

Methods for Non-invasive Trustworthy Estimation of Arterial Blood Pressure

by

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Abstract

The trustworthiness of the blood pressure (BP) readings acquired by oscillometric home-based monitoring systems is a challenging issue that requires patients to see the doctor for trusted measurements, especially those who are obese or have cardiovascular diseases such as hypertension or atrial fibrillation. Even with the most accurate monitors one may get different readings if BP is repeatedly measured. Trusted BP readings are those measured with accurate devices at proper measurement conditions. The accurate monitors need an indicator to assure the trustworthiness of the measured BP. In this work, a novel algorithm called the Dynamic Threshold Algorithm (DTA) is proposed that calculates trusted boundaries of the measured systolic and diastolic pressures from the recorded oscillometric waveforms. The DTA determines a threshold from the heart rate of subjects to locate the oscillometric pulse at the mean arterial pressure ($PULSE_{MAP}$) and uses the peak, trough, and pressure of the located pulse to calculate the trusted boundaries.

In terms of accuracy, a modeling approach is employed to estimate BP from the arterial lumen area oscillations model in the diastolic region (ALA-based). The model requires compliance parameter ' c ' to estimate BP. To this end, a pre-developed linear regression model between ' c ' and the corresponding amplitude ratio of the $PULSE_{MAP}$ is employed to evaluate ' c '. The proposed method uses ' c ' and estimates BP by minimizing differences between peak and trough amplitudes of the actual and corresponding simulated waveforms.

The proposed DTA and ALA-based methods were tested on two datasets of healthy subjects and one dataset of sick subjects with cardiovascular diseases, and results were validated against corresponding references and compared with two popular maximum amplitude and maximum/minimum slope algorithms. Mean absolute error (MAE) and standard deviation of errors (STDE) are used to evaluate and compare the results. For healthy subjects, the MAE of the estimated systolic (SBP) and diastolic (DBP) blood pressures was improved up to 57% and 57% with an STDE of 55% and 62%, respectively. For sick subjects, the MAE was improved up to 40% and 29% with an STDE of 36% and 20% for SBP and DBP, respectively.

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List of Abbreviations

ABP	Arterial Blood Pressure
AF	Atrial Fibrillation
AHA	American Heart Association
AI	Augmentation Index
ALA	Arterial Lumen Area
ANSI/AAMI	American Association for the Advancement of Medical Instrumentation
BHS	British Hypertension Society
BP	Blood Pressure
CDC	Cuff Deflation Curve
CP	Cuff Pressure
CP _e	Cuff Pressure at beginning of the oscillometric pulse
CP _s	Cuff Pressure at end of the oscillometric pulse
DBP	Diastolic Blood Pressure
DBP2	Lower Limit for Trusted Diastolic Blood Pressure
DTA	Dynamic Threshold Algorithm
ECG	Electrocardiogram
EHS	European Society of Hypertension
HBMS	Home-Based Monitoring Systems
ICU	Intensive Care Unit
ISO	International Organization for Standardization
LAA	Linear Approximation Algorithm
MAA	Maximum Amplitude Algorithm
MAE	Mean Absolute Error
MAP	Mean Arterial Pressure
MAP2	Mean Arterial Pressure Estimated by DTA
ME	Mean Error
MMSA	Maximum/Minimum Slope Algorithm
NIBP	Non-Invasive Blood Pressure
OMW	Oscillometric Waveform
OMW _{act}	Oscillometric Waveform Derived from the Actual Trace

OMW _{sim}	Simulated Oscillometric Waveform
OMWE	Oscillometric Waveform Envelope
OMWE _{max}	Maximum Amplitude of the Oscillometric Waveform Envelope
OMW _{sim}	Simulated Oscillometric Waveform
P _{a_pk}	Arterial Pressure at Peaks of the Oscillometric Waveform
P _{a_sim}	Simulated Arterial Pressure
P _{a_tr}	Arterial Pressure at Troughs of the Oscillometric Waveform
P _c	Cuff Pressure
PC	Personal Computer
PEP	Pre-ejection period
pk	Peak of the Oscillometric Pulses
pk_ratio _{act}	Actual Peaks Ratio of the two successive Oscillometric Pulses
pk_ratio _{sim}	Simulated Peaks Ratio of the two successive Oscillometric Pulses
PPG	Photoplethysmography
P _t	Transmural Pressure
PTT	Pulse Transit Time
PTT _{pk}	Pulse Transit Time from the Peaks of the Oscillometric Pulses
PTT _{tr}	Pulse Transit Time from the Troughs of the Oscillometric Pulses
PTT _{zc}	Pulse Transit Time from the Zero-crossings of the Oscillometric Pulses
PULSE _{MAP}	Oscillometric Pulse at MAP
PWV	Pulse Wave Velocity
PWV _a	Pulse Wave Velocity from Heart to Arm (Cuff)
PWV _c	Pulse Wave Velocity Underneath the Cuff
R	Amplitude Ratio of the Oscillometric Pulse at MAP
R _{act}	Amplitude Ratio of the Actual Oscillometric Pulse at MAP
R _{sim}	Amplitude Ratio of the Simulated Oscillometric Pulse at MAP
RI	Reflection Index
S1-S5	Korotkoff sounds
SBP	Systolic Blood Pressure
SBP2	Upper Limit for Trusted Systolic Blood Pressure
SCA	Slope Change Algorithm

SDBP	Sub-diastolic Blood Pressure
STDE	Standard Deviation of Errors
SI	Stiffness Index
SSBP	Supra-systolic Blood Pressure
tr	Trough of the Oscillometric Pulses
TR	Threshold
zc	Zero-crossings of the Oscillometric Pulses

Chapter 1

Introduction

Blood pressure (BP), the pressure of the blood against the walls of the vessels, causes blood to flow into the vessels [1]. BP is required to circulate the oxygenated blood throughout the body in order to supply oxygen to living cells. Blood is oxygenated through the lungs and circulated throughout the body at each heartbeat. The blood circulation system of the human body is illustrated in Fig. 1.1.

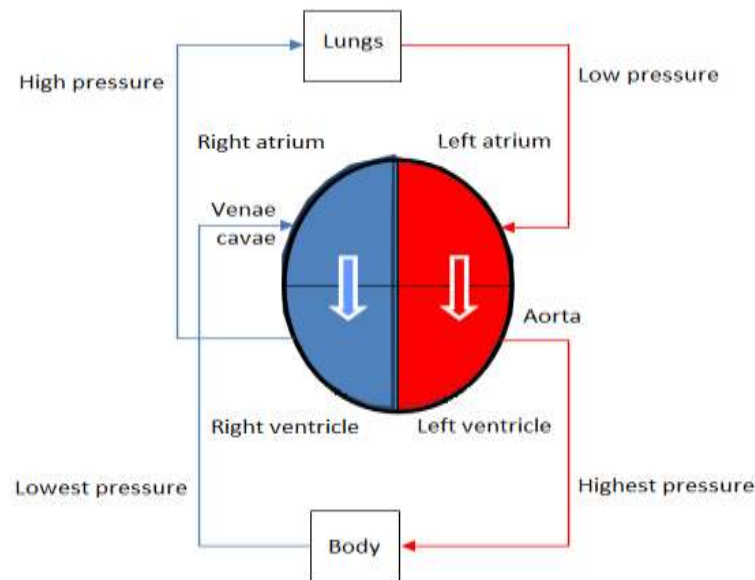


Fig. 1.1. Blood circulatory system of the body.

During the left ventricle contraction, BP in the arteries reaches its highest pressure, which is called systolic BP (SBP), while the lowest pressure, established during ventricle relaxation period, is called diastolic BP (DBP) [1]. BP is measured in millimeters of mercury (mmHg). Normally, BP in healthy adults is lower than 120 mmHg and higher than 80 mmHg, which is referred to as 120 over 80 among physicians [2]. As BP is the force of pushing the blood from the aorta into the distributing arteries, blood cannot supply the whole body if BP is too low. Conversely, with too high a BP, vessels may be injured, so BP should be maintained at its optimum level [3]. The buffering capacity of large arteries is critical to delivering a steady blood

flow to the periphery. Arterial BP, as a function of time with the approximate time intervals of systolic and diastolic phases, is shown in Fig. 1.2.

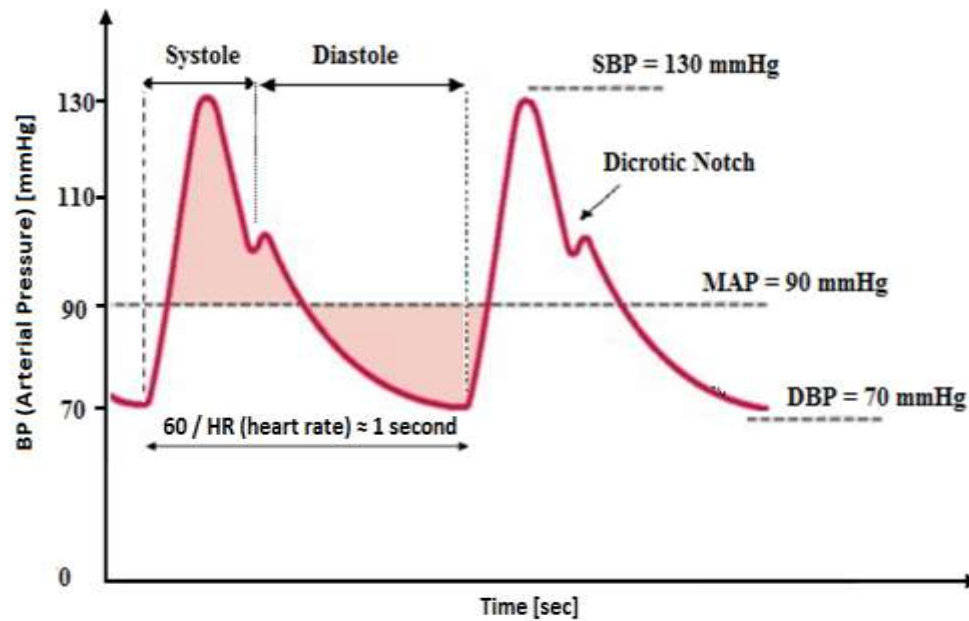


Fig. 1.2. Arterial blood pressure with the approximate time intervals.

BP is one of the most commonly measured physiological parameters that provide a vital measure of a subject's health condition. In recent years, BP measurement has been subject to increasing consideration because it is useful in the detection of cardiovascular diseases such as hypertension and heart attacks.

The history of BP measurement goes back to 1733 when Stephen Hales, a British veterinarian, recorded the BP of animals using brass pipes. A brass pipe that was one-sixth of an inch in diameter was inserted into the left crural artery about three inches from a dog's belly to which, by means of another brass pipe that was adapted to it, a nine feet long glass tube of nearly the same diameter was fixed. Hales observed the blood rise and fall at each heartbeat in the tube after untying the ligature on the artery [4].

The sphygmomanometer, which is a traditional non-invasive BP measurement instrument, was developed by Scipione Riva-Rocci, an Italian physician, in 1896 [4]. An arm cuff was used to obstruct the flow of the brachial artery, and a manometer built from a U-shaped glass tube filled with mercury was used to indicate the SBP during the cuff deflation period. The measurement techniques have developed over time, which is addressed in background section of this thesis.

Nowadays, home-based monitoring systems (HBMS) have made it possible for patients to measure BP at home non-invasively. Although the accuracy of the measurements by HBMS devices is not comparable to invasive methods, they are popular for their convenience and are widely used at home by patients. Meanwhile, researchers are working on the accuracy issue, which is part of the focus of this research, to provide reliable BP readings.

There are some factors that affect the optimum values of systolic, diastolic, and mean arterial pressures, such as age, density of blood, compliance of the vessels, drugs, diet, disease, etc. Moreover, BP changes over 24 hours, as well. For example, BP drops during sleep and increases while being awake. According to the British Hypertension Society study, there is a normal variation of BP over 24 hours for healthy subjects. Normal BP variation of a healthy subject over 24 hours is illustrated in Fig. 1.3.

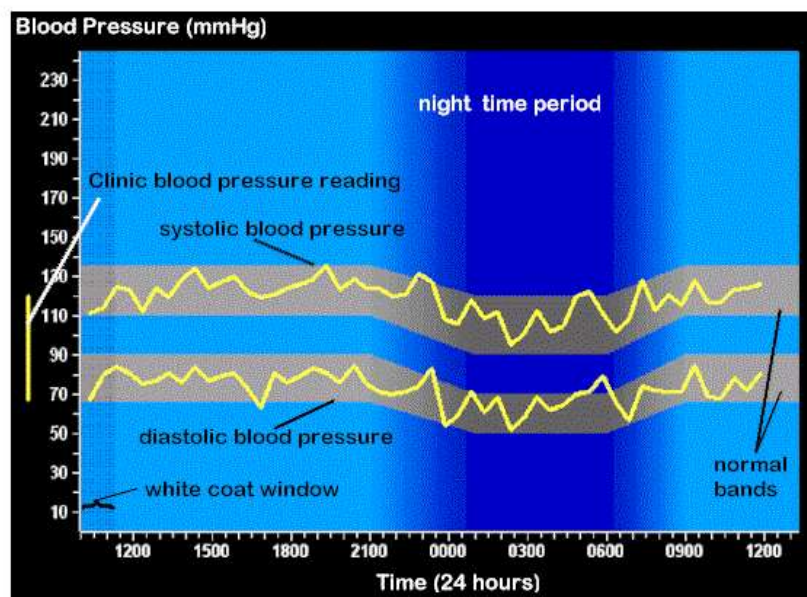


Fig. 1.3. Normal blood pressure variation at regular intervals over 24 hours for healthy subjects. The vertical yellow line segment adjacent to the Y axis represents the clinic blood pressure obtained for that patient. The horizontal grey bands represent the accepted normal limits for systolic and diastolic blood pressures. Vertical (blue) bar on the left of the graph represents the "white coat" window, when the presence of medical staff with their white coats makes the patient anxious and affects the blood pressure. Adapted from British Hypertension Society (BHS) CAL-Unit website, "<http://www.abdn.ac.uk/medical/bhs/booklet/dipper.htm>". Used with permission.

Furthermore, BP changes with mood, such as whether one is happy or upset. The medical term for high BP is hypertension. Hypertension is highly prevalent in the general population,

particularly in elderly patients. During the first stages of chronic hypertension, the cardiac output is raised while the total peripheral resistance remains normal; over time, the cardiac output drops to normal levels while the total peripheral resistance increases. According to PhysiologyWeb studies [145], normal arterial BP is between 90–119 mmHg for SBP and 60–79 mmHg for DBP. Hypertension happens when SBP and DBP exceed 140 and 90 mmHg, respectively (see Table 1.1).

Hypertension is dangerous because it makes the heart work too hard, and it is correlated to atherosclerosis (hardening of the arteries) and increases the risk of heart diseases and stroke [5, 6]. Daily monitoring of BP provides vital feedback and helps to prevent hypertension. It also removes the white coat hypertension and masked hypertension problems [7]. Therefore, observation of BP is vitally important.

Table 1.1: Normal and abnormal arterial blood pressure values.

Classification	DBP (mmHg)	SBP (mmHg)
Hypotension	< 60	< 90
Normal	60 – 79	90 – 119
Pre-hypertension	80 – 89	120 – 139
Stage 1 Hypertension	90 – 99	140 – 159
Stage 2 Hypertension	≥ 100	≥ 160

In conclusion, continuous monitoring of BP is crucial, especially for patients with chronic cardiovascular diseases such as hypertension and atrial fibrillation. On the other hand, seeing the doctor for each measurement is not comfortable for patients. As a solution, HBMS devices are available so that patients with no expertise can monitor BP themselves at home. The problem of HBMS devices is that they cannot provide trusted measurements if patients fail to consider the proper measurement conditions, or if the device itself is not accurate. Moreover, patients have no idea about the trustworthiness of the measured BP and do not know whether to accept the readings or not, since one may read different pressures at repeated measurements. Trustworthiness of BP readings is based on the accuracy of the monitoring devices and measurement conditions. To this end, I have addressed both problems in this research and have proposed solutions to increase the accuracy of BP readings and provide required indicators to alert the examiners about the trustworthiness of the measured BP. Details are explained in

Chapters 3 and 4, while the sections prior to Chapter 3 provide the necessary background to understand the details of my proposed solutions.

1.1 Background

BP measurements are classified into two methods: invasive and non-invasive methods. The invasive approach is one of the gold standards because it can give the most accurate reading of beat-to-beat BP. It is often used when continuous monitoring is required in an Intensive Care Unit (ICU) or during surgeries. This method is called direct measurement because it uses a catheter over a needle, which is inserted into the patient's artery to measure BP directly. A pressure-transducing system connected to the catheter senses the BP [1]. The basic components of the system are the intra-arterial cannula, tubing (incorporating an infusion system), pressure sensor, microprocessor, display screen, and mechanism for zeroing and calibration [4]. This method provides both numerical and graphical information. Although it is continuous and accurate, it makes patients uncomfortable. Invasive measurements tamper with the subject's BP control system, such that measurements performed with this method cannot show the BP of the same relaxed normal subject. Also, it has to be supervised continuously because it may cause severe bleeding if the measurement system is disconnected. Furthermore, it is difficult to operate and there is possibility of infection and pain. Such issues are why non-invasive methods must be considered.

Non-invasive methods measure BP indirectly. One of the conventional non-invasive methods is auscultation, which can be performed by a physician or trained person. A cuff is wrapped around the arm of the subject at the same height as the heart and inflated by an air pump until the artery underneath the cuff is completely occluded. Next, the cuff is gradually deflated by the examiner while listening to the Korotkoff sounds with a stethoscope to identify SBP and DBP values [8]. This method cannot be performed in noisy environments and requires expertise and is thus limited to the doctor's office. There are other non-invasive methods, such as oscillometry [10, 11], Doppler ultrasound sphygmomanometry [9], plethysmography [12], tonometry [13], and vascular unloading [14].

Oscillometry estimates systolic and diastolic pressures and is the most popular non-invasive method that can be implemented relatively easily in automated BP measurement devices.

Oscillometry is implemented in automatic monitors and allows individuals to perform self-monitoring BP at home and even in noisy environments, unlike the auscultatory method [8]. Oscillometry is similar to the auscultatory technique but uses a pressure sensor inside the monitoring box of the cuff system to record BP oscillations instead of listening to Korotkoff sounds. The recorded pressure waveform over the cuff deflation time is known as the cuff deflation curve (CDC). An Oscillometric waveform (OMW) is then extracted from the CDC by different methods, such as the detrending method or through the application of appropriate filters. The amplitude of the oscillometric pulses increases to a maximum value over the cuff deflation period and decreases over further cuff deflation. Different BP estimation algorithms are available to estimate SBP, DBP, and the mean arterial pressure (MAP) from the OMW [15]. The maximum amplitude algorithm (MAA) is the most popular oscillometric algorithm that estimates SBP and DBP from the maximum amplitude of the oscillometric waveform envelope (OMWE) by adopting two empirical constants known as systolic and diastolic ratios. The empirical ratios might be different over individuals, so considering constant ratios for all patients is a main problem in the MAA that considerably affects the accuracy of the estimated BP. To this end, coefficient-free algorithms are recommended to address this problem because they do not adopt any empirical constants to estimate BP.

Coefficient-free BP estimators are comprehensive methods that estimate BP from CDC recordings. These methods are recommended because they estimate BP without adopting any empirical ratios. Accuracy of the coefficient-free estimators is a challenging issue, which is the main focus of this research. Accuracy of the BP readings is also affected by improper measurement conditions of the patients during the measurement. Errors arising from the measurement conditions are known as the measurement condition error. In order to minimize the measurement condition error, BP can be measured repeatedly and estimated from weighted-average calculations over a number of measurements. The procedure reduces the measurement error, but it is time consuming and still untrustworthy because inaccurate measurements might be involved in averaging too.

In this research, a novel technique called the Dynamic Threshold Algorithm (DTA) is proposed to determine the trustworthiness of the BP measurements and eliminate the measurement conditions error by rejecting the false measurements. DTA can determine the

trustworthiness of the measured BP immediately after the BP is estimated. Both improper measurement conditions and inaccurate estimation algorithms contribute to untrustworthy BP readings. Assuming that the estimation algorithm is accurate, the DTA determines and eliminates untrustworthy BP readings caused by measurement condition errors.

The remaining parameter that can cause inaccurate BP readings is the estimation algorithm implemented in automated oscillometric monitors. The estimation algorithm processes the input CDC recordings and provides the BP. Several coefficient-free methods are available in the literature that are relatively accurate. They are covered in the literature review section of this thesis. One of the most popular coefficient-free estimators, called the Maximum/Minimum Slope Algorithm (MMSA), is selected to be compared with our proposed BP estimation method.

In this research, a novel method is proposed that also estimates BP from the arterial lumen area (ALA) oscillations model in the diastolic region. Moreover, trustworthiness of the estimated BP is determined by applying the DTA to the estimated results, so the proposed methods together provide trusted BP readings that are more accurate than the compared methods.

