CUFF-FREE BLOOD PRESSURE ESTIMATION USING SIGNAL PROCESSING TECHNIQUES

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Abstract

Since blood pressure is a significant parameter to examine people's physical attributes and it is useful to indicate cardiovascular diseases, the measurement/estimation of blood pressure has gained increasing attention. The continuous, cuff-less and non-invasive blood pressure estimation is required for the daily health monitoring. In recent years, studies have been focusing on the ways of blood pressure estimation based on other physiological parameters. It is widely accepted that the pulse transit time (PTT) is related to arterial stiffness, and can be used to estimate blood pressure.

A promising signal processing technology, Hilbert-Huang Transform (HHT), is introduced to analyze both ECG and PPG data, which are applied to calculate PTT. The relationship between blood pressure and PTT is illustrated, and the problems of calibration and re-calibration are also discussed. The proposed algorithm is tested based on the continuous data from MIMIC database. To verify the algorithm, the HHT algorithm is compared with other used processing technique (wavelet transform). The accuracy is calculated to validate the method. Furthermore, we collect data using our own developed system and test our algorithm.

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Finally, this thesis is dedicated to my parents, who always give me inspiration, support, and encouragement.

To my parents.

Contents

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List of Abbreviations

SBP	systolic blood pressure
DBP	diastolic blood pressure
PTT	pulse transit time
ECG	electrocardiogram
PPG	photoplethysmogram
AAMI	The Association for the Advancement of Medical Instrumentation
HHT	Hilbert-Huang Transform
EMD	empirical mode decomposition
IMF	intrinsic mode function
FANFARE	Falls And Near Falls Assessment Research and Evaluation

Chapter 1

Introduction

1.1 Background

Blood pressure carries a great deal of information about people's physical attributes. In recent years, blood pressure has been paid increasing attention because it is useful to indicate cardiovascular diseases, such as hypertension, heart attack and asthma. Blood pressure is the pressure of blood against the walls of the arteries as the blood is circulating in the arteries [1]. It is the driving force of pushing blood to flow in the vessels. The history of blood pressure measurement can be traced back to the year of 1733. Stephen Hales, a British veterinarian, recorded blood pressure of animals by using brass pipes [2]. In 1896, the traditional blood pressure instrument known as a sphygmomanometer was developed by an Italian physician Scipione Riva-Rocci [2].

Systolic blood pressure (SBP) is the peak pressure in the arteries when the blood flows from the ventricles to the arteries, which occurs near the end of the cardiac cycle as the ventricles are contracting. Diastolic blood pressure (DBP) is the minimum pressure in the arteries during ventricular diastole, which occurs near the beginning of the cardiac cycle when the ventricles are full of blood [1]. The metrical unit of blood pressure is called millimeters of mercury (mmHg). Normal blood pressure in adults is lower than 120/80 mmHg [3].

As blood pressure is the power of blood flowing down the aorta and into distributing arteries, blood could not supply the whole body if blood pressure is too low. On the contrary, the vessels might be injured by the too high blood pressure, or even some abnormities of the heart happen [4]. Some factors, such as stature, age, density of blood, posture, resistance of vessel, drugs, diet, disease, etc., could affect the blood pressure. Moreover, it changes during the day. When one is asleep, blood pressure is lowest and it increases as one is awake. It can also change with the mood. Blood pressure is so important because it is a valuable indication of body status. Due to the high stress of the modern society, increasing numbers of people have hypertension, especially, the elderly. It is said that hypertension happens in more than half of all Americans aged 65 years or older [5]. Hypertension, defined as the value of SBP/DBP is higher than 140/90 mmHg, can cause heart attacks, strokes and other problems. Hypertension is also a major cause of disability, and it is an important risk factor for death, about 7.5 million deaths per year (13% of all deaths) [6]. Daily monitoring of blood pressure provides vital feedback to the prevention of hypertension. The daily blood pressure monitoring removes the white coat hypertension and masked hypertension problems. And it is more convenient for patients and may lead to better blood pressure control [7]. Therefore, observation of blood pressure is really essential.

1.2 Conventional approaches to measure blood pressure

The approaches to measure blood pressure can be classified into invasive and non-invasive methods. The invasive blood pressure measurement is a gold standard which can give more accurate reading of beat-to-beat blood pressure. It is often used when rapid changes of blood pressure are anticipated, or the long-term recording of blood pressure is required. This invasive method uses catheter over a needle to insert in patient's artery to measure blood pressure directly. A needle with catheter is entered into the vessel first, and when the blood flows through the needle, the catheter is advanced over the needle into the vessel. The pressure-transducing system connects with the catheter [1]. The basic components of the system are intra-arterial cannula, tubing (incorporating an infusion system), transducer, microprocessor and display screen, and mechanism for zeroing and calibration [2]. Both numerical and graphical information are available by this continuous invasive method. Although it is continuous and accurate, it makes patients uncomfortable. It needs close supervision because it might cause severe bleeding if the measurement system is disconnected. Moreover, it is difficult to operate and there is the possibility of infection and pain. Therefore, it is desirable to develop the non-invasive method.

The existing non-invasive methods to measure blood pressure include non-continuous methods, which contain auscultatory and oscillometric methods, and continuous methods, which contain arterial tonometry, plethysmography and pulse transit time (PTT)-based method [8]. The auscultatory method is based on a blood pressure cuff placed around the arm of the subject to stop the blood flow in the artery. The Korotkoff sounds can be detected as the slow deflation of the blood pressure cuff with a stethoscope placed on the brachial artery. The systolic blood pressure is determined as the pressure of the inflated cuff when Korotkoff sounds are first detected, while the cuff pressure when Korotkoff sounds become muffled or disappear represents the diastolic blood pressure. As the heart beats are actually felt by an operator, this method is still acceptable rather than the invasive way. However, the Korotkoff sounds are difficult to detect for patients who are in low-flow state and it also needs a trained person to detect the Korotkoff sounds [9]. Sometimes, the Korotkoff sounds do not disappear for some patients, which means one could not identify the diastolic blood pressure.

Similar to the auscultatory method, the oscillometric method also requires a blood pressure cuff around the arm of the patients to stop the blood flow. A pressure transducer is used to record the pressure instead of detecting the Korotkoff sounds. Arterial pulsations cause oscillations in the cuff pressure. The cuff pressure is equal to the mean arterial pressure when the oscillations are at their maximum and the systolic blood pressure and diastolic blood pressure are estimated from the mean blood pressure and the oscillation pattern [10]. For this method, one has to make sure the measurement position of the subject's arm is at the same level of the heart. Otherwise, it would give a false result. Therefore, doctors prefer three measurements in a row to get more accurate results. Moreover, it does not work well for the patients who have irregular heart beats. These two methods using cuffs can not provide continuous measurement of blood pressure with the cuff inflation and deflation.

In recent years, the non-invasive blood pressure monitors have been widely applied in hospitals and clinics. However, clinical research studies have shown that the difference between direct blood pressure and non-invasive blood pressure by various monitors is within 5 mmHg on average [11]. They also demonstrate that the difference could be 37 mmHg by the non-invasive blood pressure measurement. Therefore, the non-invasive blood pressure measurement should be further investigated with different methods or some consecutive measurements by a non-invasive blood pressure monitor. Moreover, the cuff size should be proper to an individual. A too large cuff will cause inaccurately low results whereas a too small cuff will lead to inaccurately high results. The width of a cuff should be equal to

40% of the arm circumference [11]. Inaccurate recordings of blood pressure could happen under some conditions, like highly irregular or rapid cardiac rhythms. As the oscillometric method is dependent on the regular cardiac rhythms, some subject movements or external movements such as that from an ambulance transport can disturb the measurements.

The continuous and cuff-less measurement of blood pressure is desirable for home health-care or easing workload of clinicians at hospitals. Tonometry can determine beat to beat arterial blood pressure by adjusting the pressure required to the artery located between a tonometer and a bone. It was firstly invented in 1963 [12]. This system includes four basic steps and applies a tissue stress sensor. The continuous diaphragm of the tissue stress sensor is placed against a tissue with an artery nearby, and the sensor is used to bear against the tissue. Then, the monitor portion on the sensor is determined and the stress caused by the arterial pulsations is detected at the monitor portion. It is able to offer the continuous pressure waveform but it is subject to the relatively high cost compared with a conventional sphygmomanometer and its accuracy is decreased by the high sensitivity to sensor position and wrist movements [13]. The plethysmographic method measures the change in volume of blood in an extremity, which is caused by the arterial pulsations [1][14]. A finger cuff is applied to detect the minimum pressure and maintain a constant finger blood volume. The changes of finger blood volume are detected and the cuff pressure is adjusted to track the blood pressure. But this method does not work for patients with low peripheral perfusion, hypothermia or low-flow states [1].

1.3 Methods of blood pressure measurement/estimation using signal processing techniques

The continuous, cuff-less and non-invasive measurement of blood pressure is more desirable for people to regularly monitor their blood pressure. In recent years, the estimation of blood pressure using other physiological parameters has been studied extensively. In this section, these methods are reviewed in terms of the main idea, the results, the advantages and the limitations of each method. Particularly, PTT, photoplethysmographic signal and heart rate are considered in this section.

1.3.1 The blood pressure measurement based on pulse transit time

It is commonly accepted that PTT can be regarded as an index of arterial stiffness, and has been employed as an indirect estimation of blood pressure [15]. PTT can be measured as the time interval between the peak of R wave of the electrocardiogram (ECG) and a characteristic point at predetermined thresholds of the photoplethysmogram (PPG) in the same cardiac cycle, which is the blood propagation period from the aortic valve to a peripheral site. ECG describes and records the electrical activity of the heart by detecting and amplifying the tiny electrical changes using the skin electrodes, and it consists of P wave, QRS complex and T wave. Each part of ECG waveform has its physical meaning. The QRS complex of it represents the ventricular contraction, corresponding to the depolarization of the right and left ventricles. PPG measures the volume change of blood in an organ. It is obtained by a pulse oximeter by illuminating the skin and measuring the light amount of either transmitted or reflected. The starting point of PTT is the R wave peak of ECG, and mainly there are several different choices of the ending point [16]. Figure 1.1 gives the definition of PTT.

PTT was originally applied in the area of blood pressure estimation by Gribbin et al. in 1976. Since then, researchers have studied the mechanism and feasibility of this method. In 1979, Obrist discussed that PTT can be used as an index of blood pressure [17]. Lane studied the relationships between PTT and SBP, DBP, and mean arterial blood pressure by experiments in 1983 [18]. They found the correlations were dependent on individuals. Different expressions have been derived to characterize the relationship between the blood pressure and the PTT. Most effective ones are Moens-Korteweg's [19] and Bramwell-Hill's [20], which have been widely used and extended. Essentially, the elasticity of an artery was early recognized to be related to the velocity of the volume pulses propagating through it [21][22]. When blood pressure goes up, the arterial compliance decreases, and the pulse wave velocity is higher, PTT is reduced. Therefore, the PTT-based method is to apply the relationship to estimate blood pressure.

The pulse wave velocity PWV is defined by Moens and Korteweg as a function of such factors as the thickness of vessel wall t, the elasticity of the arterial wall, the density of blood ρ and the interior diameter of the vessel d. The equation is shown as follows [19]:

$$PWV = \sqrt{\frac{tE}{\rho d}}, \tag{1.1}$$

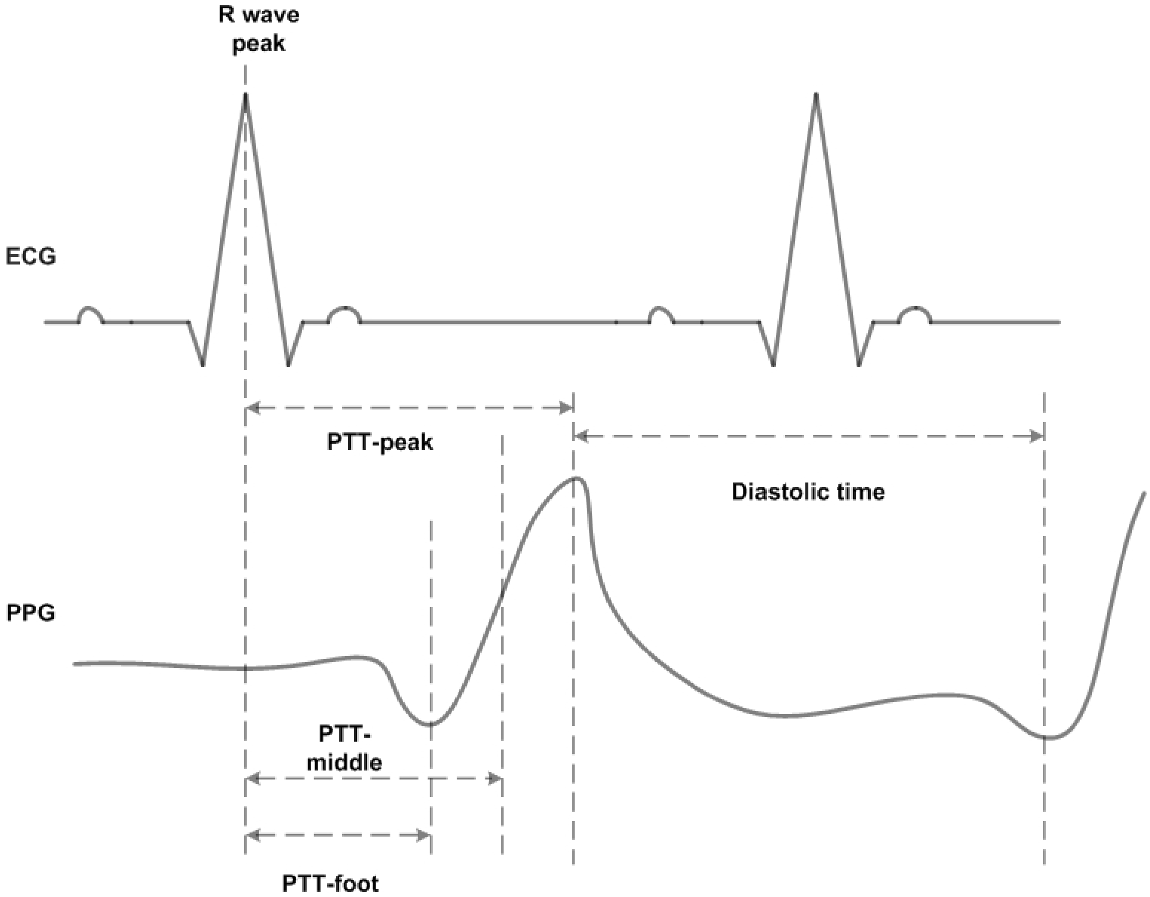

Figure 1.1: The definitions of different PTTs. PTT-peak, PTT-middle and PTT-foot are the time intervals measured from the R-wave peak of ECG to the peak, middle and foot of PPG, respectively. Diastolic time is from the peak to the foot of PPG.

where E stands for the Young's modulus describing the elasticity of the arterial wall, and generally it is not a constant. Further, the Young's modulus E was described by Geddes as $E = E_0 e^{\alpha P}$ [19], where E_0 is the modulus of the zero pressure, α is a constant that depends on the vessel, varying from 0.016 mmHg^{-1} to 0.018 mmHg^{-1}, P is the blood pressure, and e is 2.71828. Then we have

$$PWV = \sqrt{\frac{tE_0 e^{\alpha P}}{\rho d}}. \tag{1.2}$$

In the work, the relationship formula developed in [23] based on the above Moens-Korteweg formula will be applied.

