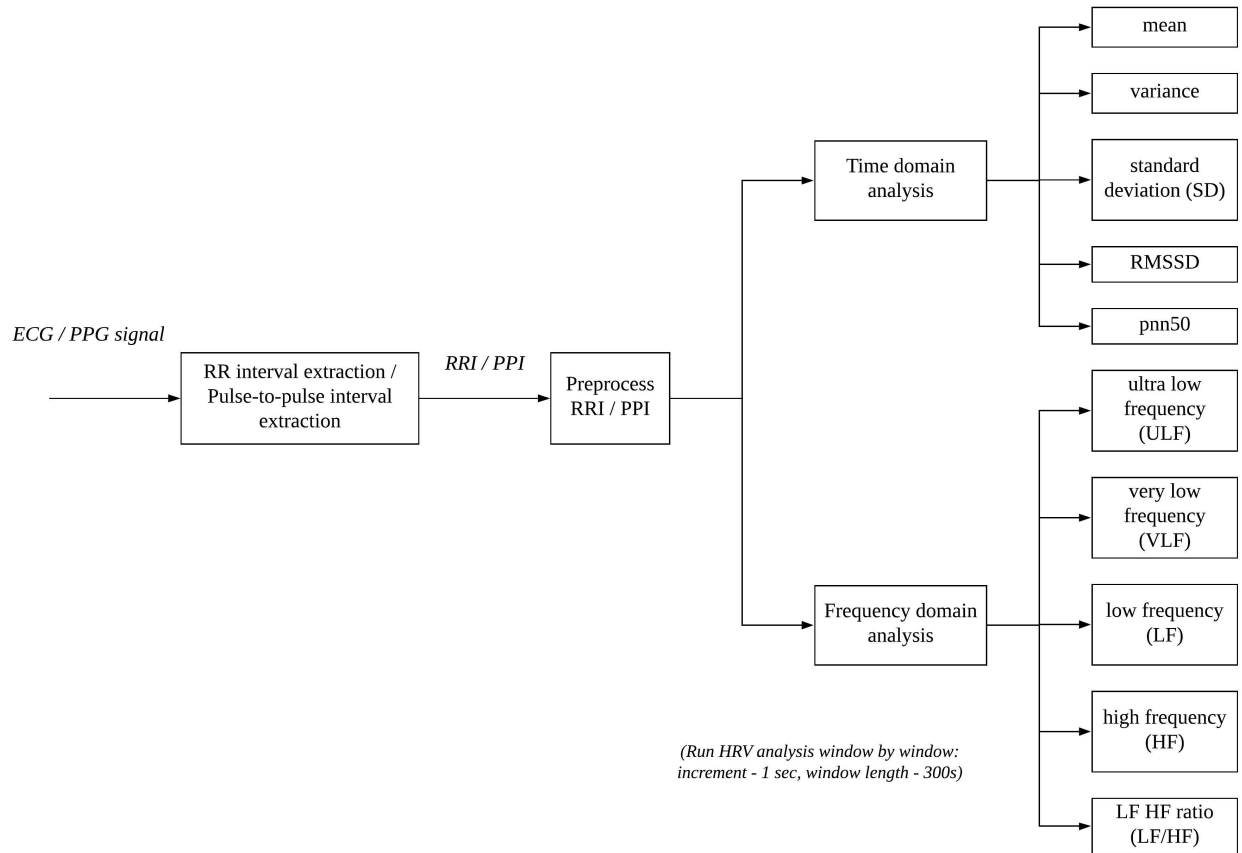
Figure 2.4: Heart rate variability (HRV) analysis process

2.2.1 Characteristic Points Extraction from ECG Signal

Before an ECG peak or onset is located, the corresponding QRS complex should be detected first so that the detection algorithm will not wrongly extract the characteristic points of the P wave or T wave. [46] provided an ECG peak detection

algorithm aiming at utilizing the slope, amplitude, and width information to detect the QRS complex. Figure 2.5 shows the block diagram, and Figure 2.6 shows one of the detection results.

The missed peaks are detected by adjusting the threshold level. Two levels of thresholds are set, and when the QRS complex has not been identified for a specific time interval, the higher threshold is replaced by the lower one in case there are missed QRS complexes. However, this technique can only be applied to regular heartbeats.
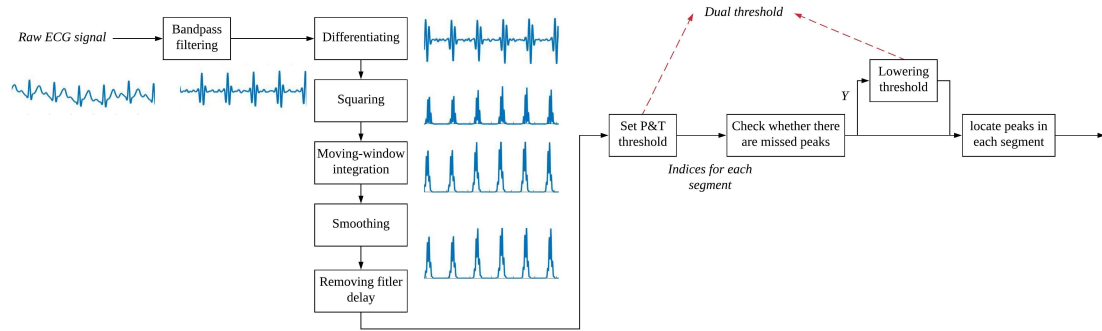
Figure 2.5: ECG signal peak detection process

Employ R peak as the characteristic point for RRI extraction will have the disadvantage that peak location tend to be affected by the morphology of QRS complexes, such as axis shifts or with abnormal patterns, which will lead to the inaccuracy of peak locations and the unreliable result for HRV analysis or ECG-blood pressure delay time studies [47].

On the contrary, onset can avoid the problem above and with the benefit that indicates the location for the beginning of ventricular excitation.
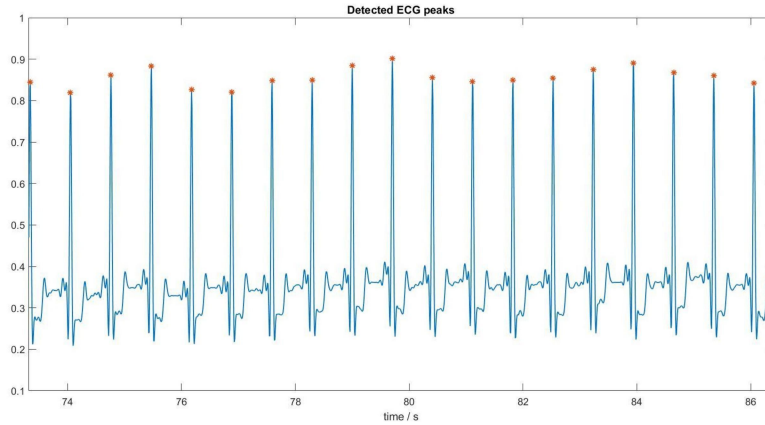
Figure 2.6: Peak detection result for ECG signal

Paper [48] exhibits a robust algorithm to detect the onset and duration of QRS complexes. It applies a curve length transform based on [49] to transfer QRS location and width information to curve length signal. Figure 2.7 shows the block diagram, and Figure 2.8 shows one detection result.

2.2.2 Characteristic Points Extraction from PPG Signal

Typical PPG pulse wave can be divided into two parts, the rising part, which is referred to as anacrotic phase, and the subsequent decreasing part, which is referred to as catacrotic phase [20].

Corresponding to each RR interval of the ECG signal, which is considered the "true" instantaneous heart cycle length, the pulse-to-pulse interval in the PPG signal also represents the heart cycle length. The exact position of PPI depends on the definition of its boundary and the algorithm used to detect it [16]. Three options
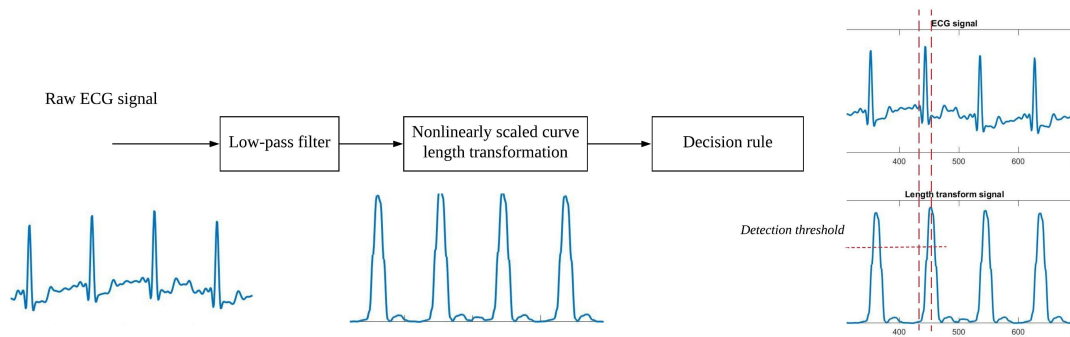
Figure 2.7: ECG signal onset detection process: ECG signal is transferred to a curve length transformed signal through integrating the signal slope information. After the curve length transformation, pulses are located using a threshold. The corresponding onset point of each pulse is found around the threshold crossing point of each pulse.
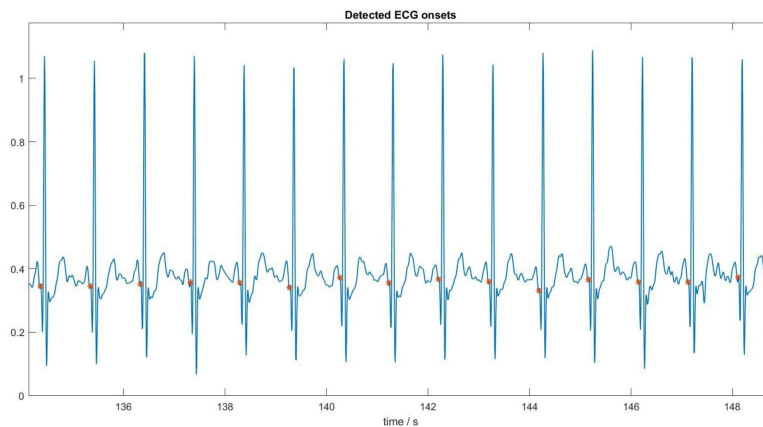
Figure 2.8: Onset detection result for ECG signal

that can be used as the boundary point of PPI: the beginning of the anacrotic or the catacrotic phase, that is, the onset point or the peak point of pulse, and the

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maximum first derivative point, which represents the steepest part of the upstroke [20]. There are some comparative studies in [50, 51].

[43] proposed a PPG pulse onset detection method, which applies a windowed and weighted slope sum function to detect pulse and extract features.

Figure 2.9 shows the onset detection process and Figure 2.10 shows one detection result.
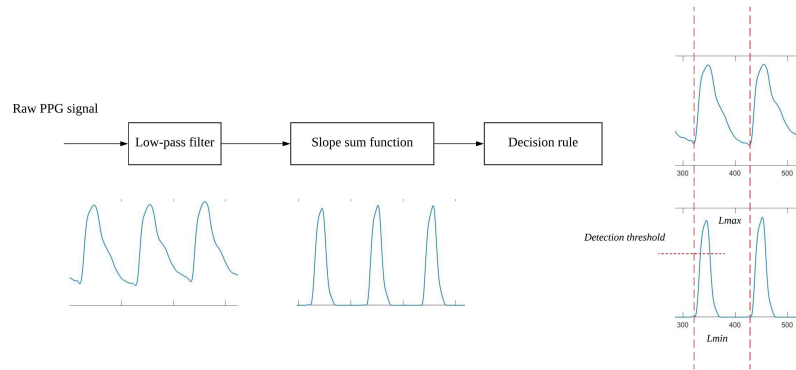
Figure 2.9: PPG onset point detection process
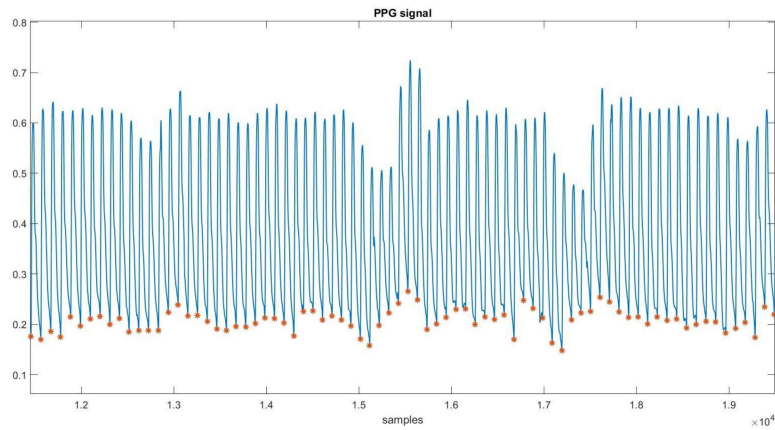
Figure 2.10: Onset detection result for PPG signal

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This method is used to extract the onset point of PPG pulses. Due to the shape of pulses, the peak of each pulse is located at the highest point between two adjacent onsets.
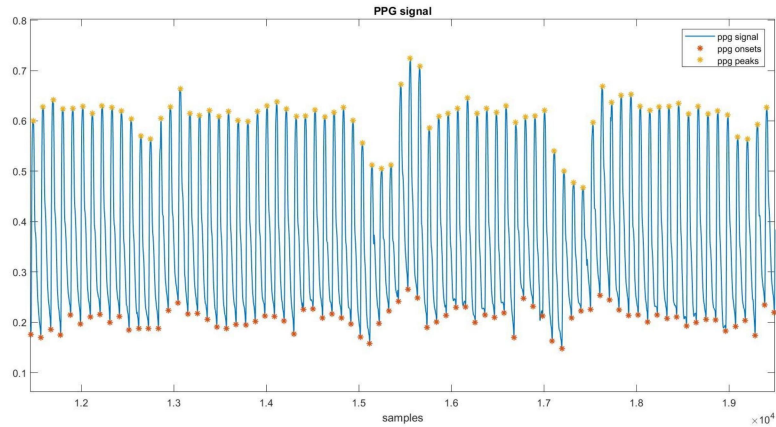
Figure 2.11: Peak detection result for PPG signal

With the lowest point and highest point of each pulse, other characteristic points that locate on the slope can be extracted correspondingly.
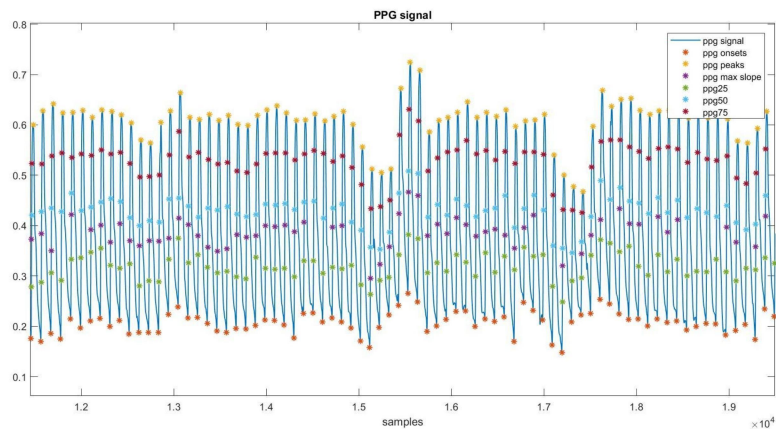
Figure 2.12: Other characteristic points detection result for PPG signal

2.2.3 Calculation of Signal Quality Index

Signal quality analysis is used to assess whether reliable heart rates can be obtained from ECG and PPG signals collected using wearable sensors. Several studies have introduced different signal quality indices (SQIs) to evaluate the cardiovascular signal quality and discussed its application to the reduction of false alarm in the intensive care unit (ICU) [52–55]. In this thesis, to reserve high-quality segments that can be used to extract reliable HRV variables, the signal quality indices for ECG and PPG signal are calculated before implementing HRV analysis.

2.2.3.1 ECG SQI Calculation

The following SQIs are introduced in previous researches [52–54]:

Table 2.3: Commonly used signal quality index (SQI)

Name	Description	Calculation	Evaluation criterion
kSQI	The fourth moment (kurtosis) of the signal	$kSQI = E[\frac{(X-\mu)^4}{\sigma^4}]$	Expect the good ECG to be highly non-Gaussian
sSQI	The third moment (skewness) of the signal	$sSQI = E[\frac{(X-\mu)^3}{\sigma^3}]$	Expect ECG to be highly skewed
pSQI	The relative power in the QRS complex	$pSQI = \frac{\int_{5Hz}^{15Hz} P(f)df}{\int_{5Hz}^{40Hz} P(f)df}$	Expect most of the power to be in the 5 - 15 Hz band

bSQI	The fraction of beats detected by one QRS detection method that are matched with beats detected by another QRS detection method
rSQI	The ratio of the number of beats detected by two QRS detection method

As ECG QRS complex detection has been performed using two different methods, one is the P&T method in Chapter 2.1.1 [46] and another one is using curve length transform in Chapter 2.1.2 [48], and P&T method is less sensitive to noise than the one using curve length transform [55], the difference between their detection results indicates the noise of signal. Thus, in the PhysioNet toolbox, $bSQI$, which calculates the ratio of beats detected by two detection methods synchronously, is applied.

2.2.3.2 PPG SQI Calculation

Paper [56] proposes a PPG signal quality assessment method using dynamic time warping (DTW), multiple-template matching, and a heuristic fusion algorithm. This method first builds a PPG interval dynamic template by detecting and averaging the regular intervals in a 30-sec window in which the PPG signal is segmented to intervals by their onset points. Then the correlation coefficient between each PPG interval and this template is calculated. As intervals in PPG signal changes in length, this paper applies several methods to fit the interval with the template: direct correlation (extract the segment that begins at the characteristic point and

with the same length of template), linear interpolation and resampling of the segment to match the template, and the dynamic time warping (DTW) to stretch the nonlinear time-base and trace an optimal path to minimize the cumulative distance between the beat and the template.

The results of these signal quality measurements are all on a scale of 0 to 1, where approaching one is with high signal quality and approaching 0 is with poor signal quality. The signal quality of PPG pulses is determined by the mean value of the three results.

2.3   Data Preprocessing

2.3.1   Database

This thesis aims at comparing the agreement between ECG signal generated HRV and PPG signal derived PRV concerning different ECG and PPG characteristic points, as well as discussing the possibility of using arterial blood pressure information to refine PRV and increase its agreement to HRV. The PhysioNet's Medical Information Mart for Intensive Care (MIMIC) III [57], which is collected from bedside patient monitors in intensive care units (ICU) is applied as a source for ECG, PPG, and arterial blood pressure (ABP) signal.

2.3.2   Preprocessing Progress

99 data sessions from 20 subjects with cardiovascular disease (CVD), while all of them with arterial blood pressure signal, 103 data sessions from 19 subjects

not with cardiovascular disease (Non-CVD), and 85 data sessions from 19 non-CVD subjects with arterial blood pressure signal are used, and for each sample, after passing low-pass filter, it is divided to 5-min segments and segments with high-quality ECG and PPG signal are preserved for characteristic points comparison, while segments with high-quality ECG, PPG, and ABP signal are preserved for PRV refinement.

According to the signal quality calculation criterion mentioned above, if 85% of the cycles have high quality for the 5-min segment's ECG and PPG, as well as the ABP signal if needed, then this segment is considered high quality and could be used for the following analysis.

The preprocessing block diagram is shown below:
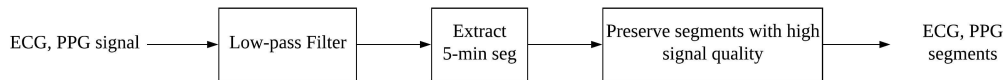
Figure 2.13: Block diagram of preprocessing raw data

Chapter 3: Comparison of PPG Characteristic Points

The definition of ECG RR intervals and PPG pulse-to-pulse intervals varies if using different characteristic points as the boundary point of intervals. Generally, the agreement between corresponding HRV and PRV using different characteristic points to generate RRI or PPI also changes. Studies have discussed the differences caused by the locations of PPG pulse-to-pulse intervals [26, 58]. However, [26] only focused on the comparison results using different pulse detection methods. Although different detection methods detect different pulse characteristic points, this paper didn't focus on the location in detail. For another study in [58], it compared the agreement using different PPG characteristic points. However, it didn't delve into the PPG signals to discuss why there will be such results.