1.2 Motivation

Regular monitoring of BP is required to control health conditions and allows the early detection of cardiovascular diseases such as hypertension and hypotension. Inaccurate BP measurements might have important consequences on health, especially when inaccuracy exceeds 5 mmHg. The most accurate measurements are performed by invasive methods that require specific equipment in hospitals, so patients need to see the doctor in a controlled environment for invasive BP measurements. Non-invasive BP measurements are an alternative solution to this problem that enables patients to monitor themselves at home. Automated oscillometric devices measure BP non-invasively. BP oscillations are recorded from the pulsation of the brachial artery wall as the cuff is deflating, from supra-systolic BP (SSBP), which is the maximum cuff pressure (CP) required to completely occlude the vessel underneath the cuff, to sub-diastolic BP (SDBP), which is the minimum CP at which the cuff system can read the BP oscillations. Different algorithms are employed to estimate BP from the specific characteristics of the recorded oscillations. Most non-invasive automated oscillometric devices employ MAA to calculate SBP and DBP from maximum amplitude of the OMW by applying

systolic (r_s) and diastolic (r_d) ratios, known as characteristic ratios [19]. There are not definite values for ratios, and different manufacturers use different ratios to estimate SBP and DBP from the MAP that are specific to the design of their monitors. The oscillometric determination of the MAP is more accurate than the estimation of systolic and diastolic pressures because ratios vary with subjects, and the empirically determined constants cannot be used for all subjects to estimate SBP and DBP. This problem affects the accuracy of the MAA [20-23]. Coefficient-free based monitoring devices avoid characteristic ratios and are more accurate when estimating BP over a broader range of subjects, including patients with specific health conditions, but their complexity increases the manufacturing cost.

Accuracy of the non-invasive BP measurements is an important factor. Even with the most accurate automated devices, there are some considerations that have to be taken into account to measure BP accurately. Otherwise, the measurements are not trusted and should be ignored by the examiner. Improper cuff size is the most common source of measurement conditions error that affects the accuracy of the measured BP. According to the American Heart Association (AHA) standards, cuff bladder width should be at least 40% of the arm circumference measured at the greatest diameter of the arm, and its length should be at least 80% of the arm circumference at its greatest point. Proper positioning of the patient during measurement is another consideration that affects the measurement conditions error. Subjects should sit comfortably in a chair with their arm positioned at the heart level. Moreover, a noisy or cold environment can increase BP and make a measurement conditions error. Motion artifacts are another source of the measurement conditions error. Furthermore, BP variability is an unavoidable source of measurement conditions error and is always present. Typically, BP can vary up to 20 mmHg over 24 hours (Fig. 1.3), but during the measurement we may see up to 2 mmHg of BP variability [143]. It means that even with an experienced nurse measurement using the most accurate BP monitors in hospitals, we may see up to 2 mmHg error in BP readings. Measurement errors result in inaccurate CDC recordings and become more important when added to the errors arising from BP estimation algorithms that convert CDC to BP readings.

In this research, novel methods are proposed as solutions to provide accurate and trusted BP readings. The ALA-based method is proposed as a coefficient-free BP estimation method to provide accurate BP readings. Trustworthiness of the measurements is determined with another

algorithm called the DTA. The proposed DTA determines trusted boundaries of the subject's BP and evaluates the trustworthiness of the estimated BP by comparing the estimated BP with the determined trusted boundaries and providing appropriate indicators so that the examiner will know the trustworthiness of the measured BP and can decide whether to trust the measurement or not. The proposed ALA-based method is coefficient-free and accurate, so the DTA mostly reflects the measurement conditions error. Therefore, the examiners can measure BP accurately by only considering the proper measurement conditions.

The proposed ALA-based method requires a compliance parameter ' c ' prior for estimation of BP. I have proposed two approaches to evaluate the compliance parameter ' c '. First, ' c ' was determined by a complex optimization process (P1). Next, the procedure was replaced by a previously derived linear regression model, which is proposed in this research and estimates ' c ' directly from the amplitude ratio of the oscillometric pulse at MAP ($PULSE_{MAP}$). Two approaches have the same results, and due to simplicity of the second approach, I evaluated ' c ' from the derived linear regression model.

A recently developed BP estimation algorithm that estimates BP from pulse transit time (PTT) and CP dependency [24] is coefficient-free and accurate but is very sensitive to noise and requires a noise removal procedure to remove noise from PTTs prior to estimation of BP. Removing the noise from biological signals such as BP or PTTs requires complex procedures that increases the manufacturing cost. In this research, the DTA is applied and trusted boundaries are determined to estimate BP directly from the noisy transit times. Therefore, the old BP estimation algorithm is simplified by eliminating the noise removal procedure, and BP is estimated even more accurately.

1.3 Contributions

As stated before, increasing the accuracy of the automated oscillometric monitors is the focus of this research. Oscillometric monitors estimate BP in two main steps. The first step provides CDC recordings, and the next step estimates BP from the recorded CDC using an estimation method. In order to get accurate BP readings, I considered both steps individually. Factors, such as the posture of the subject's arm, comfort of the subject, temperature of the room, correct wrapping of cuff around the upper arm, noise, or motion artifacts, are known as measuring

condition factors that contribute to measurement conditions error. Measurement conditions error provides noisy and untrusted CDC, and results in inaccurate BP readings in the second step. BP estimation methods estimate BP from input CDC recordings, so it is important to provide trusted CDC recordings for the implemented estimation methods in oscillometric BP monitors.

In this research, a novel algorithm called the DTA is proposed to determine the trustworthiness of the estimated BP. The DTA employs peak (pk) and trough (tr) information of the OMW pulse at MAP and determines upper (SBP2) and lower (DBP2) limits for the acceptable BP readings. These limits are known as trusted boundaries in this research. The estimated SBP and DBP are compared with the estimated trusted boundaries to evaluate the trustworthiness of the measured BP. The measured BP is trusted if the estimated SBP and DBP are inside the trusted boundaries, and it is not trusted if outside the trusted boundaries. The untrusted BP readings are rejected, and patients have the option to repeat the measurement for a trusted BP reading. If the measurement rejection persists, the patient would have to seek professional medical attention.

In terms of the accuracy, a model-based coefficient-free method was conceived and validated in this research. The new method estimates SBP and DBP from the peak and trough information of the actual and corresponding simulated OMW pulses in the diastolic region. A simulated oscillometric waveform is constructed from the ALA oscillations model in the diastolic region where arterial pressure is greater than or equal to the CP. The proposed method estimates BP by minimizing the sum of the squared differences between peak and trough amplitudes of the actual (OMW_{act}) and corresponding simulated (OMW_{sim}) OMW pulses. The unknown parameters of the model are reduced mathematically and optimized in three procedures to increase the efficiency of the optimization process and provide accurate BP readings, compared to the literature [25]. Since the compliance parameter ' c ' is an important parameter of the ALA model that affects the estimation process of the BP considerably, it is estimated in the first step in order to subsequently tune the ALA model to the specific patient's characteristics.

The CP-PTT dependency underlies a set of BP estimation methods [24]. These methods are accurate and practical, but the electrocardiogram (ECG) signals have to be acquired synchronously along with the CDC recordings. The method is very sensitive to noise and it is mandatory to remove noise before any processing of the PTTs. Removing the noise from

biological signals requires complex procedures, which are impractical for being embedded in portable devices. To this end, an improvement is proposed in this research that simplifies the old method by replacing the DTA with a noise removal procedure to estimate BP from noisy transit times even more accurately. The proposed method employs trusted boundaries of the recorded CDC and narrows down the searching domains of the maximas of the PTTs over the cuff deflation period. This approach reduces the risk of finding false maximas, so the estimated BP is more accurate.

1.4 Scholarly Outputs

- 1- I. Koohi, I. Batkin, V. Z. Groza, S. Shirmohammadi, H. R. Dajani, S. Ahmad, "A Robust Blood Pressure Estimation Method Based on the Arterial Lumen Area Oscillations Model," *IEEE Transactions on Instrumentation and Measurement (TIM)*, under publication, Feb. 2017.
- 2- I. Koohi, S. Ahmad, I. Batkin, V. Z. Groza, S. Shirmohammadi, H. R. Dajani, "Dynamic Threshold Algorithm to Evaluate Trustworthiness of the Estimated Blood Pressure in Oscillometry," *IEEE Instrumentation & Measurement Magazine*, vol. 19, issue 5, Oct. 2016.
- 3- I. Koohi, I. Batkin, V. Z. Groza, S. Shirmohammadi, H. R. Dajani, S. Ahmad, "Coefficient-Free Blood Pressure Estimation Based on Arterial Lumen Area Oscillations in Oscillometric Methods," in *9th Int. Symp. on Intelligent Signal Processing (WISP)*, Siena, Italy, May 2015.
- 4- I. Koohi, S. Ahmad, I. Batkin, V. Z. Groza, S. Shirmohammadi, H. R. Dajani, Emil M. Petriu, "Method for Evaluation of Trustworthiness of Oscillometric Blood Pressure," in *IEEE Int. Workshop Medical Measurements and Applications (MeMeA)*, Turin, Italy, May 2015.

1.5 Thesis Organization

This thesis is organized in six chapters. Chapter 1 includes the introduction, background, motivation, and contributions.

In chapter 2, the relevant literature is reviewed, and oscillometry, which is the focus of this research, is addressed along with the most popular BP estimation algorithms.

In chapter 3, a novel algorithm called the Dynamic Threshold Algorithm (DTA) is proposed to estimate the trusted boundaries of the given BP recordings in order to determine the trustworthiness of the oscillometric BP readings.

In chapter 4, a novel coefficient-free method (ALA-based) is proposed to estimate BP from the ALA oscillations model in the diastolic region. The proposed method provides accurate BP readings by processing three integrated procedures (P1-P3). The compliance parameter ' c ', which is one of the requirements of the ALA-based method, is estimated through an optimization process by procedure P1. The estimated parameter ' c ' is accurate, but P1 is time consuming and increases complexity of the method. In order to simplify the method and estimate ' c ' with the same accuracy, a linear regression model is developed to estimate parameter ' c ' of the ALA model directly from the amplitude ratio of the oscillometric pulse at MAP (R_{act}). The estimated parameter ' c ' is used by the ALA-based method to estimate BP. Finally, the DTA is employed to determine trustworthiness of the estimated BP.

In chapter 5, the DTA is employed to address the complexity of the recently proposed coefficient-free estimation algorithm that estimates BP from the CP and PTT dependency. The old method is complex, because requires noise removal procedure to clean the pulse transit times prior to estimation of the BP. The improved method estimates BP from noisy transit times without cleaning the signals, more accurately. This work is applicable if an ECG is recorded along with the BP recordings.

In chapter 6, all the methods are summarized and discussed as a brief review of the research.

In chapter 7, the thesis is concluded and future works are directed.

Chapter 2

Literature Review

BP is the force exerted by the blood on the vessel walls as the blood flows through the arterial tree after each heartbeat. BP is an oscillating wave for each cardiac cycle with a minimum and maximum value. Maximum pressure occurs when the heart is completely contracted, and it is called SBP. Conversely, pressure drops to its minimum value during the heart relaxation period, which is called DBP. The average BP at each cardiac cycle is estimated and called the MAP. Systolic, diastolic, and mean arterial pressures are known as BP and measured in mmHg [27–28]. Accuracy of the measurements is crucial [29–31], and there is always a trade-off between accuracy and the manufacturing cost of the device. To this end, different methods have been proposed and are increasing from day to day to reach a minimum price with the maximum accuracy. Generally, methods of measuring BP are categorized as either an invasive and non-invasive method.

A. Invasive Method

The most common invasive method performs intra-arterial measurement using a cannula [32]. A short parallel-sided cannula is passed into the radial artery. Constant infusion of saline is provided through a tubing system attached to the cannula. As shown in Fig. 2.1, BP waveform inside the artery is transmitted through the liquid within the tubing system to a diaphragm that moves according to transmitted BP waveform. Mechanical movement of the diaphragm is converted to the equivalent electrical signal by a transducer. Both numerical and graphical information are available by this continuous invasive method. This method is often used when rapid changes of BP are anticipated or when the long-term recording of BP is required. This method requires ICU facilities, which are normally provided by hospitals, because there is always a high risk of infection and internal bleeding, and more importantly because it requires highly trained personnel to perform the measurement [33–34].

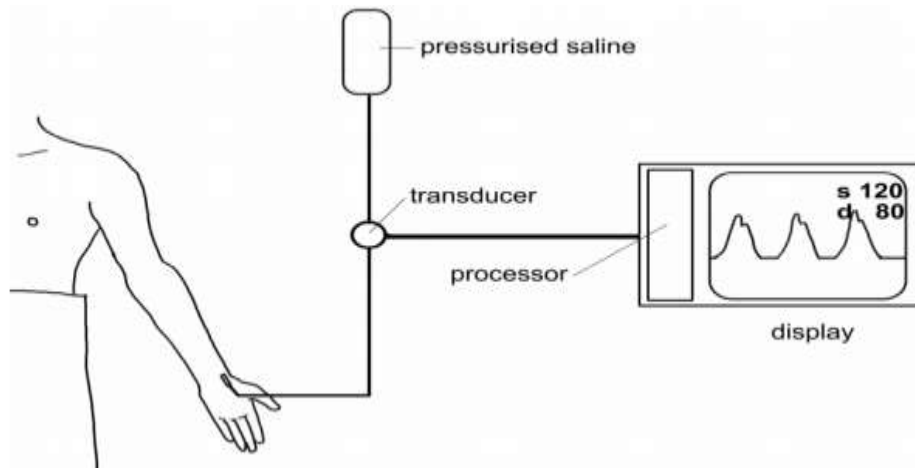


Fig. 2.1. Invasive blood pressure measurement setup.

B. Non-Invasive Methods

There are several non-invasive methods, which are safer and quicker than the invasive methods and require less expertise to perform [35–44]. They are grouped into manual and automated methods. Palpation and auscultation are two common manual methods. There are several automated methods that utilize an automated device to measure BP automatically by simply pushing a button. These methods are categorized as continuous and sampling methods. Continuous methods record beat-to-beat arterial BP (ABP) continuously, while sampling methods estimate SBP, DBP, and sometimes the MAP during a specific period of time that is less than a minute. Oscillometry is one of the most commonly used sampling methods.

2.1 Oscillometry

Oscillometry is the most commonly used non-invasive automated method, which is the focus of this research. This method is similar to the auscultatory method in principle but uses a pressure sensor inside the monitoring box to record the small oscillations of the cuff instead of listening to Korotkoff sounds. The main components of the measurement system are the cuff and pressure sensor. An inflatable cuff is wrapped around the arm or wrist with a pressure sensor inside the monitoring box. As shown in Fig. 2.2, the cuff is inflated by a pump up to supra-systolic blood pressure (SSBP) where the sensor detects no oscillations because the blood flow is blocked, as the artery underneath the cuff is completely flat and occluded. The cuff is then gradually deflated through a valve with a constant deflation rate, and cuff pressure (CP) pulses are recorded until the CP drops to the sub-diastolic blood pressure (SDBP) where no oscillations are detected again by the sensor. The recording time from SSBP to SDBP is the deflation period,

and recorded pulses are called the oscillometric waveform (OMW). The CP CDC has two components: the OMW induced by arterial BP pulses and the deflating CP: $CDC(t) = CP(t) + OMW(t)$

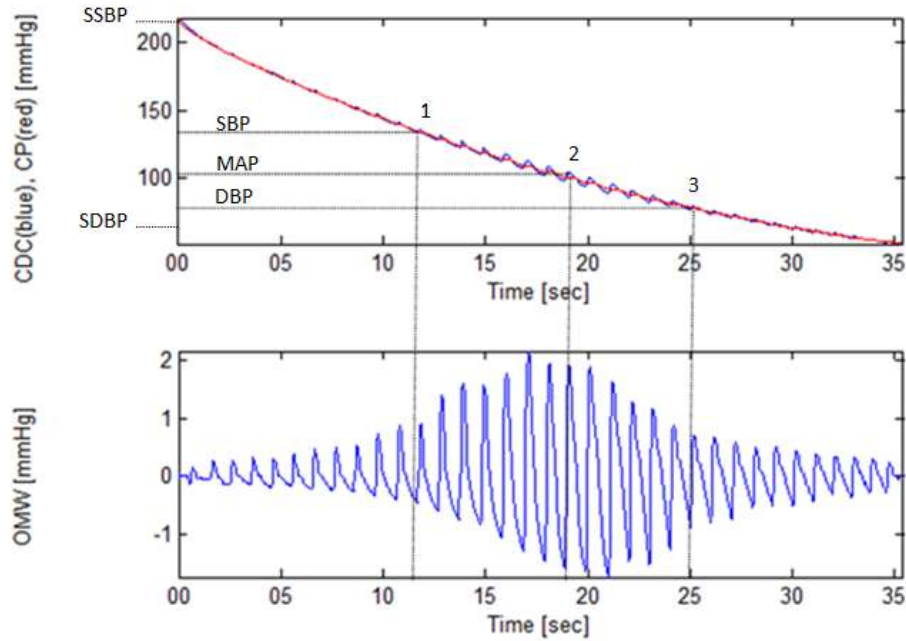


Fig. 2.2. Oscillometric Method. Systolic pressure is detected (point 1) where there is a transition from small amplitude oscillations at SSBP to increasing cuff pressure amplitude. The cuff pressure oscillations increase to a value (point 2) at MAP where pk-tr of the oscillating pulse attains maximum.

Several algorithms are employed to estimate BP indirectly from the CP recording over the cuff deflation period. Recording time is normally less than a minute, and approximately 60 OMW pulses are recorded during the measurement (Fig. 2.2). Depending on the adopted algorithms, different characteristics like peaks, troughs, phases, and the morphology of OMW pulses are analyzed to estimate BP indirectly.

Several algorithms are proposed to extract the OMW from the CDC signal, such as detrending and filtering methods. In the detrending method, a line of best fit that represents the CP is subtracted from the CDC [46] to obtain the OMW_D . Fitting the line requires locating the beginning of each individual oscillometric pulse on the deflation curve CDC and then joining these points. This trend line also produces an estimate of decreasing CP.

The filtering method uses either a low-pass or band-pass filter to extract the OMW (OMW_F). The CP can be extracted by a low-pass filter with a cutoff frequency of 0.5 Hz, and it is

subtracted from the CDC to obtain the OMW. The OMW can be obtained directly from the CDC by adopting a high-pass filter with cutoff frequencies from 0.5 to 20 Hz [47, 48].

The main difference between detrending and filtering methods is that if the CP is properly estimated by detrending, then each pulse of produced OMW should start at zero and no point in the OMW should ever be negative [45, 46]. OMWs extracted from both detrending and filtering methods are illustrated in Fig. 2.3.

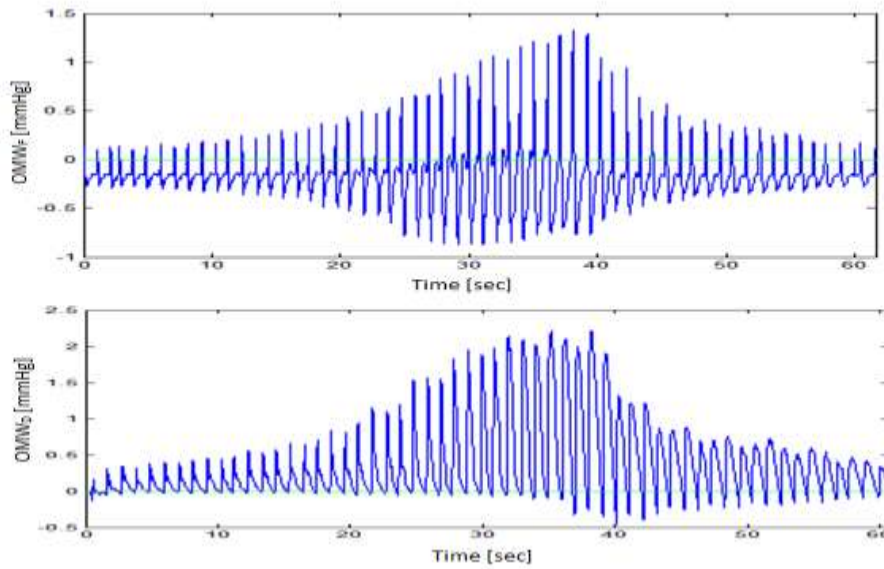


Fig. 2.3. Oscillometric waveforms obtained from CDC. (top) by filtering method. (bottom) by detrending method.

In oscillometry, the amplitude of the OMW increases to a maximum over the cuff deflation and then decreases with further deflation, which is shown in Fig. 2.2. Decrement in amplitudes is caused by the reduction of the force applied from the artery to the cuff bladder after the maximum amplitude of the CP pulses is detected. Peaks and troughs of oscillating pulses carry important information and are used to identify BP [49-53]. The oscillometric waveform envelope (OMWE) shown in Fig. 2.4 is constructed by subtracting the trough of the OMW pulses from the peak of the same pulses and then applying curve fitting to the maximums of the pulses. Cuff pressure at which the OMWE attains maximum amplitude is equal to the MAP with good accuracy [50].

Different algorithms are employed to estimate systolic and diastolic pressures from the OMWE [15, 54]. Some of the most popular algorithms are discussed below.