Bramwell and Hill have found that the propagation velocity of the pulse wave in the artery filled with blood is related to the volume-pressure relationship of the artery, with the assumption that the artery is an elastic tube filled with an incompressible and invisible liquid, which can be written as [20]:

$$PWV = \sqrt{\frac{V}{\rho}\frac{\Delta P}{\Delta V}}, \tag{1.3}$$

where PWV is the velocity of pressure wave, V is the volume of the tube, ρ is the density of the blood, ΔV is the volume change, and ΔP is the change in the distending pressure. The velocity of pressure wave can also be described as $PWV = \frac{L}{T}$, where L is the length of the pulse wave propagation along the artery, and T represents the pulse transit time. Therefore, the velocity of local pressure wave can be readily estimated by using this equation. It requires no knowledge of the thickness and diameter of the vessel, or of the elasticity of the arterial wall, but only the rate of increase of volume with pressure, which is simply and directly observable. The compliance, C, which represents how much the change in the volume is in response to a given change in the distending pressure:

$$C = \frac{\Delta V}{\Delta P}. \tag{1.4}$$

Thus, PTT can be written in terms of compliance and volume [24]:

$$(\frac{L}{T})^2 = \frac{V}{\rho C}. \tag{1.5}$$

According to the above discussion, the blood pressure is inversely proportional to PTT, and the relationship between them is individual-dependent, thus, many researchers apply the linear regression in estimating the blood pressure [25]: first, the coefficients of the model are identified based on the experimental data; second, the model is used for blood pressure estimation.

According to the Association for the Advancement of Medical Instrumentation (AAMI), an organization responsible for the safety and efficacy of medical instrumentation, blood pressure estimation, for both SBP and DBP, must have an absolute value of error mean less than 5 mmHg and the error standard deviation less than 8 mmHg. Most researchers use this standard to verify their results.

In 1981, Geddes et al. measured diastolic blood pressure and pulse arrival time to analyze the relationship using 10 anesthetized dogs. They showed PTT detected in different locations along the vessel was highly related to diastolic time [26]. Marie et al. found out that PTT was highly related to blood pressure during dynamic and static exercise [27]. Okada analyzed some factors (age, SBP, DBP, phospholipid) that might be related to pulse wave velocity in 1988. The transmission time used in his work was obtained from fingertip to toe tip [28]. ECG, the peripheral plethysmographic wave and the intra-aortic pressure were studied by Franchi et al. in 1996. They obtained the correlation between the pressure and two delays, from ECG R-wave to the aortic pulse and from aortic pulse to ear lobe pulse [29].

In the 2000s, PTT-based blood pressure estimation method gained a great deal of attention. In 2002, Nitzan et al. compared the time delay between ECG R wave and the arrival time at the toe with the time difference from the finger to the toe, which were both related to pulse wave velocity. Both of them showed high correlation with SBP, which with the correlation coefficients -0.670 and -0.515, respectively [20]. Fung et al. applied the kinetic energy of the wave and the gravitational potential energy on the study of the relationship between the PTT and blood pressure in 2004 [30]. In the same year, Lass et al. proposed that it was possible to estimate the beat to beat systolic arterial blood pressure based on PTT during the exercise [31]. The auscultatory method was used at the end of each recording minute to measure blood pressure and a continuous measurement Finapres was also applied to record the beat to beat blood pressure during the test. Park et al. introduced some other physical parameters (weight and arm length) together with PTT to estimate unspecified people's SBP in 2005. The model gave the acceptable results compared with the standard by AAMI [32]. Ahlstrom investigated if this method can be used in hemodialysis patients. The results showed the large sudden pressure changes like in sudden hypovolemia can be detected [15]. Foo et al. got the results that SBP had the strongest correlation with vascular transit time, which was measured from PPG and phonocardiography. The regression equation of blood pressure and vascular transit time was modeled in the project, and it showed DBP and mean blood pressure could also be estimated by vascular transit time [33].

In [34], the system of collecting ECG and PPG was introduced, and the non-invasive continuous blood pressure was measured. A novel adaptive algorithm for calibrating non-invasive PTT measurements to arterial blood pressure was presented in [35]. This new algorithm allowed complete calibration of PTT to BP without the use of an oscillometric blood pressure cuff or external pressure sensor. It used the natural motion to do the calibration. The natural motion includes varying the height of the sensor relative to the heart to alter hydrostatic pressure at the measurement site and adjusting proximal joint posture to vary the external arterial pressure at the measurement site. The techniques of analyzing pulse wave velocity were discussed by Boutouyrie et al. in 2009 [36]. They reviewed the methods of measuring PTT and the available devices to measure pulse wave velocity.

The main work of [25] was to determine which time parameters from ECG and PPG were better to estimate SBP and DBP, respectively. The results showed that PTT calculated between ECG R-wave and maximum first derivative PPG was strongly related to SBP, and diastolic time, which was from PPG, had better performance to determine DBP. Moreover, for SBP, individual regression method was more accurate. There was not much difference for DBP.

Heart rate was introduced to estimate blood pressure combined with pulse arrival time in [37]. The results showed better performance compared with the method only using pulse arrival time for the blood pressure estimation. Moreover, they analyzed the effect of skew and jitter on blood pressure estimation. They talked about the methods of initial calibration (least-squares algorithm), adaptive re-calibration (RLS algorithm recursions), enhancing robustness (keeping the parameters within certain limits), and fixing the bias.

The study in [38] aimed to test if PTT can be used to estimate SBP during steady state exercise. The results showed that PTT reflected the changes of blood pressure, cardiac output and arterial stiffness during steady state exercise, but should not be applied as the only index of blood pressure estimation. In the experiments, twelve male subjects cycled for 70 mins in three different conditions. Meanwhile, ECG, PPG, blood pressure, cardiac output and respiratory frequency were measured. The results showed the changes of PTT was related with SBP (r=-0.66), however, the regression analysis showed that SBP only described 29 % of the observed variability in PTT.

Foo and Wilson [39] reviewed the clinical applications of PTT-based method and the advantages and limitations of it. It could be applied in respiratory sleep studies and cardiovascular studies, and it had potential to use for small infants during critical care. Comparing with the conventional non-invasive blood pressure measurements, the PTT method provides the beat to beat readings. Multiple readings might minimize the white-coat effect and increase the probability of hypertension investigation. In addition, the conventional methods also face the problems of selecting the proper cuff size and position to ensure the accuracy.

In recent years, two research groups have studied the method, which are led by Zhang in Chinese University of Hong Kong, and by Muehlsteff in Philips Research Europe, respectively. The results of them will be discussed in the following parts.

Starting with the year of 2005, the group of Zhang analyzed the relationship between PTT and other cardiovascular variabilities, especially blood pressure. They collected continuous blood pressure, ECG and PPG signals from 11 healthy persons. The results indicated PTT can be used to estimate BP for the healthy static body state [16]. In [9], they found out that the PTT-based method had the potential to be applied in wearable devices, compared with the standard of AAMI.

In 2006, they began to consider exercises in their project. They compared the results with the measurements by Finometer, and there was only occasional discrepancy during the recovery period [13]. As the PTT-based method is dependent on individuals, they introduced a model that solved the individualized calibration problem. Hand elevation was used to obtain the individualized coefficients, which made the estimation more accurate and robust [40]. Because the experiments carried out before indicated that the contact force between the PPG sensor and the fingertip affected the values of PTT, they studied the pressure of the sensors by theoretical modeling in 2007. In the theoretical model, a nonlinear arterial Pressure-Volume curve described the bio-mechanical property of the finger arterial wall. Based on the simulation results, it was obvious to see that if the applied contact force increased, PTT went up. So they were suggesting the sensor applied on the fingertip should be carefully controlled in the experiments to guarantee the PTT values [21].

Another attention was paid to the pre-ejection period effect on the estimation of blood pressure based on the PTT method in 2008. They systematically observed and verified the inclusion of pre-ejection period in PTT for this non-invasive blood pressure estimation [41]. In [42], they found the median correlation of beat to beat PTT and invasive blood pressure was reduced from -0.73 to -0.63 as the number of the beats went up from 15 to 360. Since the relationship between blood pressure and PTT changed with time, frequent calibration was required to estimate beat to beat blood pressure. Least-squares regression was used to estimate BP in the first test and a repeatability test carried out half year later in [43]. Blood pressure in the repeatability test was also estimated using the regression coefficients in the first test. The results in the first and repeatability tests illustrated that after exercises, blood pressure increases and PTT decreased, and SBP was strongly related to PTT. However, the regression coefficients obtained firstly could not be applied to estimate blood pressure accurately.

In [44], they analyzed the influence of running on the PTT-based blood pressure estimation. The results showed that SBP was more closely related to PTT-foot than to PTT-peak, and re-calibration was needed during the continuous exercises. They arranged the experiments with four main periods: Pre-exercise, Post-exercise 1 (after 3 min of 10km/h running), Post-exercise 2 (after 3 min of 8km/h running) and Recovery. The exercises affected blood pressure estimation using PTT because exercises influenced the geometric and elastic properties of arteries which were related to PTT. The results showed re-calibration was needed because the influence of exercises could last more than 30 min and the dependance of arteries on the intensity of exercises.

Philips Research Laboratories Europe also explored this topic. In 2006, they investigated the effect of pre-ejection period on pulse arrival time more than PTT [45]. In [46], they indicated that the effect of PTT and pre-ejection period on blood pressure estimation. The results showed that SBP was highly related to pulse arrival time which was the combination of PTT and pre-ejection period. They applied the PTT-based method to a wearable body sensor network in 2008. The device and the wireless data transmission were discussed in [47]. They studied the influence of posture on the PTT measurement. The context information on posture and physical activity was required in the application of the

PTT-based method [48].

As PTT has been accepted as a main indication of blood pressure estimation, the PTT-based blood pressure estimation method has been applied in some health monitor systems. In 2000, Heard et al. tested the DxTek monitor, which uses the PTT-based non-invasive and continuous blood pressure estimation [49]. They recorded blood pressure using DxTek monitor, oscillometric method and intra-arterial method in intensive care unit patients. The results that they found out was the DxTek monitor could give an accurate recording of blood pressure of intensive care unit patients compared with the oscillometric method. A wireless body sensor network was developed by Espina et al. in 2006 [50]. The wireless body sensor network provides continuous cuff-less blood pressure monitoring based on the PTT-based method. The measure positions are waist for ECG and ear for PPG.

The Wearable Intelligent Sensor and System for e-Health was developed in 2006 [51]. It can monitor the continuous health condition and display it. Moreover, treatment and alarming are conducted if needed. The health-shirt, which is part of the system, is wearable. In their test experiment, Finometer was employed to measure the continuous blood pressure as a reference. The continuous biological signals, including ECG, PPG, SBP and DBP, were recorded for 15 mins, which included pre-exercise for 5 mins, riding on a bicycle for 5 mins and rest for 5 mins. The results showed that the error of the estimated blood pressure was quite large. The smart vest, a wearable multi-parameter remote physiological monitoring system, was developed to monitor ECG, PPG, heart rate, body temperature, galvanic skin response, SBP and DBP [52]. In the blood pressure estimation, it applied the PTT-based method.

It is worth noting that PTT-based blood pressure estimation method has gained much focus. It gives promising results by the previous study. The signal processing procedure would be studied to improve the accuracy of this method.

1.3.2 The blood pressure measurement based on photoplethysmogram signal

From the previous introduction, the estimation of blood pressure based on PTT can be recognized as an accurate non-invasive and cuff-less method. However, it requires two independent channels to measure the time interval, which increases inconvenience to users and the probability of errors' occurring. Due to these, some attempts are made to estimate blood pressure just based on PPG signal. PPG is a volumetric measurement of an organ using a pulse oximeter.

The PPG signal can be analyzed in both time domain and frequency domain to estimate blood pressure. Teng and Zhang chose four features of PPG signals, which were width of 2/3 pulse amplitude, width of 1/2 pulse amplitude, systolic upstroke time and diastolic time, to find an optimal feature for estimating blood pressure [53]. In the analysis of PPG signals, continuous wavelet transform was used to solve the problems of unclear foot position and foot position shift. Linear regression line in the form of $y = ax + b$ was established for SBP and DBP respectively using the data of some trials, and then, some other trials from the same subject were applied to estimate blood pressure. The results showed that the systolic upstroke time and diastolic upstroke time from the PPG signals have higher correlation with blood pressure. In general, there is better performance in DBP estimation, with the mean differences using systolic time and diastolic time, respectively, but worse performance in SBP estimation [53].

A new feature, normalized harmonic area, which is obtained from PPG signal in the frequency domain, has been showed that it has high correlation with blood pressure by Yan and Zhang [54]. In this method, the discrete period transform algorithm, which is good at solving low frequency signals such as PPG signals (approximately 0.1-10 Hz), is used to calculate the spectrum of each beat in frequency domain. The results of the experiment, which involved 28 healthy volunteers, aged 24-30 years, shows normalized harmonic area has more significant correlation with blood pressure and smaller error than both PTT and diastolic time. The mean differences and standard deviations of SBP and DBP are 0.37 ± 4.3 mmHg and 0.47 ± 4.8 mmHg [54]. However, the physiological mechanisms of the relation are needed to be explored. Later, they did more research on the PTT-based method.