Therefore, in this chapter, PRV's agreement to ECG peak generated HRV using 6 different characteristic points: onset point, 25% of maximum amplitude point, 50% of maximum amplitude point, 75% of maximum amplitude point, maximum slope (local maxima of pulse's first derivative) and peak point, will be compared and discussed. Also, for comparison, ECG onset points generated HRV will also be calculated and used for PRV and HRV comparison. The dataset is divided into subjects with cardiovascular diseases (CVD subjects) and subjects without cardio-

vascular diseases (Non-CVD subjects) and the agreement between PRV and HRV will be calculated separately to observe the difference.
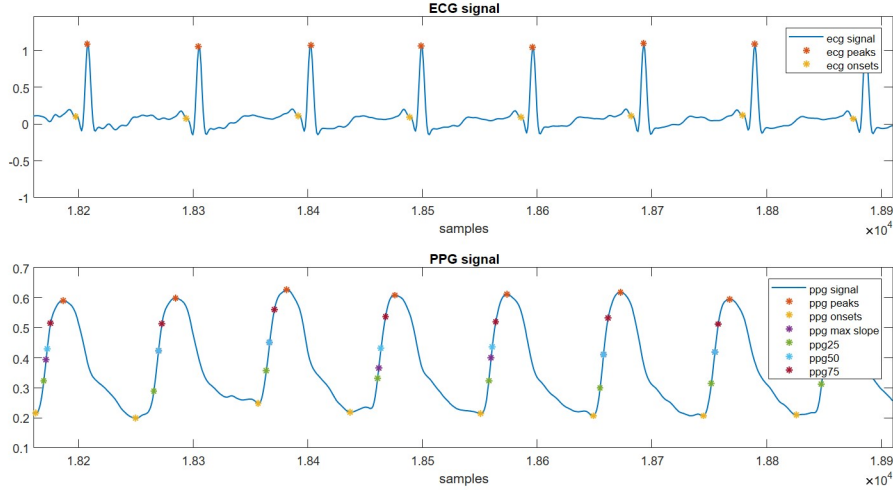
Figure 3.1: Different characteristic points for ECG and PPG signal

Figure 3.2 is the block diagram of the comparison process. PPI and RRI indicate the interbeat interval signal extracted from the ECG and PPG signal respectively.

3.1 Signal Preprocessing

3.1.1 Calculation of Interbeat Interval Signals

The characteristic points of ECG and PPG signal are extracted first and are then used to generate interbeat interval (IBI) signals.

Suppose there are two cardiac signals: the ECG signal $signal_{ECG}(i)$ and the PPG signal $signal_{PPG}(i)$. The characteristic points of ECG QRS complex and PPG
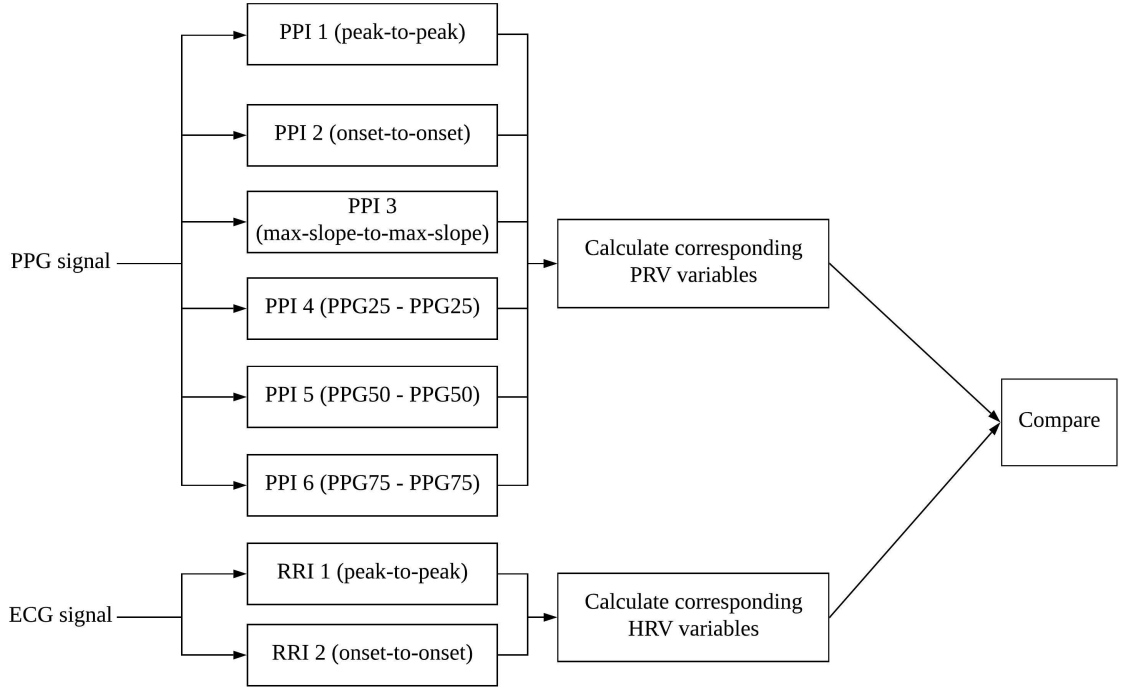
Figure 3.2: Block diagram for PRV and HRV comparison

pulse are extracted (take peak points as example): $peak_{ECG}(n), n = 1, 2, ..., N_1$, where N_1 is the number of peaks detected in this ECG segment, and $peak_{PPG}(n), n = 1, 2, ..., N_2$, where N_2 is the number of peaks detected in this PPG segment.

The IBI signals are calculated correspondingly:

$$IBI_{ECG}(n) = peak_{ECG}(n+1) - peak_{ECG}(n), n = 1, 2, ..., N_1 - 1 \qquad (3.1)$$

$$IBItime_{ECG}(n) = peak_{ECG}(n+1), n = 1, 2, ..., N_1 - 1 \qquad (3.2)$$

$$IBI_{PPG}(n) = peak_{PPG}(n+1) - peak_{PPG}(n), n = 1, 2, ..., N_2 - 1 \qquad (3.3)$$

$$IBItime_{PPG}(n) = peak_{PPG}(n+1), n = 1, 2, ..., N_2 - 1 \qquad (3.4)$$

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where $IBI(n)$ for ECG and PPG signal is the length of each cycle or each cardiac interval, the boundary of which is indicated by the characteristic point used, and $IBItime(n)$ is the corresponding time of each interval. When calculating HRV or PRV, intervals within a time window are utilized.

Figure 3.3 and Figure 3.4 show the $IBI(n)$ extracted from the ECG signal and PPG signal.
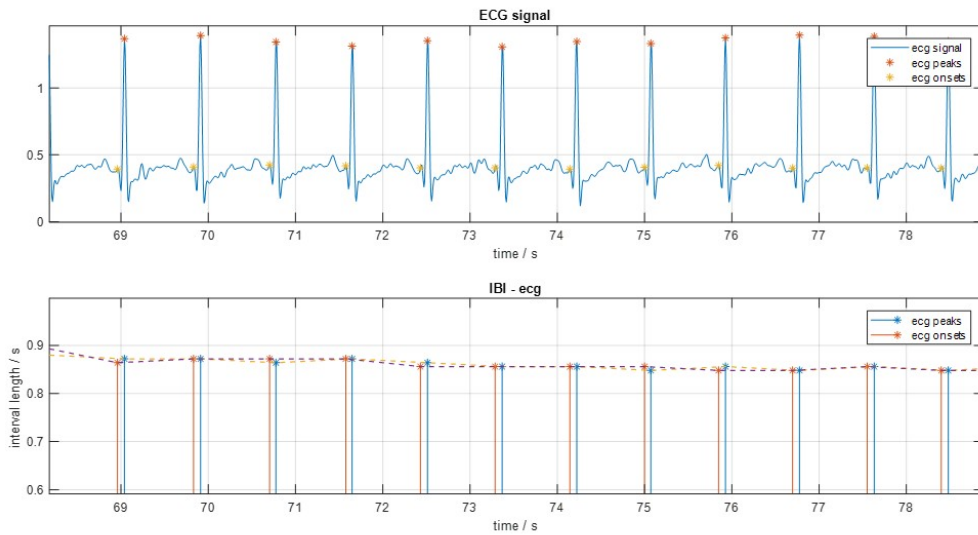
Figure 3.3: Interbeat interval (IBI) signal extracted from ECG signal

3.1.2 Preprocessing of Raw Interbeat Interval Signals

IBI signals will be preprocessed before running HRV analysis and calculating HRV and PRV variables. Each interval represents one cardiac cycle in ECG and PPG signal. Figure 3.5 shows the block diagram of preprocessing raw IBI signals.

Preprocessing IBI signal is to ensure the ECG IBI signal and PPG IBI signal are synchronized, that is, for each ECG interbeat interval and PPG interbeat in-
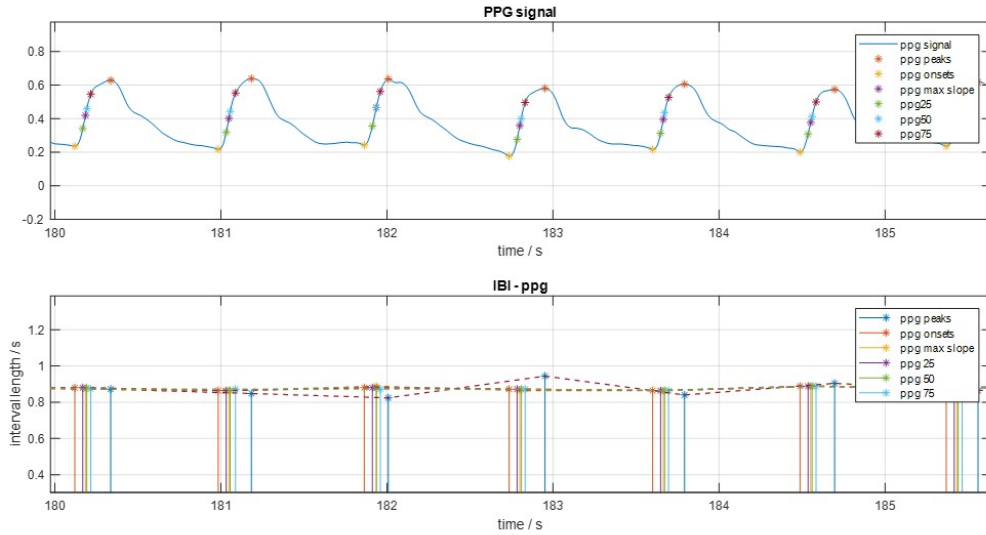
Figure 3.4: Interbeat interval (IBI) signal extracted from PPG signal
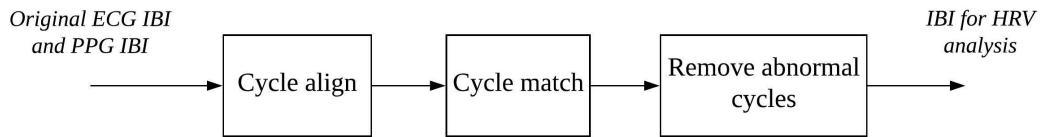
Figure 3.5: Preprocessing raw interbeat intervals (IBI) signal

terval, they correspond to the same cardiac cycle. To explain in detail, this means that it's the same cardiac cycle that causes the changes in ECG signal, transports through the vascular path from heart to the point where PPG is gathered and finally induces variations in the PPG signal.

The alignment is done first by shifting the IBI locations ($IBItime(n)$) in a limited range and finding the shift index that PPG IBI locations ($IBItime_{PPG}(n)$) with the lowest mean-squared error to the ECG IBI locations ($IBItime_{PPG}(n)$). This process is used to reduce the misalignment between ECG and PPG signal that

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may be due to measurement errors.

Then, each ECG interval is matched with its corresponding PPG interval by searching the PPG intervals within a time window around it and the PPG interval that has the minimum distance preserved. As a result, extra pulses in the PPG signal caused by noises, disturbances, or measurement issues will be excluded from heart rate variability analysis.

The last step of preprocessing is to remove abnormal beats in the ECG signal and PPG signal. Intervals that are too small or too large (smaller or larger than a given lower limit or upper limit), intervals that change over a percentage compared to the median value of adjacent five intervals, which can all be considered as unphysiological, will be removed. The parameters used for identifying abnormal intervals are from the PhysioNet toolbox [44, 45]. Finally, the normal intervals in ECG and PPG signal can be used for heart rate variability analysis.

Figure 3.6 indicates the result of each step.

3.2 Comparison of Pulse Rate Variability and Heart Rate Variability

With the normal interbeat intervals from ECG and PPG signal, HRV analysis is run for each segment using a sliding analysis window. The window length is 10 seconds, and the increment of the window is 1 second. Therefore, the total number of analysis windows is $\frac{seg\_length-(window\_length-increment)}{increment}$, which is around 290 for a 5-min segment.

Then the HRV or PRV variables are calculated. Each analysis window will
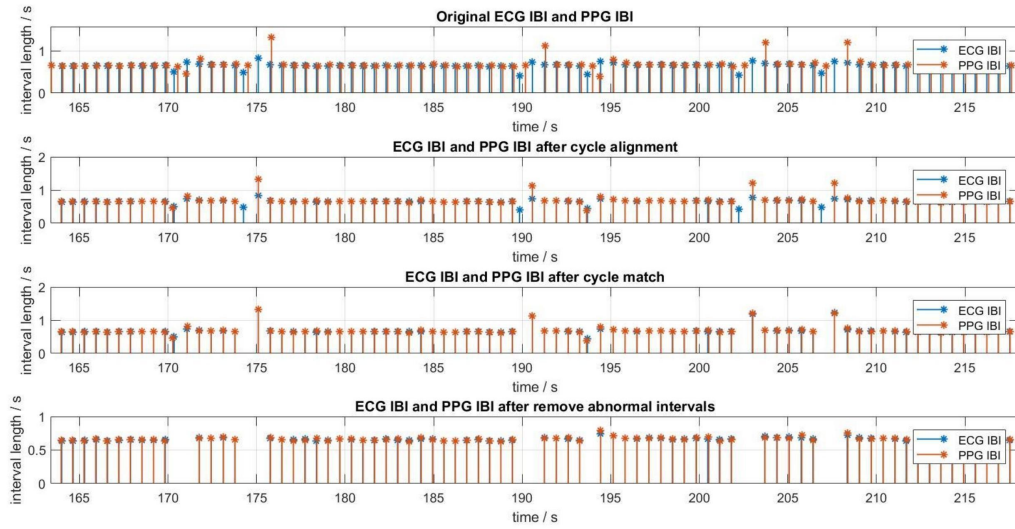
Figure 3.6: Interbeat interval (IBI) plot after each preprocessing step

generate one value for each HRV variable, and each HRV variable will finally form an array, the length of which is the number of analysis windows, reflecting the cardiac system status over time and can be used for analysis and comparison.

In the following part of this section, the HRV and corresponding PRV variables will be calculated and the results of using different PPG characteristic points: PPG onset, PPG 25% point, PPG 50% point, PPG 75% point, PPG max slope point, and PPG peak, will be compared and discussed in detail. As a reference, the difference between the ECG IBI series and PPG IBI series generated from different characteristic points will also be calculated and compared.

3.2.1 Statistical Methods for Comparison

The agreement between ECG and PPG interbeat intervals and the correspond-
ing HRV and PRV variables is evaluated using the Pearson correlation coefficient
(PCC) and normalized root-mean-square error (NRMSE).

Pearson correlation coefficient between sample x and sample y, usually repre-
sented by $r_x y$, is calculated using the following formula:

$$r_x y = \frac{\sum_{i=1}^{n}(x_i - \bar{x})(y_i - \bar{y})}{\sqrt{\sum_{i=1}^{n}(x_i - \bar{x})^2}\sqrt{\sum_{i=1}^{n}(y_i - \bar{y})^2}} \qquad (3.5)$$

where n is the sample size, x_i, y_i are samples, $\bar{x} = \frac{1}{n}\sum_{i=1}^{n} x_i$ is the sample mean,
which is the same for $\bar{y}$.

$r_x y$ has a value ranging from +1 to -1 and measures the correlation between
sample x and sample y, where $+1$ means positive linear correlation, -1 means
negative linear correlation and 0 means no linear correlation.

For our PRV and HRV agreement measurement, the closer the Pearson corre-
lation coefficient approaching 1 or -1, the more the PRV variable is correlated with
the HRV variable through the analysis windows.

Normalized root-mean-square error (NRMSE) is used to compare samples with
different scales. It is calculated as below:

$$NRMSE(x, y) = \frac{RMSE}{\bar{x}} = \frac{\sqrt{\frac{\sum_{i=1}^{n} n(x-y)^2}{n}}}{\bar{x}} \qquad (3.6)$$

where x is the reference sample. The NRMSE is expressed as a percentage, and
smaller values represent less residual variance.

When comparing PRV and HRV variables, as well as IBI signals, the lower the NRMSE, the smaller the difference between ECG variables and PPG variables.

3.3   Comparison Result of Subjects with Cardiovascular Diseases (CVD)

There are 1578 5-min segments extracted from the cardiac signals of subjects with cardiovascular diseases.

3.3.1   Interbeat Interval Signal Comparison

For each PPG characteristic point, it will generate an interbeat interval array, the size of which is the number of intervals and the value of which is the length of intervals. The array is then compared with the ECG IBI array by calculating mean PCC and mean NRMSE over all of the 5-min segments.

Table 3.1 and Table 3.2 show the comparison result of ECG and PPG IBI signals:

Table 3.1: PCC and NRMSE between ECG IBI and PPG IBI (ECG peaks) for CVD subjects

	PP	PO	PM	P25	P50	P75
mean PCC	0.4010	0.2706	0.3534	0.3525	0.3704	0.3709
mean NRMSE	0.0272	0.0444	0.0312	0.0266	0.0246	0.0248

where the meaning of abbreviations in the headline of tables is that P represents peaks, O represents onsets, M represents max slope points, 25 represents the 25% of max amplitude points, 50 represents the 50% of max amplitude points, and 75 represents the 75% of max amplitude points. The first letter corresponds to the ECG

Table 3.2: PCC and NRMSE between ECG IBI and PPG IBI (ECG onsets) for
CVD subjects

	OP	OO	OM	O25	O50	O75
mean PCC	0.3603	0.2408	0.3156	0.3182	0.3321	0.3283
mean NRMSE	0.0287	0.0456	0.0328	0.0283	0.0265	0.0269

signal characteristic point used for comparison, and the second letter indicates the PPG characteristic point used for comparison. Therefore, for example, PP indicates the comparison between ECG peak-derived IBI and PPG peak-derived IBI and PO indicates the comparison between ECG peak-derived IBI and PPG onset-derived IBI.

Figure 3.7 shows the plot of the mean PCC and NRMSE of different comparisons.
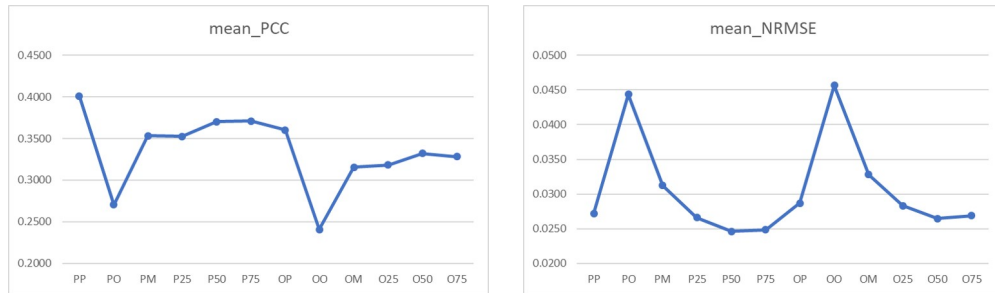
Figure 3.7: Agreement comparison of different ECG and PPG characteristic points
for CVD subjects - (left) mean PCC, (right) mean NRMSE

From the calculated mean PCC and mean NRMSE between different ECG and PPG characteristic points, a preliminary conclusion can be reached that PPG peak-derived IBI has the highest mean PCC, and that is followed by PPG 50% points, PPG 75% points, PPG 25% points and PPG max slope points, while PPG onset-derived IBI has the lowest mean PCC. There is a slight difference concerning mean NRMSE. PPG 50% points, PPG 75% points, and PPG 25% points have comparable and the smallest mean NRMSE among all PPG characteristic points,

which are followed by PPG peaks, PPG max slope points, and PPG onsets-derived IBI has the largest mean NRMSE when comparing with ECG IBI.

When considering the difference between ECG peaks and ECG onsets, it is relatively small compared to the discrepancies between PPG characteristic points. However, the plots and data still indicate the ECG peak-derived IBI has higher mean PCC and lower mean NRMSE than ECG onset-derived IBI when comparing with PPG IBIs, which means that PPG-derived IBIs are more approaching to ECG peak-derived IBI rather than ECG onset-derived IBI.