2.1.1 Maximum Amplitude Algorithm (MAA)

The MAA is the most popular oscillometric algorithm that estimates SBP and DBP from the maximum amplitude of the OMWE ($OMWE_{max}$) by utilizing systolic and diastolic ratios (r_s , r_d) [55]. These ratios are empirically predetermined and can accurately estimate SBP and DBP from the $OMWE_{max}$ in most healthy subjects [56]. The CP at the $OMWE_{max}$ is equal to the MAP with a good accuracy [48]. The left side of the $OMWE_{max}$ is known as the systolic region, and the right side is the diastolic region. The systolic and diastolic pressures are equal to the CPs at which the amplitude of the OMWE becomes equal to the $OMWE_{max}$ multiplied by r_s and r_d , respectively. The OMWE and the corresponding SBP, MAP, and DBP are illustrated in Fig. 2.4.

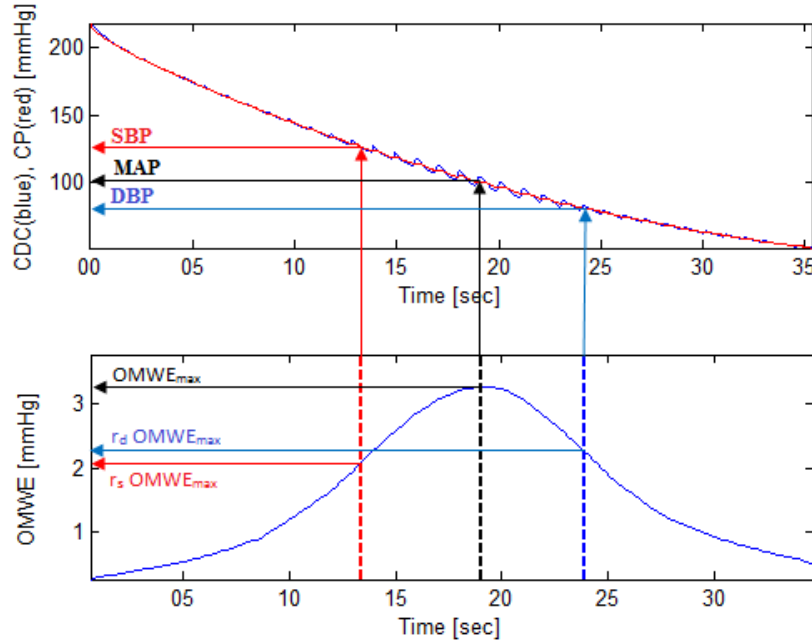


Fig. 2.4. MAA algorithm. (top) CDC and the estimated SBP, MAP, and DBP. (bottom) OMWE. Systolic and diastolic points are located on OMWE and mapped to CDC to find SBP and DBP.

The systolic ratio reported in the literature ranges from 0.45 to 0.75, and the diastolic ratio ranges from 0.69 to 0.83 [47]. These ratios could change between different cardiovascular health conditions, age, and genders [17, 26], while in monitoring devices, the same ratios are used for all subjects. Moreover, ratios differ between devices and are dependent on manufacturing properties of the devices. As a result, due to the sensitivity of the method to variations in BP waveform, pulse pressure, and compliance, the systolic and diastolic pressures cannot be precisely determined from the constant ratios.

2.1.2 Linear Approximation Algorithm (LAA)

The Linear Approximation Algorithm (LAA) was developed by Medero in a 1996 US patent [57]. This algorithm operates similar to the MAA but utilizes a triangle obtained from the OMWE. As shown in Fig. 2.5, the triangle is obtained by approximating the OMWE with two lines of best fit in the systolic and diastolic regions.

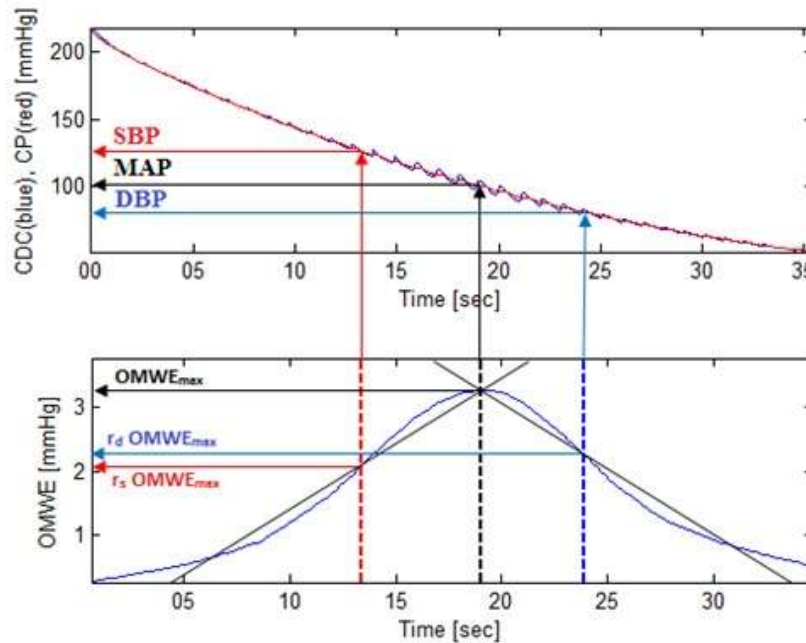


Fig. 2.5. LAA algorithm. (top) CDC and the estimated SBP, MAP, and DBP. (bottom) OMWE. Systolic and diastolic points are located on triangle and mapped to CDC to find SBP and DBP.

The maximum amplitude of the triangle corresponds to the MAP, and points corresponding to SBP and DBP are found by multiplying r_s and r_d to the $OMWE_{max}$ in systolic and diastolic regions, respectively. The systolic and diastolic pressures are equal to the CPs at which the amplitude of the OMWE becomes equal to the $OMWE_{max}$ multiplied by r_s and r_d , respectively [57]. This method has the same disadvantage as the MAA in terms of adopting empirical constant ratios because systolic and diastolic pressures are determined based on constant empirical ratios that could be different for different subjects.

2.1.3 Maximum/Minimum Slope Algorithm (MMSA)

This algorithm is coefficient-free and estimates systolic and diastolic pressures from the slope of the OMWE in systolic and diastolic regions, respectively [58-63]. This is an advantage

because no empirical ratios are adopted in this method for BP estimation. Drzewiecki et al. [20, 40] has analyzed the derivative of the OMWE against CP and found that the first derivative (slope) of the OMWE reaches a maximum value equal to SBP in the systolic region and a minimum value equal to DBP in the diastolic region. The maximum and minimum of the first derivative of the OMWE correspond to systolic and diastolic pressures, respectively. These extrema are the inflection points where the second derivative is 0. The oscillometric waveform envelope, along with the first derivative of the envelope at systolic and diastolic regions, is presented in Fig. 2.6.

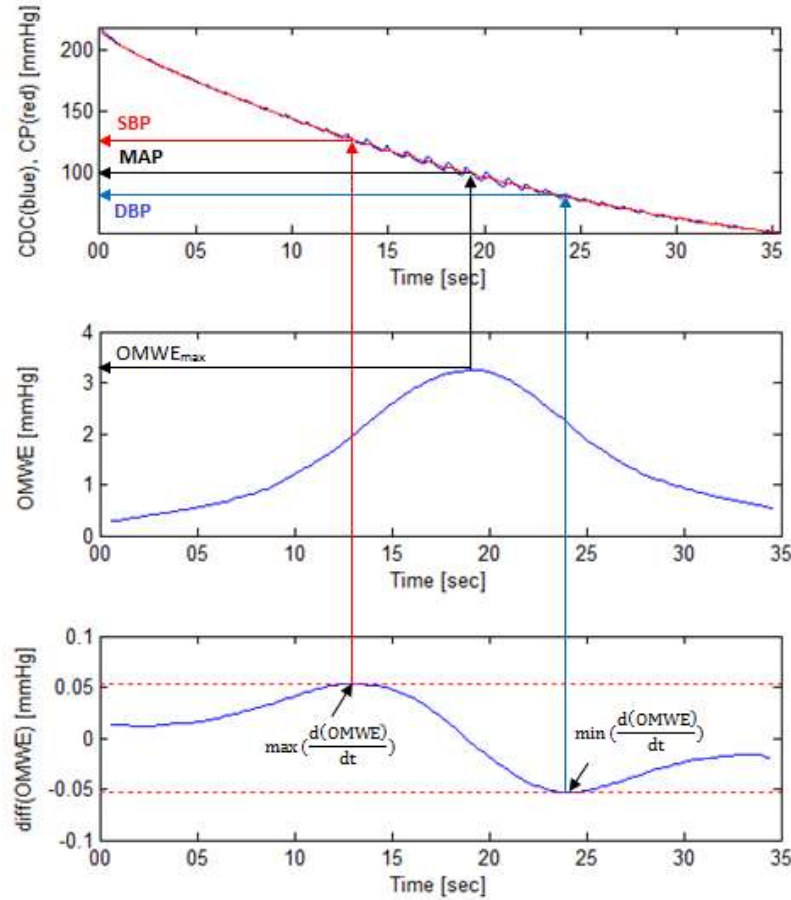


Fig. 2.6. MMSA algorithm. (top) CDC and the estimated SBP, MAP, and DBP. (Middle) OMWE. (bottom) First derivative of the OMWE with maximum and minimum values of the derivative in systolic and diastolic regions respectively. Systolic and diastolic points are located on first derivative of the OMWE and mapped to CDC to find SBP and DBP.

Similar to the MAA and LAA, this method is still very sensitive to noise, artifacts, and muscle contractions caused by breathing, and it requires a noiseless environment and good quality of the

OMW to perform well because it is based on the derivative of the oscillometric envelope. The MMSA is arguably the second-most well-known algorithm, just behind the MAA [62].

2.1.4 Pulse Morphology

This method studies the change in morphology of the oscillometric pulses as a function of CP [64]. Typical pressure blood pulse is illustrated in Fig. 2.7.

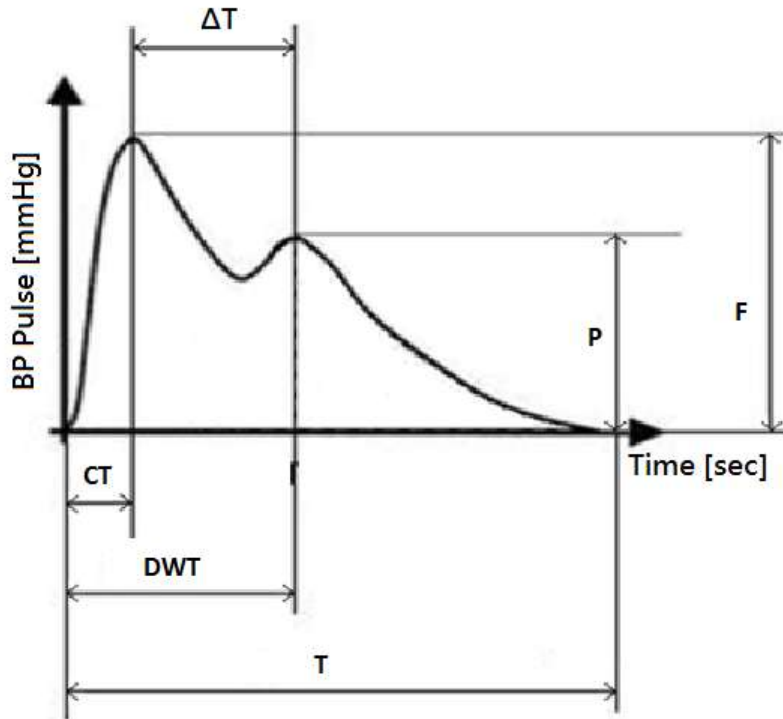


Fig. 2.7. Typical blood pressure pulse.

Specific features, such as stiffness index (SI), augmentation index (AI), reflection index (RI), total duration of pulse (T), $\Delta T/T$ ratio, crest time (CT), dicotic wave time (DWT), relative crest time (RCT), relative dicotic wave time (RDWT), time delay parameter (DT), systolic/diastolic slope, and systolic area are derived from individual oscillometric pulses, and their changes are studied over the cuff deflation time in equations 2.1–2.6.

The stiffness index can be considered as a direct measure of large arteries' stiffness [65, 66].

$$SI = \frac{h}{\Delta T} \quad 2.1$$

The augmentation index is a percentage of the pulse pressure [66–68]. In older subjects, increasing heart rate results in pulse pressure amplification, which is not associated with any change in aortic or other larger arteries' stiffness, and it can be determined by looking at the augmentation index [69, 70].

$$AI = 100 \left[\frac{F - P}{F} \right] * 100\% \quad 2.2$$

The reflection index determines the percentage of the reflected pulse waves from the peripheries to the measuring site during the diastole phase of the heart. It is influenced by the stiffness of the arteries and is linearly proportional to age. The reflection wave makes the second peak (P), which is compared to the first peak (F) to determine RI [66, 68].

$$RI = 100 \left[\frac{P}{F} \right] * 100\% \quad 2.3$$

The time difference between two successive peaks over the total duration of the pulse makes an important ratio denoted by the $\Delta T/T$ ratio. This ratio changes with age due to the change in stiffness of the arteries and disappearance of the dicrotic notch in older subjects. It is used to measure stiffness of the large arteries [69, 71].

There are some important timings of the pulse that change over the deflation time, and characterized trends carry important information that can be used to determine BP and even some of the cardiovascular diseases. Crest time is the time delay between the beginning of the pulse and the first peak at which the left ventricle reaches maximum pressure.

Dicrotic wave time is the time delay between the beginning of the pulse and the second peak constructed by the reflected wave.

Relative parameters of crest time and dicrotic wave time are derived as indicated in (2.4) and (2.5).

$$RCT = \frac{CT}{DWT} \quad 2.4$$

$$RDWT = \frac{DWT}{T} \quad 2.5$$

The time delay parameter is the difference of DWT and CT [66, 72].

$$DT = DWT - CT \quad 2.6$$

The slope between the systolic and diastolic peak is also an important feature because it changes due to the position and amplitude of the second peak, which is constructed by the reflected wave. Aging and cardiovascular diseases change the amount and timing of the reflected wave, so systolic/diastolic slopes can be useful in the classification of different groups. The systolic area, which is the area under the systolic curve, is calculated from the beginning of the pulse to the systolic peak. This area changes due to elastic properties of the large arteries and can be useful in diagnosing and classifying cardiovascular diseases [71].

Depending on the feature used, the extracted features attain a global maximum or minimum at CP equal to the MAP and two local maxima or minima at systolic and diastolic regions equal to SBP and DBP [73]. Currently there is no physiological and theoretical basis for estimating BP based on pulse morphology, and results are not validated sufficiently.

2.1.5 Pulse Transit Time Analysis

This method characterizes the PTT of individual pulses against CP pulses and estimates BP based on the temporal position of the maximum point of the characterized PTTs. PTT is the delay that is taken by the pressure pulse to travel from the heart to the measuring site [29]. In practice, PTT is measured from ECG R_peaks to certain points of the recorded oscillometric pulses (see Fig. 2.8). One can employ ECG R_peaks as a reference to measure transit times, because it corresponds approximately to the opening of the aortic valve.

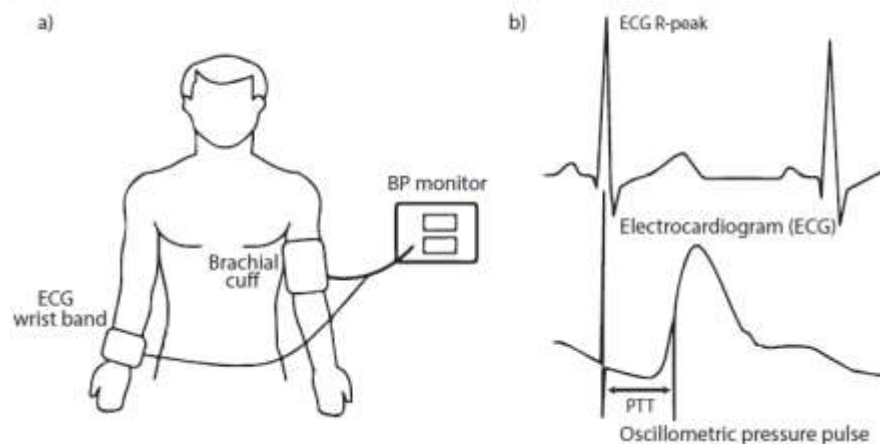


Fig. 2.8. (a) ECG setup to measure pulse transit times. (b) Pulse transit time which is the time delay from the ECG R_peak to specific point of the OMWE pulse such as zero-crossing point. Adapted from Ph.D. thesis of Mohamad Forouzanfar, “A Modeling Approach for Coefficient-Free Oscillometric Blood Pressure Estimation”, University of Ottawa, 2014. Used with permission.

Generally, the certain defined points are peaks, troughs, and zero-crossings of each oscillometric pulse, and three vectors of PTT_{pk} , PTT_{tr} , and PTT_{zc} are characterized in time with the deflating cuff for each recordings. Several techniques are proposed in the literature to estimate BP from PTTs. BP can be obtained from the existing correlation between PTT and BP [74, 75] by constructing a regression model between PTT and BP adopted from another independent method as reference for the BP [76–86]. This method needs calibration by a sphygmomanometer prior to each measurement and requires references of BP to construct the regression model. Moreover, the estimated pressures are not accurate due to the weak correlation between BP and PTT [87–89].

BP can be estimated from CP-PTT dependencies too. Three vectors of PTT_{pk} , PTT_{tr} , and PTT_{zc} are employed to estimate BP from PTTs. Each vector has a maximum point in time that corresponds to SBP, DBP, and the MAP, respectively. Cuff pressure at which the PTT_{pk} , PTT_{tr} , and PTT_{zc} vectors become maximum is equal to SBP, DBP, and the MAP, respectively [78, 26].

The PTT-based methods are extremely sensitive to noise. Breathing is an important source of noise that deviates transit times considerably from their true temporal positions. Moreover, nonlinear behavior of the elastic properties of the vessel is another issue that results in undesired deviations in PTTs. Removing the noises of any kind is required as a solution, but it makes the method too complex and time consuming to function accurately.

2.2 Standards for Automated BP Monitors

The first standard for evaluating the accuracy of sphygmomanometers (ANSI/AAMI SP10) was published in 1987 by the American Association for the Advancement of Medical Instrumentation [90, 91]. Next, a protocol was devised by the British Hypertension Society (BHS) in 1990 [92, 93] and later by the European Society of Hypertension (EHS) [94], which was then used as basis for the international protocol [95].

According to the ANSI/AAMI standard, the mean difference between different BP readings measured by oscillometric monitors must be less than 5 mmHg with the standard deviation of less than 8 mmHg for 85% of the measurements and with the 20–250 mmHg range. Also, accuracy for 95% of the measurements should be better than 10 mmHg.

In 2009, ANSI/AAMI, together with the International Organization for Standardization (ISO), announced the latest standards for automated BP monitoring devices [96]. In these protocols, the non-invasive auscultatory and the invasive intra-arterial methods are considered as the golden standard references. If the auscultatory method is used to provide the references, a dataset of a minimum of 255 recordings is required for both ANSI/AAMI/ISO and BHS protocols. Recordings are obtained from 85 subjects with at least three measurements per subject. References are obtained from averaging the two simultaneous or sequential nurse stethoscope readings. At least one minute of delay is required between each automated recordings and the respective nurse observations for sequential reading option. If the invasive method is used to provide the references, ANSI/AAMI requires a dataset of a minimum of 150 recordings obtained from 15 subjects. One to three minutes of delay should be considered between each automated recordings and respective invasive references.

The ASMI/AAMI/ISO protocol determines the accuracy of the BP monitoring devices over 255 recordings by two indicators: the mean error (ME) and the standard deviation of errors (STDE). According to the standard, the ME of the recordings should be less than or equal to 5 mmHg with the STDE less than or equal to 8 mmHg. The BP estimation method with a small ME and large STDE can still be unreliable and inaccurate. For more reliability, the mean absolute errors (MAE) of recordings is used to show the overall accuracy of the device.

According to the BHS standard, BP monitoring devices are classified into four grades from A to D, where A denotes the best accuracy. These grades represent the cumulative percentage of readings falling within 5, 10, and 15 mmHg. As shown in Table 2.1, grades in the BHS protocol are less strict than in the ANSI/AAMI standard. Grades are specified separately for systolic and diastolic BPs. A device must achieve at least a grade B to fulfill the BHS standard. The BHS protocol does not recommend invasive measurements as the reference.

Table 2.1: BHS grading classification.

Grade	Absolute difference between reference and test device		
	≤ 5 mmHg	≤ 10 mmHg	≤ 15 mmHg
A	60%	85%	95%
B	50%	75%	90%
C	40%	65%	85%
D	Worse than grade C		

Chapter 3

Dynamic Threshold Algorithm and Trustworthiness of the Blood Pressure Readings

There are many automated monitoring devices that can measure BP accurately, but some conditions are required to be considered prior to the measurements, which means that even the most accurate automated monitoring devices may show inaccurate pressures if the measurement conditions are not considered. According to the ANSI/AAMI SP10 guidelines [91], measurement should be done with the subject comfortably resting in a chair with their hand on a table leveled with the heart. The temperature of the environment should not be cold, since it causes the BP to be overestimated. Noises of any kind and motion artifacts also contribute to considerable errors. Most of the time patients are not aware of the mentioned measurement conditions or even how well they are applying them, so may get wrong BP readings accordingly.