The estimation of blood pressure only based on PPG signal requires more studies on its relation between blood pressure and PPG, which results in that more research and publications are focusing on PTT-based methods.

1.3.3 The blood pressure measurement based on heart rate

Biologically, heart rate is the number of heart beats per minute. It is related to blood pressure. The two main determinants of blood pressure are cardiac output, which is the volume of blood pumped by heart per minute, and systemic blood vessel's resistance, which is determined by many factors, including vasomotor tone in arterioles, terminal arterioles, or precapillary sphincters [55]. Blood pressure can be expressed as:

$$BP = CO \times SVR, \tag{1.6}$$

where BP is blood pressure, CO is cardiac output and SVR is systemic vascular resistance. Moreover, the cardiac output can be deduced by the stroke volume and heart rate as following:

$$CO = HR \times SV, \tag{1.7}$$

where HR is heart rate and SV is the stroke volume. Then, according to these two equations, blood pressure has the correlation with heart rate as shown:

$$BP = SV \times SVR \times HR. \tag{1.8}$$

Type-2 fuzzy system has been introduced in this method by Mahmood, Al-Jumaily and Al-Jaafreh [56]. As well known, type-2 fuzzy system is one of the most significant techniques to deal with high uncertainty, sensitive and non-linear problem [57]. So this type-2 fuzzy system is used to estimate blood pressure using heart rate as the input. Al-Jaafreh and Al-Jumaily set up different type-2 fuzzy systems to estimate systolic blood pressure and diastolic blood pressure respectively, which both use heart rate as the inputs. And then, the mean arterial blood pressure is calculated by SBP and DBP using the equation as the following:

$$MBP = DBP + \frac{1}{3} \times (SBP - DBP). \tag{1.9}$$

The design of a type-2 fuzzy system for the estimation of blood pressure includes four steps, i.e. fuzzification, rules, inference engine and output process [56]. Firstly, the input HR is fuzzified into five grades. If the heart rate has non-zero membership value in two grades, assign it with higher membership grade. Secondly, the rule, which has "If" and "Then" part, is applied. Next, the inference engine applies the fuzzy rules on truth values of input variables to obtain a corresponding output. The widely used methods are minimum t-norm and product t-norm. The scale of output blood pressure applies the product t-norm inference method. Finally, the method named center of sets was used to reduce the type of the system, and then, the defuzzifier uses the mid point of type reduced sets as the output value.

The results based on 30 adult healthy subjects showed that the mean differences and standard deviations of SBP, DBP and MBP are 3.8 ± 12.8 mmHg, -5.0 ± 8.6 mmHg and 4.6 ± 10.3 mmHg [58]. In order to obtain better results, the fuzzy logic system can be programmed into a micro-controller. The type-2 fuzzy system achieves encouraging outcomes, which the absolute value of mean differences of SBP, DBP and MBP are less than 5 mmHg. However, the error standard deviation needs to be improved to meet the standard of AAMI.

It can be obviously seen that using heart rate to estimate blood pressure based on type-2 fuzzy system has worse accuracy.

1.3.4 Summary

The methods of measuring blood pressure have been reviewed as above. The continuous, non-invasive and cuff-less method is more desired with considering the regular measurement of blood pressure necessarily. The estimation of blood pressure based on other physical parameters has a potential because of its convenience and accuracy. One of the most widely used parameters is PTT, which would be focused on.

1.4 Contributions and outline

1.4.1 Objectives and contributions

As blood pressure is one of the most vital signs for clinical use and the continuous non-invasive cuff-less blood pressure estimation is desirable in wearable health devices, PTT-based blood pressure estimation is discussed in our work. We propose the following research topics in the thesis:

- **PTT-based blood pressure estimation using Hilbert-Huang Transform:** In the method of PTT-based blood pressure estimation, signal processing is one of the crucial parts. Due to the inherent nonlinear and non-stationary properties of the ECG and PPG signals, Hilbert-Huang Transform (HHT) technique can be applied to process the signals and improve the accuracy of the estimation. The theory of the HHT algorithm is introduced and our algorithm is discussed.

- **Testing PTT-based blood pressure estimation on elderly:** Since the daily monitoring of blood pressure for elderly is really demanded, we focus on applying the PTT-based blood pressure estimation using the HHT algorithm to older adults. Some details of the method, such as the correlation of blood pressure and PTT, the ending point of PTT, and re-calibration are analyzed. To verify our algorithm, the wavelet transform is applied to compare with the HHT algorithm. Moreover, the Multi-innovation Recursive Least Square algorithm is applied to estimate the unknown parameter vector. Its application to elderly is studied to guarantee the acceptable results.

- **The application of PTT-based blood pressure estimation to the data by the developed device:** Continuous ECG and PPG can be recorded by the device developed in the FANFARE project. By applying HHT algorithm, the data are analyzed to obtain PTT values. Based on the equations in Chapter 3, the changes of blood pressure are calculated and its relationship with PTT is studied.

The main contributions of the thesis can be briefly summarized as follows:

- To the best of our knowledge, the HHT technique is, for the first time, applied to the PTT-based blood pressure estimation method. Due to the nonlinear and non-stationary properties of the physiological signals, the introduction of HHT algorithm could improve the results.

- We verify that the PTT-based blood pressure estimation method can be used in elderly. According to the comparison of the wavelet transform, the accuracy can validate our algorithm. To improve the results of re-calibration, the Multi-innovation technique is introduced to the Recursive Least Square.

- Both ECG and PPG data are collected by the developed device, and the proposed algorithm is tested based on the data.

For the sake of concentrating on the development of the PTT-based blood pressure estimation method, the main theme of the thesis is to apply a proper signal processing technique to smoothen signals for the acceptable accuracy, especially for the elderly.

1.4.2 Outline of the thesis

As the background of blood pressure measurement and the review of continuous cuff-free blood pressure estimation has been presented in the previous part, the remainder of the thesis is organized as follows:

Chapter 2 gives the introduction of the HHT algorithm. Other signal processing techniques are reviewed, and the properties of HHT algorithm are discussed.

Chapter 3 presents the HHT algorithm and the application to PTT-based blood pressure estimation. The HHT algorithm is firstly introduced and algorithm is developed and presented, and finally, the results are illustrated.

Chapter 4 highlights that the proposed algorithm can be applied to older adults. HHT is used on the data from MIMIC database, and the comparison with wavelet transform is illustrated. In addition, the choice of the ending point and the relationship between blood pressure and PTT are presented. Multi-innovation technique is used to improve the accuracy of the re-calibration.

In Chapter 5, the developed data collection system is introduced, and the analysis of the data is discussed. The results of the relationship between blood pressure and PTT based on the collected data is given in this chapter.

The conclusion is provided in Chapter 6. Some suggestions for the future work on PTT-based blood pressure estimation are summarized also.

Chapter 2

Hilbert-Huang Transform

Signal processing plays a vital part in the PTT-based blood pressure estimation. It is obvious that if a proper technique is applied to analyze the signals, the accuracy in this point can be improved. To provide a more efficient method of filtering of a signal from noise for nonlinear, non-stationary data, Huang, et al. [59][60] introduced a new approach called the Hilbert-Huang Transform (HHT). To understand the promising Hilbert-Huang Transform well, a review of other signal analysis methods will be firstly given.

2.1 Non-stationary signal processing techniques

In digital signal processing area, Fourier spectral analysis is a vital technique [61]. Generally speaking, Fourier spectral analysis is used to break the complicated signals into a sum of simpler pieces. Due to the outstanding characters that Fourier spectral analysis has, it has gained lots of attention and has been applied to all kinds of applications, such as physics, mathematics, probability, statistics, acoustics, optics and signal processing. Although it is valid under usual conditions, there are some inherent shortcomings: the system must be linear and stationary. The linear system must meet two requirements: superposition and homogeneity. Linear systems have the features and properties that are much easier than nonlinear systems. Although some natural phenomena can be approximated by linear systems or a sum of linear systems, most physical systems are inherently nonlinear. In this case, Fourier spectral analysis may cause some problems, giving some inaccurate results. In addition to linearity, Fourier spectral analysis must also be applied in stationary process. It is defined as a random process that joint probability distribution does not depend on the location of the sample. Some parameters such as the mean and covariance do not change with time. Most signal processing techniques require the property of stationarity. However, few data in practice can satisfy this requirement.

The spectrogram is another basic signal processing technique. It uses a short-time Fourier Transform, so the data should satisfy piecewise stationary, which the non-stationary data could not always meet [62]. Moreover, it is hard to choose the window size. This method is of limited use.

The wavelet analysis is a common tool for extracting information from data. Wavelet transform can be considered as a form of time-frequency representation [63]. It has gained extreme attention of some fields. Many applications are in edge detection and image analysis. However, wavelet analysis is non-adaptive, which means once the basic wavelet is selected, all the data have to be analyzed using it. Moveover, the leakage generated by the limited length of the basic wavelet function makes the quantitative definition of the energy-frequency-time distribution difficult. Despite these demerits, wavelet analysis still has been applied to analyzing the non-stationary data. Some researchers introduced it to the PTT-based blood pressure estimation [30][34][53]. So this technique will be considered as a comparison in our work.

Some other miscellaneous techniques also have some inherent shortcomings. Since all the discussed methods fail in one way or another, a good technique for the PTT-based blood pressure estimation is needed to be introduced to guarantee the results.

2.2 The advantages of Hilbert-Huang Transform

HHT can overcome the limitations of the above mentioned methods. It can analyze the nonlinear and non-stationary data. HHT is the first adaptive method for measuring things that do not stay still and do not follow regular patterns. The result is a more precise definition of particular events in time-frequency space, and a more meaningful interpretation of underlying dynamic processes that can be obtained by historical methods [64]. HHT is a combination of the empirical mode decomposition (EMD) method and Hilbert Transform. By EMD, the complicated data can be decomposed into a collection of function components. The energy-frequency-time distribution of the decomposed data is created by the Hilbert Transform. The key point of this method is the introduction of EMD, which can decompose data into a number of intrinsic mode functions (IMF). IMF is a function having the same numbers of zero-crossing and exterma, and symmetric envelops defined by the local maxima and minima respectively. This method is highly efficient and adaptive, and it is applicable to nonlinear and non-stationary data.

HHT consists of two steps. Firstly, the EMD method is used to obtain finite IMFs. Secondly, with the Hilbert Transform, the IMFs yield instantaneous frequencies as functions of time. Finally, the Hilbert Spectrum can be obtained, which is an energy-frequency-time distribution. Since the decomposition is based on the local characteristic time scale of the data, it is applicable to nonlinear and non-stationary processes. The detailed dynamics characteristic of a nonlinear system through the instantaneous frequency can be examined using this technique. The main flow of the HHT algorithm is shown in Figure 2.1.

With the attractive advantages, HHT has successfully found a wide variety of applications: Basic nonlinear mechanics, climate studies, earthquake engineering, geophysical exploration, submarine design, structural damage detection in bridges and buildings, speech signal processing and satellite data analysis.

2.3 The theory of Hilbert-Huang Transform

According to the properties of HHT algorithm, it is applied to our work to solve the signal processing problem. The whole theory of HHT is introduced in this section. The Hilbert Transform and two significant concepts, including instantaneous frequency and intrinsic mode functions, are discussed first. Then, the Hilbert-Huang Transform is introduced.

2.3.1 Hilbert Transform

The Hilbert Transform is an operator which starts from a real function and produces a function in the same domain. A real function and its Hilbert Transform are related to each other. A strong analytic signal, which can be written with an amplitude and a phase, is together created by the real function and its Hilbert Transform. The derivative of the phase can be called as the instantaneous frequency.

For an arbitrary time series, $f(t)$, its Hilbert Transform $\widehat{f}(t)$ can be expressed as [64]

$$\widehat{f}(t) = \frac{1}{\pi} P \int \frac{f(\tau)}{t-\tau} d\tau, \tag{2.1}$$

where P represents the Cauchy principal value. The conjugate pair $f(t)$ and $\widehat{f}(t)$ can create the analytic signal $Z(t)$ as

$$Z(t) = f(t) + i\widehat{f}(t) = a(t)e^{i\mu(t)}, \tag{2.2}$$

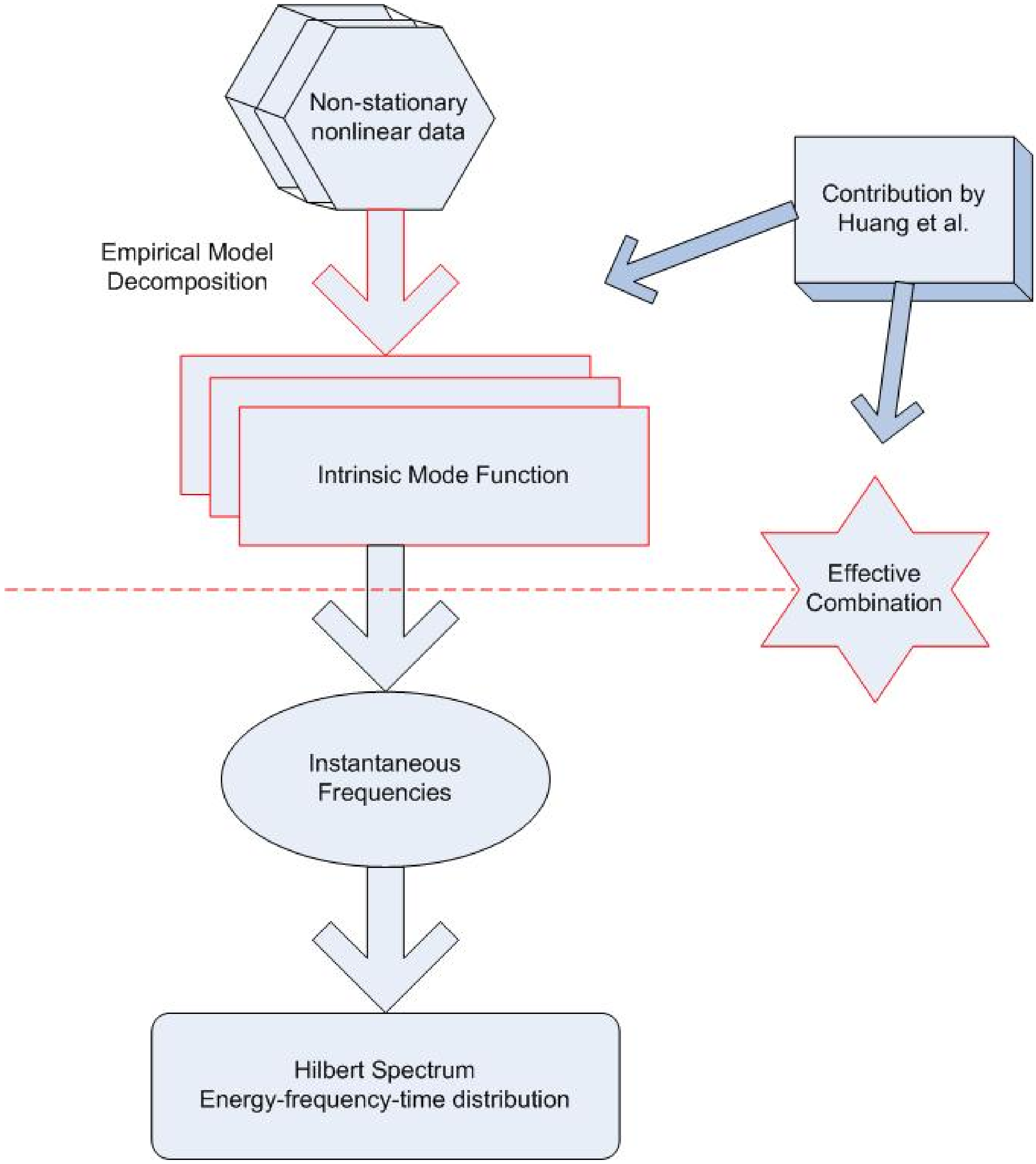

Figure 2.1: The brief idea of HHT.