Figure 3.8 - Figure 3.13 exhibit the different PPG IBI signals comparing with the ECG peak-derived IBI signal of one sample, and visualize the difference of PPG characteristic points and the discrepancies between the PPG IBI signal and ECG IBI signal using plots.
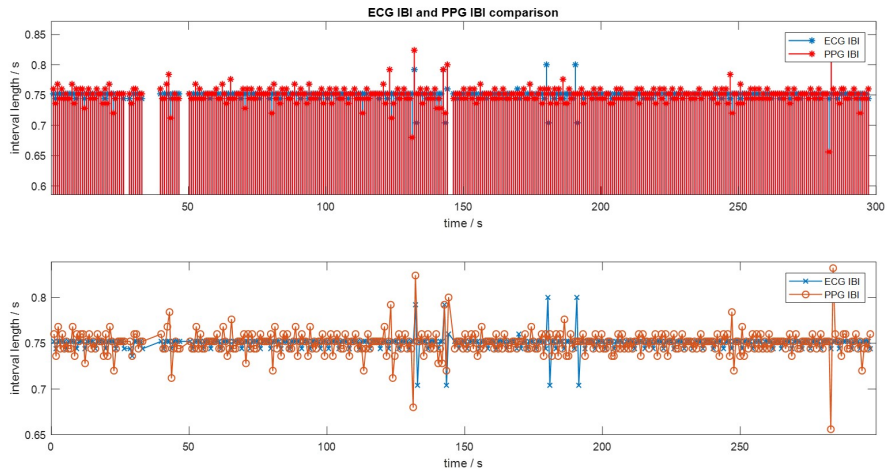
Figure 3.8: Comparison of ECG peak-derived IBI and PPG peak-derived IBI for CVD subjects: NRMSE = 0.0188, PCC = 0.1801

While ECG IBI signal has a relatively low variation, PPG IBI signal obtained from different characteristic points has different agreement to ECG IBI signal. The distinctions between the ECG IBI and PPG IBI signal will lead to the disagreement between HRV and PRV variables.
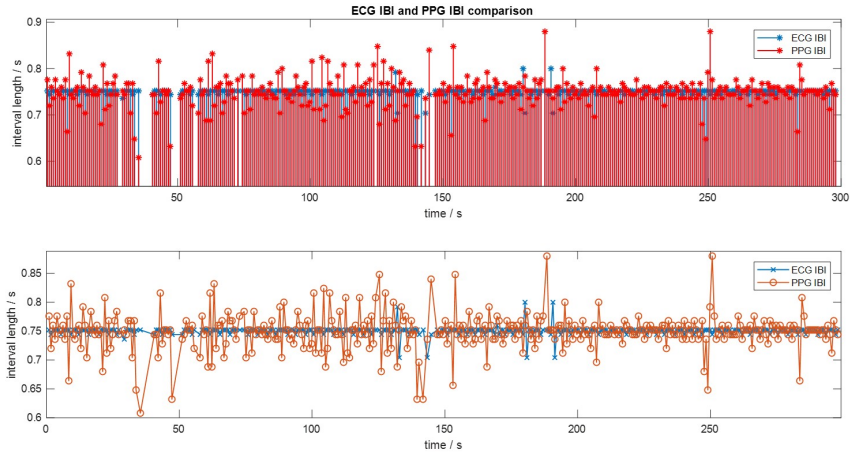
Figure 3.9: Comparison of ECG peak-derived IBI and PPG onset-derived IBI for CVD subjects: NRMSE = 0.0442, PCC = -0.0503
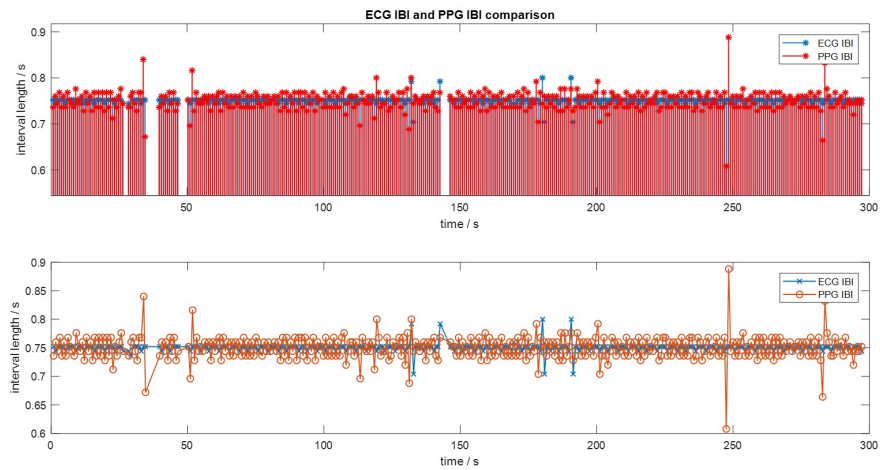
Figure 3.10: Comparison of ECG peak-derived IBI and PPG max slope points derived IBI for CVD subjects: NRMSE = 0.0291, PCC = 0.0893

3.3.2 Heart Rate Variability and Pulse Rate Variability Variables Comparison

The ECG IBI and PPG IBI signal are then used to calculate HRV variables and PRV variables. The calculation for each variable will generate an array that contains the value of the variable and the length of which is the number of analysis
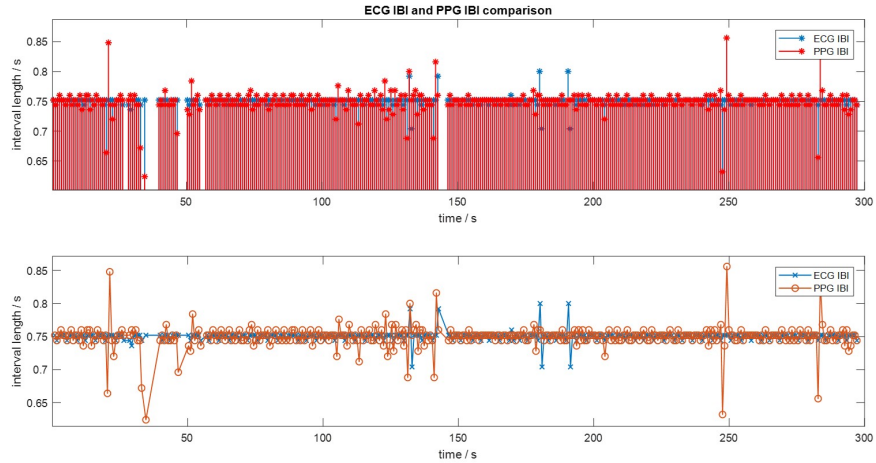
Figure 3.11: Comparison of ECG peak-derived IBI and PPG 25% max amplitude points derived IBI for CVD subjects: NRMSE = 0.0252, PCC = 0.0877
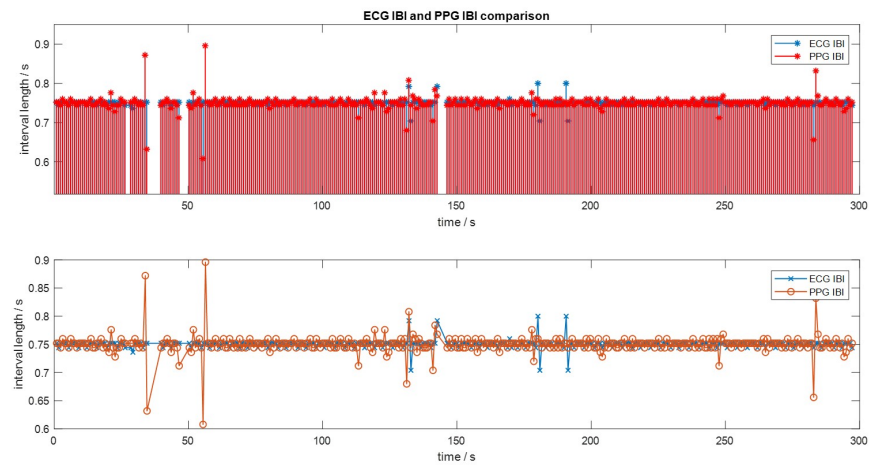
Figure 3.12: Comparison of ECG peak-derived IBI and PPG 50% max amplitude points derived IBI for CVD subjects: NRMSE = 0.0247, PCC = 0.1083

windows used for HRV analysis. These arrays from the ECG signal and the PPG signal are compared by the PCC and NRMSE between each other.

Table 3.3 and Table 3.4 show the comparison result of time domain variables for HRV measurements.
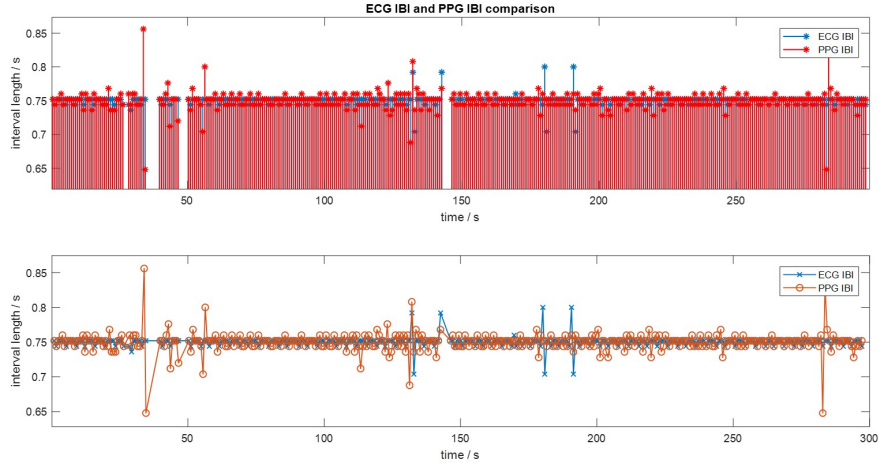
Figure 3.13: Comparison of ECG peak-derived IBI and PPG 75% max amplitude points derived IBI for CVD subjects: NRMSE = 0.0197, PCC = 0.172

Table 3.3: Mean PCC between time domain variables of HRV and PRV derived from different characteristic points for CVD subjects

mean PCC	mean	variance	SD	RMSSD	pnn50
PP	0.6376	0.4983	0.5011	0.4702	0.5255
PO	0.5755	0.3158	0.3256	0.2937	0.3261
PM	0.6289	0.4433	0.4494	0.4066	0.4609
P25	0.6230	0.4497	0.4664	0.4414	0.5201
P50	0.6308	0.4894	0.5026	0.4753	0.5499
P75	0.6378	0.4858	0.4993	0.4723	0.5461
OP	0.6359	0.4787	0.4800	0.4462	0.4828
OO	0.5775	0.3261	0.3321	0.2963	0.3168
OM	0.6240	0.4410	0.4422	0.3964	0.4317
O25	0.6183	0.4369	0.4474	0.4224	0.4839
O50	0.6288	0.4728	0.4806	0.4540	0.5146
O75	0.6332	0.4693	0.4766	0.4476	0.5056

Table 3.4: Mean NRMSE between time domain variables of HRV and PRV derived from different characteristic points for CVD subjects

OP	0.0044	17.3129	1.9615	2.1144	11.3032
OO	0.0073	39.1696	4.0219	4.3488	16.6480
OM	0.0045	17.9801	2.4335	2.7122	9.8592
O25	0.0045	14.6052	1.8605	1.9747	8.3048
O50	0.0042	11.5316	1.5988	1.6893	7.8069
O75	0.0041	11.5822	1.5975	1.7036	7.7847

where the notations are the same as mentioned in section 3.3.1.

Figure 3.14 presents the plot of mean PCCs and mean NRMSEs.

Figure 3.14: Agreement comparison of time domain variables for CVD subjects - (left) mean PCC, (right) mean NRMSE

During IBI signal comparison, when comparing with ECG peak derived IBI signal, PPG IBI signal has higher mean PCC and lower mean NRMSE than comparing with ECG onset derived IBI signal. When considering PRV variables, comparing with ECG peak derived HRV has higher mean PCC but also higher mean NRMSE.

For PPG characteristic points, peaks, max slope points, 25% max amplitude points, 50% max amplitude points and 75% max amplitude points tend to have a similar scale of PCC for the mean length of pulse-to-pulse intervals, while onsets have relatively lower PCC comparing to other characteristic points for this variable. The

mean NRMSEs of mean pulse-to-pulse interval length for six characteristic points are similar and all very low. This result is due to the reason that for the PPG signal, the mean interval length has a high agreement to that of the ECG signal. Therefore, the difference in mean interval length among using these characteristic points are relatively small.

The value of other variables differs on a comparatively large scale. For variables except for pnn50, peak-derived PRV has a larger mean PCC than other characteristic points, which is followed by that of 75% max amplitude point and 50% max amplitude point, and then 25% max amplitude point and max slope point. Onset-derived PRV has the lowest mean PCC. For pnn50, PRV from 50% max amplitude point and that from 75% max amplitude point have a higher agreement to the pnn50 values of HRV than other characteristic points. While PRV from the peak and 25% max amplitude point have less high mean PCC values, this is followed by that of max slope point, and onset derived PRV still has the lowest mean PCC for this variable.

The performance of different characteristic points for mean NRMSE is relatively similar to that for mean PCC among other time domain variables. Generally, 25% max amplitude point of PPG pulse, 50% max amplitude point, and 75% max amplitude point have the lowest mean NRMSE among all PPG characteristic points. Peak and max slope point have slightly higher mean NRMSE comparing to them, and PRV variables calculated from PPG onsets have the highest mean NRMSE.

In general, for time domain variables, peak, 50% max amplitude point and 75% max amplitude point derived PRV have the highest agreement to that of HRV

calculated from ECG signal, and that from PPG onsets has the lowest agreement.

Then the frequency domain variables are calculated and compared. Table 3.5 and Table 3.6 display the detailed results.

Table 3.5: Mean PCC between frequency domain variables of HRV and PRV derived from different characteristic points for CVD subjects

mean PCC	ULF	VLF	LF	HF	LF/HF
PP	0.4496	0.4538	0.5133	0.4975	0.3135
PO	0.3001	0.3045	0.3656	0.3231	0.2665
PM	0.4021	0.4063	0.4763	0.4374	0.2536
P25	0.3925	0.3973	0.4623	0.4477	0.3351
P50	0.4128	0.4172	0.4790	0.4776	0.3441
P75	0.4178	0.4226	0.4880	0.4801	0.3420
OP	0.4292	0.4342	0.5038	0.4768	0.2915
OO	0.2984	0.3033	0.3700	0.3302	0.2456
OM	0.3880	0.3930	0.4688	0.4329	0.2355
O25	0.3664	0.3714	0.4412	0.4345	0.3129
O50	0.3855	0.3907	0.4598	0.4602	0.3140
O75	0.3843	0.3896	0.4654	0.4637	0.3087

Table 3.6: Mean NRMSE between frequency domain variables of HRV and PRV derived from different characteristic points for CVD subjects

mean NRMSE	ULF	VLF	LF	HF	LF/HF
PP	49.8524	50.4746	41.5769	17.6052	1.9991
PO	98.9788	100.7254	91.0357	40.8598	2.0033

PM	54.8596	55.7823	47.7263	17.6654	2.2715
P25	50.4989	51.4471	45.5944	16.1969	1.9385
P50	41.7894	42.4781	35.0760	13.0803	1.9699
P75	42.9430	43.5054	36.2208	13.4670	1.9603
OP	43.5685	44.1312	34.4166	16.1770	1.9514
OO	87.9111	89.2593	77.3221	38.1688	1.9398
OM	44.0152	44.6965	37.2984	16.0404	2.1222
O25	38.2392	38.7465	31.8380	14.0561	1.9008
O50	34.5933	35.0309	26.3336	11.1794	1.9412
O75	33.4328	33.9072	26.2551	11.3596	1.9347

where the notations are the same as mentioned before.

Figure 3.15 presents the plot of mean PCCs and mean NRMSEs.
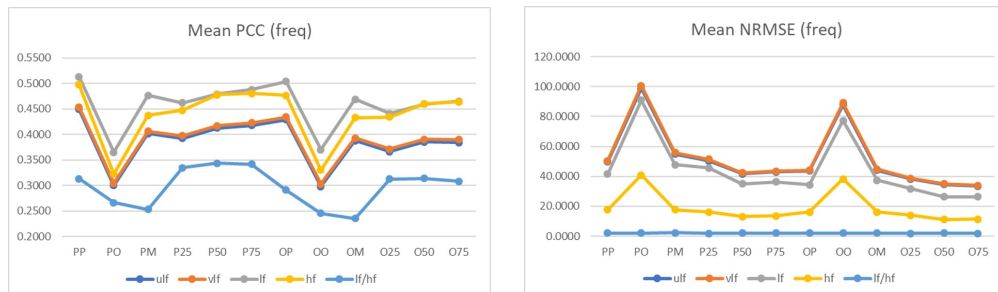
Figure 3.15: Agreement comparison of frequency domain variables for CVD subjects
- (left) mean PCC, (right) mean NRMSE

From frequency domain variables, the mean PCC of comparing with ECG peak-generated HRV is slightly higher than that of comparing with ECG onset-generated HRV, and the mean NRMSE is higher as well.

Comparing the mean PCC of frequency domain variables, except for LF/HF,

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peak-derived PRV has the highest mean PCC, and max slope point, 25% max amplitude point, 50% max amplitude point and 75% max amplitude point have relatively lower PCC, while onset-derived PRV variables have the least correlation to HRV variables. For LF/HF, 25% max amplitude point, 50% max amplitude point, 75% max amplitude point derived PRVs all have high mean PCC, and the mean PCC of peak derived PRV is comparatively lower. Onset and max slope point derived PRV have the lowest mean PCC among all characteristic points.

The mean NRMSE of LF/HF remains small and similar for all PPG characteristic points. Meanwhile, the mean NRMSE of other frequency domain variables ranges on a large scale and differs among characteristic points. 50% max amplitude point derived PRV and 75% max amplitude point derived PRV have the lowest mean NRMSE, and the mean NRMSE of peak, 25% max amplitude point and max slope point derived PRV is higher than that. Onset has the highest mean NRMSE among all of the PPG characteristic points.

3.3.3   Result Analysis

The agreement between PRV and HRV for subjects with cardiovascular diseases (CVD) is relatively low, indicating by the low mean PCC and the high mean NRMSE that with many values greater than 1. This finding is due to the HRV characteristic of this situation as reduced HRV is usually associated with cardiovascular diseases. Besides, the interval length variance of the ECG signal only depends on cardiac status, while the interval length variance of the PPG signal will also

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be affected by pulse transit time variance, random noises during pulse transfer and detection noises. The variables that involve interval length variation, such as variance, SD, RMSSD in the time domain, LF, HF in the frequency domain, will have larger values in PRV variables calculation. Furthermore, as HRV for CVD subjects decreases, the interval length variation in the ECG signal is relatively low. Therefore, the variables regarding interval length change will have small values in HRV analysis. The relatively low amount of HRV variables and the relatively large value of PRV variables cause the small mean PCC and large mean NRMSE among all characteristic points.

Below are two examples that could represent the situation when ECG interval length variation is low and when ECG interval length variation is high.
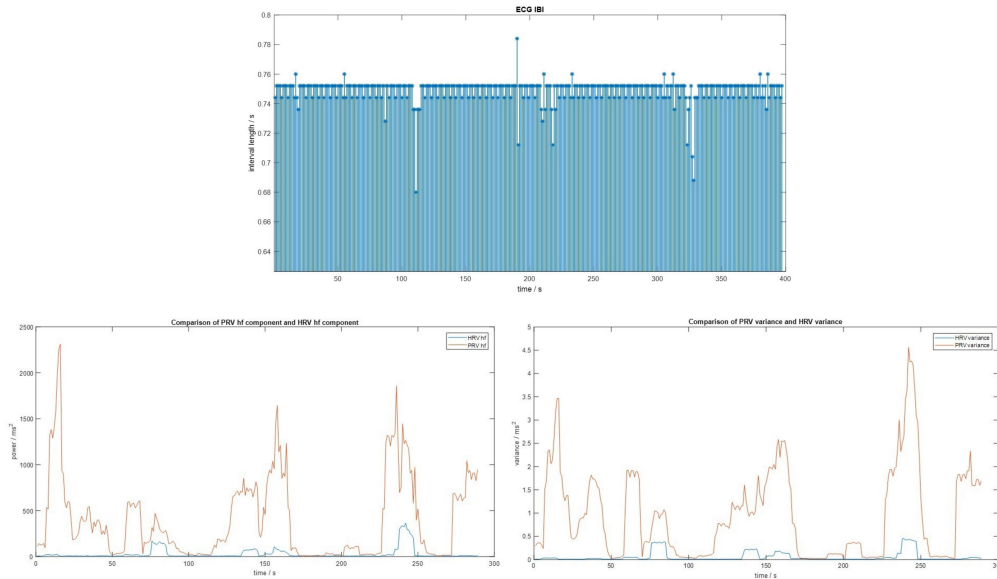
Figure 3.16: Comparison of PRV variables and HRV variables when ECG intervals have low variations: (top) Plot of ECG interbeat intervals, (Bottom left) Comparison plot of PRV variance and HRV variance (NRMSE = 22, PCC = 0.53), (Bottom right) Comparison plot of PRV HF component and HRV HF component (NRMSE = 19.6, PCC = 0.38). The plots demonstrate that the PRV variable and HRV variable have a similar trend although PRV has a few disturbances, however, as ECG interval length remains nearly constant for some segments, there are many low values for these two variables. Therefore, when evaluating the agreement between HRV and PRV using statistical methods, the PCC will have relatively low value, and the NRMSE will have a high value.
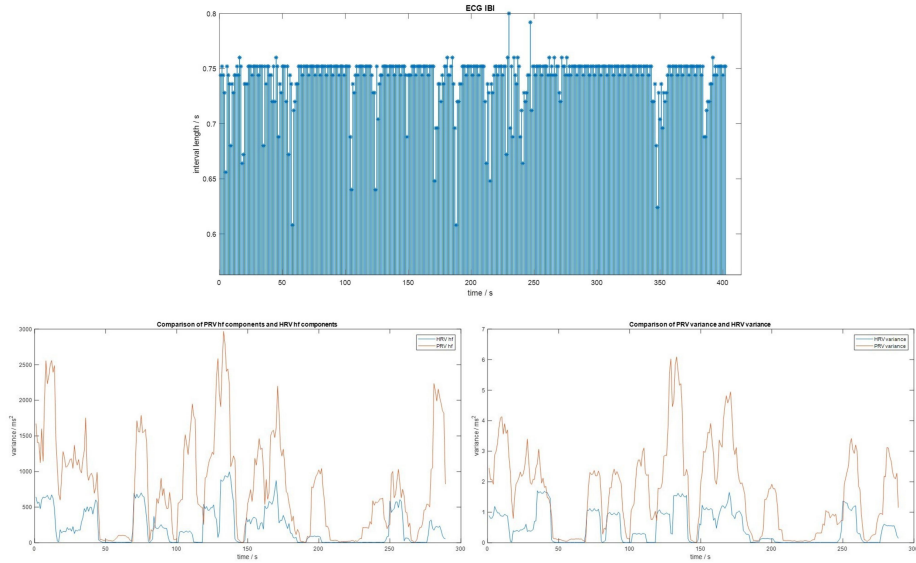
Figure 3.17: Comparison of PRV variables and HRV variables when ECG intervals have high variations: (top) Plot of ECG interbeat intervals, (Bottom left) Comparison plot of PRV variance and HRV variance (NRMSE = 1.58, PCC = 0.73), (Bottom right) Comparison plot of PRV HF component and HRV HF component (NRMSE = 3.67, PCC = 0.68). When ECG interval length has a larger variance, the NRMSE reduces greatly, and the PCC improves. Generally, PPG variables have a similar trend with ECG variables but with larger amplitude due to the disturbances.