Even with accurate BP measurements, there is always a 1–2 mmHg natural variability present during the BP measurement (Fig. 1.3). BP variability is caused by short-term changing of nonlinear properties of the cardiovascular system, such as vessel compliance, at measuring time. Although the contribution of the vessel compliance variability is small, it becomes important when added to the effect of other sources of measurement conditions error. To this end, complementary systems are required for oscillometric BP monitors in order to determine trustworthiness of the measured BP. This will increase the accuracy of the BP readings. Generally, subjects can repeat the BP measurements and average the results over the number of measurements, which is time consuming and still untrusted, since false measurements also contribute to an average. In this chapter, a novel algorithm called the Dynamic Threshold Algorithm (DTA) is proposed to determine the trustworthiness of the BP readings immediately after the BP is estimated. This will help the examiner, whether they repeat the measurement or stay with the trusted BP reading.

The DTA analyzes the oscillometric pulse at the MAP and estimates the amplitude ratio (R) of the oscillometric pulse at the MAP, which is used to evaluate the upper and lower trusted limits of the BP readings. Although, SBP and DBP are important measurements in BP diagnosis,

it is the MAP that drives blood through the vasculature system from the arteries to arterioles, capillaries, venules, veins, and back to the heart. MAP is a time-weighted average of the BP pulses in large systemic arteries. MAP is also a function of amplitude and duration of the BP pulses (Fig. 1.2).

There is little difference between the MAP in the aorta and large systemic arteries, because resistance against the blood flow is lower in large arteries. That's why the brachial artery in the upper arms is used to measure BP. MAP is approximately constant but may vary due to BP variability over 24 hours. MAP is a function of heart rate, rate of blood flow out of the large arteries to smaller arteries and arterioles, and arterial wall compliance. If the ventricles would spend an equal length of time in the systole and diastole phases, the MAP could simply be estimated as the mathematical average of systolic and diastolic pressure values. In reality, the ventricles spend approximately one-third of their time in the systole and two-thirds in the diastole phase. Therefore, a simple average of the systolic and diastolic pressure values is not a correct estimate of the MAP. Instead, a simple approximation (3.1) is typically used to estimate the MAP [8, 47].

$$MAP = DBP + \frac{SBP - DBP}{3} \quad 3.1$$

The MAP approximation equation is required to estimate trusted boundaries of the measured BP. The model in (3.1) is improved in (3.2) by contributing the heart rate (HR) of the subjects [140]. The upgraded model is more accurate than the previous approximation. The DTA is based on the MAP approximation in (3.2).

$$MAP = DBP + (0.33 + 0.0012HR)(SBP - DBP) \quad 3.2$$

We defined the threshold (TR) as an OMW specific parameter given by peak to trough amplitude of the oscillometric pulse at the MAP ($PULSE_{MAP}$). The TR is estimated from the improved MAP approximation model (3.2), and it is used as a reference to locate the $PULSE_{MAP}$ for each subject. The peak to trough amplitude ratio of each OMW oscillometric pulse of a given subject is compared to the TR, and the $PULSE_{MAP}$ is located from the closest ratio to the TR. The TR is different for subjects with different HR, so it is called the dynamic threshold. The upper and lower limits for trusted SBP and DBP are determined by the DTA (Fig. 3.3).

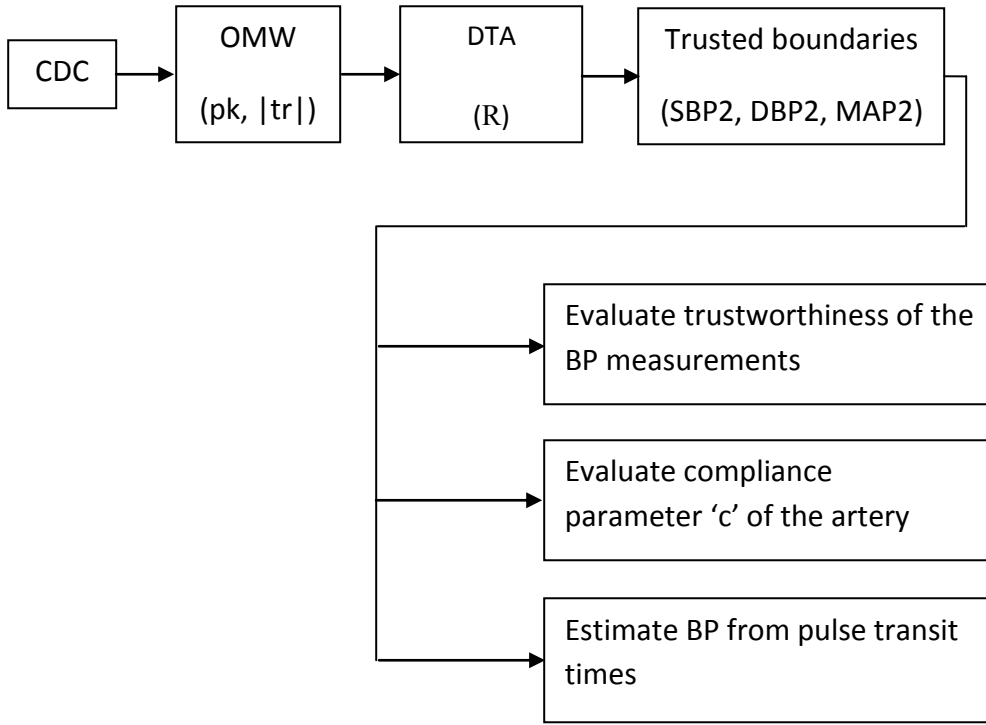


Fig. 3.1. Three applications of the Dynamic Threshold Algorithm (DTA).

The upper limit for trusted SBP is denoted by SBP2, and the lower limit for trusted DBP is denoted by DBP2. The trusted range for trusted SBP is from SBP2 to MAP2 (SBP2-MAP2), and the trusted range for DBP is from MAP2 to DBP2 (MAP2-DBP2). In this research, I have proposed methods based on the three different applications of the DTA presented in Fig. 3.1.

The first application of the DTA evaluates the trustworthiness of the measured BP.

The second application evaluates the compliance parameter ' c ' of the brachial artery. I have used ' c ' in chapter 4 to estimate BP from the ALA oscillations model.

The third application of the DTA improves the recently proposed BP estimation algorithm [26] that estimates BP from pulse transit times (PTTs).

3.1 Dynamic Threshold Algorithm (DTA)

Starting from the deflating cuff pressure (CP), the DTA locates the $PULSE_{MAP}$ and determines the trusted boundaries of the estimated SBP and DBP. The DTA is based on the MAP approximation model (3.2) at which the MAP is approximated in terms of the SBP, DBP, and HR of the subjects. The peak (pk_{MAP}) and trough ($|tr_{MAP}|$) amplitudes of the $PULSE_{MAP}$ are respectively proportional to the estimated systolic and diastolic differences from the MAP, with a proportional constant factor k (3.3, 3.4).

$$SBP - MAP = k \cdot pk_{MAP} \quad 3.3$$

$$MAP - DBP = k \cdot |tr_{MAP}| \quad 3.4$$

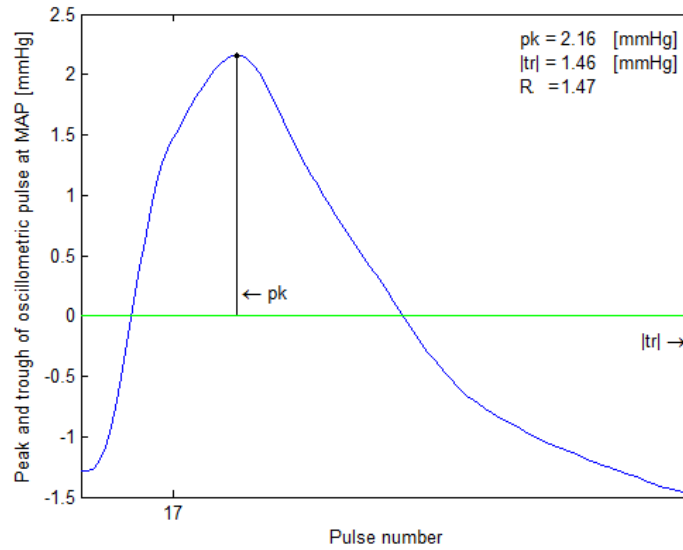


Fig. 3.2. OMW pulse at MAP ($PULSE_{MAP}$) with peak (pk), absolute value of trough ($|tr|$), and estimated amplitude ratio of the oscillometric pulse at MAP (R).

In order to find the TR, which is the peak to trough amplitude ratio (R) of the oscillometric pulse at the MAP, we employed the MAP approximation model (3.2) and replaced SBP and DBP with $k \cdot pk_{MAP}$ and $k \cdot |tr_{MAP}|$, respectively (3.5, 3.6). As shown in (3.6), the TR should be always less than 2. If we ignore the contribution of the HR, the TR will become approximately equal to 2. All estimations in the DTA are only valid at a specific instance in time at which the cuff deflating pressure becomes equal to the MAP.

$$MAP = DBP + (0.33 + 0.0012HR)(SBP - DBP) \quad 3.5$$

$$MAP = k \cdot |tr_{MAP}| + (0.33 + 0.0012HR)(k \cdot pk_{MAP} - k \cdot |tr_{MAP}|) \quad 3.6$$

$$TR = \frac{k \cdot pk_{MAP}}{k \cdot |tr_{MAP}|} = \frac{1 - (0.33 + 0.0012HR)}{0.33 + 0.0012HR} < 2 \quad 3.7$$

The peak and trough amplitudes of the oscillometric pulse at the MAP are proportional to the systolic and diastolic pressures, respectively [8]. The χ_s and χ_d parameters used in 3.8–3.12 are proportional constants for each measurement that are used to estimate the peak and trough amplitudes of the oscillometric pulse at the MAP from the SBP and DBP, respectively. The pressure of the oscillometric pulse at the MAP (MAP2) is estimated by averaging the cuff pressures at the starting (CP_s) and the end points (CP_e) of the located $PULSE_{MAP}$, and substitutes MAP in (3.2). Also, SBP and DBP in (3.2) are replaced with $\chi_s \cdot pk_{MAP}$ and $\chi_d \cdot |tr_{MAP}|$, respectively (3.8, 3.9). To determine the trusted boundaries, we need the optimum values of χ_s and χ_d . In other words, we should increase χ_s and decrease χ_d to their optimum values. If χ_s becomes more than its optimum value, we cannot detect the inaccurately estimated SBP, because the upper limit will be expanded by mistake and the inaccurate SBP will be considered as the trusted SBP. Conversely, if χ_s becomes less than its optimum value, there is a risk to consider the accurate estimated SBP as inaccurate pressure, so χ_s should be optimum to be able to determine the trusted boundary for the estimated SBP. Similarly, χ_d should be optimum, too. Otherwise, we will have the same issues this time for the estimated DBP. In order to find the optimum value of the proportional constants, we repeated the experiment with $\chi_s > \chi_d$, $\chi_d > \chi_s$, and $\chi_s = \chi_d$. Each time, we estimated trusted boundaries, found the outliers or the untrusted measurements, removed the outliers from the dataset, and validated the results against the corresponding references. The most accurate results were observed when χ_s was equal to χ_d . Therefore, with the equal proportional constants ($\chi_s = \chi_d = \chi$), χ is estimated as shown by equations 3.8–3.12.

$$SBP = \chi_s \cdot pk_{MAP} \quad 3.8$$

$$DBP = \chi_d \cdot |tr_{MAP}| \quad 3.9$$

$$\text{With } \chi_s = \chi_d = \chi : \quad 3.10$$

$$MAP2 = |\chi \cdot tr_{MAP}| + (0.33 + 0.0012HR)(\chi \cdot pk_{MAP} - \chi \cdot |tr_{MAP}|) \quad 3.11$$

$$\chi = \frac{MAP2}{(0.33 + 0.0012HR)pk_{MAP} + [1 - (0.33 + 0.0012HR)]|tr_{MAP}|} \quad 3.12$$

Starting from the OMW in Fig. 3.3., the threshold (TR—which is the amplitude ratio of the oscillometric pulse at the MAP) is estimated from (3.7). If we ignore the contribution of the HR, the TR will become approximately equal to 2. So, with the contribution of the HR, the TR will be always less than 2. Amplitude ratios of all oscillometric pulses (R_{vec}) of an OMW recording are calculated in order to be compared with the TR and locate the PULSE_{MAP}.

After locating the PULSE_{MAP}, the amplitude ratio of the located pulse (R) is calculated along with the MAP2 pressure for further analysis. The mean BP estimated from the pulse at the MAP ($MAP2$) is calculated by averaging the CPs at starting (CPs) and end (CPe) points of the PULSE_{MAP}. The peak (pk_{MAP}), the absolute value of the trough ($|tr_{MAP}|$), and the pressure of the PULSE_{MAP} ($MAP2$), are used to calculate the proportional constant (χ) by replacing SBP and DBP with $\chi \cdot pk_{MAP}$ and $\chi \cdot |tr_{MAP}|$ in (3.2), respectively. The constant χ is used in (3.13, 3.14) to estimate the trusted boundaries SBP2 and DBP2.

$$SBP2 = \chi \cdot pk_{MAP} \quad 3.13$$

$$DBP2 = \chi \cdot |tr_{MAP}| \quad 3.14$$

In theory, we could stop here and use the trusted boundaries to determine the trustworthiness of the BP readings. In practice, due to the nonlinear properties of the brachial vessel compliance and the cuff bladder over measurements, we need to apply corrections to the estimated boundaries. The relative distance of R from the TR is calculated as a constant (d) and applied to the estimated boundaries to find the practical trusted ranges (3.15–3.17).

$$d = |R - TR| / TR \quad 3.15$$

$$SBP2 = SBP2 + d \cdot SBP2 \quad 3.16$$

$$DBP2 = DBP2 - d \cdot DBP2 \quad 3.17$$

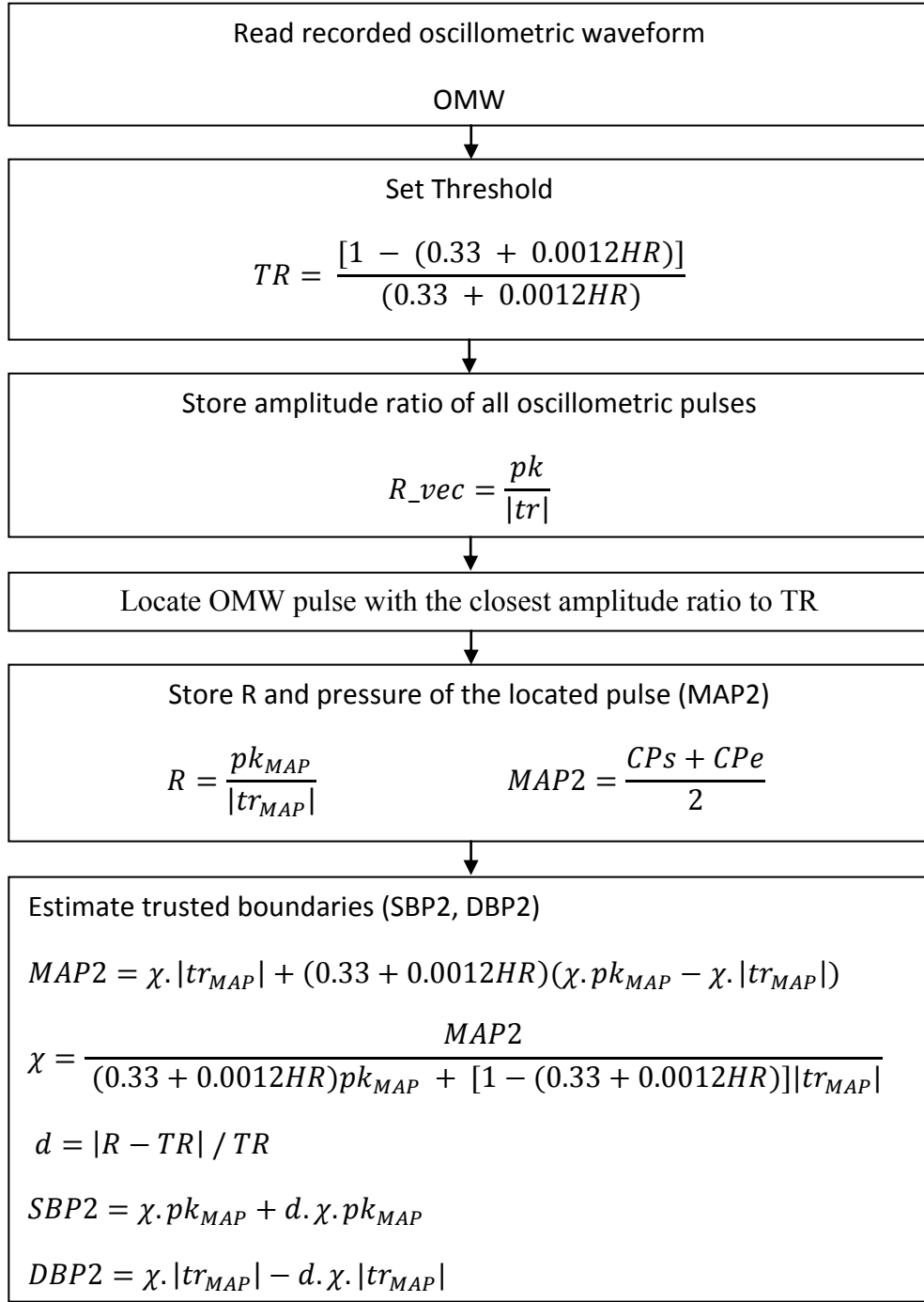


Fig. 3.3. Dynamic Threshold Algorithm (DTA).

3.1.1 Trustworthiness Evaluation of the Blood Pressure Measurements

The DTA estimates the trusted boundaries (SBP2, DBP2) to determine the trustworthiness of the estimated BP (SBP, DBP). Trustworthiness evaluation of the estimated BP is possible for all estimation algorithms—such as MAA, and MMSA. Trustworthiness of the measured BP is determined by comparing the estimated BP with the estimated trusted boundaries. As illustrated in Fig. 3.4., the estimated SBP should be between SBP2 and MAP2 in order to be considered as a trusted SBP, while a trusted DBP should be between MAP2 and DBP2. Finally, the trusted measurement is a BP reading with both systolic and diastolic pressures inside the trusted boundaries.

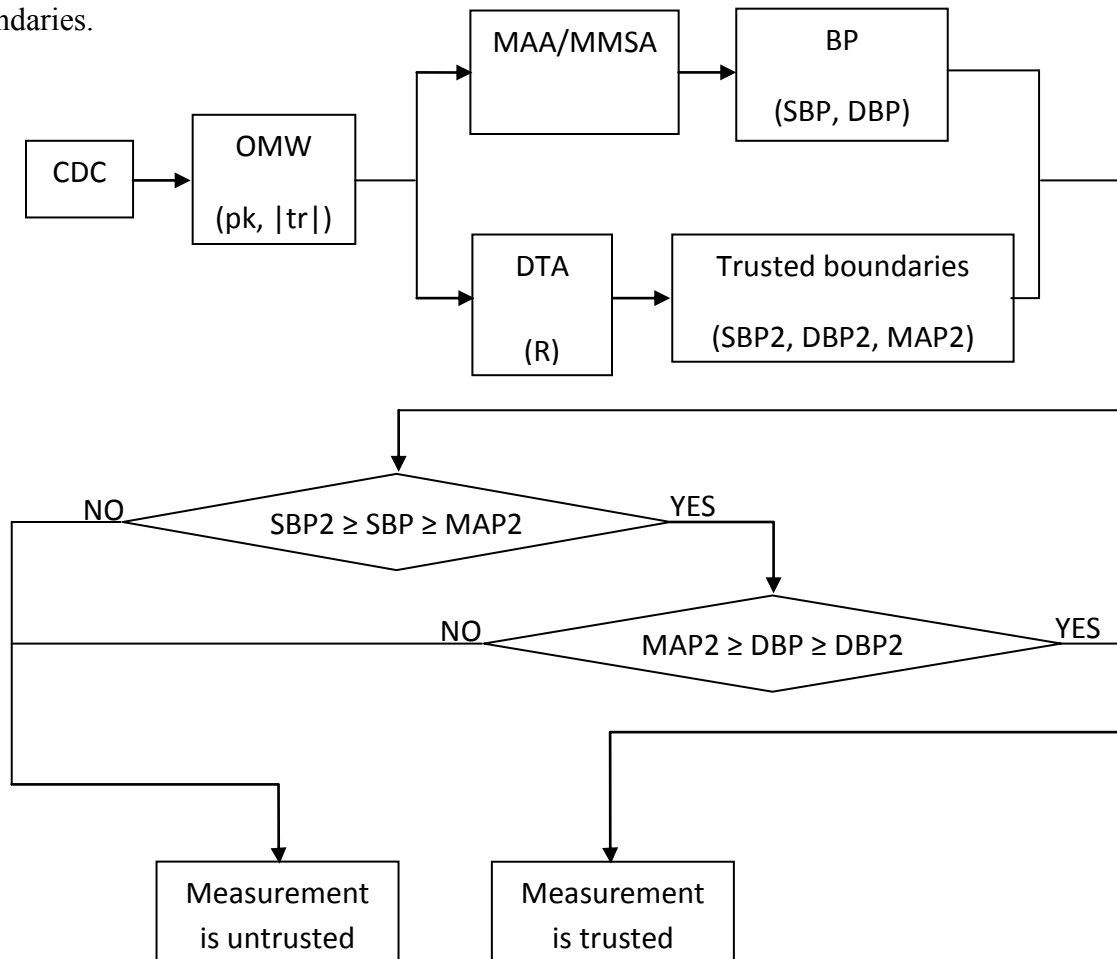


Fig. 3.4. Trustworthiness evaluation of the measured BP.