in which

$$a(t) = [f^2(t) + \widehat{f}^2(t)]^{\frac{1}{2}}; \tag{2.3}$$

$$\mu(t) = arctan(\frac{\widehat{f}(t)}{f(t)}). \tag{2.4}$$

Equation 2.1 describes the Hilbert Transform as the convolution of $f(t)$ with $1/t$. It can pinpoint the local properties of $f(t)$. The analytic signal gives the local nature, both the amplitude and phase information in equation 2.2.

2.3.2 Instantaneous frequency

Instantaneous characteristics of signals gain lots of interested from researchers. The instantaneous energy or the instantaneous envelope of the signal is already accepted, whereas the idea of the instantaneous frequency is not clearly defined. Two basic difficulties with accepting the notion of the instantaneous frequency are as follows:

- **The effect of the Fourier spectral analysis:** Under the framework of the traditional Fourier analysis, the frequency is determined as the sine or cosine function through the whole length of the data with certain amplitude. Extending from this definition, the instantaneous frequency still has to involve the sine or cosine function. Hence, at least one full oscillation of a sine or a cosine wave is needed to define the local frequency value. Based on this logic, nothing shorter than a full wave will make sense. Furthermore, such a definition would not be applicable for non-stationary data whose frequency changes from time to time. The analysis of this difficulty, on the other hand, motivates us to jump out of the framework of the Fourier analysis to hunt for new tools, especially for non-stationary and non-linear signal analysis.

- **The non-unique way of the definition of instantaneous frequency:** There are numerous ways of defining the imaginary part, however, the Hilbert Transform defines the instantaneous frequency in a unique way as

$$\omega(t) = \frac{d\mu(t)}{dt}. \tag{2.5}$$

  There is still considerable controversy in the definition of instantaneous frequency.

We have to impose the restrictive conditions on the data to acquire the meaningful instantaneous frequency. The restrictive condition is that the real part of the Fourier Transform has to have only positive frequency, which is still global. Therefore, a local condition instead of the global one is developed to obtain the instantaneous frequency. Taking a sine function as an example, the instantaneous frequency can be defined only if the function is restricted to be symmetric locally with respect to the zero mean level. This local restriction gives us a hint of the way of decomposing the data into components so that the instantaneous frequency can be defined. To this end, we are naturally led to a class of functions, called IMF, whose instantaneous frequency can be defined.

In summary, physically, the necessary conditions to define the meaningful instantaneous frequency are that the functions are symmetric with respect to the local zero mean, and have the same numbers of zero crossings and extrema [60].

2.3.3 Intrinsic mode functions

The IMF is determined by satisfying these two conditions:

- The number of the extrema must be equal to the number of the zero crossings in the whole data set or differ at most one.
- The mean value of the local maxima envelope and the local minima envelope is zero at any point. This condition is the local requirement modified from the global one.

In order to obtain the instantaneous frequency, the data can be decomposed into IMF components according as the conditions, and the instantaneous frequency can be defined by each IMF component. The EMD method is applied to decompose the data into IMFs.

2.3.4 Hilbert-Huang Transform

Firstly, the EMD method, which can deal with the non-stationary and non-linear data, is used to obtain the IMFs. This method is adaptive and efficient. The sifting procedure of the method can be summarized as follows:

- **Step 1:** Find out the envelopes determined by the local maxima and minima respectively. All the local extrema are detected first, and then a cubic spline line is used to link all the local maxima to get the upper envelope. The lower envelope is obtained in the same way. All the data should be between the upper and lower envelopes. Then we have:

$$f(t) - m_1 = h_1, \tag{2.6}$$

where $f(t)$ indicates the data, m_1 represents the mean of the upper and lower envelops, and h_1 is considered as the first component.

- **Step 2:** We take h_1 as the data, then

$$h_1 - m_{11} = h_{11}. \tag{2.7}$$

Repeat the sifting procedure k times until h_{1k} is an IMF:

$$h_{1(k-1)} - m_{1k} = h_{1k}. \tag{2.8}$$

The first IMF component from the data can be expressed as:

$$c_1 = h_{1k}. \tag{2.9}$$

- **Step 3:** To make sure that the IMF components have enough physical sense of both amplitude and frequency, the standard deviation, SD, calculated from the two consecutive sifting results, is used as a criterion to stop the sifting procedure.

$$SD = \sum_{t=0}^{T} [\frac{|h_{1(k-1)}(t) - h_{1k}(t)|^2}{h_{1(k-1)}^2(t)}]. \tag{2.10}$$

Normally, SD is set between 0.1 and 0.3.

- **Step 4:** Separate c_1 from the data by

$$f(t) - c_1 = r_1, \tag{2.11}$$

where r_1 indicates the residue.

- **Step 5:** Repeat the above procedures to get the IMF components.

$$r_1 - c_2 = r_2, \cdots, r_{n-1} - c_n = r_n. \tag{2.12}$$

The predetermined value of substantial consequence can be used as the criterion to stop the sifting process. Or, no more IMF can be extracted because the residue, r_n, stays monotonic.

Finally we would get

$$f(t) = \sum_{i=1}^{n} c_i + r_n. \tag{2.13}$$

Once the IMF components are obtained, it will be straightforward to apply the Hilbert Transform to each component, and get the instantaneous frequency through equation 2.5. After conducting the Hilbert Transform to each IMF component, the original data can be demonstrated as:

$$f(t) = \sum_{j=1}^{n} a_j(t) e^{i \int \omega_j(t) dt}. \tag{2.14}$$

The residue, r_n, is not considered because it is either a constant or a monotonic function.

2.4 Summary

To sum up, the HHT algorithm is a promising method to solve the non-linear and non-stationary data. Both ECG and PPG signals are inherently non-linear and non-stationary due to lots of interference, and the data are changing with time due to the physiological status [65][66][67]. So the HHT is employed to process the ECG and PPG signals to estimate the PTT.

Chapter 3

Pulse transit time-based blood pressure estimation using Hilbert-Huang Transform

PTT-based blood pressure estimation has received considerable attention. The PPG sensor was developed in [68]. In [40], some important factors that could affect the accuracy of the estimation method were explored. The wavelet transform was employed to detect the peak value of the signals and then calculated the PTT [30][34][53]. However, most of the existing methods in the literature have not fully considered the inherent nature of the nonlinear and non-stationary properties of the measured ECG and PPG signals when applying different kinds of signal processing techniques. In this section, we aim to process the measured signals by using the Hilbert-Huang Transform (HHT) that can effectively process the nonlinear and non-stationary signals [69].

3.1 Algorithm description

3.1.1 PTT estimation

HHT is applied to process the ECG and PPG signals, respectively, to obtain the intrinsic mode functions. To achieve so, we need to accurately determine the time instance of the R wave peak in the ECG signal, and recognize several related characteristic points in the PPG signal. First, the IMFs are obtained using the EMD procedure. Second, the signal without noise is reconstructed by ignoring the IMFs corresponding to noise part. Third, each interested IMF is compared with the rebuilt signal to see which one shows better performance on the time instance. The logic flowchart to decompose the input signal into successive IMFs is illustrated in Figure 3.1. The spline interpolation is applied to get the maximal and minimal envelopes based on the maximal and minimal points. Then, the IMF components can be obtained using the standard deviation as a criterion, which is used to make sure that each IMF has enough physical meaning. The process to obtain IMF is stopped when the maximal and minimal envelopes could not be detected.

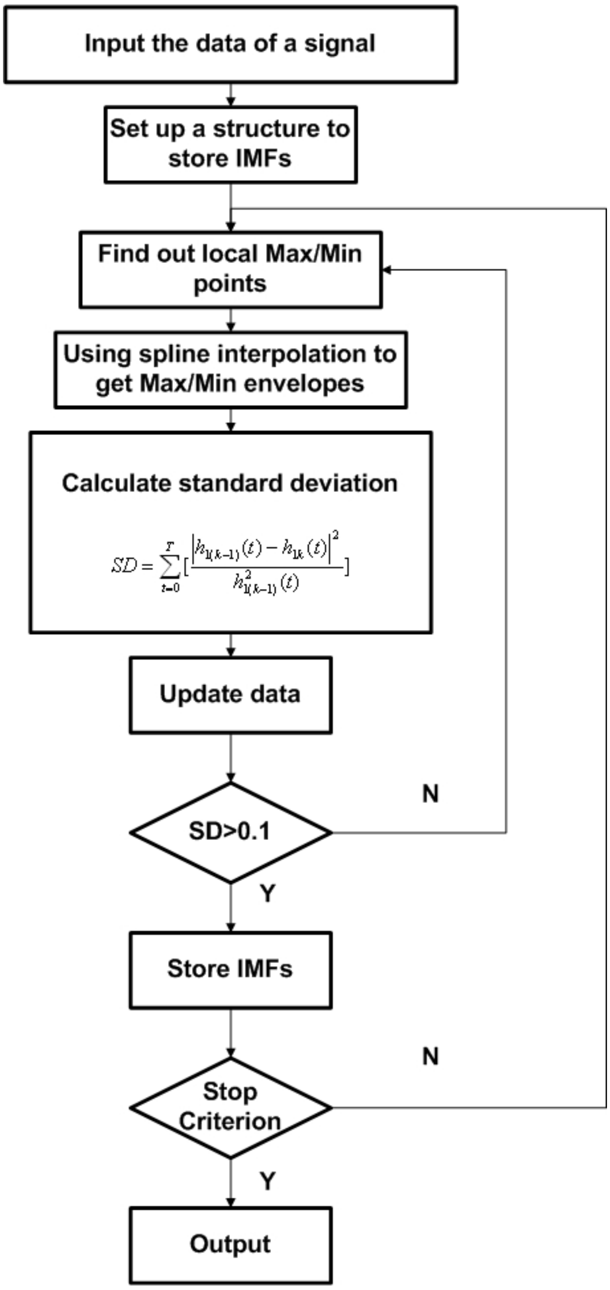

Figure 3.1: The logic flowchart to decompose the input signal into successive IMFs.

Generally, PTT is defined as the time interval between the R wave peak of ECG and the peak of PPG in the same cardiac cycle [32].

3.1.2 The estimation of blood pressure

The mathematical expression that describes the relationship between the blood pressure and the pulse wave velocity PWV are given in the Moens-Korteweg equation:

$$PWV = \sqrt{\frac{tE}{\rho d}}, \tag{3.1}$$

where t represents the vessel wall thickness, ρ indicates the blood density, and d is the interior diameter of the vessel. According to the derived results of [23], the pulse wave velocity can be described by the distance L for the pulse wave to transit and the transit time T as:

$$PWV = \frac{L}{T}. \tag{3.2}$$

The elastic modulus is indicated as:

$$E = E_0 e^{\alpha P}, \tag{3.3}$$

where E_0 is the modulus as the pressure is zero, α is dependent on the vessel, and P is the blood pressure. Substituting equations 3.2 and 3.3 into the Moens-Korteweg formula, we have

$$\frac{L}{T} = \sqrt{\frac{tE_0 e^{\alpha P}}{\rho d}}, \tag{3.4}$$

then it follows that

$$P = \frac{1}{\alpha}[\ln \frac{L^2 \rho d}{tE_0} - 2\ln T]. \tag{3.5}$$

If the changes in the wall thickness and the diameter of the vessel with respect to the change in blood pressure are negligible, and the change in the modulus E_0 is slow enough, the change of blood pressure, which is linearly related to the change in the PTT, can be described as:

$$\triangle P = -\frac{2}{\alpha T} dT. \tag{3.6}$$

Remark 3.1. It can be seen that the change of blood pressure is related to the PTT. After accurately estimate the PTT, the variation of blood pressure can be readily calculated using (3.6).

3.2 Results

In this section, for the measured ECG and PPG signals, which are collected at 256 Hz in World Wide Electronic Technology Ltd., the HHT method is applied to estimate the PTT, and further calculate the change of blood pressure.

The original signals and the empirical mode decomposition components are listed in Figure 3.2 and Figure 3.3, respectively. The C_i indicates each IMF component obtained by EMD method in the time domain. By applying the criteria of $SD = 0.1$, which is used to guarantee that each IMF has enough physical meaning, the ECG is decomposed into seven components C_1-C_7, while the PPG is decomposed into nine components C_1-C_9.