Therefore, for subjects with cardiovascular diseases, PPG pulse peak, 50% max amplitude point, 75% max amplitude point all can generate PRV with high PCC and low NRMSE comparing to HRV, while peak-derived PRV has higher PCC than other two locations and 50% max amplitude point, 75% max amplitude point derived PRV has relatively lower NRMSE. On the contrary, max slope point and

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onset derived PRV has a worse agreement to HRV. Moreover, this result matches the result of comparing IBI signals generated from different characteristic points.

In this situation, when comparing the ECG IBI and PPG IBI signal, PPG IBI signal is more approaching to IBI signal calculated from ECG peaks. But the comparison of PRV variables indicates that the PCC between PRV and ECG peak derived HRV is higher, although the mean NRMSE is also higher.

3.4 Comparison Result of Subjects without Cardiovascular Diseases (Non-CVD)

There are 1763 5-min segments extracted from the cardiac signals of subjects without cardiovascular diseases.

3.4.1 Interbeat Interval Signal Comparison

The mean PCC and mean NRMSE between ECG IBI array and PPG IBI array generated from difference characteristic points over all of the segments are calculated.

Table 3.7 and Table 3.8 show the result of ECG and PPG IBI comparison:

Table 3.7: PCC and NRMSE between ECG IBI and PPG IBI (ECG peaks) for non-CVD subjects

	PP	PO	PM	P25	P50	P75
mean PCC	0.6522	0.5487	0.6226	0.6820	0.7077	0.6955
mean NRMSE	0.0179	0.0279	0.0199	0.0159	0.0143	0.0151

Table 3.8: PCC and NRMSE between ECG IBI and PPG IBI (ECG onsets) for
non-CVD subjects

	OP	**OO**	**OM**	**O25**	**O50**	**O75**
mean PCC	0.5651	0.4816	0.5386	0.5855	0.6041	0.5989
mean NRMSE	0.0220	0.0313	0.0238	0.0206	0.0194	0.0197

the notations are the same as mentioned before.

Figure 3.18 shows the plot of the mean PCC and NRMSE.
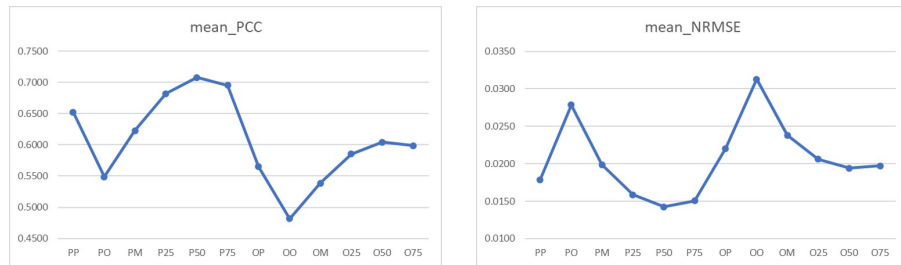
Figure 3.18: Agreement comparison of different ECG and PPG characteristic points

for non-CVD subjects - (left) mean PCC, (right) mean NRMSE

For subjects without cardiovascular diseases, when comparing the agreement
of PRV that derived from different characteristic points with HRV, it is revealed in
the plots and data that:

For mean PCC, 50% max amplitude point > 75% max amplitude point > 25%
max amplitude point > peak > max slope > onset

For mean NRMSE, 50% max amplitude point < 75% max amplitude point <
25% max amplitude point < peak < max slope < onset

The comparison result above indicates that 50% max amplitude point derived
PRV has the highest agreement to HRV among all the characteristic points and this

followed by the 75% max amplitude point, 25% max amplitude point, peak, and the other points. Characteristic points that have a higher agreement to HRV are all on the slope of PPG pulse, except for max slope point. This conclusion is different from the conclusion drawn in the last section for subjects with cardiovascular diseases that characteristic point derived PRV with a higher agreement to HRV is either that from 75% max amplitude point, 50% max amplitude point (points on pulse slope), or peak.

Besides, there is a difference between ECG peak derived HRV and ECG onset derived HRV. In general, the mean PCC between ECG IBI that derived from ECG onsets and PPG IBI is lower than that derived from ECG peaks, and the mean NRMSE between ECG onsets-derived IBI is higher, which leads to the result that PRV is more approaching to ECG peak-derived HRV rather than onset-derived HRV.

Figure 3.19 - Figure 3.24 exhibit example plots of different PPG IBI signals comparing with ECG peak-derived IBI signal.

3.4.2 Heart Rate Variability and Pulse Rate Variability Variables Comparison

HRV analysis variables for ECG signal and PPG signal of different characteristic points are also calculated and compared. The agreement is evaluated based on the mean PCC and mean NRMSE.

Table 3.9 and Table 3.10 show the comparison result of time domain variables
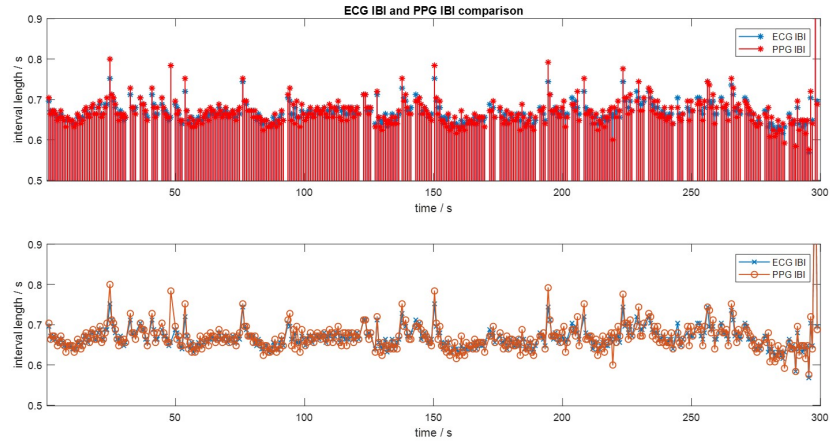
Figure 3.19: Comparison of ECG peak-derived IBI and PPG peak-derived IBI for

non-CVD subjects: NRMSE = 0.0229, PCC = 0.9247
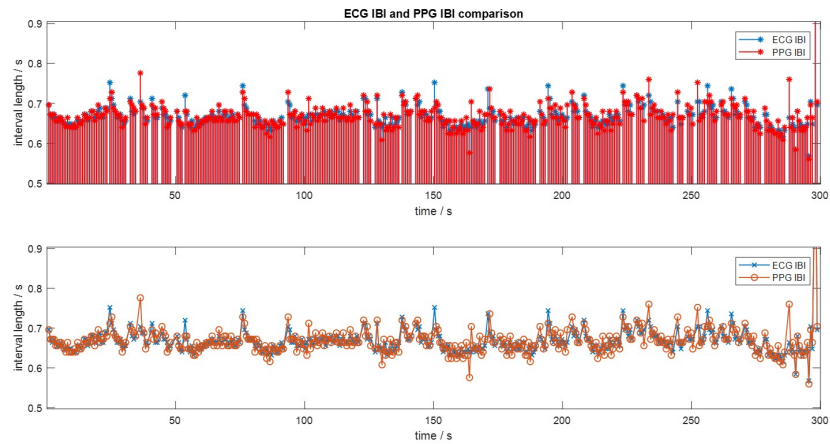
Figure 3.20: Comparison of ECG peak-derived IBI and PPG onset-derived IBI for

non-CVD subjects: NRMSE = 0.0255, PCC = 0.8872

for HRV measurements.

Table 3.9: Mean PCC between time domain variables of HRV and PRV derived from

different characteristic points for non-CVD subjects

mean PCC	mean	variance	SD	RMSSD	pnn50
PP	0.9654	0.7500	0.7519	0.6666	0.5812
PO	0.9178	0.6043	0.6241	0.5498	0.4973
PM	0.9601	0.6948	0.6984	0.5964	0.5434
P25	0.9669	0.7488	0.7701	0.6896	0.6357
P50	0.9754	0.8175	0.8232	0.7401	0.6798
P75	0.9711	0.7930	0.7957	0.7031	0.6226
OP	0.9450	0.6763	0.6806	0.5825	0.4996
OO	0.9023	0.5724	0.5831	0.4958	0.4342
OM	0.9413	0.6392	0.6405	0.5252	0.4655
O25	0.9503	0.6843	0.6992	0.6064	0.5272
O50	0.9547	0.7337	0.7372	0.6364	0.5458
O75	0.9527	0.7237	0.7276	0.6226	0.5342

Table 3.10: Mean NRMSE between time domain variables of HRV and PRV derived from different characteristic points

mean NRMSE	mean	variance	SD	RMSSD	pnn50
PP	0.0038	2.3495	0.7311	1.0065	10.4131
PO	0.0063	5.9968	1.2972	1.8058	14.7610
PM	0.0043	2.9190	0.8765	1.2398	8.1665
P25	0.0035	1.9787	0.5824	0.8050	5.4780
P50	0.0031	1.3404	0.4601	0.6352	4.2542
P75	0.0034	1.6800	0.5536	0.7823	5.7475
OP	0.0050	1.5022	0.5468	0.7086	3.3516
OO	0.0072	3.7034	1.0105	1.2744	5.7618

OM	0.0054	1.7167	0.6200	0.7746	2.8559
O25	0.0047	1.4494	0.5488	0.6889	2.3813
O50	0.0045	1.1439	0.4713	0.5886	2.0223
O75	0.0046	1.1747	0.4562	0.5744	2.1727

where the notations are the same as mentioned before.

Figure 3.25 presents the plot of mean PCC and mean NRMSE.
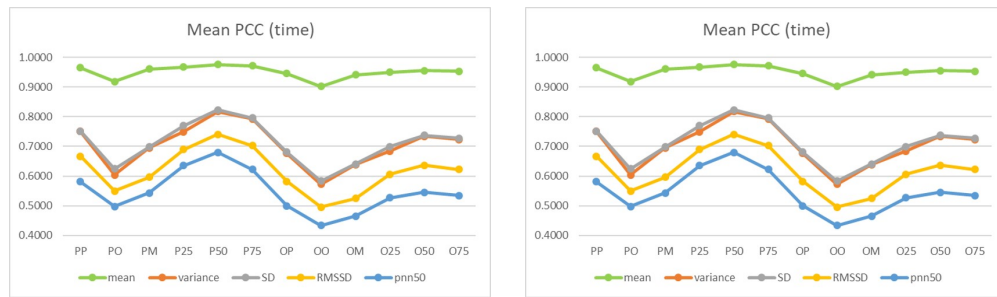
Figure 3.25: Agreement comparison of time domain variables for non-CVD subjects - (left) mean PCC, (right) mean NRMSE

The figures and data demonstrate that using ECG peak as the characteristic point has higher mean PCC and higher mean NRMSE than using ECG onset as the characteristic point for subjects without cardiovascular diseases.

For PPG characteristic points, the agreement of all time domain variables, except for mean interval length, is similar and matched with the result we get from ECG IBI and PPG IBI comparison. We conclude that 50% max amplitude point derived PRV generally has the highest agreement to HRV (highest PCC and lowest NRMSE), and it is followed by 75% max amplitude point, 25% max amplitude point, peak, max slope point, and onset. Onset derived PRV tends to have a worse
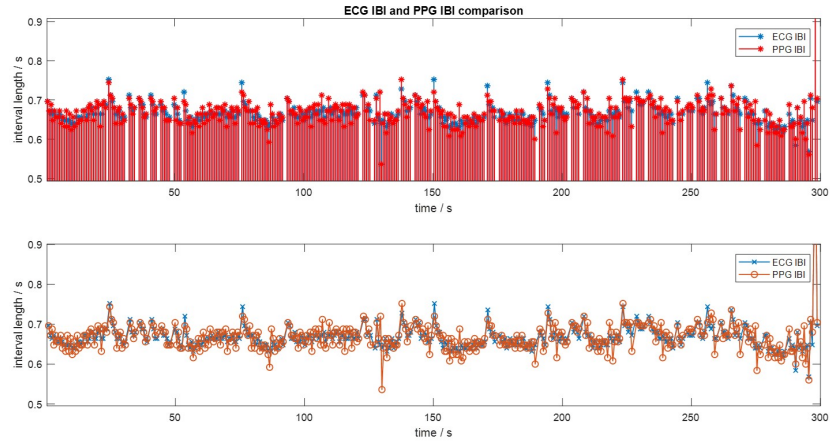
Figure 3.21: Comparison of ECG peak-derived IBI and PPG max slope points derived IBI for non-CVD subjects: NRMSE = 0.0277, PCC = 0.8712
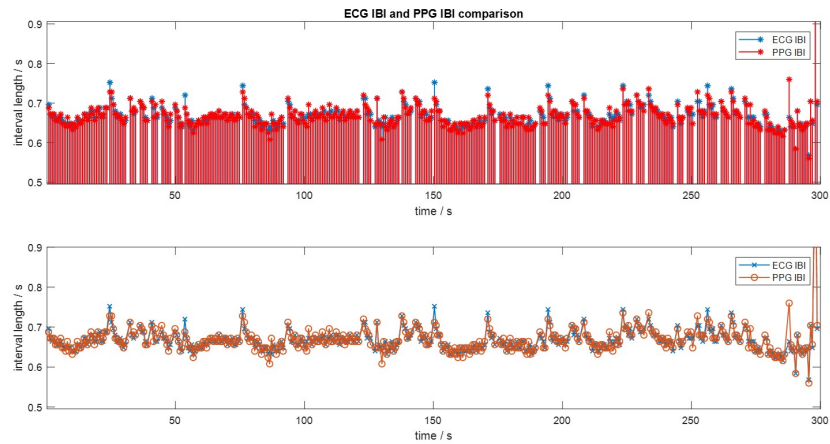
Figure 3.22: Comparison of ECG peak-derived IBI and PPG 25% max amplitude points derived IBI for non-CVD subjects: NRMSE = 0.0164, PCC = 0.9510

agreement than all other points.

Frequency domain variables are then calculated and compared. Table 3.11 and Table 3.12 display detailed results.
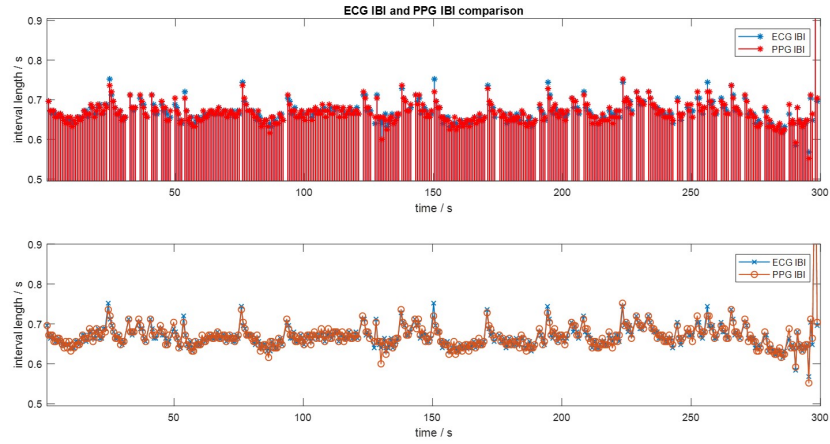
Figure 3.23: Comparison of ECG peak-derived IBI and PPG 50% max amplitude points derived IBI for non-CVD subjects: NRMSE = 0.0126, PCC = 0.9706
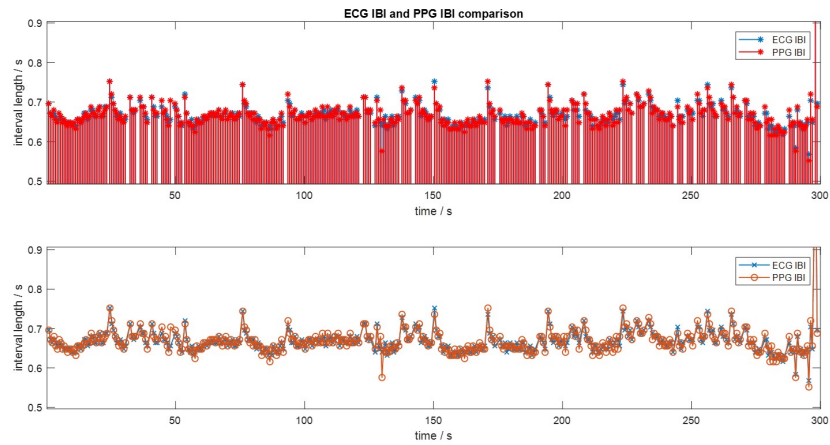
Figure 3.24: Comparison of ECG peak-derived IBI and PPG 75% max amplitude points derived IBI for non-CVD subjects: NRMSE = 0.0139, PCC = 0.9671

Table 3.11: Mean PCC between frequency domain variables of HRV and PRV derived from different characteristic points for non-CVD subjects

mean PCC	ULF	VLF	LF	HF	LF/HF
PP	0.7169	0.7217	0.7268	0.4260	0.5260
PO	0.5781	0.5836	0.5735	0.3431	0.4881
PM	0.7074	0.7126	0.7219	0.4010	0.5135
P25	0.7278	0.7321	0.7264	0.4257	0.5791
P50	0.7648	0.7686	0.7705	0.4700	0.5842
P75	0.7578	0.7619	0.7676	0.4639	0.5717
OP	0.6572	0.6632	0.6756	0.3674	0.4625
OO	0.5387	0.5450	0.5475	0.3131	0.4276
OM	0.6447	0.6510	0.6715	0.3542	0.4554
O25	0.6551	0.6606	0.6684	0.3698	0.4912
O50	0.6874	0.6927	0.7057	0.4003	0.4998
O75	0.6872	0.6928	0.7087	0.3939	0.4967

Table 3.12: Mean NRMSE between frequency domain variables of HRV and PRV derived from different characteristic points for non-CVD subjects

mean NRMSE	ULF	VLF	LF	HF	LF/HF
PP	2.9269	2.8654	2.8269	7.1132	1.0284
PO	7.6531	7.4776	7.7696	26.4475	1.0635
PM	2.9480	2.8785	2.8584	7.4030	1.0565
P25	2.7317	2.6765	2.7073	7.6300	0.9801
P50	2.2837	2.2377	2.2175	5.3028	0.9732
P75	2.3619	2.3111	2.2539	5.3414	0.9789

OP	2.4462	2.4049	2.1642	3.2833	1.4596
OO	5.1268	5.0386	4.9207	12.5846	1.4939
OM	2.4504	2.4081	2.1434	3.5376	1.3797
O25	2.5061	2.4629	2.2915	3.7335	1.6120
O50	2.1358	2.0983	1.8645	2.7539	1.6453
O75	2.1588	2.1191	1.8695	2.6779	1.5329

where the notations are the same as mentioned before.