3.2 Experimental Results

I have employed three different datasets—DS1, DS2, and DS3 [Appendix B - Datasets]—to test the DTA, and measure level of improvements achieved by the DTA for each dataset. The DS1 and DS3 are provided by Biosign Technologies Inc., and Health Parametrics Inc. (HPI), respectively, while the DS2 is provided using the InBeam prototype designed and built by our research group at the University of Ottawa [Appendix A - Pilot Study]. Two estimation algorithms—the MAA and MMSA—are used to estimate BP. The MAA used empirical ratios to estimate SBP and DBP from maximum amplitude of the OMWE. The systolic and diastolic ratios in the MAA are tuned to best fit the employed dataset, so estimated BP may seem more accurate compared to the MMSA, which is coefficient-free and estimates SBP and DBP from maximum and minimum slopes of the OMWE. Coefficient-free estimation algorithms such as the MMSA are more reliable, because they are not tuned for a specific range of subjects and can be used over broader range of subjects. Estimation algorithm is not the focus of this section, but the DTA can read the estimated BP regardless of how accurate it is and improve it by rejecting the untrusted measurements. All datasets include reference SBP and DBP for each estimated pressure, so estimated SBP and DBP are validated against corresponding references for each measurement. The mean absolute error (MAE), and the standard deviation of errors about the mean (STDE), is calculated for each dataset before and after applying the DTA. The DTA is applied to the estimated pressures in order to determine the untrusted recordings (called outliers). Outliers are removed from the datasets, and pressures of the cleaned datasets are estimated again. Estimated SBP and DBP from the cleaned datasets are validated against corresponding references again. Finally, validated results before and after removing the outliers are compared, and levels of improvements are determined in terms of the MAE and STDE.

DS1 and DS2 are obtained from healthy subjects, while DS3 is obtained from sick subjects some with chronic cardiovascular diseases such as hypertension and atrial fibrillation. DS1 is provided by Biosign Technologies Inc. and comprised of 425 oscillometric recordings obtained from a collection of 85 healthy subjects composed of 48 males and 37 females aged from 12 to 80 years old. Reference SBP and DBP are provided by averaging two independent simultaneous readings by two nurses using the auscultatory method and a double stethoscope. Nurse references

are the golden standard references, so DS1 is more important to analyze the validated results and contribution of the DTA. Moreover, DS1 includes more recordings and a variety of ages, which is more suitable as pilot study. In DS1, the cuff deflation curve (CDC) and the CP are recorded for each subject, and the detrending method is used to extract the OMW for the CDC by subtracting the CP from the CDC (3.18). OMWE is obtained by subtracting the peak of each oscillometric pulse from the corresponding trough (3.19). OMWE is used by the MAA and MMSA to estimate BP.

$$OMW = CDC - CP \quad 3.18$$

$$OMWE = pk - tr \quad 3.19$$

Each subject in DS1 has 5 trials recorded in a row with a 1 minute break between consecutive measurements. The SBP and DBP of all trials are estimated by the MAA and MMSA estimation algorithms and validated against corresponding references. Next, the DTA is applied, trusted boundaries of each trial are determined, estimated pressures are compared with trusted boundaries, outliers are detected and removed from the experiment, remaining trials are validated against corresponding references, and results are compared over each estimation algorithm to determine levels of improvements in accuracy after removing the outliers. The validated results before and after removing the outliers are shown in Table 3.1, along with the level of the improvements achieved by the DTA.

Table 3.1: Validated results and improvements by DTA for DS1.

DS1		Results from MAA [mmHg]						Results from MMSA [mmHg]					
		Before removing the outliers		After removing the outliers		Reduced error %		Before removing the outliers		After removing the outliers		Reduced error %	
		SBP	DBP	SBP	DBP	SBP	DBP	SBP	DBP	SBP	DBP	SBP	DBP
Subject with outlier	MAE	9.3	2.6	7.8	2.5	16	3.5	19	7.8	13	4.0	35	49
	STDE	3.1	1.3	2.5	0.2	20	85	9.2	12	0.5	4.5	95	61
425 Rec's	MAE	7.5	5.6	7.3	5.0	2.7	10	14	7.0	12	5.7	16	19
	STDE	6.8	4.8	5.4	4.6	21	4.5	10	6.3	7.1	4.9	30	23

The DS2 is provided using the InBeam prototype designed and built by our research group at the University of Ottawa and comprised 150 oscillometric recordings obtained from 10 healthy subjects that included 6 males and 4 females aged from 24–63 years old. The ECG is recorded simultaneously with BP. Reference SBPs and DBPs are provided by an FDA-approved arm monitor (Omron HEM-790IT). The monitor was calibrated with a nurse before application. DS2 was employed to test the DTA and to evaluate the results' improvements.

In DS2, the OMW was obtained from the recorded CDC using a 2nd order band-pass digital Butterworth filter with the lower cut-off frequency of 0.5 Hz and upper cutoff frequency of 20 Hz. A local maxima detection technique [15] was employed to detect the peaks and troughs of the oscillometric signal. The lower cut-off is set 0.5 Hz to stop cuff deflating pressure and pass all frequency components of the recorded CDC. Moreover, the upper cut-off frequency is set to 20 HZ in order to keep high frequency components of the recorded CDC and reject the high frequency noises induced from the environment. The order of the filter affects the width of the transition band, and the more we increase the order, the more we need the cascade filtering stages in our design. The order of 2 is good enough for our case.

Peaks and troughs were then used to construct the OMWE by subtracting the troughs from the peaks of each oscillometric pulse (Fig. 3.5.).

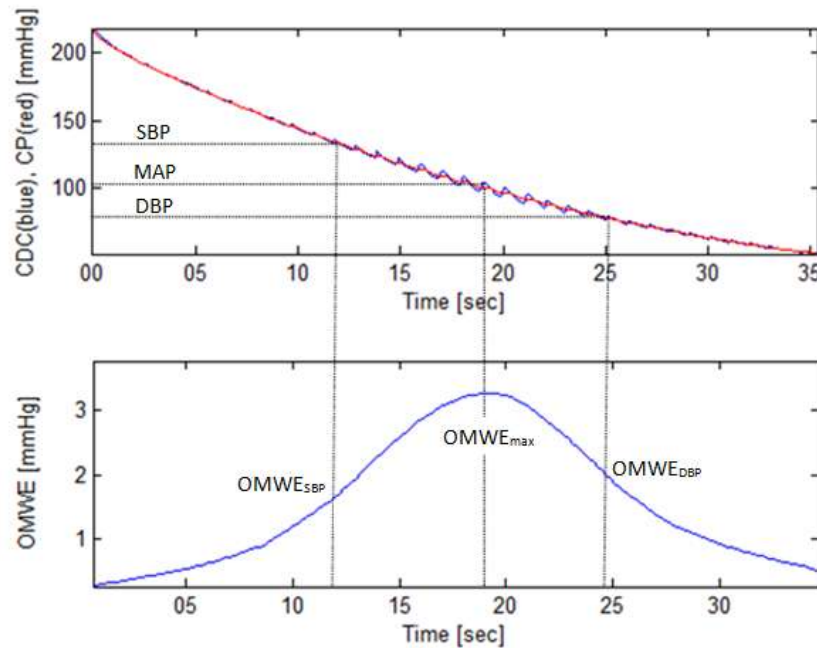


Fig. 3.5. An example of the cuff deflation curve (CDC) waveform, and oscillometric waveform envelope (OMWE). $OMWE_{max}$: Maximum amplitude of the OMWE that corresponds to the position of the mean arterial pressure (MAP). $OMWE_{SBP}$: Amplitude of the OMWE that corresponds to the position of systolic blood pressure (SBP). $OMWE_{DBP}$: Amplitude of the OMWE that corresponds to the position of diastolic blood pressure (DBP).

The OMWE is smoothed and used by the MAA to derive SBP and DBP from the maximum amplitude of the envelope using systolic and diastolic empirical ratios. The MAP is equal to the CP at $OMWE_{max}$ [48]. Systolic and diastolic pressures are estimated from the $OMWE_{max}$ by applying the empirical systolic (r_s) and diastolic (r_d) ratios [55]. The systolic and diastolic pressures are equal to CP at $OMWE_{SBP}$ and $OMWE_{DBP}$, respectively (3.20, 3.21).

$$OMWE_{SBP} = r_s \cdot OMWE_{max} \quad 3.20$$

$$OMWE_{DBP} = r_d \cdot OMWE_{max} \quad 3.21$$

Each subject in DS2 had 15 trials. Some subjects showed outliers and some didn't. Validated results before and after removing the outliers are shown in Table 3.2, along with the level of the improvements by the DTA.

Table 3.2: Validated results and improvements by DTA for DS2.

DS2		Results from MAA [mmHg]						Results from MMSA [mmHg]					
		Before removing the outliers		After removing the outliers		Reduced error %		Before removing the outliers		After removing the outliers		Reduced error %	
		SBP	DBP	SBP	DBP	SBP	DBP	SBP	DBP	SBP	DBP	SBP	DBP
Subject with outlier	MAE	9.5	1.8	9.3	1.8	1.9	1.0	6.0	1.8	5.9	1.7	1.6	4.0
	STDE	2.3	0.9	2.0	0.8	7.9	17	2.8	0.9	2.3	0.8	16	9.3
150 Rec's	MAE	5.7	3.4	5.4	3.3	3.8	1.2	6.2	4.6	6.1	3.7	1.0	20
	STDE	4.6	2.8	4.2	2.7	7.4	1.5	5.1	4.8	5.0	3.0	2.1	38

The DS3 comprises 78 oscillometric recordings obtained from 13 sick subjects with chronic cardiovascular disease composed of 5 males and 8 females aged from 46–85 years old. The ECG is recorded simultaneously with BP. Reference SBPs and DBPs are provided by the popular and professional FDA-approved arm BpTru monitor (BPM-100).

In DS2, the oscillometric waveform signal was obtained from filtering the recorded CDC. The dataset is provided by Health Parametrics Inc. (HPI). Each subject in DS2 had six trials. Some subjects showed outliers and some didn't. Validated results before and after removing the outliers are shown in Table 3.3, along with the level of the improvements by the DTA.

Table 3.3: Validated results and improvements by DTA for DS3.

DS3		Results from MAA [mmHg]						Results from MMSA [mmHg]					
		Before removing the outliers		After removing the outliers		Reduced error %		Before removing the outliers		After removing the outliers		Reduced error %	
		SBP	DBP	SBP	DBP	SBP	DBP	SBP	DBP	SBP	DBP	SBP	DBP
Subject with outlier	MAE	11	14	9.2	13.4	15	4.9	8.2	5.3	6.3	3.3	23	38
	STDE	6.6	5.2	2.4	4.2	63	20	5.7	4.2	4.9	1.4	13	66
78 Rec's	MAE	12	8.5	12	6.6	4.6	21	9.0	7.9	7.2	5.9	20	25
	STDE	8.4	5.2	7.5	4.2	9.8	19	8.9	5.3	6.3	4.9	30	7.0

3.3 Results and Discussion

The amplitude ratio is the ratio of the peak over the absolute value of the trough of one oscillometric pulse, which is calculated for all oscillometric pulses by the DTA. The amplitude ratio of the actual oscillometric pulse at the MAP is denoted by R and is used to determine the trusted boundaries (SBP2, DBP2) from the input CDC recordings. The trusted boundaries are compared with the estimated BP by the MAA and MMSA algorithms. Both the MAA and MMSA algorithms are validated against corresponding references for all datasets (DS1-DS3) prior to applying the DTA. Next, the DTA is applied to the estimated results, and trusted boundaries are estimated for all recordings. Trusted boundaries are compared with the estimated BP by the MMA and MMSA, and outliers are determined and removed from the datasets. The remaining datasets are validated against corresponding references again and are compared with the validated results of the original dataset including the outliers. The amplitude ratio of the OMW pulses versus the CP of one recording is illustrated in Fig. 3.6.

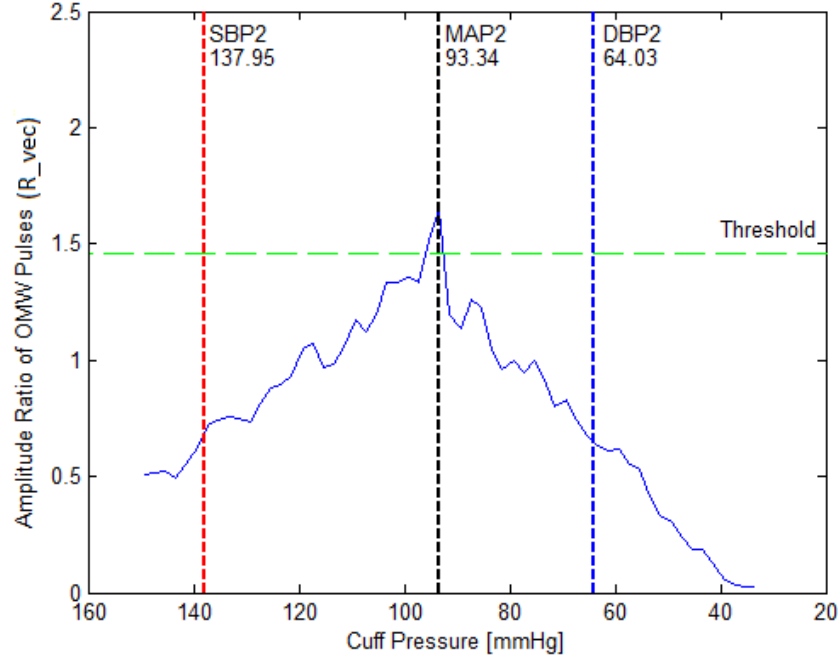


Fig. 3.6. Amplitude ratio of the OMW pulses versus cuff pressure for one recording.

The estimated SBP and DBP by the MAA for the specific recording shown in Fig. 3.6 was 112.04 mmHg, 67.11 mmHg respectively, while it was 118.24 mmHg, 66.83 mmHg when estimated by the MMSA. The trusted boundaries for estimated SBP and DBP are SBP2=137.95 mmHg and DBP2=64.03 mmHg. Therefore, the estimated blood pressures by both algorithms are trusted for this sample recording because they are inside the trusted boundaries.

Validated results before and after removing the outliers are shown in Tables 3.1–3.3 for DS1–DS3 respectively. The level of improvements by the DTA are also estimated and shown in the tables. Regardless of the estimation algorithms or employed datasets, whether it is for healthy or sick subjects, important improvements in accuracy were observed after applying the DTA and validating the remaining trusted recordings. The number of determined outliers for both the MAA and MMSA estimation algorithms over all datasets are listed in Table 3.4. According to the observations, maximum improvement happens when we remove all determined outliers. Meaning, if we fail to remove all outliers, the improvements shown in Tables 3.1–3.3 will decrease accordingly.

Table 3.4: Outliers detected by DTA for MAA, MMSA over all datasets.

Number of outliers	BP estimation algorithms			
	MAA		MMSA	
	SBP	DBP	SBP	DBP
For DS1	129	49	213	75
For DS2	6	0	4	9
For DS3	38	0	27	0

3.4 Conclusion

Estimation algorithms implemented in oscillometric monitors can improve the accuracy of the measured BP if one observes the proper measurement conditions, such as room temperature, posture of the subject's body, hand positioning level to heart, and proper usage of the cuff, as explained before. Therefore, we may get inaccurate BP readings if we fail to consider the proper measurement conditions. Improper measurement conditions affect the accuracy of the measurement. The examiners may get different results if they repeat the measurement, so they may be confused how to trust the measured BP. We need complementary software implemented in the oscillometric devices to determine the trustworthiness of the measured BP and inform the examiners whether the measured BP is trustable or not.

The DTA is the proposed solution that determines a threshold from HR, peak, and trough information of the oscillometric waveform and estimates trusted boundaries for acceptable (trusted) BP. The estimated SBP and DBP are compared with the trusted boundaries and will be considered trusted if both the SBP and DBP are inside the trusted boundaries. Otherwise, the measured BP is untrusted and will be rejected accordingly. Subjects have the option to improve the measurement conditions and repeat the measurements until they read a trusted measurement. The DTA estimates trusted boundaries directly from the OMW, so it is independent of the estimation algorithms.

In order to determine the trustworthiness of the BP readings, we need to estimate BP first. The MMA and the MMSA are employed as two popular estimation algorithms to estimate BP from the recorded CDC. The MMA adopts two empirical ratios to estimate SBP and DBP from maximum amplitude of the OMWE. These ratios are tuned to best fit the employed dataset,

while the MMSA is coefficient-free and estimates SBP and DBP from the maximum and minimum slope of the OMWE without adopting any empirical ratios, so it is applicable for broader range of subjects even if the measured BP is less accurate compared to the MMA. As stated before, BP estimation algorithms are not the focus of this chapter, so the DTA is applied to detect outliers and clean the datasets regardless of the accuracy of the estimated BP. The objective of this chapter is to apply the DTA on measurements, remove outliers from the datasets, and compare the accuracy of the results estimated by MAA, and MMSA estimation algorithms of the cleaned datasets with corresponding results before removing the outliers, and finally evaluate the level of improvements achieved by the DTA.

The DTA was applied to DS1, which was comprised of 425 recordings obtained from 85 healthy subjects, and corresponding results have been listed in Table 3.1. According to the observations, the MAE of the estimated BP by the MAA was improved up to 2.7% and 10%, and the STDE was improved by 21% and 4.5% for SBP and DBP, respectively. Similarly, the MAE of the estimated BP by the MMSA was improved up to 16% and 19%, and the STDE was improved by 30% and 23% for SBP and DBP, respectively. Furthermore, improvements as percentage of the reduced errors were considerable over individual subjects in some cases.

Also, the DTA was applied to DS2, which was comprised of 150 recordings obtained from 10 healthy subjects, and corresponding results have listed in Table 3.2. According to the observations, the MAE of the estimated BP by the MAA was improved up to 3.8% and 1.2%, and the STDE was improved by 7.4% and 1.5% for SBP and DBP respectively. Similarly, the MAE of the estimated BP by the MMSA was improved up to 1.0% and 20%, and the STDE was improved by 2.1% and 38% for SBP and DBP respectively. Furthermore, improvements were considerable over individual subjects in some cases.

Finally, the DTA was applied to DS3 that was comprised of 78 recordings obtained from 13 sick subjects with cardiovascular diseases, and corresponding results have listed in Table 3.3. According to the observations, the MAE of the estimated BP by the MAA was improved up to 4.6% and 21%, and the STDE was improved by 9.8% and 19% for SBP and DBP respectively. Similarly, the MAE of the estimated BP by the MMSA was improved up to 20% and 25%, and

the STDE was improved by 30% and 7.0% for SBP and DBP respectively. Furthermore, improvements were considerable over individual subjects in some cases.

In conclusion, regardless of the estimation algorithms and whether the subject is healthy or sick, even for patients with chronic conditions such as hypertension, atrial fibrillation, or obese subjects—the DTA determines the trustworthiness of the measured BP and provides enough information for the examiner to decide whether to repeat the measurement or stay with the trusted measurement.

Chapter 4

Modeling Approach for BP Estimation

Most of the oscillometric methods estimate BP from the envelope of the oscillometric waveforms, so they fail to estimate BP accurately for all subjects, especially for patients with cardiovascular diseases, such as atrial fibrillation, and atherosclerosis, since the pulse amplitudes may be weak or erratic [113-117]. The modeling approach is an alternative to address this problem, since it has been previously employed to estimate BP from pulse transit times (PTTs) [26, 118–120]. The most important problem of the PTT-based methods is the necessity of the electrocardiogram (ECG) signal to measure BP, which requires additional electrodes to be connected to the subject's body during the measurement. Processing ECG signals in order to acquire PTTs is another problem that defeats the simplicity of the methods. Therefore, in this chapter, the modeling approach is employed to estimate BP from the arterial lumen area (ALA) oscillations model in the diastolic region that requires no ECG. We process the peak and trough information of the oscillometric pulses in the diastolic region to estimate the BP of a given subject. The diastolic region over the cuff deflation period is the region where the arterial pressure is greater than or equal to the CP, while the systolic region is the region where the arterial pressure is less than the CP (Fig. 4.1).