The peak detection of ECG is performed on the rebuilt signal, which is reconstructed by adding C_3 to C_7 together and shows clear waveforms to detect the R-wave peaks, as shown in Figure 3.4. For the PPG, it is noticed that the third IMF of PPG shows better performance in the peak detection comparing with other functions and the rebuilt PPG signal. After detecting the peak of the signals, the time interval between ECG and PPG in the same cardiac cycle can be determined, which will be used to estimate the blood pressure.

The ECG and PPG are collected at 256 Hz and the constant parameter α is fixed as 0.017 mmHg^{-1}. The change of blood pressure can be readily calculated: Some of the estimated data are shown in Table 3.1.

Remark 3.2. A good estimation of the blood pressure variation is very useful in monitoring patients' health status, and it can be potentially applied to the fall and near-fall detection system, developed by our research team. If the base blood pressure level is known, then the estimated blood pressure can be obtained.

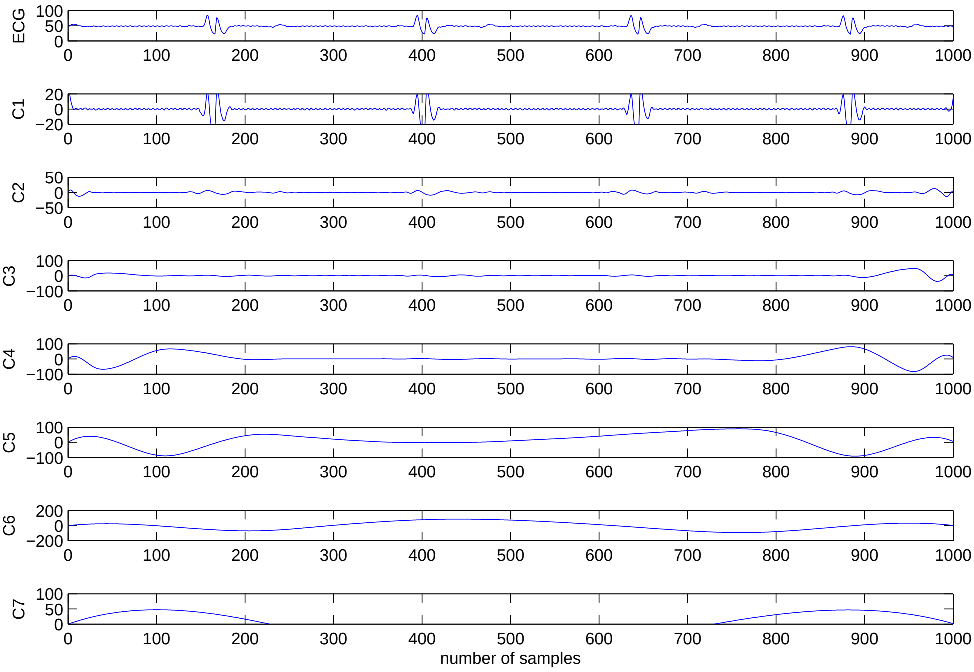

Figure 3.2: The original ECG and the empirical mode decomposition components C1-C7.

Table 3.1: The pulse transit time and the change of blood pressure.

Peak of ECG	Peak of PPG	PTT (s)	Change of BP (mmHg)
157	223	0.2578	
395	460	0.2539	1.8100
636	700	0.2500	1.8382
876	942	0.2578	-3.5651
1116	1183	0.2617	-1.7559

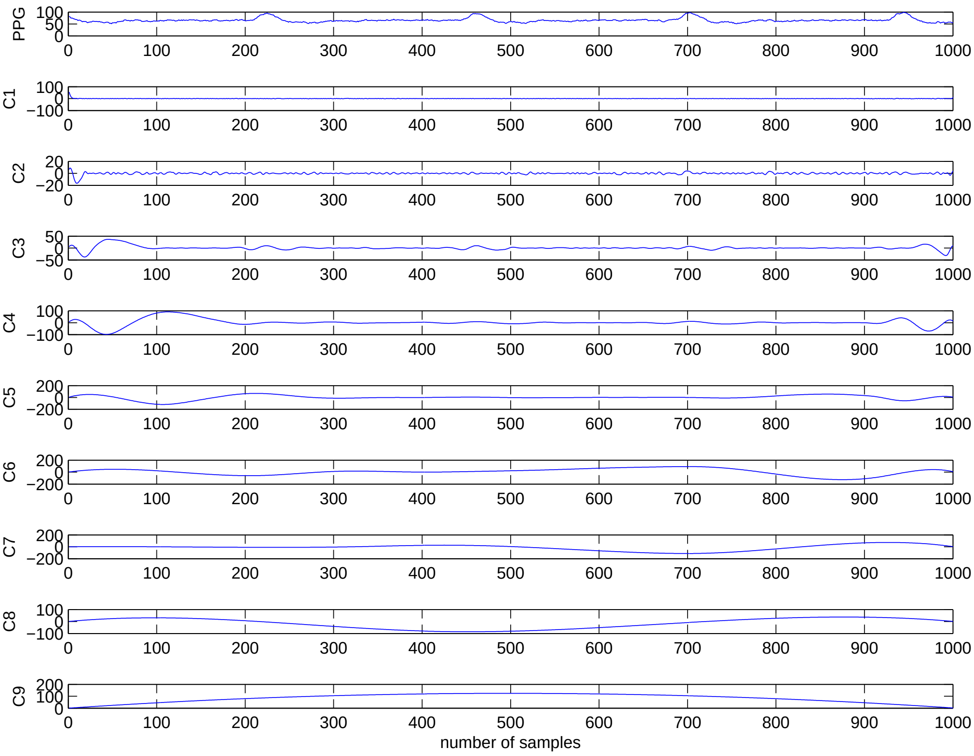

Figure 3.3: The original PPG and the empirical mode decomposition components C1-C9.

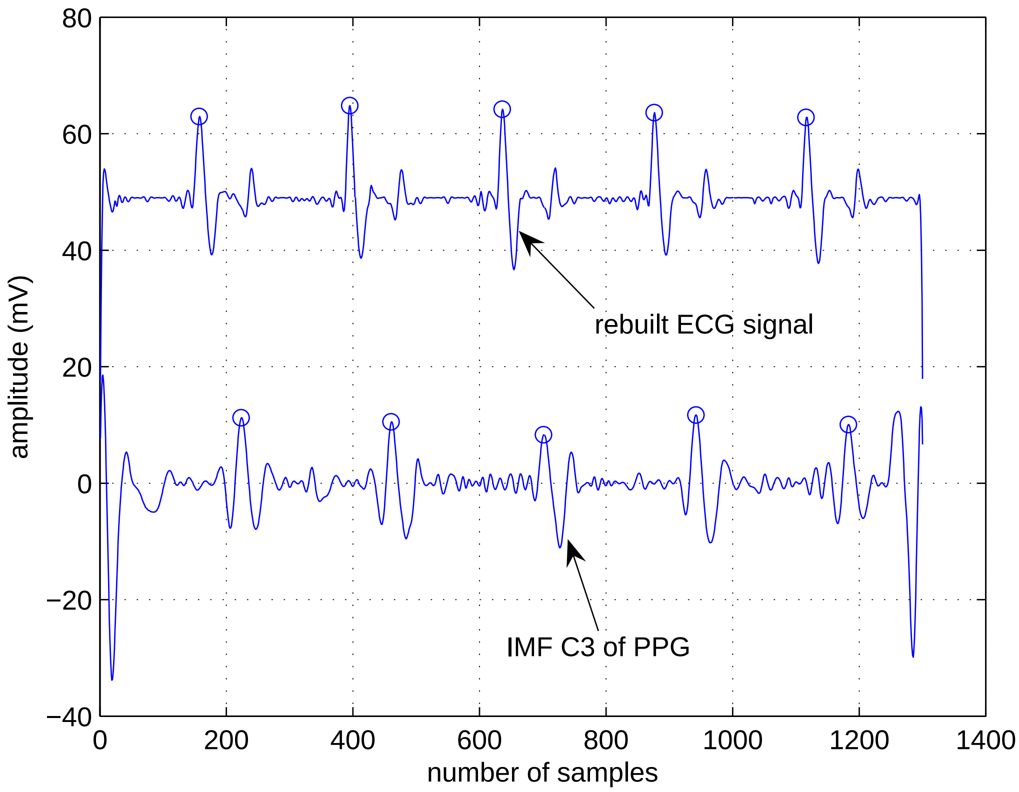

Figure 3.4: The detection of the peak based on the rebuilt ECG and IMF C3 of PPG.

3.3 Summary

In this chapter, we propose to apply the HHT to process the measured ECG and PPG signals, and further estimate the PTT, and finally calculate the variation of blood pressure. Simulation results for the measured ECG and PPG signals illustrate the effectiveness of the proposed method. It is worthwhile noting that to further explore the efficiency of this method, the real values of blood pressure should be calculated and the comparison with other signal processing techniques should be considered, which will be discussed in the following chapters.

Chapter 4

Testing pulse transit time-based blood pressure estimation on elderly

Due to the effectiveness of the HHT application in PTT-based blood pressure estimation, it is employed to the data from MIMIC database [70]. The MIMIC database includes signals and periodic measurements obtained from the bedside monitors. The data are recorded continuously, and the information of the patients can also be provided, such as gender and age. Continuous ECG, PPG are available, and blood pressure is recorded by the invasive way, which can give the continuous and accurate reading. Because elderly people are the primary objects of daily health monitor, the algorithm is tested on the data of elderly from MIMIC database. Furthermore, the values of blood pressure are included, then the accuracy can be obtained to verify our algorithm.

4.1 Algorithm description

The HHT algorithm is applied on the data from MIMIC database to obtain the filtered ECG and PPG. Then, R wave peaks of ECG and characteristic points of PPG are detected. Different PTTs are calculated and used to estimate blood pressure. Since PTT is highly related to blood pressure [9][10][13][23], the model for each individual is linearized as: $BP = a \cdot PTT + b$. Least Square algorithm is employed to determine the unknown coefficients a and b, which is considered as the calibration process. As the blood pressure values are available in the database, the estimated blood pressure results by the PTT-based method can be compared with the actual blood pressure values. The error mean, error standard deviation and correlation coefficient are presented.

After the original calibration, the different PTTs are discussed. The error mean and error standard deviation are the criteria to choose the better one. Other than the linear model, $BP = a \cdot \ln PTT + b$ is also studied. In order to verify the HHT algorithm, another popular technique, wavelet transform, is introduced for comparison. Furthermore, the re-calibration problem, which is essential to the application, is explained. The Multi-innovation Recursive Least Square algorithm is employed to re-calibrate the model and update the parameter vector.

4.1.1 Original calibration

When the PTT values are detected, original calibration is performed firstly when the method is used for blood pressure estimation. About 40 values of PTT are required for the original calibration for the acceptable outcome. Least Square algorithm [71] is a prevalent statistical method that has been widely employed in many applications. It minimizes the sum of the squares of the errors to achieve the proximal values. The original calibration in our work is accomplished through Least Square method. The procedure is stated as follows. The unknown coefficients a and b are gathered into the matrix

$$\beta = \begin{bmatrix} a \\ b \end{bmatrix} \tag{4.1}$$

for SBP and DBP respectively. We collect the blood pressure and PTT into matrices

$$Y_n = \begin{bmatrix} BP_1 \\ \vdots \\ BP_n \end{bmatrix} \tag{4.2}$$

$$X_n = \begin{bmatrix} PTT_1 & 1 \\ \vdots & \vdots \\ PTT_n & 1 \end{bmatrix}, \tag{4.3}$$

where n denotes the nth measurement.

The coefficient matrix β is obtained from the minimization of $\|Y_n - X_n\beta\|^2$:

$$\beta = [X_n^T X_n]^{-1} X_n^T Y_n. \tag{4.4}$$

Whereafter, the estimation of blood pressure $\widehat{Y}$ can be obtained from $\widehat{Y} = X\beta$, when the new measurements of PTT (X) are given.

4.1.2 Different PTT descriptions

Since blood pressure has been verified that it is related to PTT, many researchers have studied the different PTTs [16][37][44][46]. As shown in Figure 1.1, four different PTTs, from R wave peak of ECG to peak, middle, or foot of PPG respectively (PTT-peak, PTT-middle, PTT-foot), and diastolic time, are all considered in our work. We calculate the results of each one and do the comparison to testify which one should be employed in our work.

4.1.3 The relationship between blood pressure and PTT

The fact that blood pressure wave propagates through the arteries depends on the blood and the elastic properties of the arteries. There are a number of researches dictating the relationship between blood pressure and PTT. From equation 1.2 and 1.3, it is worthily noting that there is a logistic relation between blood pressure and PTT. A widely used model is $BP = a \cdot PTT + b$. Different models have been tried in other studies. In our work, we focus on the linearized model and also do the comparison with the logarithmic model, $BP = a \cdot \ln PTT + b$, which has been used in [45][42].

4.1.4 Comparison with wavelet transform processing technique

To verify the acceptable results that we obtain using HHT, they are compared with the results of wavelet transform. The wavelet transform has been used by [30][34][53]. We follow their method to filter the same data from MIMIC database, and use the same algorithm to initially calibrate the models. So the only effect on the different results is the two processing techniques.

4.1.5 Periodic re-calibration

The estimation performance of the PTT-based blood pressure method retains accurate within a certain period after the original calibration, so the periodic re-calibration is required. The periodic re-calibration is studied in terms of the requirements of AAMI.

One new measurement of SBP and DBP is used for the re-calibration. For the application, SBP and DBP can be measured by some cuff-based method. Recursive Least Square algorithm is employed to complete the re-calibration combined with the initial calibration (equation 4.4). The new records of SBP, DBP, and PTT are given, then the new parameter matrix can be calculated from the minimization of $\|Y_{n+1} - X_{n+1}\beta\|^2$:

$$\beta_{n+1} = \beta_n + L_{n+1}(y_{n+1} - x_{n+1}\beta_n), \tag{4.5}$$

$$L_{n+1} = \lambda^{-1}[X_n^T X_n]^{-1} x_{n+1}^T (1 + \lambda^{-1} x_{n+1}[X_n^T X_n]^{-1} x_{n+1}^T)^{-1}, \tag{4.6}$$

where

$$y_{n+1} = \begin{bmatrix} BP_{n+1} \end{bmatrix}, \tag{4.7}$$

$$x_{n+1} = \begin{bmatrix} PPT_{n+1} & 1 \end{bmatrix}, \tag{4.8}$$

and the range of the forgetting factor λ is $0 < \lambda \leq 1$.