Figure 3.26 presents the plots of PCCs and NRMSEs.
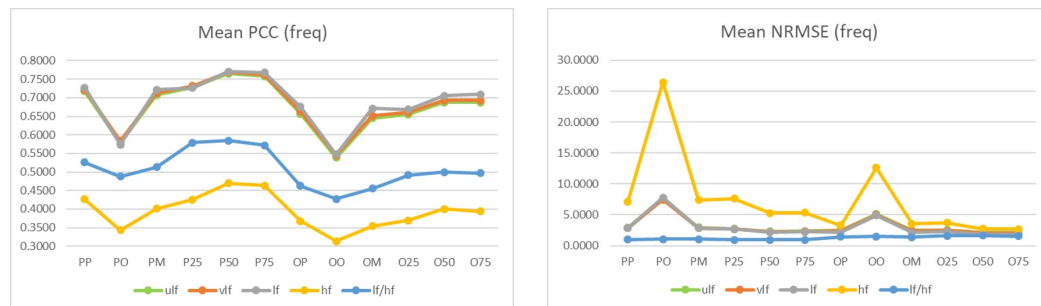
Figure 3.26: Agreement comparison of frequency domain variables for non-CVD subjects - (left) mean PCC, (right) mean NRMSE

For frequency domain parameters, PRV generated from 50% max amplitude point has the highest mean PCC between HRV parameters, and it is followed by the 75% max amplitude point, 25% max amplitude point. Peak and max slope point derived PRV have less mean PCC than the previous three characteristic points, while onset derived PRV has the least mean PCC. When considering mean NRMSE, PRV derived from 50% max amplitude point has the least difference between HRV. 75% max amplitude point, 25% max amplitude point, peak, and max slope point derived

PRV has higher mean NRMSE and onset has the highest mean NRMSE than all other PPG characteristic points.

The difference between using ECG peaks and onsets to calculate the agreement is similar to that of time domain variables.

3.4.3   Result Analysis

Unlike the situation that subjects with cardiovascular diseases (CVD), comparison results for subjects that do not have cardiovascular diseases (non-CVD) tend to be consistent for both methods and nearly all parameters.

Rather than PRV derived from PPG pulse peak has a relatively high agreement to HRV in the CVD situation, in non-CVD case, 50% max amplitude point derived PRV have the highest agreement, which means highest mean PCC and lowest mean NRMSE, among all characteristic points to gold standard HRV. Besides, 75% max amplitude point and 25% max amplitude point derived PRV also has a high agreement to HRV. Max slope point and onset derived PRV have the lowest agreement and are not recommended to use in both situations.

The comparison of the IBI signal generated from different PPG characteristic points with the ECG IBI signal also supports this conclusion.

In non-CVD cases, PPG IBI signal has higher agreement to ECG peak derived IBI signal and for PRV variables, they have higher PCC and higher NRMSE to ECG peak derived HRV than onset derived HRV, which is the same as the result in CVD situation.

3.5 Discussion and Chapter Conclusion

3.5.1 Further Analysis

There are still some points that need to be discussed.

Because of the limited sampling rate of cardiac signals, the number of points for each pulse slope is also limited. Thus locating the 25% max amplitude point, 50% max amplitude point, and 75% max amplitude point will be not accurate enough. Then why these points tend to have a better agreement than other locations, especially the max slope point, which is also on the pulse slope, and onset, which has the worst agreement in our comparison result?

Let's first compare the scale of characteristic points on the pulse slope to the maximum amplitude. Figure 3.27 and Figure 3.28 show the comparison for CVD subjects and non-CVD subjects respectively (display the scale of the pulse characteristic points location for each pulse).

Unlike max slope point, other points on pulse slope basically lie in the scale where they are supposed to be and vary in a relatively narrower scale than max slope points (smaller standard deviation). Comparing to max slope point, 25%, 50% and 75% max amplitude point are less likely to be affected by the variation of pulse shape and thus, PRV derived by these characteristic points has higher agreement than max slope point.

As the deviation of the scale of points on the slope will cause a decreasing of PRV and HRV agreement according to the observation above, the exact 50% max
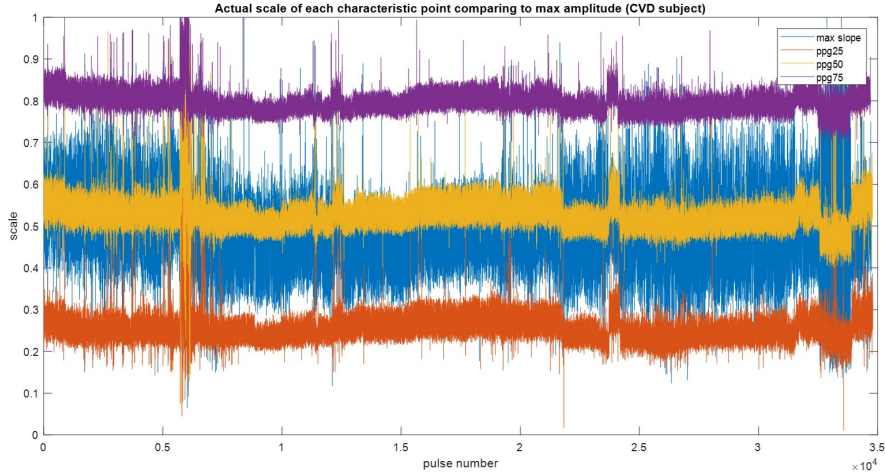
Figure 3.27: Comparison of the scale of different characteristic points on pulse slope for CVD subjects: for max slope points: mean - 0.4925, standard deviation (sd) - 0.1, for 25% max amplitude points: mean - 0.2563, sd - 0.04, for 50% max amplitude points: mean - 0.5287, sd - 0.04, for 75% max amplitude points: mean - 0.7978, sd - 0.03

amplitude point location is interpolated and compared with the 50% max amplitude points selected from the PPG signal. The interbeat interval comparison result is shown in Table

The observations above indicates that the location deviation of characteristic points on the slope will cause the decreasing of PRV and HRV agreement. Therefore, as an example, the exact location of 50% max amplitude point is interpolated using PPG signal and the derived interbeat interval signal and PRV variables are compared with that calculated from 50% max amplitude point extracted from PPG sampling points.
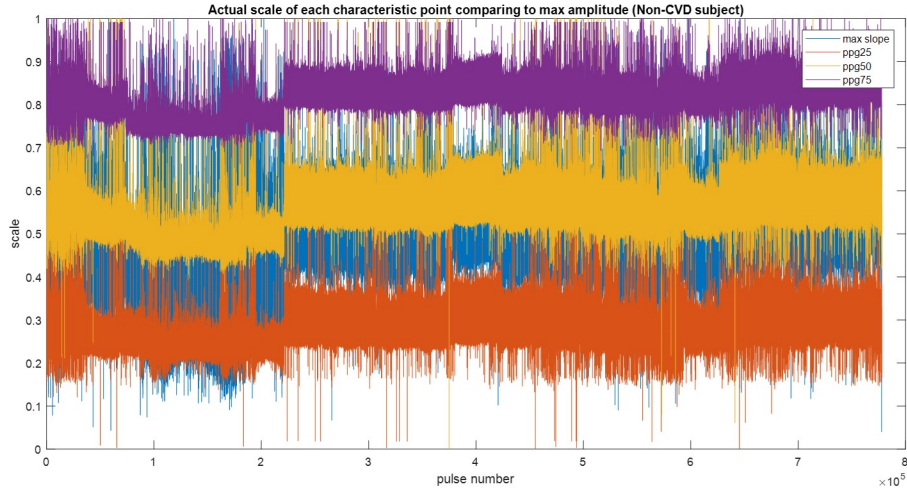
Figure 3.28: Comparison of the scale of different characteristic points on pulse slope for Non-CVD subjects: for max slope points: mean - 0.4961, standard deviation (sd) - 0.11, for 25% max amplitude points: mean - 0.2833, sd - 0.04, for 50% max amplitude points: mean - 0.5574, sd - 0.05, for 75% max amplitude points: mean - 0.8192, sd - 0.04

The IBI comparison result for CVD subjects and non-CVD subjects is shown in Table 3.13.

Table 3.13: Agreement comparison of PPG 50% max amplitude points and interpolated 50% max amplitude points

Mean PCC	ppg50	ppg50_int	Mean NRMSE	ppg50	ppg50_int
CVD	0.6020	0.6197	CVD	0.0193	0.0184
Non-CVD	0.7050	0.7283	Non-CVD	0.0143	0.0134

Table 3.14 and Table 3.15 demonstrate the comparison result of PRV variables.

Table 3.14: Agreement comparison of 50% max amplitude point and interpolated 50% max amplitude point derived PRV variables (CVD)

mean PCC	ppg50	ppg50_int	mean NRMSE	ppg50	ppg50_int
mean	0.8690	0.8724	mean	0.0034	0.0033
variance	0.7257	0.7323	variance	4.9622	4.9561
SD	0.7351	0.7418	SD	0.9427	0.9139
RMSSD	0.6922	0.7025	RMSSD	1.0673	1.0315
pnn50	0.6266	0.6308	pnn50	7.2781	7.3645
ULF	0.6865	0.6950	ULF	15.2076	14.7331
VLF	0.6905	0.6988	VLF	15.4301	14.8929
LF	0.7245	0.7322	LF	12.4293	11.8822
HF	0.5822	0.5928	HF	6.0011	5.8268
LFHF	0.5235	0.5431	LFHF	1.3542	1.3849

Table 3.15: Agreement comparison of 50% max amplitude point and interpolated 50% max amplitude point derived PRV variables (Non-CVD)

mean PCC	ppg50	ppg50_int	mean NRMSE	ppg50	ppg50_int
mean	0.9747	0.9743	mean	0.0034	0.0033
variance	0.8148	0.8168	variance	4.9622	4.9561
SD	0.8190	0.8204	SD	0.9427	0.9139
RMSSD	0.7330	0.7375	RMSSD	1.0673	1.0315
pnn50	0.6715	0.6623	pnn50	7.2781	7.3645
ULF	0.7596	0.7673	ULF	15.2076	14.7331
VLF	0.7634	0.7709	VLF	15.4301	14.8929

LF	0.7647	0.7713	LF	12.4293	11.8822
HF	0.4675	0.4831	HF	5.6410	5.2532
LFHF	0.5822	0.6038	LFHF	0.9744	1.0044

Figure 3.29 visualize the agreement relationship.
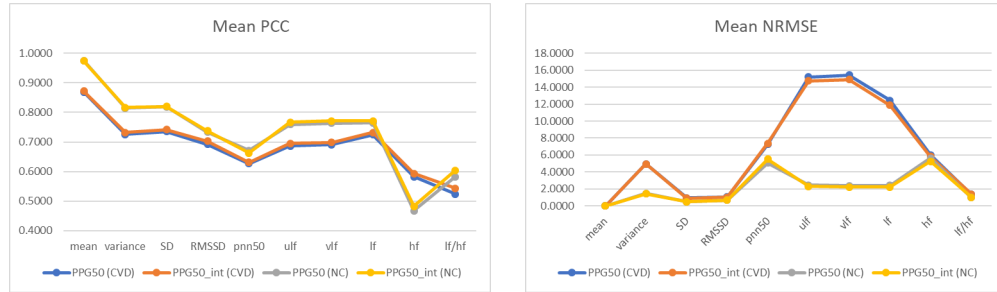
Figure 3.29: Agreement comparison of interpolated and original 50% max amplitude

point - (left) mean PCC, (right) mean NRMSE

The comparison result supports the observations that the IBI signal and PRV variables calculated from interpolated 50% max amplitude points have higher agreement to that of ECG signal than 50% max amplitude points extracted from PPG signal, with slightly higher mean PCC and slightly lower mean NRMSE.

Moreover, characteristic points on the slope, such as 25% max amplitude point, 50% max amplitude point, and 75% max amplitude point, also have the advantage that being less sensitive to turning point.

Figure 3.30 and Figure 3.31 demonstrate situations that error occurs during onset and peak detection.

As onset is located as the lowest point before the upward part of the pulse and peak is located as the highest point between the pulse rising and decreasing part,
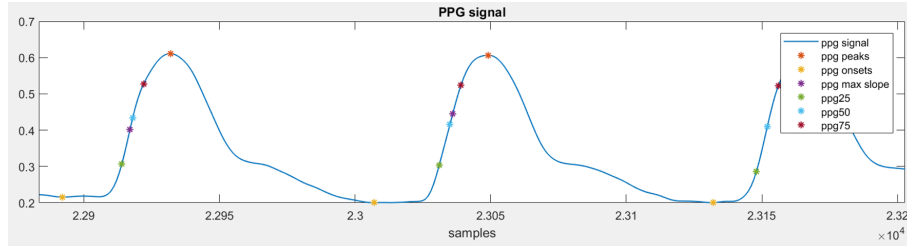
Figure 3.30: Onset detection error example
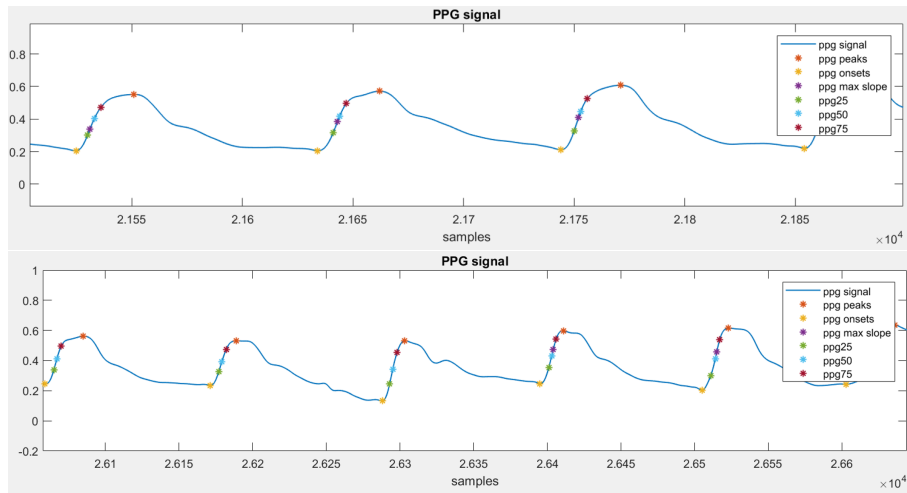
Figure 3.31: Peak detection error examples

when the turning part before the rising part, between the rising and decreasing part, is relatively plain, locating peak and onset point will bring error. A plain turning part before the pulse going upward happens more frequently than that between pulse upward and downward part. Therefore, onset derived PRV has the lowest agreement to HRV for both situations among all characteristic points.

3.5.2   Chapter Conclusion

In conclusion, for subjects with cardiovascular diseases, the peak, 50% max amplitude point, and 75% max amplitude point derived PRV has a very good agree-

ment to ECG derived HRV. 50% max amplitude point and 75% max amplitude point derived PRV has the lowest mean NRMSE, and peak derived PRV has the highest mean PCC. For subjects without cardiovascular diseases, 50% max amplitude point has the highest agreement to HRV variables and peak point is not recommended to use in this situation.

For both conditions, max slope point and onset have a relatively lower agreement than other characteristic points, which may because of max slope point's high sensitivity to pulse shape changes and onset point's easily being influenced by a plain turning part before the rising part of the pulse.

In general, 50% max amplitude point on the PPG pulse pulse is most recommended for both situations.

Chapter 4: PRV Refinement Using Arterial Blood Pressure Information

Factors that will lead to the difference between ECG IBI and PPG IBI including artifacts, noise or random fluctuations in characteristic point detection, which is discussed in Chapter 3, and variations in pulse transit time (PTT), which is correlated with blood pressure as mentioned in Chapter 2. With arterial blood pressure (ABP) signal provided in MIMIC III dataset for some subjects, the relationship between PTT and blood pressure will be modeled in this chapter, and blood pressure information will be utilized to estimate corresponding PTT and for further PPG IBI signal refinement. Then PRV variables of refined PPG IBI signal and their agreement to HRV variables are calculated and compared with the original PRV. This chapter aims at proving that with the information from blood pressure, the agreement between PRV and HRV can be improved, based on which we will continue our further researches, and observe whether there will be a difference between the refinement result for specific PRV variables.

Figure 4.1 shows the methodology of the refinement process.

PPG signal and ECG signal are preprocessed, and high-quality segments are extracted, and so as arterial blood pressure signal (ABP).
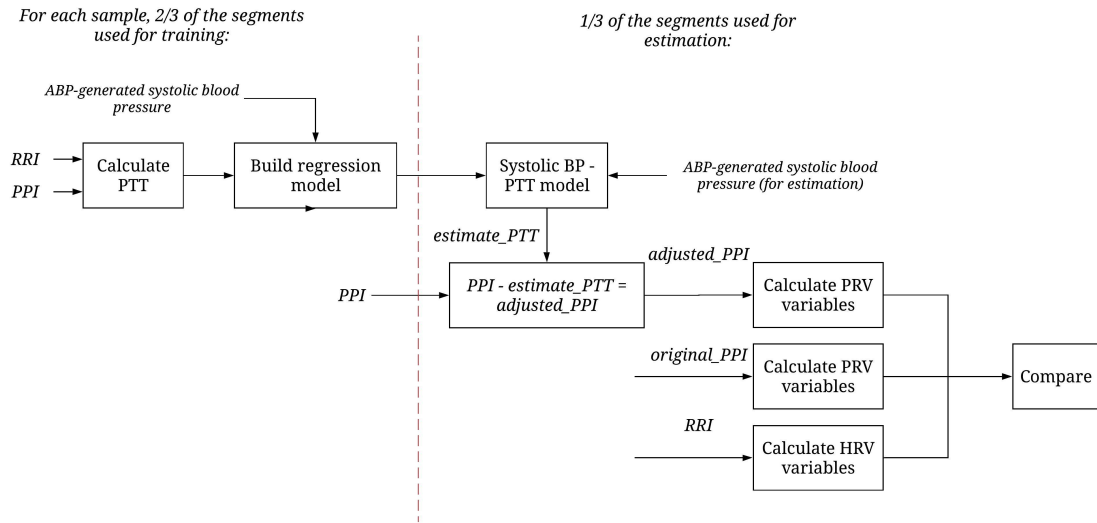
Figure 4.1: Block diagram of PPG interbeat interval refinement and PRV agreement
comparison

Figure 4.2 shows the plot of signals and characteristic points.

4.1   Signal Alignment and Pulse Transit Time Extraction

4.1.1   Signal Alignment

The process of segment preprocessing is shown in Figure 4.3. Cardiac signal segments are aligned and preprocessed first. The corresponding pulse transit time can then be calculated.

As shown in Figure 4.4, PPG characteristic points and systolic blood pressure (SBP) that are in the same cardiac cycle of ECG R peaks are extracted, and thus, signal cycles are aligned.