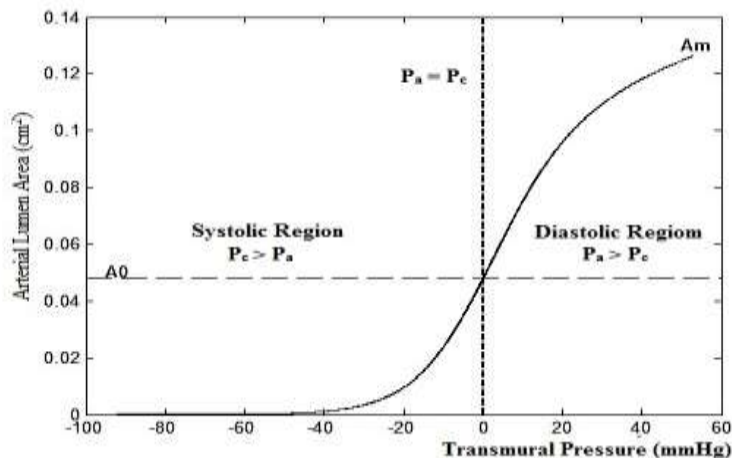


Fig. 4.1. Simulated arterial lumen area versus transmural pressure.

The ALA models for both systolic and diastolic regions are adopted from the literature [26] and are shown in (4.1), (4.2). However, for this research, we only needed the ALA oscillations model in the diastolic region (4.2)

$$A(t) = A_0 e^{aP_t(t)} \quad \text{for } P_t(t) \leq 0 \quad 4.1$$

$$A(t) = A_m - (A_m - A_0)e^{-cP_t(t)} \quad \text{for } P_t(t) \geq 0 \quad 4.2$$

where $A(t)$ is the ALA oscillations model underneath the cuff at the time instant 't'. $P_t(t)$ is the transmural pressure, which is the pressure difference between the arterial pressure ($P_a(t)$) and the CP ($P_c(t)$): $P_t(t) = P_a(t) - P_c(t)$. A_0 represents the lumen area at $P_t(t) = 0$, at which the arterial pressure becomes equal to the CP during the cuff deflation period, while A_m represents the lumen area when fully expanded. Parameters 'a' and 'c' are the compliance of the brachial artery in systolic and diastolic regions, respectively.

4.1 BP Estimation method from ALA Oscillations Model (ALA-based)

The ALA oscillations model in the diastolic region (4.2) is adopted to estimate SBP and DBP. The arterial pressures ($P_a(t)$) at peak and trough of the oscillometric pulses represent SBP and DBP respectively. The peak and trough of the simulated OMW (OMW_{sim}) pulses in the diastolic region is compared with corresponding actual pulses from the experiments (OMW_{act}), and differences are minimized in two separate procedures (P2, P3) in order to estimate the SBP and DBP, respectively.

Arterial lumen oscillations ($A(t)$) are composed of two slow-varying (A_1) and oscillating (A_2) components

$$A_1(t) = A_m - (A_m - A_0)e^{-c(MAP - P_c(t))} \quad \text{for } P_a(t) \geq P_c(t) \quad 4.3$$

$$A_2(t) = A_m - (A_m - A_0)e^{-c(P_a(t) - P_c(t))} \quad 4.4$$

$$- (A_m - (A_m - A_0)e^{-c(MAP - P_c(t))}) \quad \text{for } P_a(t) \geq P_c(t) \quad 4.5$$

$$OMW_{sim}(t) = \varphi A_2(t)$$

where $A_1(t)$ and $A_2(t)$ are the respective slow-varying and oscillating components of the lumen area model at time instant 't'. $P_a(t)$ and $P_c(t)$ represent arterial and cuff pressures, respectively.

The MAP is estimated by the DTA. Parameter ‘ c ’ represents the compliance parameter. The OMW_{sim} is the oscillometric waveform derived from the oscillating component of the ALA oscillations model. The slow-varying component $A_1(t)$ is obtained in (4.3) by replacing the arterial pressure $P_a(t)$ in (4.1) with the MAP estimated by the DTA (MAP_{DTA}). The oscillating component $A_2(t)$ in (4.4) is obtained by removing the slow-varying component from the ALA model. The slow-varying component $A_1(t)$ is influenced by the deflating CP, while the oscillating component $A_2(t)$ is the simulated BP oscillations, and it is comparable to the corresponding OMW_{act} if multiplied by a proportional factor φ (4.5).

The least square method is used to optimize the unknown parameters of the ALA model during the optimization process. Although we can initialize φ with any positive number, in the optimization process it was empirically set to 40 in order to reduce the optimization iterations because it has been observed that the actual oscillometric waveforms’ amplitude were approximately 40 times the corresponding simulated waveforms over all measurements. The purpose of adopting the ALA model is to construct the OMW_{sim} , which is the simulated version of the actual oscillometric waveform. The OMW_{sim} can simulate the corresponding actual recording if the MAP and $P_c(t)$ in the model are replaced with corresponding values from the actual recording, and lumen area parameters A_0 , A_m , and ‘ c ’ are replaced with the optimized values, so we need to optimize A_0 , A_m , and compliance parameter ‘ c ’ prior to the BP estimation.

The simulated ALA oscillations ($A(t)$) and its components ($A_1(t)$ and $A_2(t)$) are illustrated in Fig. 4.2. The oscillating component ($A_2(t)$) is linearly proportional to the OMW_{sim} which starts from zero where the CP is at the SSBP and the artery underneath the cuff is completely occluded. Next, increases exponentially and attains maximum at $P_a(t) = P_c(t)$, and decreases exponentially with the further cuff deflation, and finally stays at a constant level. The slow-varying component ($A_1(t)$) is the lumen area at $P_c(t)=MAP$, so it has no oscillations and just reflects the cuff deflating influence on $A(t)$, and it is used to be subtracted from $A(t)$ and to extract the oscillating component ($A_2(t)$).

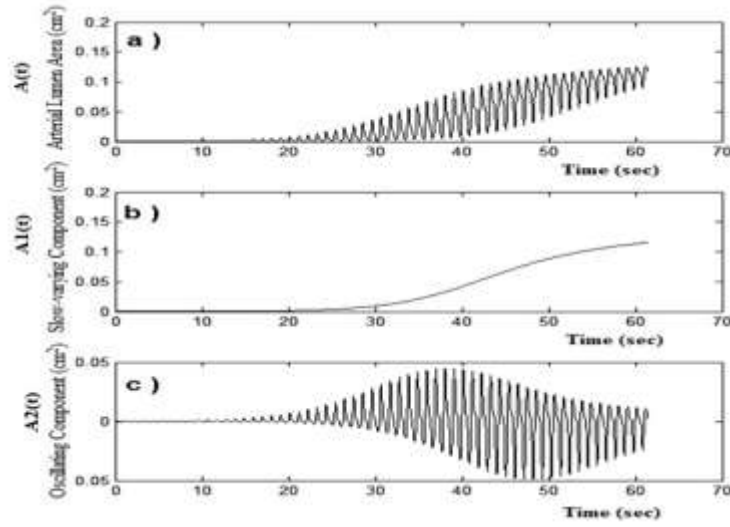


Fig. 4.2. (a) Simulated arterial lumen area. (b) Slow-varying component which is influenced by deflating cuff pressure. (c) Oscillating component that reflects the intra-arterial blood pressure oscillations.

The proposed ALA-based method is based on the mathematical model of the ALA in the diastolic region. The oscillometric waveform is extracted from the ALA model (4.3–4.5) and is used to optimize the unknown parameters ‘ c ’ (compliance parameter), A_0 (lumen area at MAP), A_m (maximum lumen area), P_a (arterial pressure) of the ALA model such as to estimate SBP and DBP accordingly. The known parameters are the MAP, which is estimated by the DTA, and $P_c(t)$, which is the deflating cuff pressure. The proportional constant φ is set equal to 40 for all measurements. In this research, a sequence of three integrated procedures (P1-P3) was developed to optimize the unknown parameters of the ALA model. The peak and trough amplitudes of actual and corresponding simulated OMW pulses in the diastolic region are compared to optimize the unknown parameters of the employed ALA model. The least squares method is employed to minimize sum of the squared differences between the actual and corresponding simulated waveforms and optimize the unknown parameters of the model. The results are the compliance parameter ‘ c ’ in procedure P1; A_m , A_0 , and SBP in procedure P2; and DBP in procedure P3. Procedure P1 was developed to optimize the parameter ‘ c ’ of the ALA model and estimate the compliance parameter by minimizing the absolute difference between successive peak ratios of the actual and corresponding simulated OMW pulses in the diastolic region. The estimation of compliance parameter ‘ c ’ allows for adapting the measurement to the specific arterial stiffness of the subject, thus addressing the rigidity of other measurement

algorithms, such as the most popular coefficient-based MAA. Procedure P2 employs peak information of the actual and simulated OMW pulses and the compliance parameter ‘ c ’ provided by P1 to optimize three unknown parameters A_0 , A_m , and P_{a_pk} . The P_{a_pk} is the arterial pressure at peaks of the OMW pulses, so the optimized value of P_{a_pk} will be considered as the SBP. Similarly, procedure P3 adopts trough information of the actual and corresponding simulated OMW pulses and the estimated compliance parameters ‘ c ’, A_0 , and A_m to estimate the DBP. Estimated DBP is the optimized value of the arterial pressure at troughs (P_{a_tr}) of the OMW pulses. Fig. 4.3 illustrates the cooperation of the three procedures, along with the optimized unknown parameters at each step of the work.

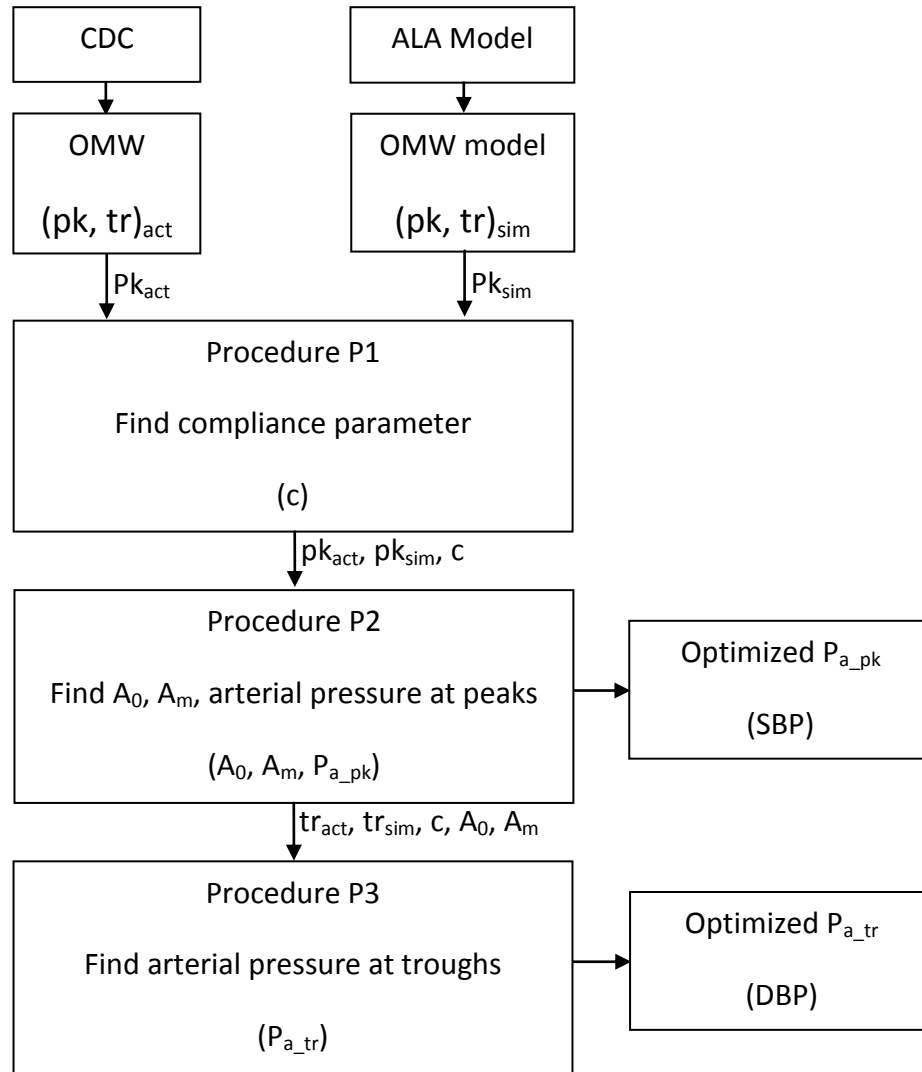


Fig. 4.3. ALA-based BP evaluation method in the diastolic region.

4.1.1 Evaluation of the Compliance Parameter (Procedure 1)

The compliance parameter of the ALA-based model is estimated from the peaks of the OMW pulses in the diastolic region, where the CP influence on vessel compliance is small and the elasticity of the vessel underneath the cuff can be measured more accurately. The proposed modeling approach is based on the lumen area oscillations of the brachial vessel underneath the cuff, so the vessel should oscillate under minimum external CP, which is possible in the diastolic region. Therefore, the diastolic region is used to estimate the compliance parameter ‘ c ’ of the employed ALA model.

The peaks of the actual OMW pulses are available from the experiments. The ALA oscillations model in the diastolic region (4.2) is employed to construct the corresponding simulated OMW pulses. Parameter ‘ c ’ of the model is determined by minimizing the sum of the squared differences between the actual and simulated peaks in the diastolic region. The unknown parameters of the ALA model are reduced prior to the optimization process in procedure P1. To this end, mathematical simplification in (4.6–4.10) is accomplished to eliminate two unknown parameters (A_0 , A_m) by dividing the values of two successive peaks of the simulated OMW pulses and estimate simulated peak ratios (pk_ratio_{sim}). Similarly, the actual peak ratios (pk_ratio_{act}) are estimated from the division of the corresponding two successive peaks from the experiments (4.11). Finally, parameter ‘ c ’ is determined as compliance parameter by minimizing the absolute differences between the actual and simulated peak ratios.

$$\frac{OMW_{sim}(t)}{A_m - A_0} = \varphi \cdot \left\{ \left(\frac{A_m}{A_m - A_0} - e^{-c(P_a(t) - P_c(t))} \right) - \left(\frac{A_m}{A_m - A_0} - e^{-c(MAP - P_c(t))} \right) \right\} \text{ for } P_a(t) \geq P_c(t) \quad 4.6$$

$$\frac{OMW_{sim}(t)}{A_m - A_0} = \varphi \cdot \{ e^{-c(MAP - P_c(t))} - e^{-c(P_a(t) - P_c(t))} \} \text{ for } P_a(t) \geq P_c(t) \quad 4.7$$

$$\frac{pk_{sim_i}}{A_m - A_0} = \varphi \cdot \{ e^{-c(MAP - P_{c_i})} - e^{-c(P_{a_i} - P_{c_i})} \} \text{ for } P_a(t) \geq P_c(t) \quad 4.8$$

$$\frac{pk_{sim_{i+1}}}{A_m - A_0} = \varphi \cdot \{ e^{-c(MAP - P_{c_{i+1}})} - e^{-c(P_{a_{i+1}} - P_{c_{i+1}})} \} \text{ for } P_a(t) \geq P_c(t) \quad 4.9$$

$$pk_{ratio_{sim}} = \frac{pk_{sim_{i+1}}}{pk_{sim_i}} = \frac{e^{-c(MAP - P_{c_{i+1}})} - e^{-c(P_{a_{i+1}} - P_{c_{i+1}})}}{e^{-c(MAP - P_{c_i})} - e^{-c(P_{a_i} - P_{c_i})}} \text{ for } P_a(t) \geq P_c(t) \quad 4.10$$

$$pk_{ratio_{act}} = \frac{pk_{act_{i+1}}}{pk_{act_i}} = \frac{\text{Amplitude of the } (i+1)^{th} \text{ peak of the } OMW_{act}}{\text{Amplitude of the } i^{th} \text{ peak of the } OMW_{act}} \quad \text{for } P_a(t) \geq P_c(t) \quad 4.11$$

The objective function Of_c in (4.12) holds the sum of the squared differences between successive peak ratios of the actual and corresponding simulated OMW pulses in the diastolic region, which is minimized to optimize compliance parameter ‘c’ of the ALA model in P1.

$$Of_c = \sum_{i=1}^{\text{number of peaks}-1} \left(pk_{ratio_{act_i}} - pk_{ratio_{sim_i}} \right)^2 \quad \text{for } P_a(t) \geq P_c(t) \quad 4.12$$

where the actual and simulated peak ratios are derived from the division of the two successive peaks of the actual and simulated OMW pulses, respectively. $P_a(t)$ and $P_c(t)$ represent the arterial and cuff pressures at time instant ‘t’, respectively.

The actual and simulated peak ratios are used in Fig. 4.4 to minimize the objective function (Of_c) and to optimize parameter ‘c’ of the OMW_{sim} .

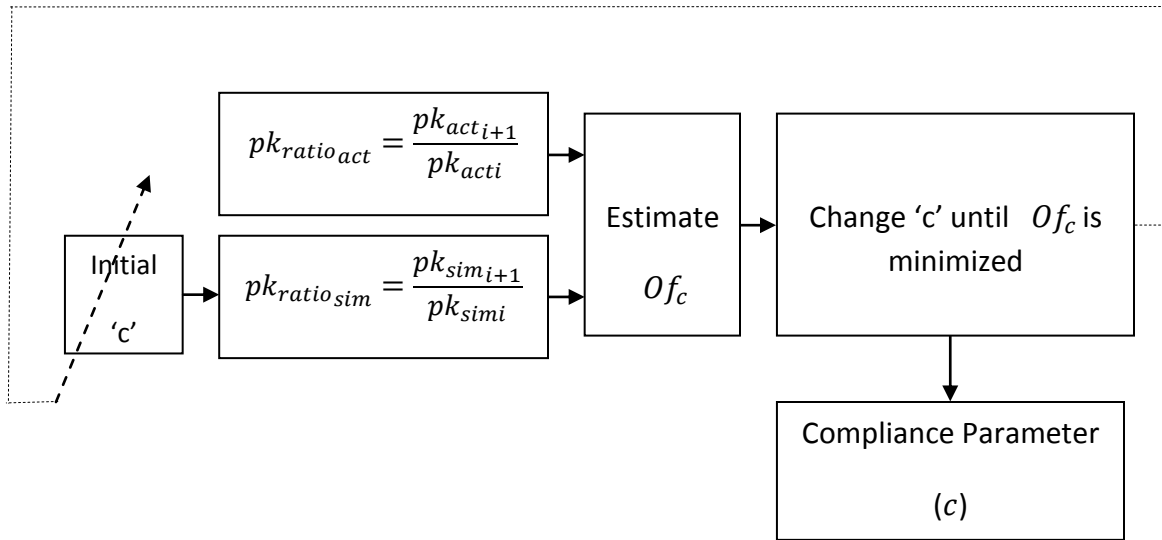


Fig. 4.4. Compliance parameter evaluation in the diastolic region (Procedure P1).

4.1.2 Evaluation of the SBP (Procedure 2)

In this procedure, the peaks of the actual of the simulated OMW pulses in the diastolic region are employed to optimize the unknown parameters of the model. Since the arterial pressure is optimized at the peak positions of the oscillometric pulses, it is denoted by P_{a_pk} . The optimized value of P_{a_pk} corresponds to the maximum value of the arterial BP, which is the SBP. Unknown

parameters (A_0 , A_m , P_{a_pk}) are optimized by minimizing the objective function Of_{SBP} . The objective function Of_{SBP} in (4.13) holds the sum of the squared differences between the actual and corresponding simulated peaks of the OMW pulses in the diastolic region, which is minimized to optimize the unknown parameters of the ALA model in P2.

$$Of_{SBP} = \sum_{i=1}^{\text{number of peaks}} (pk_{act_i} - pk_{sim_i})^2 \quad \text{for } P_a(t) \geq P_c(t) \quad 4.13$$

The known parameters of the OMW_{sim} are the cuff deflating pressure ($P_c(t)$) and the compliance parameter ' c ' estimated by the P1. The optimization process in Fig. 4.5 employs the peak of the actual and simulated OMW pulses in the diastolic region to optimize A_0 , A_m , and the arterial pressure at peaks (P_{a_pk}) by minimizing the objective function Of_{SBP} . The optimized lumen areas A_0 , and A_m are used by P3, and the optimized P_{a_pk} , which is the main output of this procedure, is considered as the SBP.