By extending the conventional standard Recursive Least Square algorithm, the Multi-innovation technique is introduced for linear regression models with unknown parameter vectors [72][73]. Since the Multi-innovation Recursive Least Square algorithm uses more than one innovation, the accuracy of the parameter estimation is expected to improve compared with the standard Recursive Least Square algorithm.

In order to improve the accuracy, a number of innovations are well used to obtain the parameter vector. The scalar innovations y_{n+1} and x_{n+1} in equation 4.5 are expanded to the innovation vectors $y_{n+1}(p,t)$ and $x_{n+1}(p,t)$:

$$y_{n+1}(p,t) = \begin{bmatrix} BP_{n+1} \\ BP_n \\ BP_{n-1} \\ \vdots \\ BP_{n-p+1} \end{bmatrix}, \tag{4.9}$$

$$x_{n+1}(p,t) = \begin{bmatrix} PTT_{n+1} & 1 \\ PTT_n & 1 \\ PTT_{n-1} & 1 \\ \vdots & \vdots \\ PTT_{n-p+1} & 1 \end{bmatrix}, \tag{4.10}$$

where p represents the innovation length.

The accuracy of the Multi-innovation Recursive Least Square algorithm can be improved because it applies not only the current data but also the past data at each iteration. In our application, besides the new measurement of SBP, DBP and PTT, some innovations from the first 40 measurements for initial calibration are also used for the re-calibration. Different lengths of innovation need to be discussed to choose the better one.

4.2 Results

In this section, the algorithm as stated before is applied on the data chosen from MIMIC database, which have the continuous ECG, PPG and blood pressure. Tables and figures of the results are shown and explained as follows.

ECG and PPG are processed using HHT algorithm and characteristic points are detected. The measured data are collected at 500 samples per second. The estimated blood pressure are compared with the actual values. PTT-peak, PTT-middle, PTT-foot and diastolic time are firstly analyzed. Due to the comparisons of error mean, error standard deviation and correlation coefficient, PTT-peak shows better performance. Table 4.1 shows the result of one subject using different PTTs to estimate blood pressure during about 10 mins. PTT-peak has the highest relation with blood pressure. In the following analysis, the PTT-peak as the estimated parameter would be used.

Table 4.2 gives the error mean and error standard deviation of different records. It can be seen that the results meet the requirements by AAMI, which is the absolute value of error mean is less than 5 mmHg and the error standard deviation is less than 8 mmHg.

Wavelet transform has been applied for comparison with HHT. The result in Table 4.3 shows that wavelet transform has better performance in error mean, but worse in error standard deviation and correlation coefficient. For the application of the PTT-based blood pressure estimation, the error standard deviation is a main consideration. The results by other studies have trouble in meeting the requirement of the error standard deviation [37][44]. In this aspect, the HHT algorithm shows better results. Moreover, it still meets the error mean standard. Therefore, the HHT is better since it meets more applicable standards. For the correlation coefficient, the PTT of HHT technique shows higher relation with blood pressure than that of wavelet transform, which is the basic of the PTT-based blood pressure estimation method. Therefore, HHT is a promising technique to employ

Table 4.1: Error mean (mean), error standard deviation (SD) and correlation coefficient (r) of different PTTs, for SBP (Top) and DBP (Bottom).

	PTT-peak	PTT-foot	PTT-middle	Diastolic time
mean (mmHg)	-0.4361	-0.6332	-0.4668	-1.9685
SD (mmHg)	3.8456	5.4934	5.2761	4.6060
r	-0.7115	-0.0899	-0.3190	0.5408

	PTT-peak	PTT-foot	PTT-middle	Diastolic time
mean (mmHg)	-0.9337	-1.0471	-0.9601	-1.5973
SD (mmHg)	1.8384	2.6646	2.6716	2.5202
r	-0.6936	0.0153	-0.2178	0.3252

Table 4.2: Error mean (mean) and error standard deviation (SD) for different individuals.

	SBP mean ± SD (mmHg)	DBP mean ± SD (mmHg)
Subject 1	-1.2701±2.4806	-0.9841±1.4776
Subject 2	0.3475±0.9199	-0.6423±0.7969
Subject 3	-0.4361±3.8456	-0.9337±1.8384
Subject 4	-0.0865±3.7995	-0.2635±2.3611
Subject 5	0.2275±3.2126	0.1025±1.6439

Table 4.3: Error mean (mean), error standard deviation (SD) and correlation coefficient (r) of Wavelet Transform (WT) and HHT.

	SBP		DBP	
	HHT	WT	HHT	WT
mean (mmHg)	-0.0865	0.0151	-0.2635	-0.2201
SD (mmHg)	3.7995	4.1703	2.3611	2.5692
r	-0.6178	-0.5502	-0.5574	-0.4845

Table 4.4: Comparisons between two models: $BP = a \cdot PTT + b$ and $BP = a \cdot \ln PTT + b$.

		mean (mmHg)	SD (mmHg)	r
SBP	$BP = a \cdot PTT + b$	-0.4361	3.8456	-0.7115
	$BP = a \cdot \ln PTT + b$	-0.4492	3.8772	-0.7050
DBP	$BP = a \cdot PTT + b$	-0.9337	1.8384	-0.6936
	$BP = a \cdot \ln PTT + b$	-0.9400	1.8477	-0.6891

for data processing.

Figures 4.1 and 4.2 show the correlation between PTT-peak and SBP and DBP, respectively. The regression line is obtained from the 40 measurements for original calibration. The 40 measurements are denoted by the circles. The dots denote the actual values obtained during the testing period. The estimated blood pressure should be in the line. From this figure, it is obviously noting that PTT-peak is highly related to SBP and DBP. And the estimated SBP and DBP based on the regression line are acceptable compared with the actual values.

The models $BP = a \cdot PTT + b$ and $BP = a \cdot \ln PTT + b$ are both studied. The same procedure is conducted including the HHT processor and Least Square algorithm-original calibration. It is shown that the linearized model gives better results, which are available in Table 4.4.

40 measurements are done to initially calibrate the PTT-BP model. Table 4.5 gives the results of different time periods. The periods of 30-mins and 60-mins can meet the

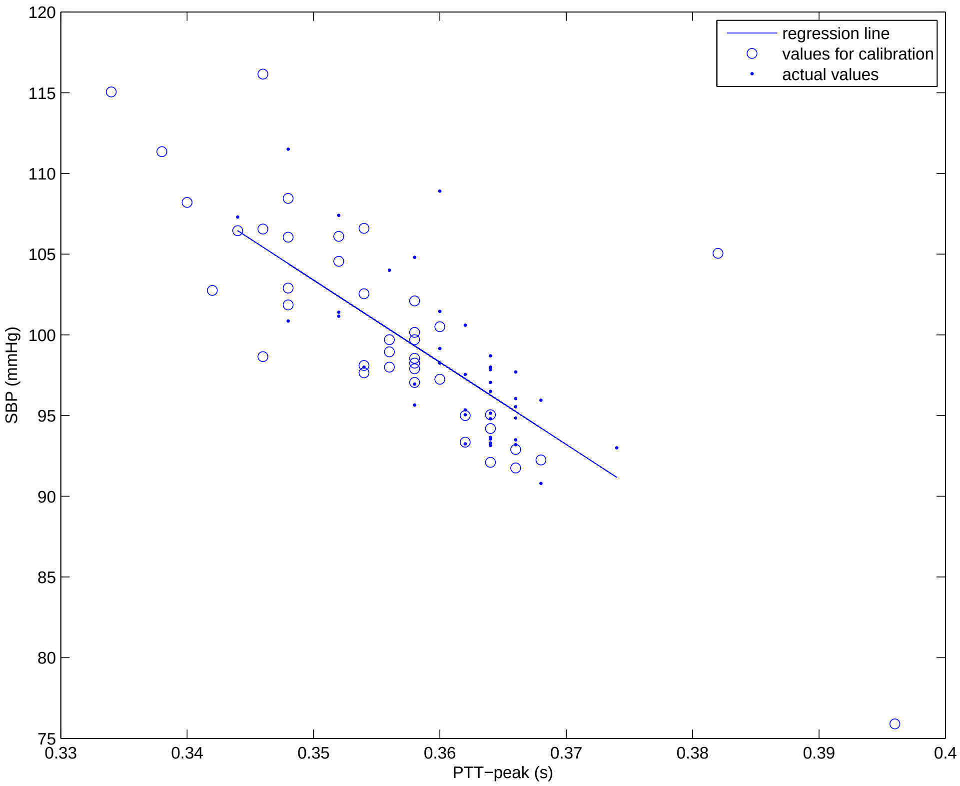

Figure 4.1: The relationship between SBP and PTT-peak.

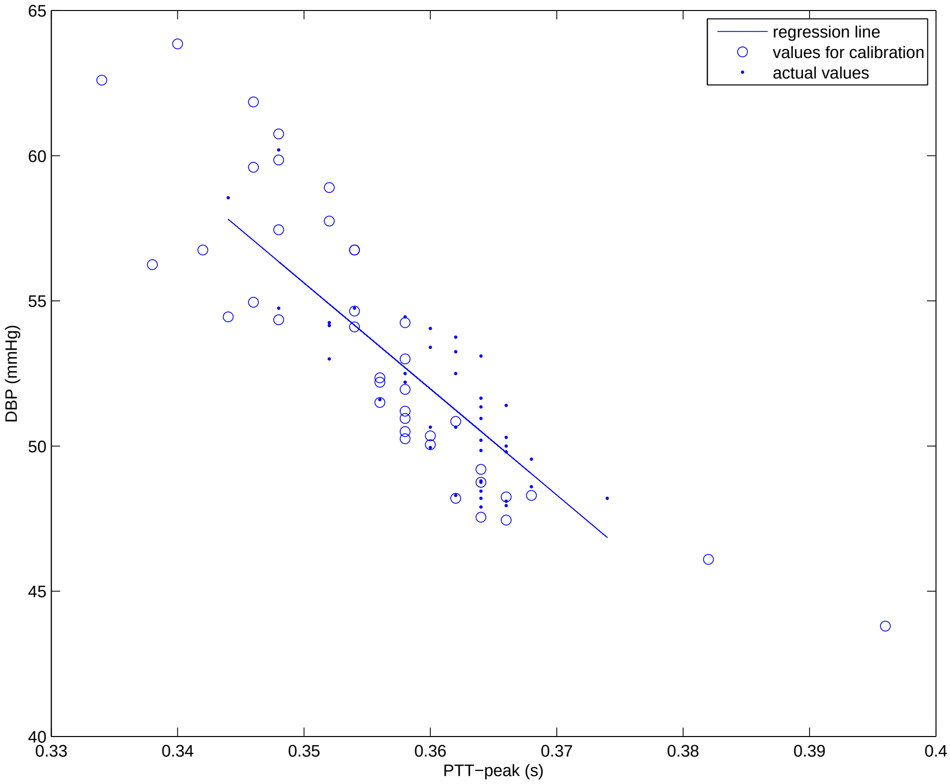

Figure 4.2: The relationship between DBP and PTT-peak.

Table 4.5: Error mean (mean) and error standard deviation (SD) for different time periods.

	SBP mean ± SD (mmHg)	DBP mean ± SD (mmHg)
30-mins	0.8071 ± 5.4775	0.3388 ± 2.9381
60-mins	-0.6336 ± 5.9834	-0.1868 ± 3.2071
90-mins	-1.7655 ± 8.1509	-1.2189 ± 4.8499

requirements by AAMI, while for the 90-mins period, the standard deviation does not satisfy, which is above 8 mmHg. The re-calibration period affects the performance of our method. Longer period will improve the practicability while shorter period will increase the accuracy. To meet the standards and achieve good recording, we select 60-mins as the re-calibration period. The error mean and error standard deviation ($mean \pm SD$) of 60-mins are -0.6336 ± 5.9834 mmHg and -0.1868 ± 3.2071 mmHg for DBP and SBP, respectively. After 1 hour, the Recursive Least Square method is applied to re-calibrate the model. The re-calibration needs one new measurement of SBP and DBP to meet the requirements by AAMI. The forgetting factor is chosen as $\lambda = 0.95$ in our work. To improve the re-calibration performance, the Multi-innovation algorithm is employed to the standard Recursive Least Square. Figures 4.3 and 4.4 show the results of error mean and error standard deviation with different innovation lengths. The x-axis indicates the innovation length p, while $p = 1$ represents the standard Recursive Least Square. The y-axis represents error mean (mmHg) and standard deviation (mmHg), respectively. It can be seen that the absolute value of error mean gives the best result at $p = 1$, while the best standard deviation occurs at $p = 5$. The results after re-calibration using standard Recursive Least Square and Multi-innovation Recursive Least Square are shown in Table 4.6. The Multi-innovation algorithm improves the error standard deviation, which is a main consideration in the PTT-based blood pressure estimation method. Therefore, in application, the algorithm with $p = 5$ gives promising result.