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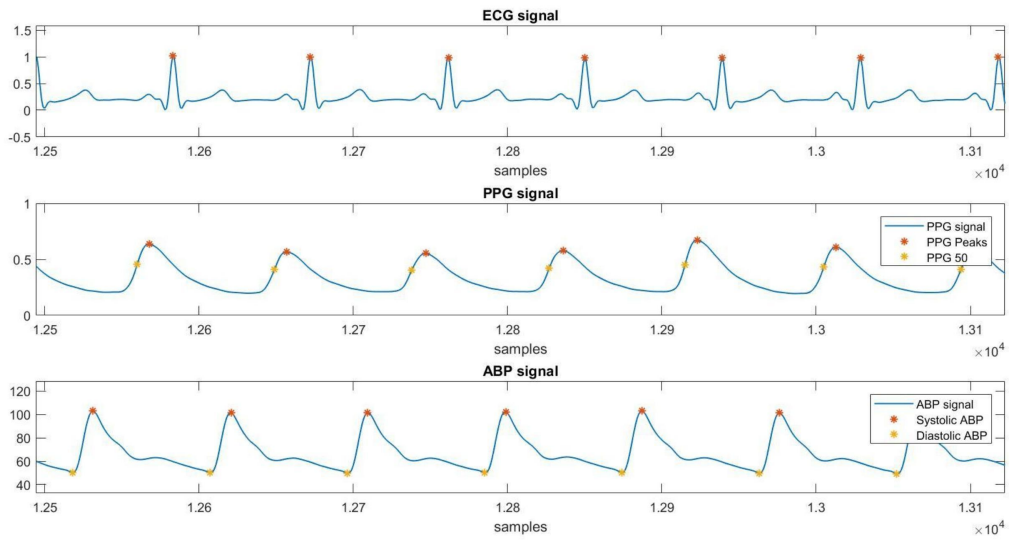
Figure 4.2: Plot of ECG signal and ECG peaks (up), PPG signal and PPG peaks, PPG 50% max amplitude points (mid), ABP signal and time of systolic BP, time of diastolic BP (down)
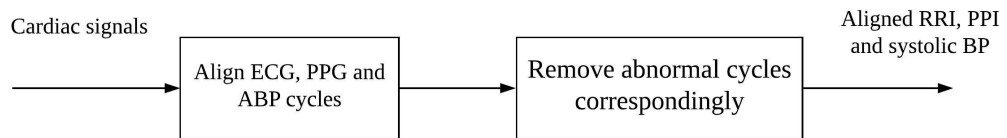
Figure 4.3: Block diagram of signal preprocessing progress

4.1.2 Pulse Transit Time Extraction

PTT can be calculated using the time difference between pulse at a proximal site to pulse at a distal location, which is usually considered as the time difference between ECG R peak and PPG characteristic points, either PPG pulse peak or the
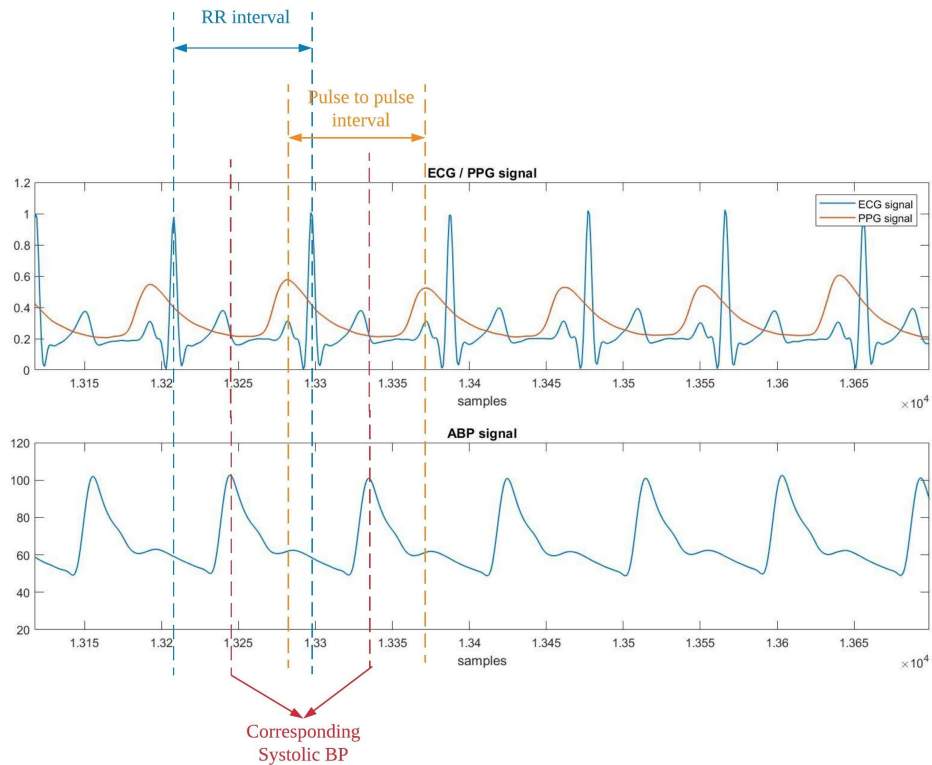
Figure 4.4: ECG, PPG, ABP waves and corresponding cardiac cycles (up) ECG and PPG waves, RR interval and corresponding pulse-to-pulse interval, (down) ABP wave and systolic blood pressure (SBP) in the corresponding cardiac cycles.

50% max amplitude point on pulse slope. Choosing 50% max amplitude point for PTT calculation is because we discussed in the last chapter that the PRV generated from this point has a high agreement to HRV comparing with other characteristic points.
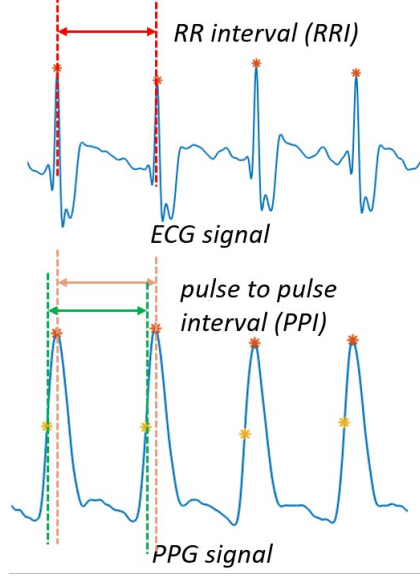
Figure 4.5: ECG RR interval and ECG pulse-to-pulse interval from two character-
istic points: pulse transit time is extracted from the time difference
between ECG R peak and corresponding PPG peak or 50% max ampli-
tude point.

4.2 Regression Model to Represent the Relationship between PTT and Systolic BP

Many models have been proposed concerning the relationship between PTT and blood pressure. To simplify the modeling process, in this chapter, a linear support vector regression (SVR) is applied, where the linear function is in the form:

$$f(x) = \omega^T \cdot x + b, \text{with} \, \omega \in \mathcal{X}, b \in R \tag{4.1}$$

solving the convex optimization problem:

$$\text{minimize } \frac{1}{2}\|\omega\|^2 \qquad (4.2)$$

$$\text{subject to } \begin{cases} y_i - \omega^T x_i - b \leq \epsilon \\[2mm] \omega^T x_i + b - y_i \leq \epsilon \end{cases} \qquad (4.3)$$

Meanwhile, a radial basis function (RBF) kernel SVR is utilized for comparison, for it has the advantage of fitting the samples to a more complex function:

$$k(\mathbf{x}, \mathbf{x}') = \exp(-\frac{\|\mathbf{x} - \mathbf{x}'\|^2}{2\sigma^2}) \qquad (4.4)$$

4.3 PRV Refinement Result for Subjects with Cardiovascular Diseases (CVD)

99 data sessions from 20 subjects with ECG, PPG and ABP signal are used for PTT-BP model training, PTT estimation and PRV refinement.

The Systolic BP - PTT model is trained session-dependently. Specifically, for each data session, take 2/3 of the segments for model training and the refinement process is applied to the rest 1/3 of the segments.

4.3.1 Refinement Sample

For CVD subjects, Figure 4.6 presents the regression model using linear kernel SVR and RBF kernel SVR of one sample.

The PTT and SBP form a linear relationship with many outliers, which may occur due to other physiological variations and disturbances. Therefore, the re-
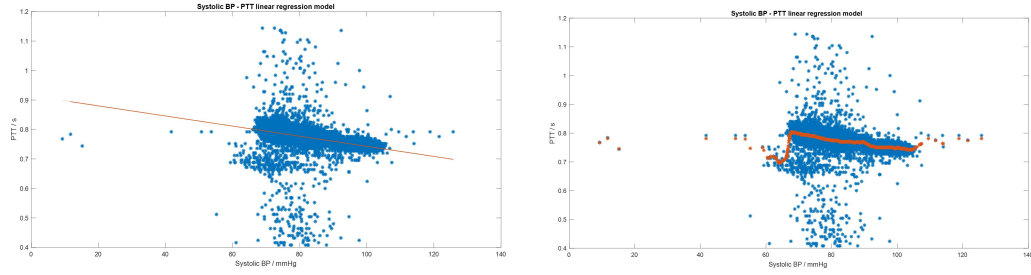
Figure 4.6: Regression model of the relationship between systolic BP and PTT for CVD subjects (left) linear kernel (right) RBF kernel

gression models built by a linear kernel or RBF kernel are similar. It can also be observed from the estimated PTT using two regression models. Figure 4.7 and Figure 4.8 compare the true PTT and estimated PTT for both linear kernel SVR model and RBF kernel SVR model, as well as the comparison of RR interval, original pulse-to-pulse interval and pulse-to-pulse interval after adjustment using estimated PTT.

It is known that subjects with cardiovascular diseases have relatively low heart rate variability. Therefore, the ECG RRI for this sample remains at an approximately constant level. Also, for this sample, PTT has small variations with some sudden fluctuations. The SVR model can estimate the PTT level but can do very little to make up for the oscillations. This adjustment, in turn, has a relatively small influence on the difference between RRI and PPI.

The regression model example and estimation result above basically reveals that due to the small variations of RR intervals and the random fluctuations, using a linear kernel or RBF kernel SVR model to estimate PTT and applying it for PRV refinement will have limited improvement. The fluctuations for the PTT-BP model

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Figure 4.7: Comparison plot of estimated PTT and adjusted PPI using the linear kernel for CVD subjects: (up) Comparison of estimated PTT using linear-kernel SVR and true PTT (down) Comparison of ECG RR interval (RRI), original PPG pulse-to-pulse interval (PPI) and PPG pulse-to-pulse interval after adjustment using estimated PTT. The mean-squared error between RRI and PPI is 0.0024, and the mean-squared error between RRI and adjusted PPI is 0.0013

are left for further study.

4.3.2 Comparison Result of Refined PRV and Original PRV

For specific parameters, the refinement result is shown in the below figures from Figure 4.9 - Figure 4.18. They present the comparison of PCC and NRMSE between HRV variables and corresponding PRV variables, PRV variables after refinement using the RBF kernel SVR model and linear kernel SVR model.

In summary, the influence of PPI adjustment differs when considering PRV parameters. Parameters that reflect long-term characteristics, such as the mean in-
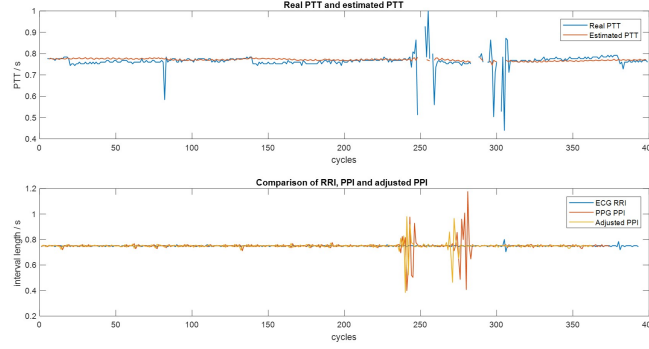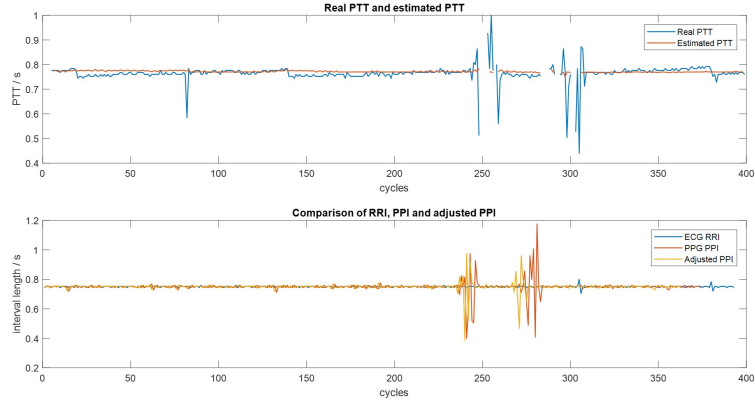
Figure 4.8: Comparison plot of estimated PTT and adjusted PPI using the RBF kernel for CVD subjects: (up) Comparison of estimated PTT using RBF kernel SVR and true PTT (down) Comparison of ECG RR interval (RRI), original PPG pulse-to-pulse interval (PPI) and PPG pulse-to-pulse interval after adjustment using estimated PTT. The mean-squared error between RRI and PPI is 0.0024, and the mean-squared error between RRI and adjusted PPI is 0.0013

terval length, ULF component and VLF component in PPI, will be improved by the adjustment, The improvement to parameters that reflect short-term characteristics is relatively small. However, there are exceptions. Parameters like RMSSD and HF component, which are considered to reflect some short-term characteristics, are also be improved in this situation.

For PRV derived from 50% max amplitude points of PPG pulses, the improvements are similar with regard to different parameters.
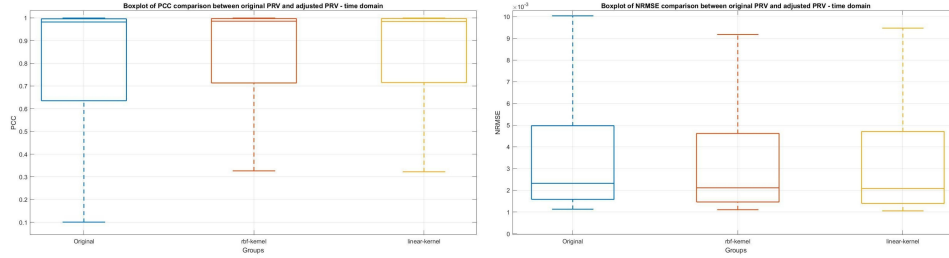
Figure 4.9: Agreement comparison of PRV parameters for CVD subjects (mean): (left) PCC comparison of mean interval length: mean: 0.7735, 0.7694, 0.7700 (Right) NRMSE comparison of mean interval length: mean: 0.0045, 0.0046, 0.0045: Although the mean value of PCC and NRMSE remains similar for all three situations, the adjustment reduces the deviation of PCC and NRMSE, indicating that the agreement between HRV and PRV about mean interval length has increased.

4.4 PRV Refinement Result for Subjects without Cardiovascular Diseases (Non-CVD)

The refinement method is then applied to subjects without cardiovascular diseases. There are 85 data sessions from 19 subjects. The results of using different kernel functions are compared with each other and are also compared with the performance of subjects with cardiovascular diseases.
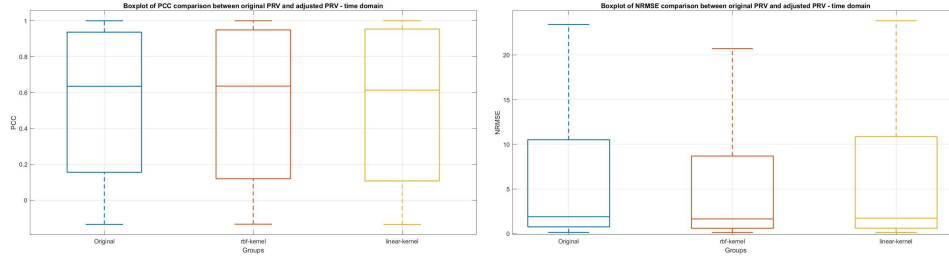
Figure 4.10: Agreement comparison of PRV parameters for CVD subjects (variance): (left) PCC comparison of interval length variance: mean: 0.5633, 0.5603, 0.5556 (Right) NRMSE comparison of interval length variance: mean: 27.54, 24.88, 25.36: The refinement has little improvement to the agreement of interval length variance, except for using the RBF kernel SVR model estimated PTT that the NRMSE has been reduced on a small scale.

4.4.1   Refinement Sample

Figure 4.19 demonstrates the linear kernel regression and RBF kernel regression of one sample.

Comparing to CVD subjects, the relationship between PTT and systolic BP is more approximate to a linear relationship. Hence, the difference between the linear kernel and the RBF kernel is more significant in this situation. Figure 4.20 and Figure 4.21 exhibit the two estimated PTTs for this sample.

For this sample, the PTT has a higher variance comparing to CVD subjects. In this situation, the estimated PTT generated from the RBF kernel SVR model tends to have a consistent trend, and the estimated PTT generated by the linear
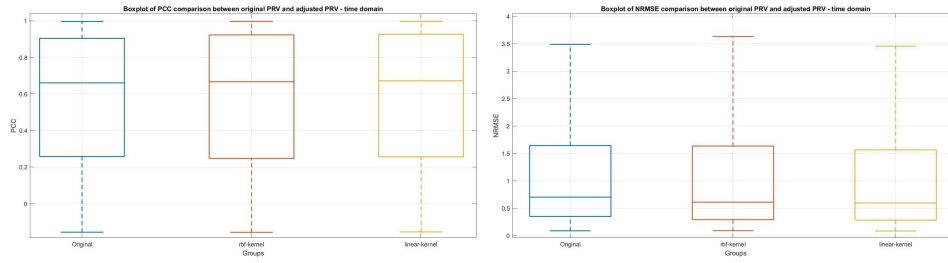
Figure 4.11: Agreement comparison of PRV parameters for CVD subjects (SD): (left) PCC comparison of standard deviation (SD) of interval length: mean: 0.5843, 0.5863, 0.5842 (Right) NRMSE comparison of interval length: mean: 1.9158, 1.8130, 1.8191: Concerning the standard deviation (SD) of interval length, the refinement has little influence on the PCC. However, the refined PRV has lower NRMSE comparing to the original one, and the linear kernel has a better result than the RBF kernel.

SVR model can remain the variance trend in blood pressure, which can reveal the variance trend in PTT to some degree. Therefore, the linear kernel generally has better performance than the RBF kernel for non-CVD subjects.

4.4.2 Comparison Result of Refined PRV and Original PRV

The comparison of agreement between HRV and original PRV, HRV and adjusted PRV using linear kernel SVR and RBF kernel SVR is shown below from Figure 4.22 - Figure 4.31. The agreement is evaluated using the value of PCC and NRMSE.

Figure 4.12: Agreement comparison of PRV parameters for CVD subjects (RMSSD): (left) PCC comparison of RMSSD of HRV and PRV: mean: 0.4055, 0.3985, 0.4045 (Right) NRMSE comparison of RMSSD of HRV and PRV: mean: 2.2644, 2.1574, 2.1643: The deviation of PCC and NRMSE both decrease after adjustment and the linear kernel SVR model has a better effect on improving PCC, while the RBF kernel SVR model has a better result on improving NRMSE. In general, after refinement, the agreement between HRV and PRV has been slightly enhanced.

Although parameters have a different amount of improvement using the estimated PTT from the SVR models, compared to subjects with cardiovascular diseases, there is an overall improvement for all HRV parameters in this situation, either parameters that reflect long-term characteristics or parameters that reveal short-term characteristics. The only parameter that could not be improved is pnn50, which is the percentage of intervals that vary from their previous intervals by 50 milliseconds. The NRMSE of this parameter has a wide range for CVD subjects as the interval length does not differ drastically in the ECG signal. For non-CVD sub-
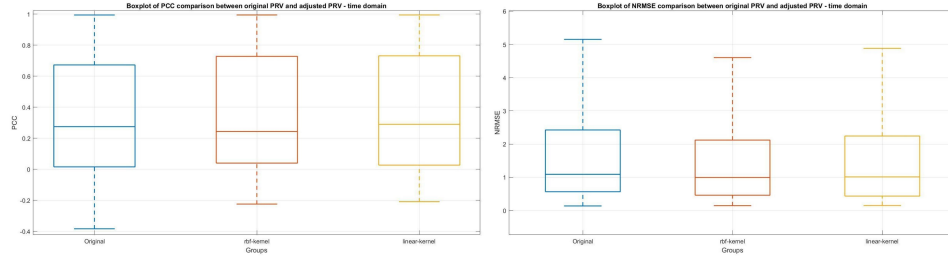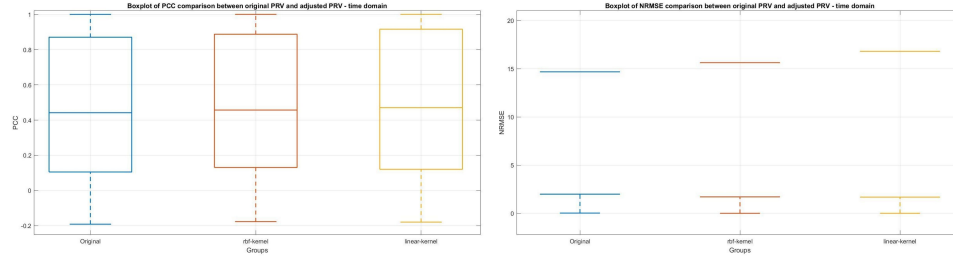
Figure 4.13: Agreement comparison of PRV parameters for CVD subjects (pnn50):
(left) PCC comparison of pnn50 of HRV and PRV: mean: 0.4983,
0.4979, 0.5097 (Right) NRMSE comparison of pnn50 of HRV and PRV:
mean: 15.78, 16.62, 16.65: The adjustment improves the PCC of pnn50,
however, due to the significant variance of NRMSE (this is because
pnn50 of HRV is relatively small), the adjustment to the NRMSE of
pnn50 does not have a very good performance

jects, the NRMSE varies in a smaller range, but it is still relatively large compared
to other parameters. This result may because pnn50 does not reveal the continuous
PTT change according to its definition, but only a summary that provides the over-
all change information. Therefore, the agreement of this parameter is hard to be
improved by our method that utilizing continuous blood pressure information. As
mentioned in the part of the SVR model example for non-CVD subjects, the linear
kernel should outperform the RBF kernel. The result of various HRV parameters
also supports this conclusion.

For PRV derived from 50% max amplitude point of PPG pulses, the origi-
nal agreement between PRV and HRV is generally higher than that obtained from

Figure 4.14: Agreement comparison of PRV parameters for CVD subjects (ULF): (left) PCC comparison of HRV and PRV ULF component: mean: 0.6787, 0.6824, 0.6842 (Right) NRMSE comparison of HRV and PRV ULF component: mean: 79.47, 80.79, 79.40: For ULF component in RRI or PPI, the adjusted PRV has similar mean PCC and mean NRMSE comparing to the original PCC. However, the deviation decreases for both measurements, while the adjustment has a more considerable improvement concerning NRMSE.

pulse peaks, which also matches what we got from the previous chapter. However, for specific HRV parameters, the improvement using PRV derived from 50% max amplitude point will differ.