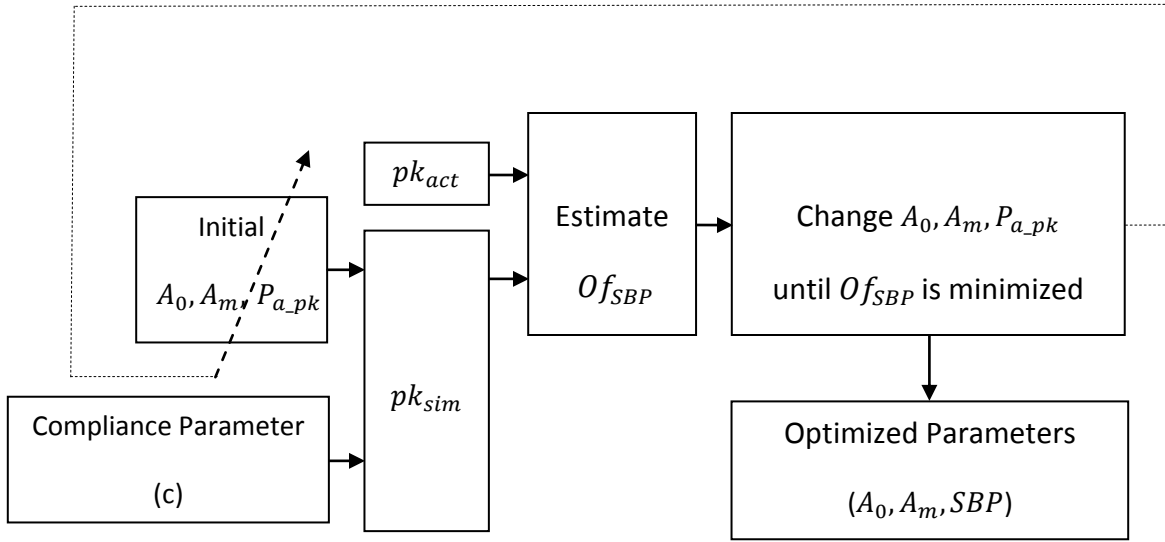


Fig. 4.5. Evaluation of the SBP in the diastolic region (Procedure P2).

4.1.3 Evaluation of the DBP (Procedure 3)

This procedure is used to determine the DBP by optimizing the arterial pressure at the trough of the OMW pulses in the diastolic region. The arterial pressure at the trough of the OMW pulses is denoted by P_{a_tr} . The troughs of the simulated OMW pulses in the diastolic region are compared with the corresponding actual troughs from the experiments, and their absolute

differences are minimized to obtain the optimized value of the arterial pressure at the troughs. The trough of the oscillometric pulses correspond to the minimum of the arterial pressure, so the optimized P_{a_tr} represents the DBP. The objective function Of_{DBP} in (4.14) holds the sum of the squared differences between actual and corresponding simulated troughs of the OMW pulses in the diastolic region, which is minimized to optimize the unknown parameter of the ALA model in P3.

$$Of_{DBP} = \sum_{i=1}^{\text{number of troughs}} (tr_{act_i} - tr_{sim_i})^2 \quad \text{for } P_a(t) \geq P_c(t) \quad 4.14$$

The optimization process of arterial pressure at troughs is illustrated in Fig. 4.6. Troughs of the actual and simulated OMW pulses are compared to optimize P_{a_tr} in the diastolic region. The compliance parameter ‘ c ’ of the OMW_{sim} is estimated by P1, while the lumen area parameters A_0 , and A_m are estimated by P2 to provide required inputs of the P3.

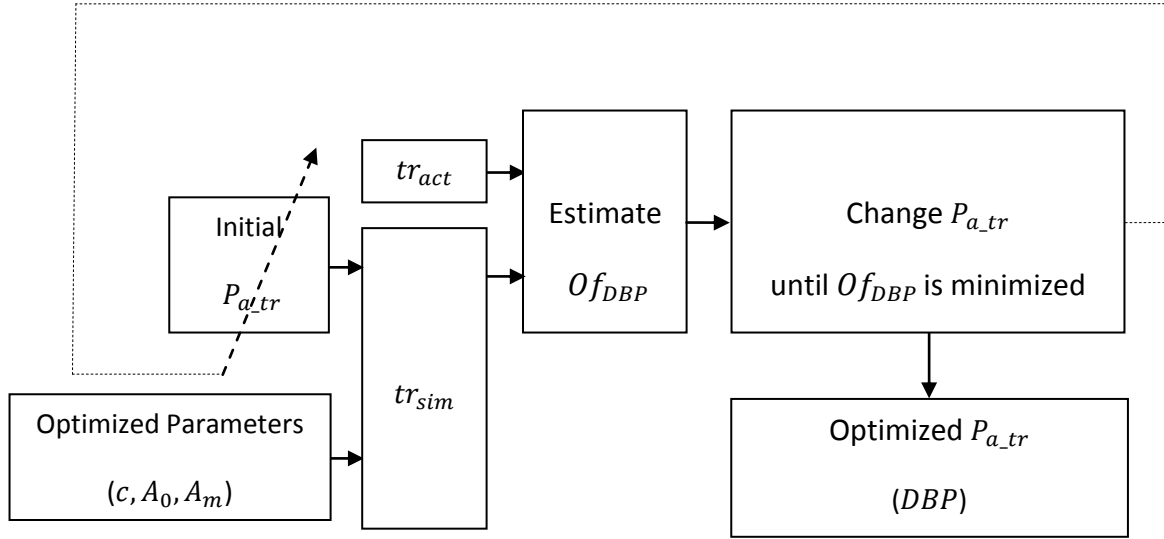


Fig. 4.6. Evaluation of the DBP in the diastolic region (Procedure P3).

4.2 Simplifying the ALA-based Method

The Procedure P1 can estimate parameter ‘ c ’ of the ALA model accurately, but the optimization process in P1 is time consuming and increases the complexity of the model. In this section, a linear regression model is proposed to estimate parameter ‘ c ’ directly from the corresponding R_{act} .

In order to derive the linear regression model, the DTA is employed to determine the actual (R_{act}) and corresponding simulated (R_{sim}) amplitude ratios of the oscillometric pulse at MAP, compare them, and optimize 'c' by minimizing the differences between R_{act} and corresponding R_{sim} over all recordings. The vessel compliance peaks at zero transmural pressure [141, 142], at which the deflating CP becomes equal to MAP. That's why parameter 'c' of the ALA model is evaluated from the OMW pulse at MAP. Finally, I investigated the correlation between parameter 'c' and corresponding R_{act} to derive a linear regression model. In order to evaluate parameter 'c', we need to construct the simulated waveform (OMW_{sim}) of the corresponding actual waveform (OMW_{act}) for each measurement. We cannot use the model in (4.2) to estimate parameter 'c', because we do not have the required unknown parameters A_0 , A_m , and $P_a(t)$. Therefore, I employed the arterial lumen area simulator in (4.18) with fewer unknown parameters [20]. One of the unknown parameters of the employed model in (4.18) is the arterial pressure ($P_a(t)$), so I employed the arterial pressure simulator [104] and constructed the simulated version of the arterial pressure of the subjects by customizing the MAP, HR, C_0 , C_1 , and $\emptyset$ of the model in (4.15) and replaced it with $P_a(t)$ in (4.19). The R_{act} is specific for each subject, so by simply replacing the R_{act} in the linear regression model in (4.25), we can find the compliance parameter of the subject. The compliance parameter 'c' is an important factor in BP measurements and is used in P2 and P3 to estimate SBP and DBP, respectively.

4.2.1 Modeling Approach to Evaluate the Compliance Parameter

The ALA model [20] requires parameters 'a', 'b', 'c', 'd', $P_a(t)$, and $P_c(t)$ to simulate the ALA oscillations (4.18, 4.19). Parameters 'a'=0.03, 'b'=3.3, and 'd'=0.08 are the cuff constants and are set with the initial values of the simulated cuff [20]. Parameter 'c' is unknown and is determined by an optimization process. The optimization process is done once in order to derive the linear regression model between R_{act} and parameter 'c'. The $P_a(t)$ is the arterial pressure waveform, which is provided by a customized arterial pressure simulator. The $P_c(t)$ is the cuff deflating pressure, which is known from the experiments. The ALA model is employed to construct the simulated oscillometric waveform (OMW_{sim}). The compliance parameter 'c' is optimized by minimizing the sum of the squared differences between R_{act} and the corresponding R_{sim} (Fig. 4.7.). The simulated arterial pressure in (4.15) is composed of fundamental frequency

and the second harmonic. In order to customize simulate arterial pressure corresponding to the actual pressure, the MAP and HR are replaced with the corresponding actual values from the experiments, and amplitudes of frequency components C_0 , and C_1 are optimized by minimizing the objective function Of_{c0c1} (see Fig. 4.12).

The lumen area model in (4.18) is constructed by employing the customized simulated arterial pressure ($P_a(t)$). The lumen area model is composed of two slow-varying and oscillating components. The slow-varying component is influenced by cuff deflating pressure and is removed from the model to obtain the oscillating component required to derive OMW_{sim} . The oscillating component is linearly proportional to OMW_{sim} by the proportional constant φ , which is initialized to 40.

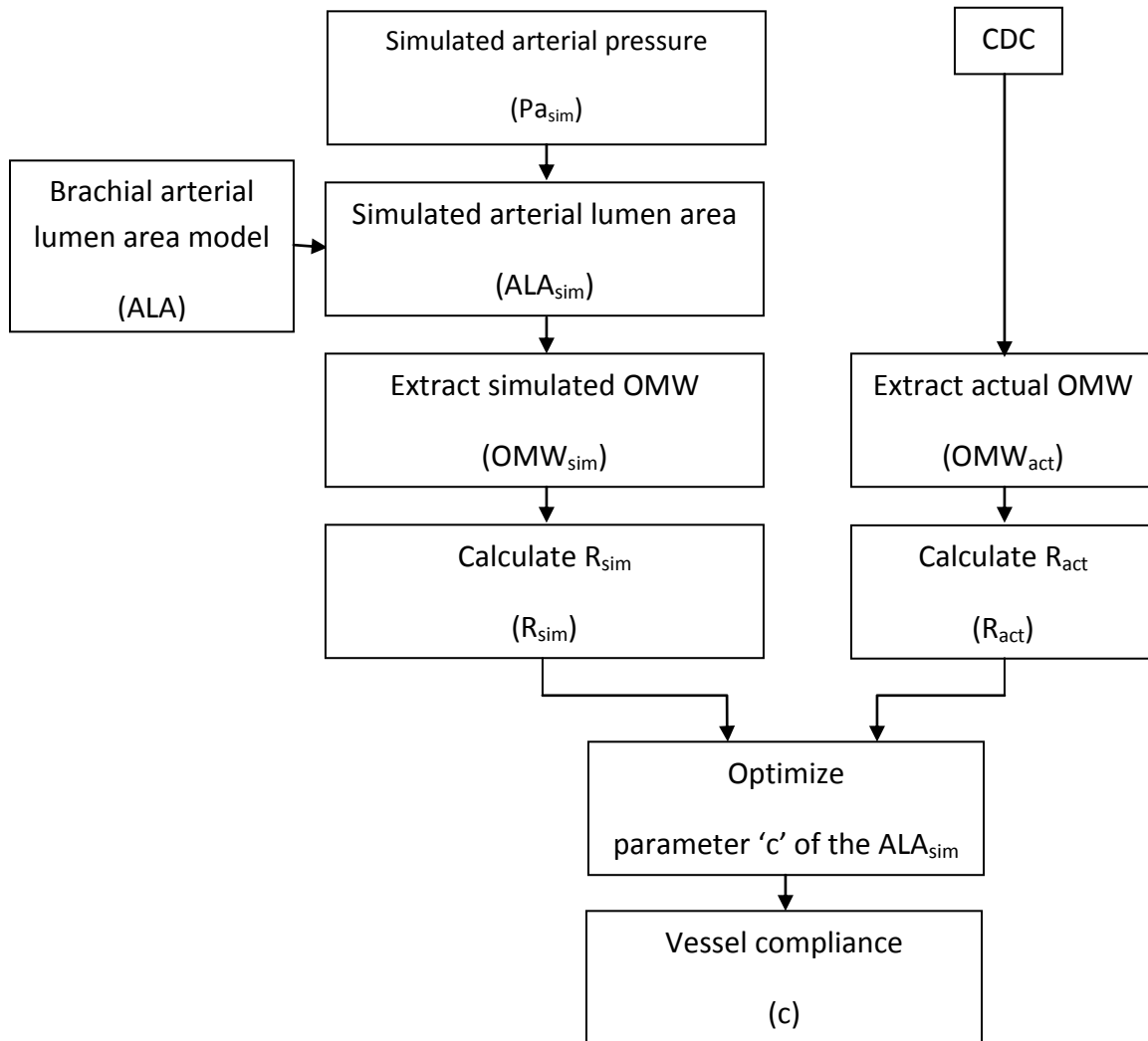


Fig. 4.7. Compliance parameter evaluation of the brachial artery.

4.2.1.1 Oscillometric Waveform Simulator

The arterial pressure model is adopted from [20]. The model requires the MAP, HR, and the fundamental and second harmonic as frequency components (4.15). To construct the simulated arterial pressure, the phase angle of the second harmonic (ϕ) is set to -1.2 radians, and the MAP is replaced by MAP_{DTA} , which is the pressure of the oscillometric pulse at the MAP estimated by the DTA. Also, HR is calculated from number of the oscillometric pulses over specific duration of time, and amplitudes of the fundamental and second harmonic (C_0 , C_1) are optimized such that the sum of the squared differences between the maximum and minimum values of the simulated arterial pressure and corresponding reference values in (4.22) is minimized. The simulator is composed of two sinusoidal waveforms to construct the arterial pressure and the reflective waveforms. A more complete model of the arterial pressure can be found in [105].

$$P_a(t) = MAP + C_0 \cos\left(2\pi \frac{HR}{60} t\right) + C_1 \cos\left(4\pi \frac{HR}{60} t + \phi\right) \quad 4.15$$

The simulated arterial pressure should simulate approximately the actual arterial pressure, so in order to validate the simulated arterial pressure, simulated systolic and diastolic pressures estimated from (4.16) and (4.17) were validated against corresponding reference values from the experiments prior to constructing the OMW_{sim} .

$$SBP_{sim} = Max(P_{a_{sim}}) \quad 4.16$$

$$DBP_{sim} = Min(P_{a_{sim}}) \quad 4.17$$

Initial settings for the arterial pressure parameters are $MAP=95$ mmHg, $C_0=10$ mmHg, $C_1=9$ mmHg, $HR=75$ beats/min, and $\phi=-1.2$ radians. With the cuff deflating from $SSBP=140$ mmHg to $SDBP=40$ mmHg and a deflation rate of 3 mmHg/sec, estimated systolic and diastolic pressures with these settings are 113.8 mmHg and 82.8 mmHg, respectively (4.16, 4.17). The initial values are used as an example to construct and show the simulated arterial pressure in Fig. 4.8.

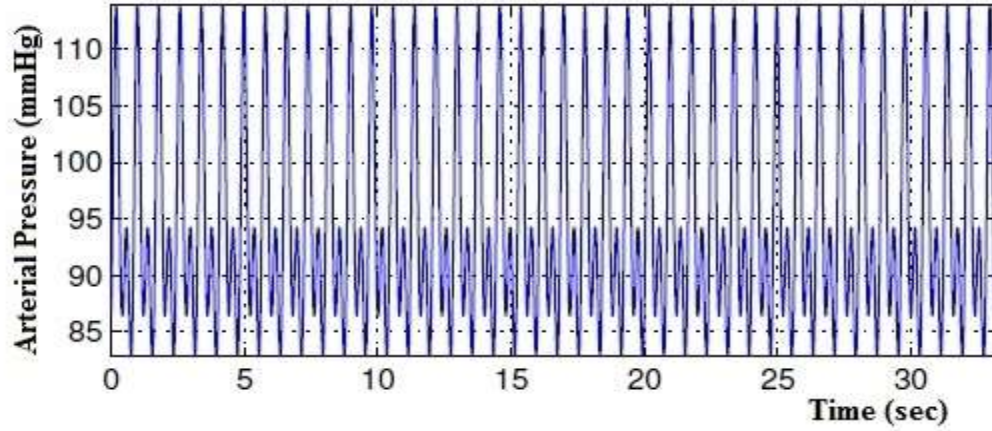


Fig. 4.8. Simulated arterial pressure waveform.

The ALA model (4.18) is a function of parameters ‘ a ’, ‘ b ’, ‘ c ’, and ‘ d ’ and the transmural pressure ($P_t(t)$) [20]. Parameters ‘ a ’, ‘ b ’, and ‘ d ’ are the simulated cuff constants and are set with their initial values. The unknown parameter of the model is the compliance parameter ‘ c ’. Initial settings for the parameters are ‘ a ’=0.03, ‘ b ’=3, ‘ c ’=0.1 mmHg⁻¹, and ‘ d ’=0.08 [20]. Transmural pressure $P_t(t)$ in (4.19) is the difference between $P_a(t)$ and the $P_c(t)$.

$$A(t) = d \frac{\ln(aP_t(t) + b)}{1 + e^{-cP_t(t)}} \quad 4.18$$

$$P_t(t) = P_a(t) - P_c(t) \quad 4.19$$

The simulated lumen area waveform ($A(t)$) is composed of two components, namely, the slow-varying component ($A_1(t)$) caused by the deflating CP and the oscillating component ($A_2(t)$) caused by the arterial pressure oscillations. The oscillating component is obtained by removing the slow-varying component from the simulated lumen area waveform (4.20).

$$A_2(t) = A(t) - A_1(t) \quad 4.20$$

The transmural pressure increases with deflating the cuff from a minimum, at which the CP is considerably greater than the arterial pressure, to a maximum, at which the CP is considerably smaller than the arterial pressure. The arterial pressure is equal to the MAP when the CP becomes equal to the arterial pressure. Fig. 4.9 illustrates the simulated transmural pressure waveform over the cuff deflation period.

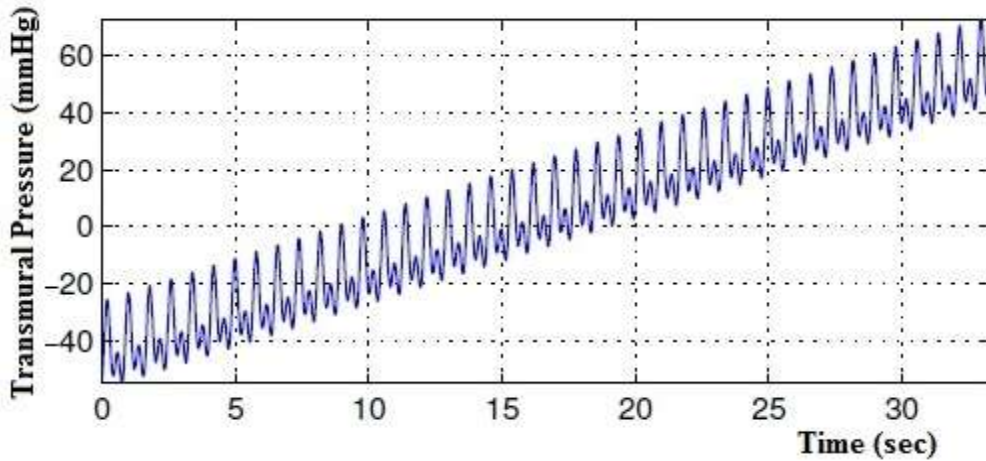


Fig. 4.9. Simulated transmural pressure waveform over cuff deflation period.

The amplitude of the oscillating component of the ALA waveform is about zero when the cuff is inflated to SSBP. The amplitude of the oscillations increases over the cuff deflation period until the CP becomes equal to the arterial pressure. Next, the amplitude decreases with further cuff deflations, because in practice, with the CP less than arterial pressure, only part of the force caused by intra-arterial pressure is transferred to the mechanical sensor of the cuff system. The amplitude continues to decrease and stays at a constant level as the cuff continues to deflate. The slow-varying component of the ALA waveform is influenced by the deflating CP. The amplitude of the slow-varying component starts from about zero and increases exponentially with a positive slope during the cuff deflation period until the CP becomes equal to the arterial pressure. With more deflation, the amplitude increases again, but with a negative slope. The point at which the slope changes from positive to negative is critical, because arterial pressure becomes equal to the MAP. The arterial pressure oscillations and the components are illustrated in Fig. 4.10.

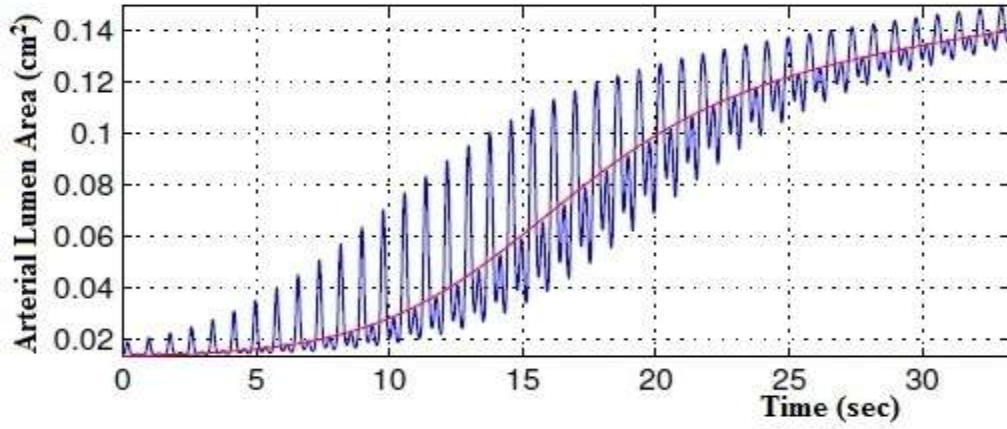


Fig. 4.10. Simulated lumen area waveform over cuff deflation period. Blue waveform is the oscillating component and red curve is the slow-varying component of the lumen area waveform.