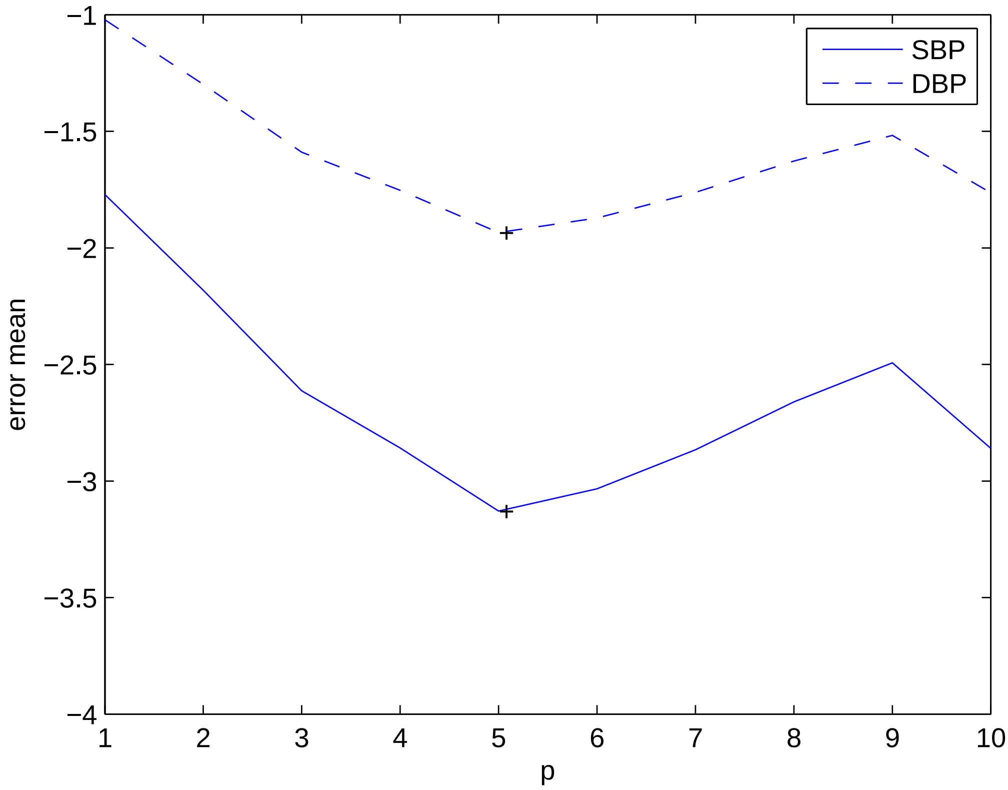

Figure 4.3: The error mean values of different innovation length.

Table 4.6: Error mean (mean) and error standard deviation (SD) for re-calibration with Multi-innovation Recursive Least Square at $p = 5$ (RE-MI), and standard Recursive Least Square $p = 1$ (RE).

	SBP		DBP	
	RE-MI	RE	RE-MI	RE
mean (mmHg)	-3.1292	-1.7714	-1.9341	-1.0222
SD (mmHg)	6.2831	6.6999	3.8470	4.1047

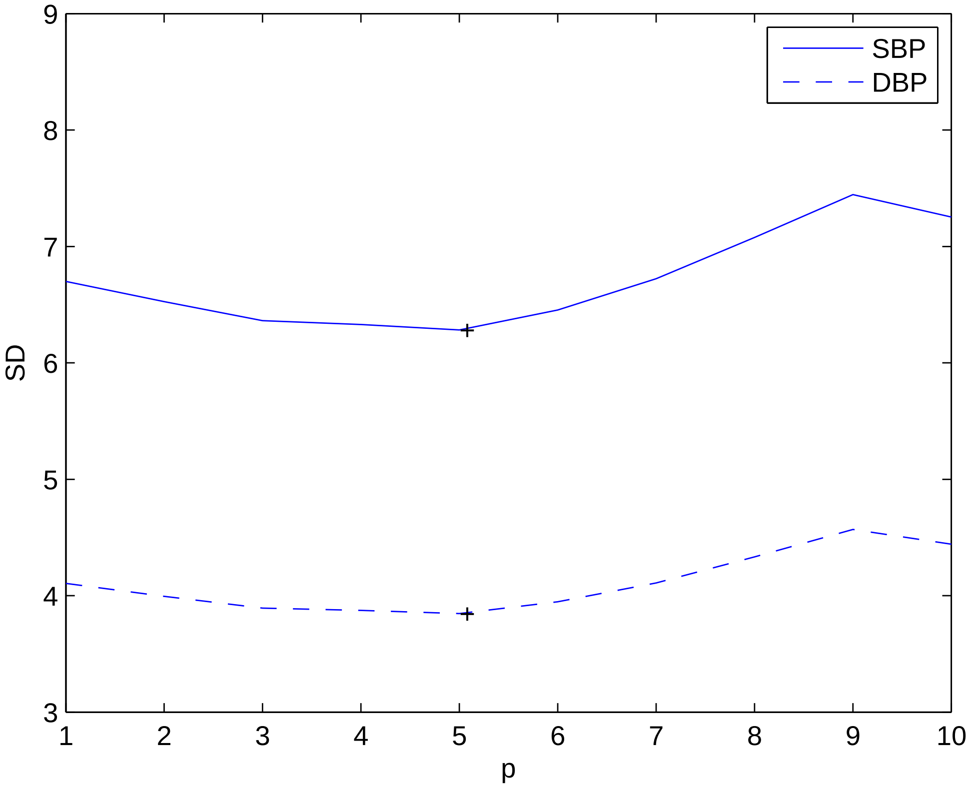

Figure 4.4: The error standard deviation of different innovation length.

4.3 Summary

The algorithm is tested on elderly data from MIMIC database in this section. The algorithm gives the acceptable results in terms of the requirements of AAMI. Compared with the wavelet transform, the result of HHT technique gives better performance in error standard deviation and correlation coefficient. The values of blood pressure are estimated based on the models that describe the relationship between blood pressure and PTT. The models are initially calibrated using Least Square algorithm and re-calibrated using Multi-innovation Recursive Least Square algorithm, which improves the result. The proper re-calibration period is discussed and picked as 60 mins. Furthermore, different PTTs are compared and PTT-peak is the best choice. Based on the standard of AAMI, our results illustrate the effectiveness of the proposed method.

Chapter 5

The application of pulse transit time-based blood pressure estimation to the data by the developed device

According to the results in previous chapters, it has been shown that the PTT-based blood pressure estimation offers promising results for continuous blood pressure monitoring. Furthermore, it is quite essential to test the proposed algorithm based on the practical data collected using the device developed in the FANFARE project. The wearable data collection system is introduced and applied to collect continuous ECG and PPG signals. The algorithm is applied on the data, and results are shown and discussed in the following parts.

5.1 System description

The data collection system, which is developed by the FANFARE (Falls And Near Falls Assessment Research and Evaluation) group at University of Saskatchewan, includes a wearable device, a coordinator connected to the computer. Figure 5.1 shows the wearable device, with sensors to measure 3-lead ECG and PPG, and the coordinator (i.e., the wireless receiver). The ECG sensor, with three leads, is placed on the chest, and the PPG sensor is put on the finger tip. The coordinator can transmit the data from the wearable device to the computer. Figure 5.2 illustrates the physical data that measured by the sensors and displayed on the computer, including ECG and PPG.

The three electrodes are placed on the subject's chest to collect ECG, and PPG sensor is placed on his/her finger tip, which will be modified to a wrist sensor. Continuous data are collected at 40 Hz when the subject wearing the sensors is sitting.

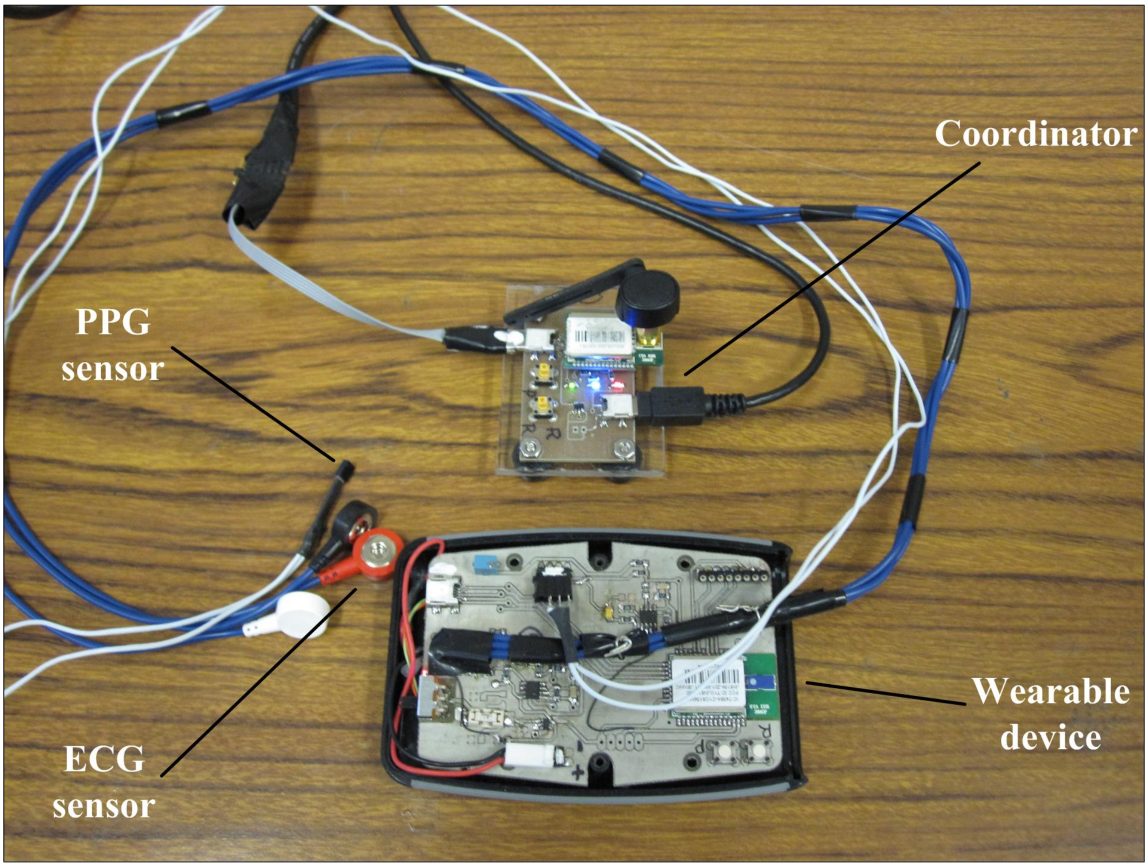

Figure 5.1: The data collection system.

5.2 Algorithm description

5.2.1 PTT estimation

Once the data is collected, the HHT algorithm is used to analyze the data. Since the definition of PTT is the time period from R-wave peak of ECG to a characteristic point of PPG, the time instance of the data is the information of our interest. The EMD method of the HHT algorithm is applied firstly to obtain the IMFs. The standard deviation is applied here to determine how many components C_i are for ECG and PPG, which is to make sure they have enough physical meaning. While the maxima and minima envelops could not be calculated, it will stop to detect IMF. Then the signal is rebuilt without the IMFs regarding to the noise parts to obtain clear data. Based on the results that we got in Chapter 4, the peak of PPG as the ending point of PTT shows better result. Thus, peaks of PPG and R-wave peaks are detected on the rebuilt data obtaining from the summation of C_i.

5.2.2 Blood pressure estimation

According to the Moens-Korteweg description (equation 1.2) of the correlation between blood pressure and PTT, and the derivation by [23], the variation of blood pressure can be calculated using

$$\triangle P = -\frac{2}{\alpha T} dT, \tag{5.1}$$

where the parameter α is 0.017 mmHg^{-1}.

From this equation, the changes of PTT can be obtained from the values of PTT and the changes of it.

5.3 Results

The results of the processed data, the determination of PTT, and the blood pressure variations are given in this section.

Figure 5.3 and Figure 5.4 illustrate the information of the original and processed ECG and PPG, respectively. The rebuilt data without noise give better information of peaks, which we are interested in. The C_i represents each IMF component obtained by EMD method. The rebuilt data is obtained by adding the components together ignoring the component C_1. Then, they show clear data to detect the peaks.

It is more reliable when the detection of peaks is performed on the clear rebuilt data, as shown in Figure 5.5. Once the peaks of the data are detected, the time period between ECG and PPG in the same cardiac cycle can be calculated. Then, it can be used to estimate blood pressure variation. The determination of PTT is a vital part in the PTT-based blood pressure estimation method.

Through the equation 5.1, the changes of blood pressure are obtained. In Figure 5.6, the relationship between PTT and the blood pressure variation can be easily seen. They are inversely related. If the value that the change of PTT divided by PTT increases, the change of blood pressure decreases, and vice versa. It is agreeable to the widely accepted concept that blood pressure is inversive-related to PTT.

5.4 Summary

The HHT algorithm is applied to process the ECG and PPG data measured by our device. After the determination of PTT, the changes of blood pressure can be estimated. If the actual continuous values of blood pressure are obtained, the estimated blood pressure based on the data collected by the developed device could be detected. The results show the application of the method to our data. It is commonly accepted that the blood pressure variation estimation is beneficial to the daily health monitor.

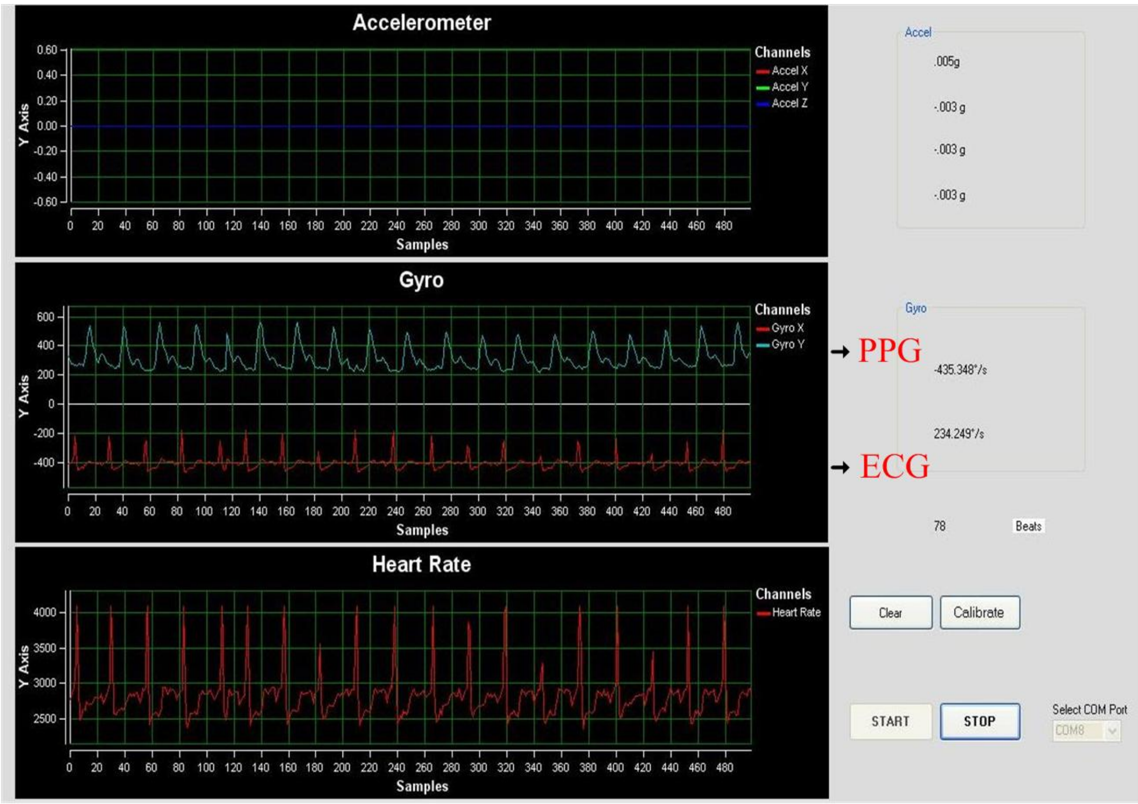

Figure 5.2: The data display.