Except for parameters such as mean interval length, ULF component and VLF component of intervals that all can be improved by a relatively large degree after refinement, there are some parameters whose agreement is significantly improved when utilizing PRV derived from 50% max amplitude point. Examples are shown in Figure 4.32 - Figure 4.34.

Figure 4.15: Agreement comparison of PRV parameters for CVD subjects (VLF): (left) PCC comparison of HRV and PRV VLF component: mean: 0.6824, 0.6858, 0.6875 (Right) NRMSE comparison of HRV and PRV VLF component: mean: 79.05, 81.19, 79.73: The adjustment to VLF component has similar result to that of ULF component.
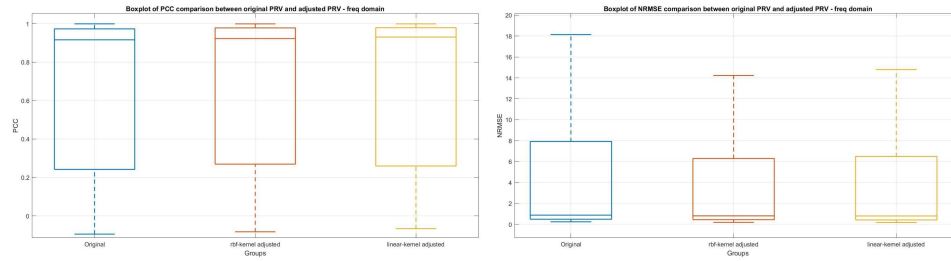

Figure 4.16: Agreement comparison of PRV parameters for CVD subjects (LF): (left) PCC comparison of HRV and PRV LF component: mean: 0.6799, 0.6830, 0.6867 (Right) NRMSE comparison of HRV and PRV LF component: mean: 70.56, 58.65, 58.38: The adjustment has limited influence on PCC between the LF component of HRV and PRV. There is an improvement to the mean NRMSE. However, the change extends the distribution range of NRMSE.
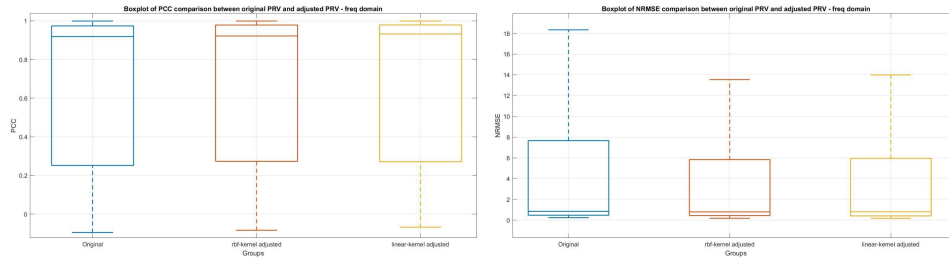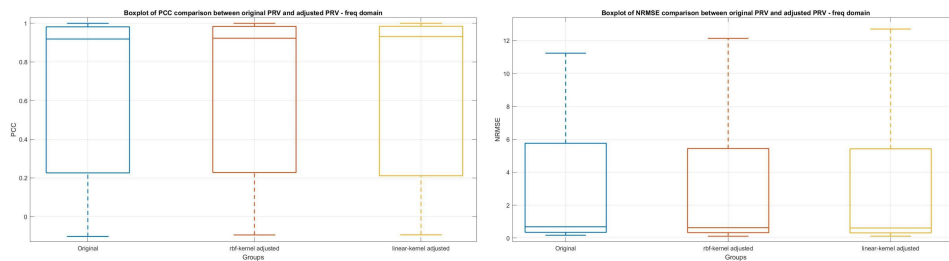
Figure 4.17: Agreement comparison of PRV parameters for CVD subjects (HF): (left) PCC comparison of HRV and PRV HF component: mean: 0.4948, 0.5183, 0.5174 (Right) NRMSE comparison of HRV and PRV HF component: mean: 29.56, 25.76, 25.86: After refinement, the PCC is improved by a relatively small amount, while the NRMSE is reduced, on a larger scale.

4.5   Result Analysis and Further Discussion

Based on the calculation and comparison in the above sections, the conclusion can be drawn that evaluating PTT using a subject-specific PTT-BP model and based on the systolic BP value per cardiac cycle and using it to refine PPG IBI signal are a feasible method. Although the refinement does not work very well on subjects with cardiovascular diseases, it can improve the agreement between PRV and HRV, as well as PPG IBI and ECG IBI, considerably for subjects without cardiovascular diseases.

Generally, variables that represent long term characteristics are likely to be improved by this method to a more significant degree than variables that represent
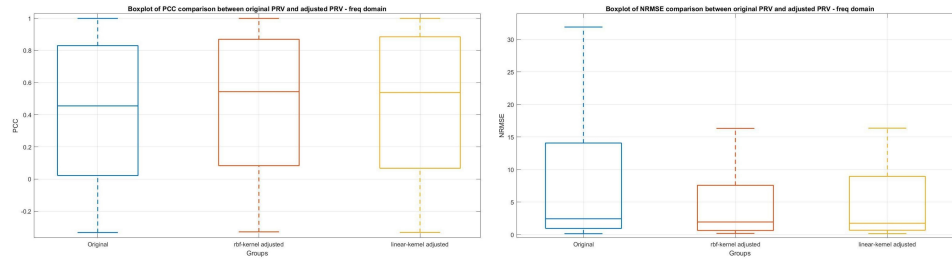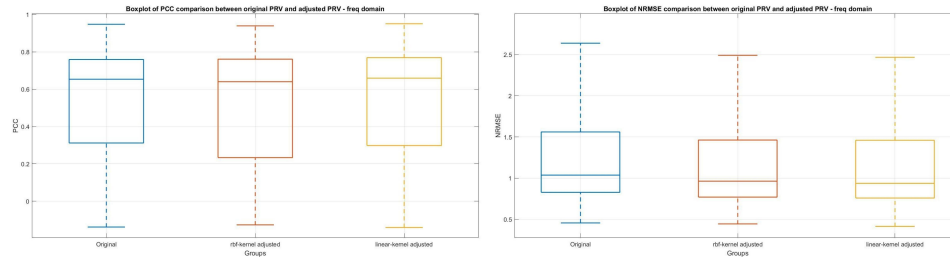
Figure 4.18: Agreement comparison of PRV parameters for CVD subjects (LF/HF): (left) PCC comparison of HRV and PRV's LF to HF ratio: mean: 0.5434, 0.5304, 0.5446 (Right) NRMSE comparison of HRV and PRV's LF to HF ratio: mean: 1.478, 1.489, 1.537: The refinement has little improvement to PRV with regard to this parameter as the mean PCC and NRMSE remain similar to that of the original PRV. Only the distribution of NRMSE is narrower after adjustment.
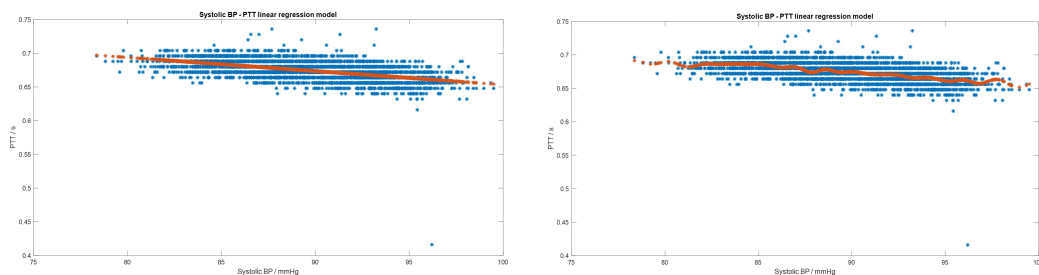
Figure 4.19: Regression model of the relationship between systolic BP and PTT for non-CVD subjects: (left) linear kernel (right) RBF kernel

short term characteristics. Meanwhile, agreement of variables that do not reflect a continuous characteristic, such as pnn50, is hard to be increased.

Comparing to peak-derived PRV, in the situation where subjects do not have cardiovascular diseases, 50% max amplitude points-derived PRV has a better agree-

Figure 4.20: Comparison plot of estimated PTT and adjusted PPI using linear kernel for non-CVD subjects: (up) Comparison of estimated PTT using linear kernel SVR and true PTT (down) Comparison of ECG RR interval (RRI), original PPI and PPI after adjustment using estimated PTT. The mean-squared error between RRI and PPI is 2.16e-04, and the mean-squared error between RRI and adjusted PPI is 9.74e-05

ment to HRV. Furthermore, the refinement works better to PRV calculated from PPG pulse 50% max amplitude points.

4.5.1 PRV Refinement Using Average Blood Pressure

Collecting continuous blood pressure signals is complicated and expensive, as the most accurate measurement is the invasive method. Although blood pressure information could help with the refinement of the PPG signal, collecting ECG signal directly may be a more convenient way. Therefore, whether average blood pressure could be used for PRV refinement is discussed in the following part.
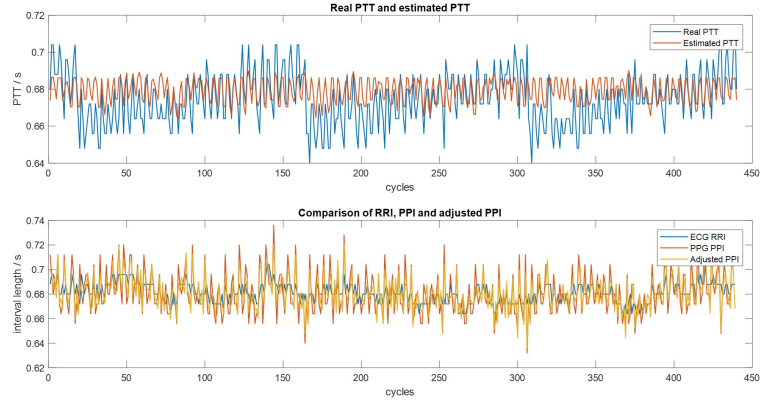
Figure 4.21: Comparison plot of estimated PTT and adjusted PPI using RBF kernel for non-CVD subjects: (up) Comparison of estimated PTT using RBF kernel SVR and true PTT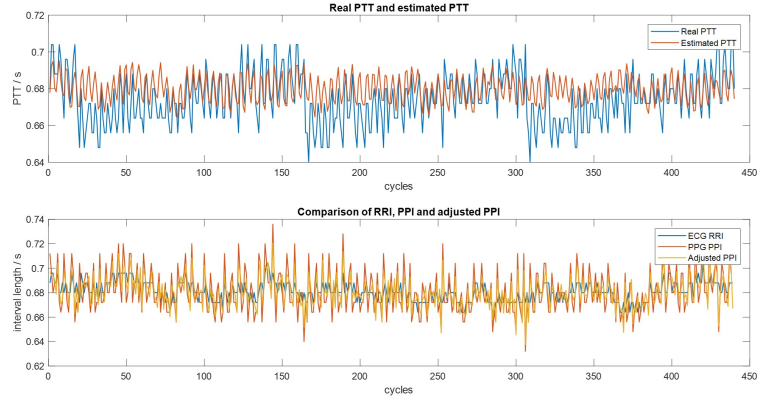 (down) Comparison of ECG RR interval (RRI), original PPI and PPI after adjustment using estimated PTT. The mean-squared error between RRI and PPI is 2.16e-04, and the mean-squared error between RRI and adjusted PPI is also 1.21e-04

Unfortunately, using average blood pressure is not as efficient as using blood pressure information per cycle. The agreement calculated after average BP refinement is shown below. The refinement process is the same as Figure 4.1 while changing the systolic blood pressure per cardiac cycle to average systolic blood pressure values calculated from three parts of the blood pressure segment.

Table 4.1 and Table 4.2 show the mean PCC and mean NRMSE between HRV and original PRV, PRV adjusted using BP per cycle and PRV adjusted using average BP for CVD subjects.

Figure 4.35 is the plot for comparison.
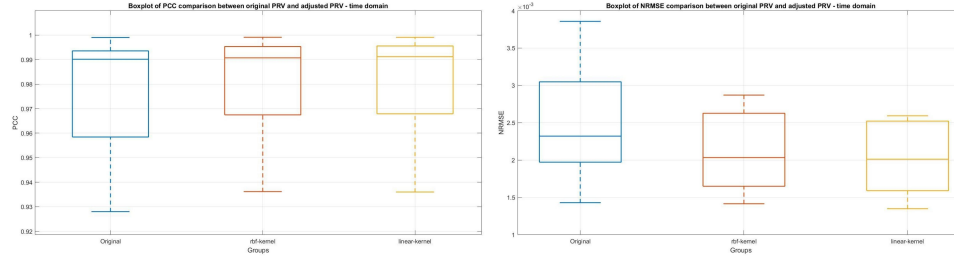
Figure 4.22: Agreement comparison of PRV parameters for non-CVD subjects (mean): (left) PCC comparison of mean interval length: mean: 0.9485, 0.9585, 0.9591 (Right) NRMSE comparison of mean interval length: mean: 0.0036, 0.0034, 0.0034. For non-CVD subjects, the agreement for mean interval length is also improved, and the improvement is more substantial comparing to the CVD situation. Besides, the linear kernel SVR has a better improvement result than the RBF kernel for this variable.

Table 4.3 and Table 4.4 exhibit the comparison result for subjects without cardiovascular diseases.

Figure 4.36 is the plots of the comparison above.

Comparing to using blood pressure per cycle, using average BP can only reduce mean NRMSE slightly and can hardly improve mean PCC. To explain this result, Figure 4.37 and Figure 4.38 show examples from CVD situation and non-CVD situation with the regression model, the estimated PTT and adjusted PPI as reference.

As average BP cannot reflect blood pressure changes over time, adjusting
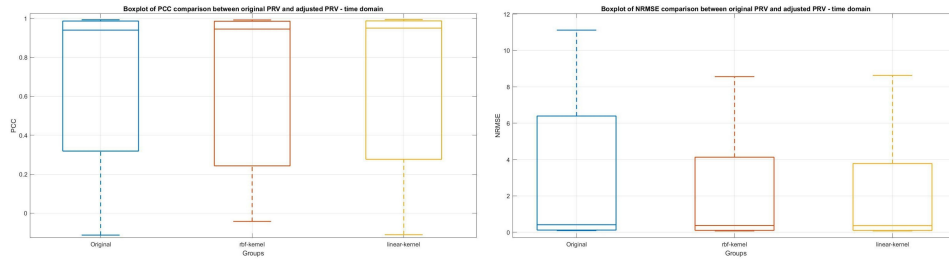
Figure 4.23: Agreement comparison of PRV parameters for non-CVD subjects (variance): (left) PCC comparison of interval length variance: mean: 0.6730, 0.6512, 0.6618 (Right) NRMSE comparison of interval length variance: mean: 14.42, 11.33, 11.20. The adjustment has a limited improvement for the PCC, but the mean NRMSE and the distribution range of NRMSE are reduced significantly.
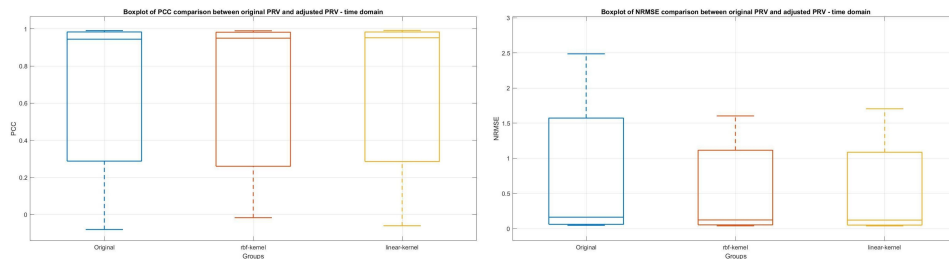
Figure 4.24: Agreement comparison of PRV parameters for non-CVD subjects (SD): (left) PCC comparison of standard deviation (SD) of interval length: mean: 0.6762, 0.6602, 0.6720 (Right) NRMSE comparison of interval length: mean: 1.021, 0.817, 0.775: The adjustment performance is similar to that of interval length variance.

Figure 4.25: Agreement comparison of PRV parameters for non-CVD subjects (RMSSD): (left) PCC comparison of RMSSD of HRV and PRV: mean: 0.6107, 0.6012, 0.6134 (Right) NRMSE comparison of RMSSD of HRV and PRV: mean: 1.296, 1.118, 1.064: The PCC improvement is relatively small, while the NRMSE decrease is more significant, and the linear kernel has better performance than the RBF kernel.
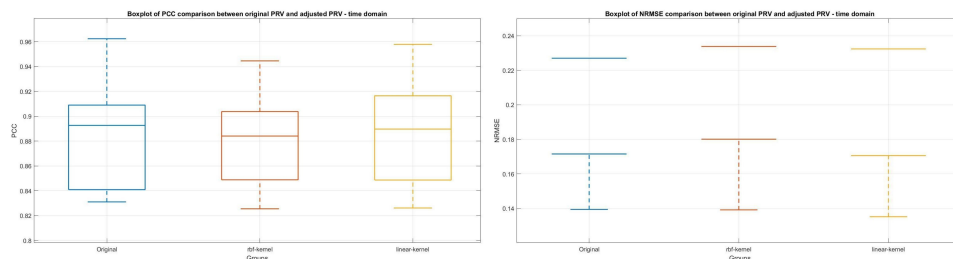
Figure 4.26: Agreement comparison of PRV parameters for non-CVD subjects (pnn50): (left) PCC comparison of pnn50 of HRV and PRV: mean: 0.8219, 0.8143, 0.8281 (Right) NRMSE comparison of pnn50 of HRV and PRV: mean: 1.568, 1.636, 1.587: For pnn50, there is not much improvement to the agreement

Figure 4.27: Agreement comparison of PRV parameters for non-CVD subjects (ULF): (left) PCC comparison of HRV and PRV ULF component: mean: 0.8185, 0.8240, 0.8264 (Right) NRMSE comparison of HRV and PRV ULF component: mean: 4.249, 2.455, 2.401: For ULF component of the intervals, PCC is improved by a small amount while NRMSE is reduced to a larger degree.
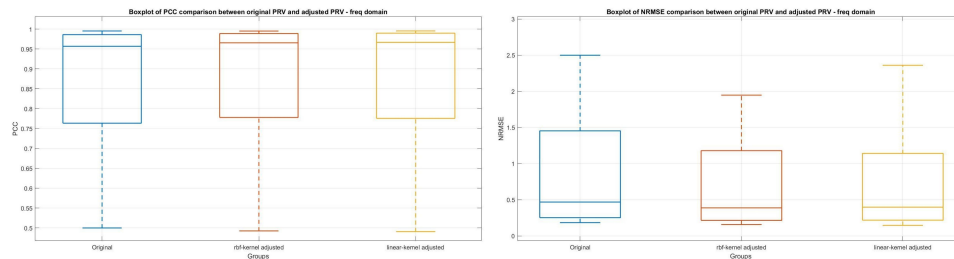
Figure 4.28: Agreement comparison of PRV parameters for non-CVD subjects (VLF): (left) PCC comparison of HRV and PRV VLF component: mean: 0.8224, 0.8270, 0.8295 (Right) NRMSE comparison of HRV and PRV VLF component: mean: 4.046, 2.377, 2.325: The refinement performance for the VLF component is similar to that of ULF component.
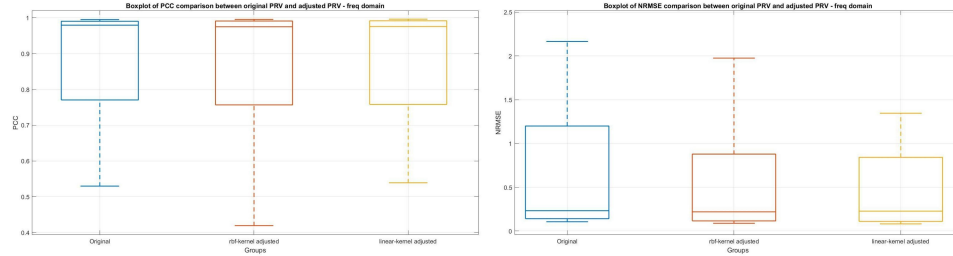
Figure 4.29: Agreement comparison of PRV parameters for non-CVD subjects (LF): (left) PCC comparison of HRV and PRV LF component: mean: 0.8262, 0.8181, 0.8230 (Right) NRMSE comparison of HRV and PRV LF component: mean: 3.612, 3.411, 3.323: The refinement has little improvement for PCC. However, the improvement for NRMSE is significant, and the linear kernel performs better than RBF kernel here.
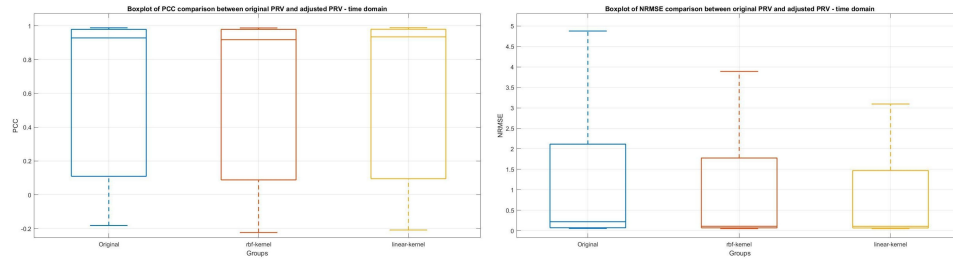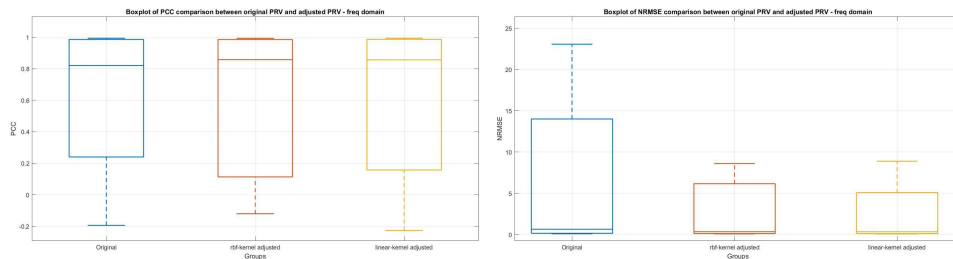