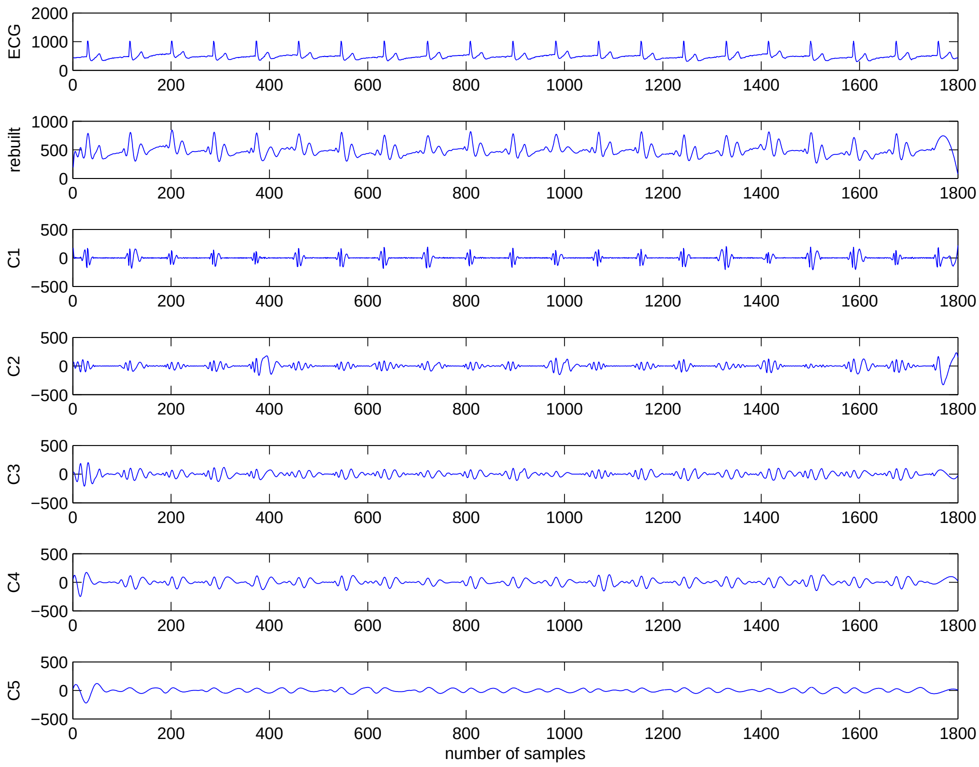

Figure 5.3: The original and rebuilt ECG and the IMF components C1-C5.

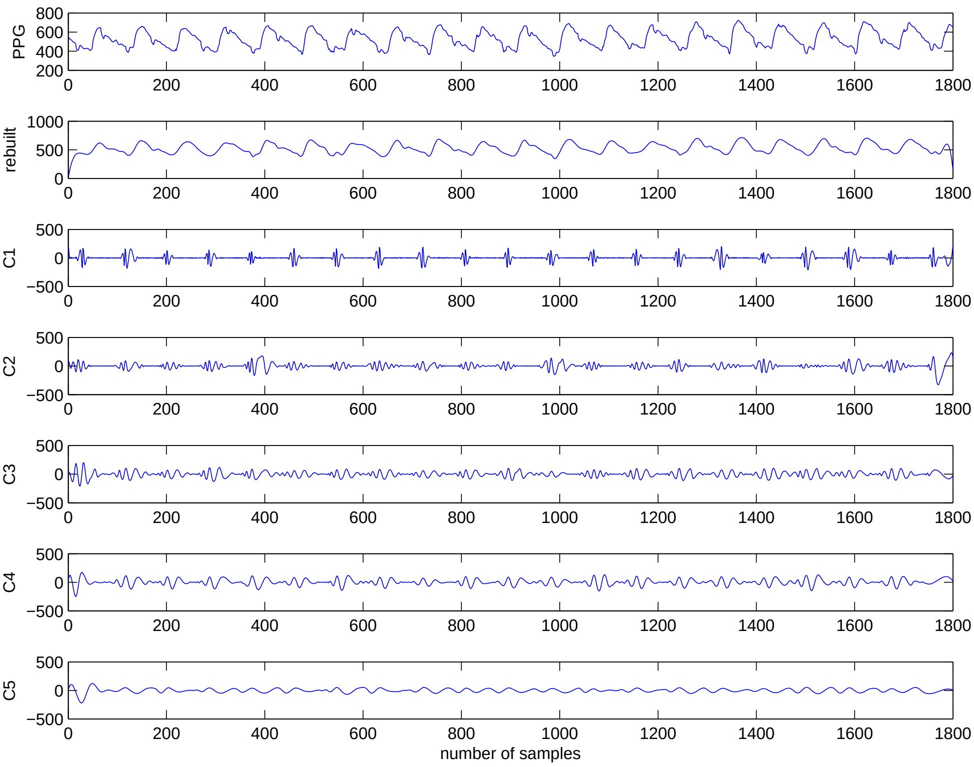

Figure 5.4: The original and rebuilt PPG and the IMF components C1-C5.

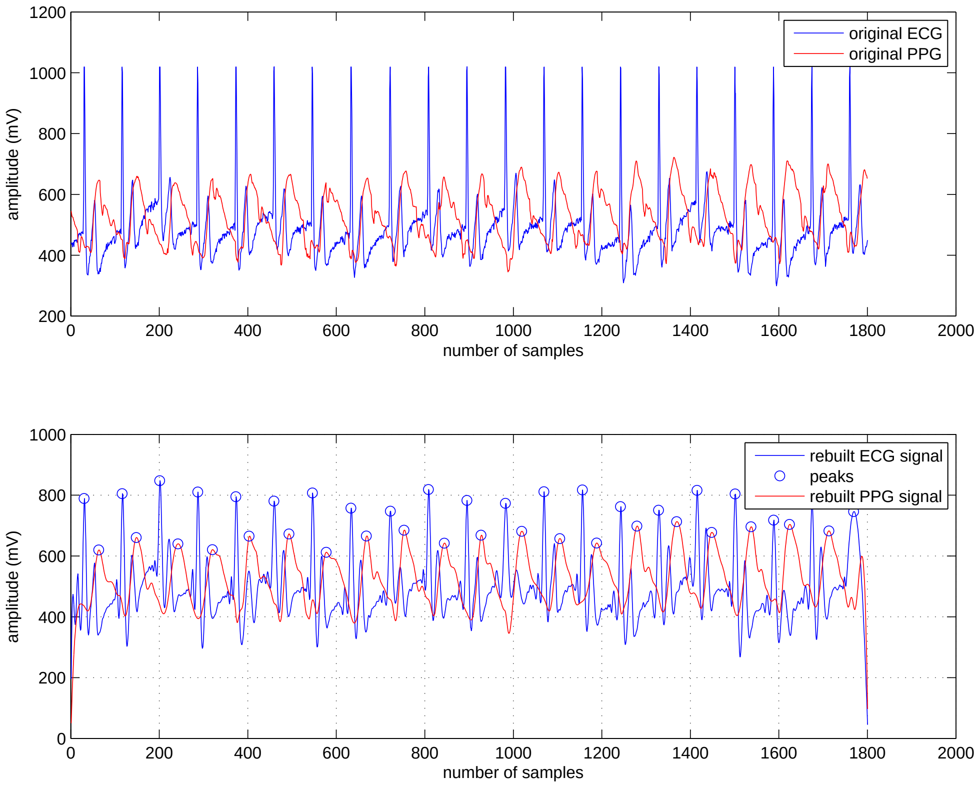

Figure 5.5: The original data and the detection of peaks based on the rebuilt data.

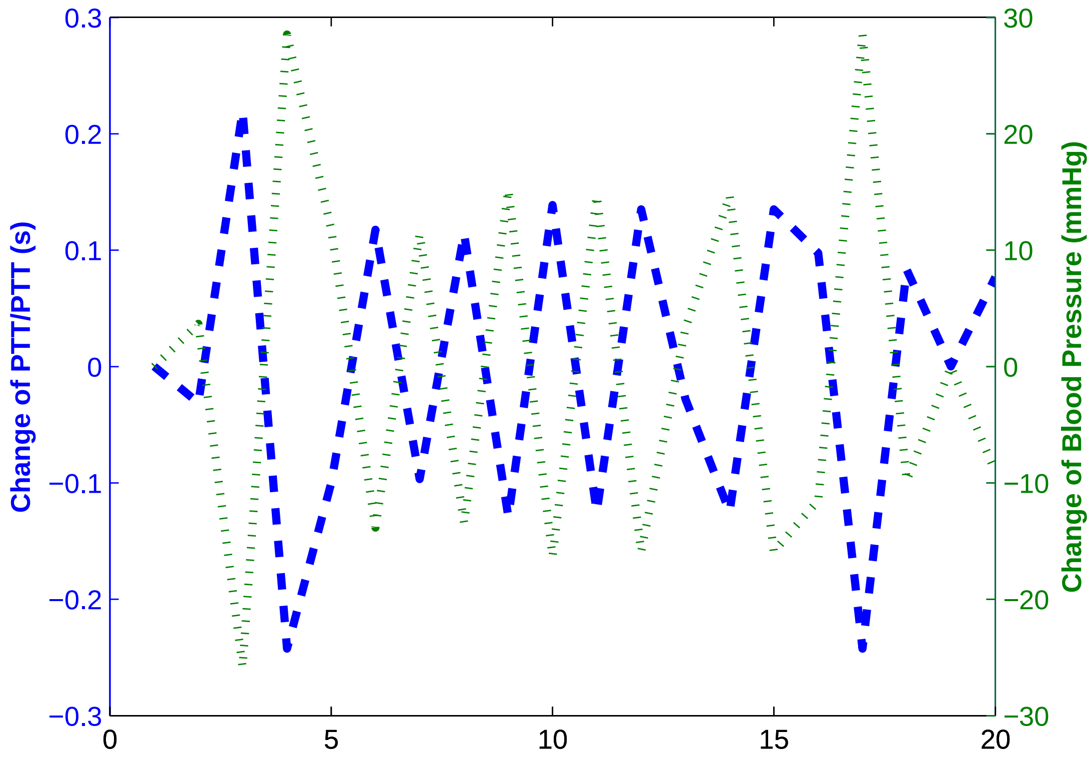

Figure 5.6: The relationship between blood pressure variation and PTT. The x-axis represents the number of cardiac pairs.

Chapter 6

Conclusions and future work

6.1 Conclusions

This thesis explores a cuff-less blood pressure estimation method using signal processing techniques. In the area of blood pressure measurement or even the health monitor field, continuous, cuff-less and non-invasive blood pressure estimation is increasingly desirable. The PTT, which is obtained from ECG and PPG signals, is a widely accepted index of blood pressure estimation. Due to lots of interferer to the physiological data, the signal processing procedure is a main consideration. The HHT algorithm is the signal processing technique that is applied to solve this problem and it shows promising results.

In the Introduction, the main existing methods of blood pressure measurement were introduced. The properties of each method were addressed. It is noting that the continuous, cuff-less and non-invasive way is highly needed.

Chapter 2 discussed the theory of HHT algorithm. The review of other signal processing techniques, and the main idea of HHT algorithm were presented.

In Chapter 3, the application of HHT algorithm to the blood pressure estimation were discussed. The results demonstrated the efficiency of the method. The blood pressure changes can be obtained, which is useful to monitor the health status.

In Chapter 4, we further studied the PTT-based blood pressure estimation method and applied it to MIMIC database, which provides the continuous ECG, PPG and blood pressure. According to the comparison with wavelet transform, it was verified that the algorithm that used HHT technique was a promising method to give higher accuracy. The definition of PTT was determined and the linearized model was calibrated and re-calibrated. Multi-innovation Recursive Least Square algorithm was applied to update the parameter vector of the model. Based on the standard of AAMI, our results were acceptable. Since the health monitoring of elderly is more required, applying our method to the old adults from MIMIC database is necessary.

In Chapter 5, our developed wearable system was highlighted. After applying our method to the measured data, the results indicated that our algorithm were applicable to our data collection system.

6.2 Future work

Our work has achieved meaningful results. Since the blood pressure estimation is an applicable problem, the various situations in the daily life should be considered.

In the blood pressure estimation method, the least square algorithm is applied to set up the model. For the least square algorithm, the independence problem should be discussed. When it is applied to the applicable systems, sometimes, it is defaulted as independence. For the re-calibration, the forgetting factor λ in the recursive least square algorithm is pre-fixed. The varying value of the forgetting factor can be further discussed to improve the performance.

At the present time, the PPG signal by our system is detected from the finger tip. However, it is not convenient for people who want to wash hands or lift things. Furthermore, the signal might be affected by the more often used fingers. Therefore, the PPG signal could be modified and obtained from other sites, like at the wrist.

This blood pressure estimation method is only dependent on ECG and PPG signals, so if the dynamic ECG and PPG are acceptable, our algorithm can be applied to the daily health monitor system. The FANFARE system is designed to collect data for fall analysis. Blood pressure is one of the most important information to supervise the health status. Thus, our algorithm could be applied to the project.

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