Figure 4.30: Agreement comparison of PRV parameters for non-CVD subjects (HF): (left) PCC comparison of HRV and PRV HF component: mean: 0.6232, 0.6101, 0.6256 (Right) NRMSE comparison of HRV and PRV HF component: mean: 15.18, 14.00, 13.79: Although the mean PCC remains nearly similar, the refinement improves it by a small amount, and the NRMSE is significantly enhanced.
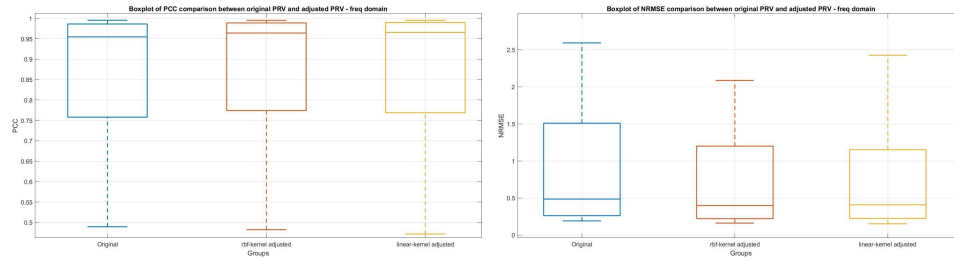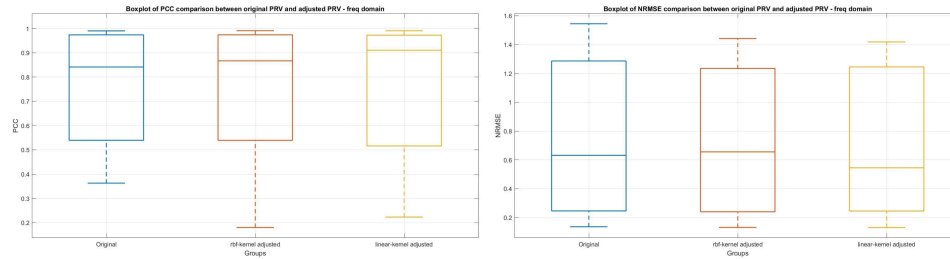
Figure 4.31: Agreement comparison of PRV parameters for non-CVD subjects (LF/HF): (left) PCC comparison of HRV and PRV's LF to HF ratio: mean: 0.7751, 0.7526, 0.7497 (Right) NRMSE comparison of HRV and PRV's LF to HF ratio: mean: 0.7270, 0.7105, 0.7084. For this parameter, the adjustment has little improvement to the PCC. However, it reduces NRMSE by a small amount.

PPG IBI signal using estimated PTT from average BP is the same as adding some constant value to it, and therefore the refinement will not make much difference to the agreement between PRV and HRV.
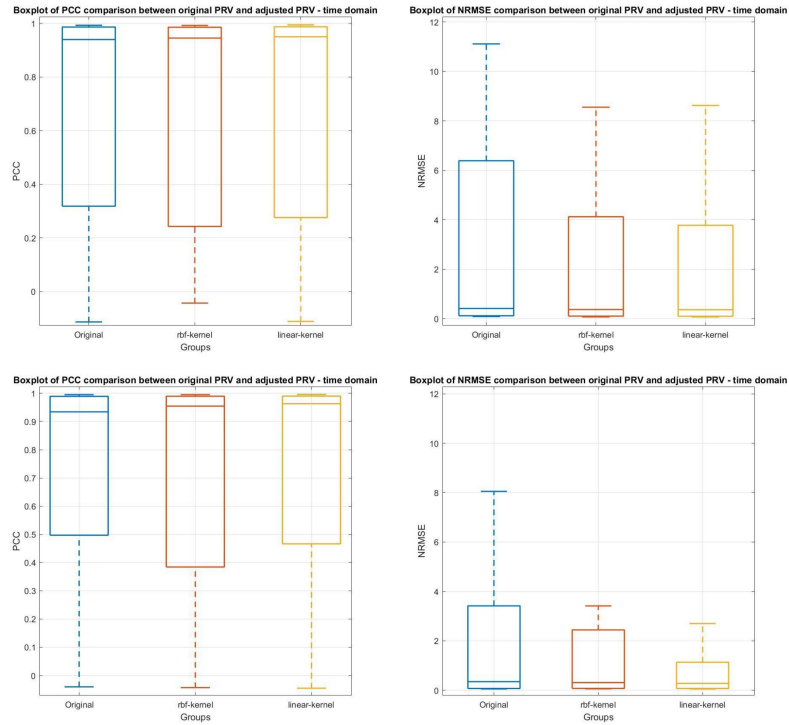
Figure 4.32: Improvement comparison of PPG peak derived PRV and PPG 50% max amplitude point derived PRV (variance): (up) Agreement of interval length variance between PPG peaks derived PRV and HRV (down) Agreement of interval length variance between PPG 50% max amplitude points derived PRV and HRV

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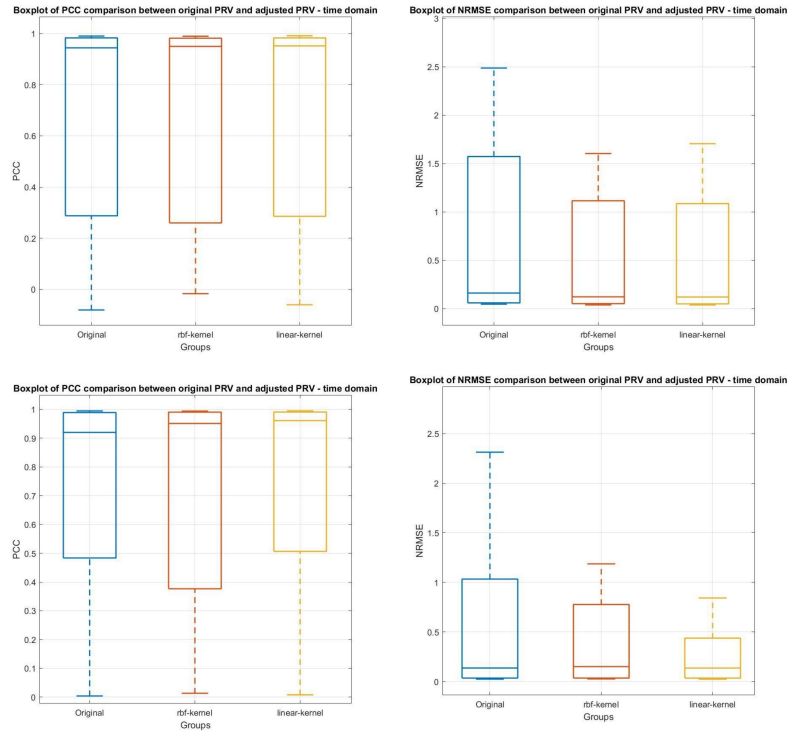
Figure 4.33: Improvement comparison of PPG peak derived PRV and PPG 50% max amplitude point derived PRV (SD): (up) Agreement of interval length standard deviation (SD) between PPG peaks derived PRV and HRV (down) Agreement of interval length standard deviation (SD) between PPG 50% max amplitude points derived PRV and HRV
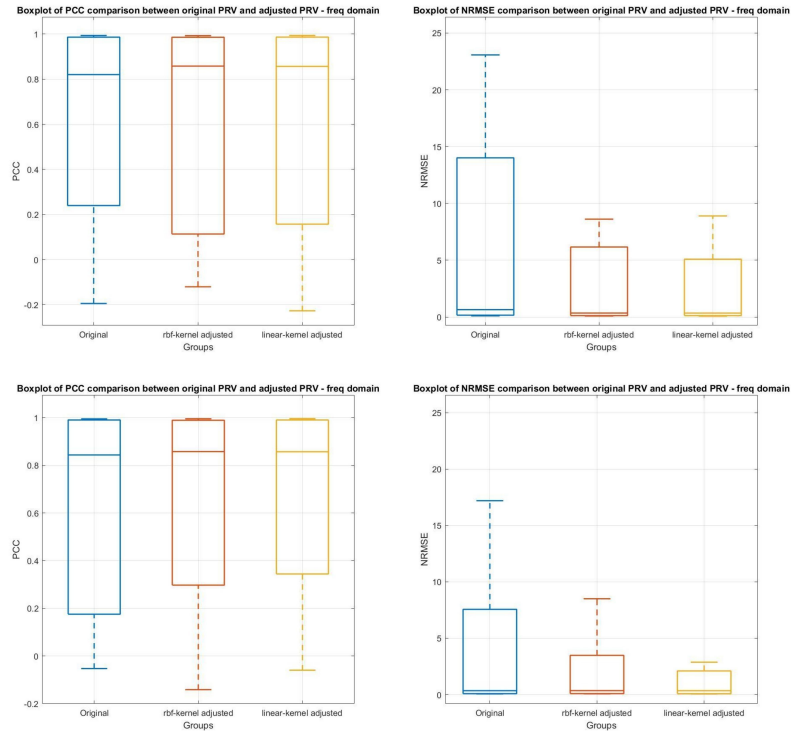
Figure 4.34: Improvement comparison of PPG peak derived PRV and PPG 50% max amplitude point derived PRV (HF): (up) Agreement of interval HF components between PPG peaks derived PRV and HRV (down) Agreement of interval HF components between PPG 50% max amplitude points derived PRV and HRV

Table 4.1: PCC comparison of PRV refinement using different kinds of blood pressure (CVD subjects)

mean PCC	Original	BP per cycle	Average BP
mean	0.7718	0.7700	0.7697
variance	0.5579	0.5556	0.5557
SD	0.5808	0.5842	0.5796
RMSSD	0.3986	0.4045	0.3949
pnn50	0.4876	0.5097	0.4797
ULF	0.6710	0.6842	0.6626
VLF	0.6740	0.6875	0.6649
LF	0.6760	0.6867	0.6719
HF	0.4900	0.5174	0.4867
LFHF	0.5416	0.5446	0.5384

Table 4.2: NRMSE comparison of PRV refinement using different kinds of blood pressure (CVD subjects)

mean NRMSE	Original	BP per cycle	Average BP
mean	0.0047	0.0045	0.0050
variance	27.99	25.36	28.71
SD	1.948	1.819	1.983
RMSSD	2.313	2.164	2.357
pnn50	16.14	16.65	16.14
ULF	79.96	79.40	79.82
VLF	80.19	79.73	80.67
LF	71.46	58.38	74.83
HF	29.98	25.86	30.69
LFHF	1.472	1.537	1.473
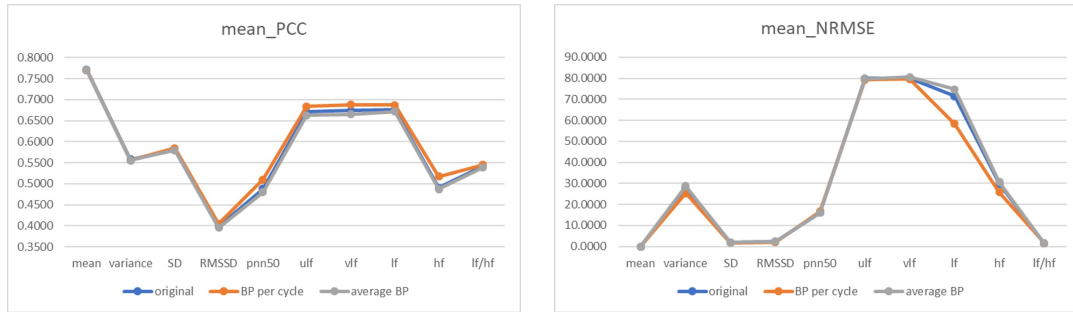
Figure 4.35: Agreement comparison of different PPG refinement method for CVD subjects - (left) mean PCC, (right) mean NRMSE

Table 4.3: PCC comparison of PRV refinement using different kinds of blood pressure (Non-CVD subjects)

mean PCC	Original	BP per cycle	Average BP
mean	0.9475	0.9591	0.9470
variance	0.6663	0.6618	0.6601
SD	0.6711	0.6720	0.6667
RMSSD	0.6074	0.6134	0.6045
pnn50	0.8178	0.8281	0.8138
ULF	0.8183	0.8264	0.8189
VLF	0.8222	0.8295	0.8226
LF	0.8260	0.8230	0.8259
HF	0.6201	0.6256	0.6181
LFHF	0.7558	0.7497	0.7575

Table 4.4: NRMSE comparison of PRV refinement using different kinds of blood
pressure (Non-CVD subjects)

mean NRMSE	Original	BP per cycle	Average BP
mean	0.0037	0.0034	0.0037
variance	14.28	11.20	14.14
SD	1.013	0.775	1.006
RMSSD	1.286	1.064	1.275
pnn50	1.544	1.587	1.522
ULF	4.223	2.401	4.185
VLF	4.021	2.325	3.986
LF	3.586	3.323	3.555
HF	15.03	13.79	14.86
LFHF	0.7261	0.7084	0.7235
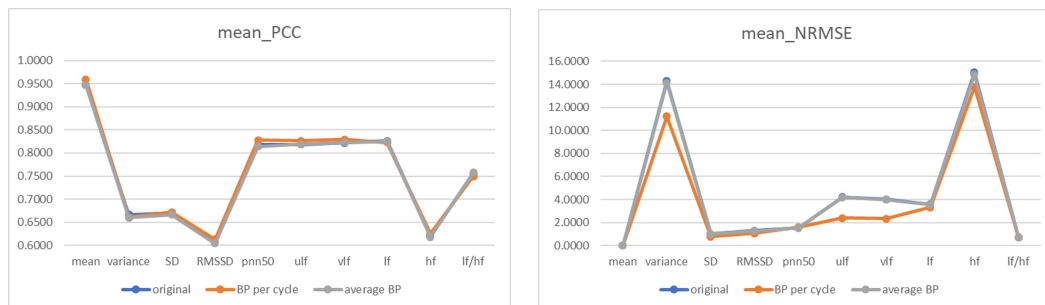
Figure 4.36: Agreement comparison of different PPG refinement method for non-
CVD subjects - (left) mean PCC, (right) mean NRMSE
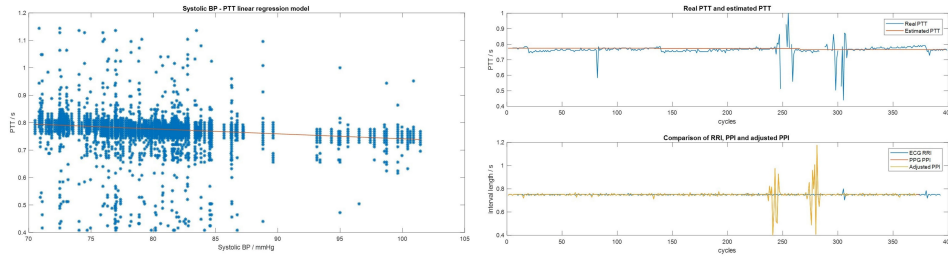
Figure 4.37: Regression model, estimated PTT and adjusted PPI for CVD subjects: (left) Linear regression model using average BP (right) PTT plots and IBI plots
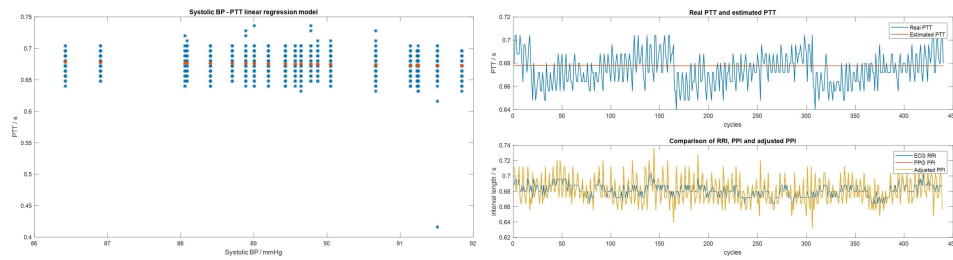
Figure 4.38: Regression model, estimated PTT and adjusted PPI for non-CVD subjects: (left) Linear regression model using average BP (right) PTT plots and IBI plots

Chapter 5: Thesis Conclusion and Perspectives

5.1 Thesis Conclusion

This thesis mainly focuses on two problems. One is comparing the agreement between HRV and PRV derived from different PPG pulse characteristic points and identifying the one with the highest agreement. This part is discussed in Chapter 3. Six characteristic points, pulse onset, pulse peak, maximum first derivative point on the slope, 25% max amplitude point on the slope, 50% max amplitude point on the slope, and 75% max amplitude point on the slope, are extracted and calculated. Furthermore, subjects with cardiovascular diseases and subjects without cardiovascular diseases are considered separately. ECG interbeat interval signal and different PPG interbeat interval signals, as well as calculated HRV parameters and PRV parameters, are used for comparison. The agreement is evaluated by the Pearson correlation coefficient and normalized root-mean-squared error between ECG IBI signal and PPG IBI signal and between ECG HRV parameters and PPG PRV parameters. The larger the PCC value, the smaller the NRMSE value, the higher the agreement. The comparison result indicates that for subjects with cardiovascular diseases, PPG peak-derived PRV has higher PCC, 50% max amplitude point and 75% max amplitude point derived PRV has lower NRMSE than other charac-

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teristic points, and all of them have a comparatively higher agreement to HRV than PRV derived from other characteristic points. For subjects without cardiovascular diseases, 50% and 75% max amplitude point derived PRV has higher agreement and peak is not recommended in this situation. For both cases, the onset and max slope point obtained PRV has a relatively low agreement.

Chapter 4 discusses the other problem of this thesis, which is about PPG refinement using arterial blood pressure information. The refinement is conducted by first building a regression function to model the relationship between PTT and systolic blood pressure value per cycle. Then PTT is estimated through the regression model and blood pressure information. PPG interbeat interval is adjusted using the estimated PTT. The refinement result is also compared to CVD subjects and non-CVD subjects separately. Besides, to figure out whether there will be a difference between pulse characteristic points, the result using PPG peak derived PRV and using PPG 50% max amplitude point derived PRV is also calculated and compared. As a comparison, the regression model applies the linear kernel and the RBF kernel separately. For CVD subjects, as the PTT does not vary much when blood pressure changes, the BP and PTT do not form a strictly linear relationship. Therefore, the improvement to the agreement between PPG IBI and ECG IBI, as well as between PRV and HRV is very limited. In this situation, parameters that reflect long-term characteristics, such as mean interval length, ULF component, and VLF component, have good improvement. However, parameters that related to short term characteristics do not have much improvement. Using PPG 50% max amplitude point derived PRV or changing kernel function to RBF have similar results. For non-CVD sub-

jects, estimated PTT contains more trend information than CVD situations. Hence, in this situation, the refinement can achieve a more considerable improvement. After adjustment, the agreement between ECG IBI and PPG IBI, and the agreement between approximately all variables of HRV and PRV are increased significantly. PPG 50% max amplitude point has more improvement for specific parameters. In this situation, the RBF kernel is outperformed by the linear kernel. As continuous blood pressure is complicated and expensive to collect, the last part of this chapter compares the result using average blood pressure to do refinement with the result before. However, as average blood pressure can only make a constant adjustment to the PPG signal, the improvement is very limited.

5.2   Future Perspectives

This research can be continued and extended in several directions.

There is still much to be improved for the regression model. We can utilize more arterial blood pressure signal features, as well as PPG, ECG signal features to build a deeper machine learning regression model to fit the PTT and BP relationship better. We hope the agreement between HRV and PRV can be further improved in this way.

As average blood pressure can not be utilized in our method and continuous blood pressure is hard to collect, we would like to build a new framework that estimating continuous blood pressure using PPG signal and apply the estimated blood pressure signal for further study of PRV refinement.

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