The slow-varying component is the lumen area waveform with the arterial pressure equal to the MAP [104], so by replacing the arterial pressure with MAP_{DTA} in (4.19), the lumen area waveform in (4.18) will become the slow-varying component. In order to obtain the simulated oscillating component of the lumen area waveform illustrated in Fig. 4.11, the slow-varying component is subtracted from the simulated lumen area waveform. The simulated OMW in (4.20) is obtained from multiplying the oscillating component by a proportional factor φ [106]. The proportional factor φ is empirically determined and initialized to 40 in this research.

$$OMW_{sim} = \varphi \cdot A_2(t) \quad 4.21$$

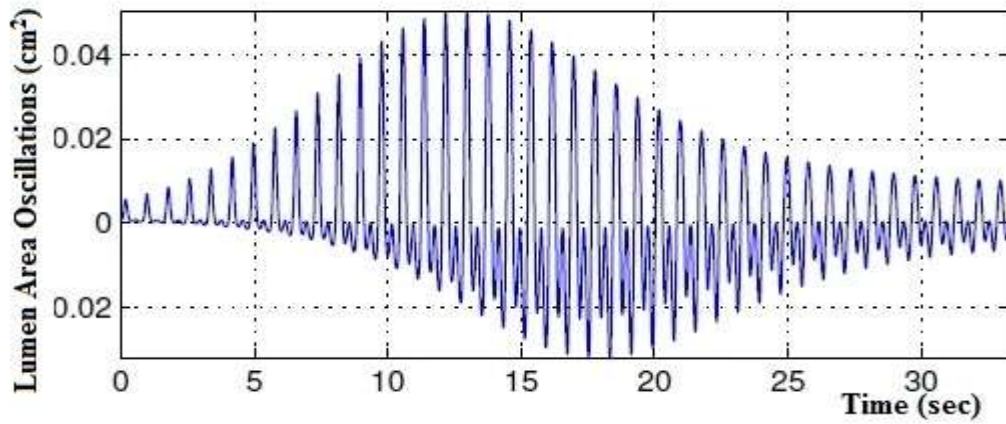


Fig. 4.11. Simulated oscillating component of the lumen area waveform.

4.2.1.2 Customizing the Simulated Oscillometric Waveforms

The Arterial Pressure Simulator should be constructed and customized prior to the estimation of the compliance parameter of the ALA model in order to simulate the OMW of a given recording. The simulated oscillometric waveforms (OMW_{sim}) are constructed in two steps. In the first step, the amplitudes of the fundamental and the second harmonic of the simulated arterial pressure (C_0 , and C_1) are optimized to simulate the arterial pressure with maximum and minimum values closest to the reference SBP and DBP, respectively. In the second step, the optimized amplitudes are employed by the ALA simulator along with the MAP and HR adopted from the corresponding actual CDC recording to construct the OMW_{sim} . The lumen area model starts with the initial parameters and optimizes parameter ‘ c ’ of the model. The least square method is employed in (4.22) to minimize the sum of the squared differences between the actual and simulated SBP and DBP in order to optimize the parameter ‘ c ’.

4.2.1.3 Optimization of C_0 , and C_1

In order to construct the simulated arterial pressure of a given recording, the arterial pressure simulator in (4.15) is constructed and customized by replacing MAP with MAP_{DTA} , HR with calculated value from the actual waveform, and C_0 and C_1 amplitudes with the optimized values. In order to optimize C_0 and C_1 , the arterial pressure simulator is initialized with the initial values of the C_0 and C_1 , and the amplitudes are optimized by minimizing the objective function Of_{c0c1} in (4.22).

The MAP_{DTA} is estimated by DTA and replaced with the MAP in (4.15). The HR is calculated from number of the oscillometric pulses over specific duration of time. The simulated systolic and diastolic pressures are calculated from the maximum and minimum of the simulated arterial pressure at each iteration of the optimization process and compared with the corresponding reference pressures to optimize amplitudes C_0 and C_1 . The least squares method is employed to optimize the amplitudes by minimizing the objective function (Of_{c0c1}). The objective function holds the sum of the squared differences between reference and corresponding simulated SBP and DBP (4.22).

$$Of_{c0c1} = (SBP_{ref} - SBP_{sim})^2 + (DBP_{ref} - DBP_{sim})^2 \quad 4.22$$

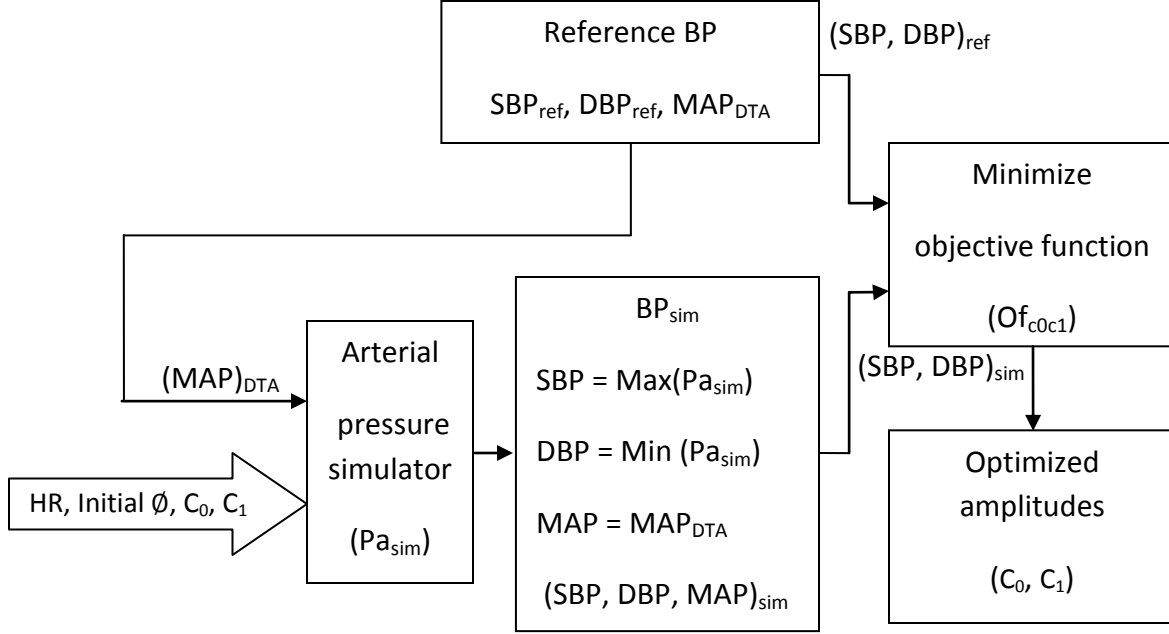


Fig. 4.12. Optimization process of C_0 and C_1 parameters of the simulated arterial pressure.

4.2.1.4 Evaluation of the Compliance Parameter

In order to evaluate the compliance parameter, the lumen area waveform is constructed by employing the ALA model in (4.18) and adopting the customized simulated arterial pressure. The deflating CP is adopted from experiments, and the transmural pressure $P_t(t)$ is constructed by subtracting the CP from the customized arterial pressure (4.19). The simulated cuff constants ‘ a ’, ‘ b ’, and ‘ d ’ are replaced with their initial values, and parameter ‘ c ’ is the only unknown parameter which is optimized and evaluated as compliance parameter. As illustrated in Fig. 4.13, the amplitude ratios of the actual and simulated OMW pulses at the MAP are compared to determine the parameter ‘ c ’ of the ALA model in (4.18).

The simulated oscillometric waveform (OMW_{sim}) is derived from the lumen area model by subtracting the slow-varying component $A_1(t)$ from the lumen area waveform $A(t)$ and multiplying the remaining oscillating component $A_2(t)$ to a proportional factor φ equal to 40 in this research (4.20, 4.21). As stated before, the slow-varying component $A_1(t)$ is obtained from

replacing the simulated arterial pressure in (4.18) with the corresponding MAP_{DTA} of a given recording (4.23).

$$A_1(t) = d \frac{\ln(a(MAP_{DTA} - P_c(t)) + b)}{1 + e^{-c(MAP_{DTA} - P_c(t))}} \quad 4.23$$

The optimized parameter ‘ c ’ of the model (4.18) is required to fit a regression line between the amplitude ratio of the oscillometric pulse at the MAP and the compliance parameter ‘ c ’. Parameter ‘ c ’ is optimized by minimizing the objective function (Of_c). The objective function holds the sum of the squared differences between the actual and corresponding simulated amplitude ratio of the oscillometric pulses at the MAP (4.24).

$$Of_c = (R_{act} - R_{sim})^2 \quad 4.24$$

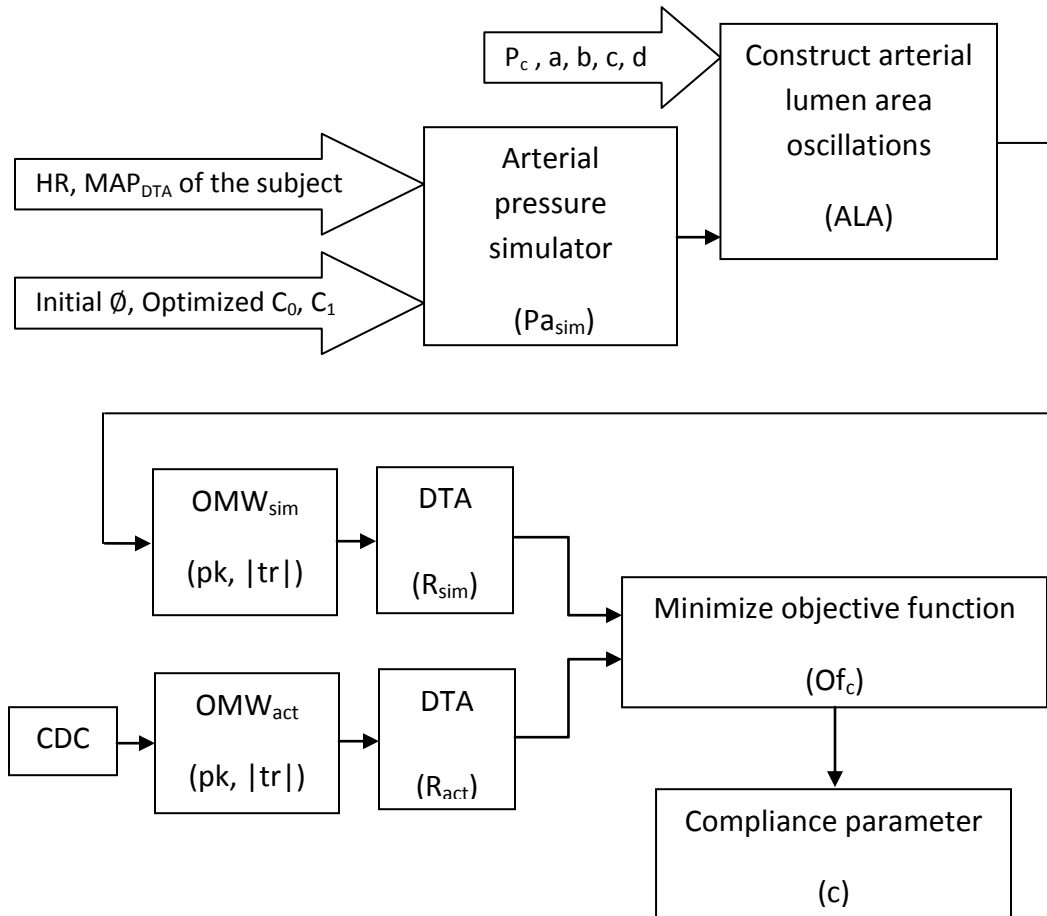


Fig. 4.13. Optimization process of the parameter ‘ c ’ of the lumen area model.

In order to derive the linear regression model between the parameter ‘ c ’ of the ALA model in (4.18) and the corresponding R_{act} from the actual waveforms, I investigated the correlation between R_{act} and ‘ c ’. According to the observations, there was a good correlation between R_{act} and ‘ c ’ for all datasets. For example, there was a correlation of 98% between parameter ‘ c ’ and the corresponding R_{act} over all measurements of the DS1. The correlation is illustrated in Fig. 4.15. This correlation is good enough to fit a regression line between R_{act} and corresponding parameter ‘ c ’ of the ALA model. Previously, parameter ‘ c ’ was estimated through a time consuming optimization procedure (P1) based on the successive peak ratios of the OMW pulses. The P1 is replaced with the derived regression model to estimate compliance parameter ‘ c ’ of the ALA model in (4.2) directly from the corresponding R_{act} .

4.3 Experimental Results

In order to provide accurate BP readings in oscillometry, an accurate coefficient-free estimation method is required to estimate BP. The estimated pressures from the accurate estimation method will be trusted if the examiners observe the proper measurement conditions. In chapter 3, the DTA was proposed to reject the untrusted measurements and provide the trusted BP readings. Both improper measurement conditions and inaccurate estimation methods contribute to the untrusted BP readings, so we need an accurate estimation method beside the DTA to finally provide trusted BP readings. In this chapter, a modeling approach is employed, and an ALA-based method is proposed to estimate BP from the lumen area oscillations model in the diastolic region. Moreover, P1 is replaced with a linear regression model to estimate the compliance parameter ‘ c ’ directly from the amplitude ratio of the oscillometric pulse at the MAP

In order to test the proposed simplified method, the recordings with maximum errors estimated by both MAA and MMSA estimation algorithms were selected from each dataset and the validated results against references were compared with the corresponding validated results estimated by the proposed simplified ALA-based method to calculate level of the improvements in accuracy by ALA-based method (see Table 4.1.).

Table 4.1: Validated results of MAA, MMSA, and ALA-based method for maximum errors.

One Rec. with max. error from each dataset		BP estimation algorithms [mmHg]				Reduced error % relative to MAA		BP estimation algorithms [mmHg]				Reduced error % relative to MMSA	
		MAA		ALA-based				MMSA		ALA-based			
		SBP	DBP	SBP	DBP	SBP	DBP	SBP	DBP	SBP	DBP	SBP	DBP
DS1	AE	88	25	51	7.0	42	72	95	43	51	8.5	47	80
DS2	AE	26	14	6.7	10	75	24	27	25	5.9	1.0	78	96
DS3	AE	43	24	25	17	44	30	47	27	14	17	71	37

Also, I have tested the proposed simplified ALA-based method on all recordings of all three datasets including the healthy and sick subjects (DS1–DS3). DS1 is composed of 425 trials acquired from healthy subjects, and each recording is referenced with corresponding nurse systolic and diastolic pressures. Table 4.2 includes validated results against the nurse for the MAA, MMSA, and ALA-based algorithm over 425 recordings. Although the developed MAA is best tuned for the dataset, the ALA-based algorithm provides much better results. The last four columns include the level of improvements provided by the ALA-based algorithm compared to the MAA and MMSA.

Table 4.2: Validated results of MAA, MMSA, and ALA-based method for DS1.

DS1		BP estimation algorithms [mmHg]						Reduced error % relative to MAA		Reduced error % relative to MMSA	
		MAA		MMSA		ALA-based					
		SBP	DBP	SBP	DBP	SBP	DBP	SBP	DBP	SBP	DBP
425 Rec's	MAE	7.5	5.6	14	7.0	5.9	3.0	21	47	57	57
	STDE	6.8	4.8	10	6.3	5.1	2.6	25	47	50	59

In order to be more confident with the accuracy of the ALA-based method, the validation process was repeated on another dataset (DS2), which was composed of 150 trials of healthy subjects. Each trial is referenced with Omron FDA-approved monitor (HEM-790IT) and calibrated with a nurse prior to the measurements. The validated results for all estimation algorithms are listed in Table 4.3, along with the level of improvements obtained with the ALA-based method compared to the MAA and MMSA.

Table 4.3: Validated results of MAA, MMSA, and ALA-based method for DS2.

DS2		BP estimation algorithms [mmHg]						Reduced error % relative to MAA		Reduced error % relative to MMSA	
		MAA		MMSA		ALA-based					
		SBP	DBP	SBP	DBP	SBP	DBP	SBP	DBP	SBP	DBP
150 Rec's	MAE	5.7	3.3	6.2	4.6	5.1	3.2	9.5	5.2	17	31
	STDE	4.6	2.8	5.1	4.8	3.6	2.6	22	6.2	30	46

The dataset DS3, provided by Health Parametrics Inc. (HPI), is composed of 78 sick subjects, some with chronic cardiovascular diseases, such as hypertension, atrial fibrillation, and stoke. Each recording is referenced by an FDA-approved BpTru BP monitor (BPM-100). The proposed ALA-based method is tested on DS3, and the results are validated against BpTru. The validated results are compared to the MAA and MMSA and shown in Table 4.4.

Table 4.4: Validated results of MAA, MMSA, and ALA-based method for DS3.

DS3		BP estimation algorithms [mmHg]						Reduced error % relative to MAA		Reduced error % relative to MMSA	
		MAA		MMSA		ALA-based					
		SBP	DBP	SBP	DBP	SBP	DBP	SBP	DBP	SBP	DBP
78 Rec's	MAE	12	8.4	9.0	7.9	7.5	6.2	39	26	17	21
	STDE	8.4	5.2	8.9	5.3	6.2	5.0	26	3.3	31	4.0

4.3.1 Trustworthiness of the BP readings in the ALA-based Method

As stated before, trustworthiness of the estimated BP is affected by either improper measurement conditions or an inaccurate BP estimation method. The simplified ALA-based method is proposed as an accurate BP estimation method, and the results are listed in Tables 4.2–4.4. Although the proposed estimation method is accurate and contributes considerably to accurate BP readings, we need to test the estimated results with the DTA to eliminate the untrusted measurements caused by improper measurement conditions. To this end, I applied the DTA to the estimated results and rejected those untrusted recordings that are measured improperly over all datasets. The validated results are shown in Tables 4.5–4.7.

The estimated results of the ALA-based method is evaluated by DTA over DS1 comprised of 425 recordings from 85 healthy subjects, and trusted results estimated by ALA-based method (trusted ALA-based method) are validated against corresponding references and compared to the validated results of MAA, and MMSA estimation algorithms. The level of improvement by trusted ALA-based method is estimated and shown in Table 4.5.

Table 4.5: Validated results of MAA, MMSA, and trusted ALA-based method for DS1.

DS1		BP estimation algorithms [mmHg]						Reduced error % relative to MAA		Reduced error % relative to MMSA	
		MAA		MMSA		Trusted ALA-based					
		SBP	DBP	SBP	DBP	SBP	DBP	SBP	DBP	SBP	DBP
425 Rec's	MAE	7.5	5.6	14	7.0	5.9	3.0	21	47	57	57
	STDE	6.8	4.8	10	6.3	4.6	2.4	32	51	55	62

Similarly, the validated results of trusted ALA-based method is compared to the validated results of MAA, and MMSA estimation algorithms over DS2 comprised of 150 recordings from 10 healthy subjects, and the level of improvement by trusted ALA-based method is estimated and shown in Table 4.6.

Table 4.6: Validated results of MAA, MMSA, and trusted ALA-based method for DS2.

DS2		BP estimation algorithms [mmHg]						Reduced error %		Reduced error %	
		MAA		MMSA		Trusted ALA-based		relative to MAA		relative to MMSA	
		SBP	DBP	SBP	DBP	SBP	DBP	SBP	DBP	SBP	DBP
150 Rec's	MAE	5.7	3.4	6.2	4.6	5.1	3.2	9.8	5.9	17	31
	STDE	4.6	2.8	5.1	4.8	3.6	2.6	22	6.6	30	46

Finally, the validated results of trusted ALA-based method is compared to the validated results of MAA, and MMSA estimation algorithms over DS3 comprised of 78 recordings from 13 sick subjects, and the level of improvement by trusted ALA-based method is estimated and shown in Table 4.7.

Table 4.7: Validated results of MAA, MMSA, and trusted ALA-based method for DS3.

DS3		BP estimation algorithms [mmHg]						Reduced error %		Reduced error %	
		MAA		MMSA		Trusted ALA-based		relative to MAA		relative to MMSA	
		SBP	DBP	SBP	DBP	SBP	DBP	SBP	DBP	SBP	DBP
78 Rec's	MAE	12	8.4	9.0	7.9	7.3	6.0	40	29	19	24
	STDE	8.4	5.2	9.0	5.3	5.4	4.1	36	20	40	21

4.4 Results and Discussion

In this research, I have proposed a BP estimation algorithm based on the lumen area oscillations model in the diastolic region. The ALA model in (4.2) is employed to construct a simulated oscillometric waveform (OMW_{sim}). The slow-varying component of the ALA model is determined in (4.3) by replacing the MAP with MAP_{DTA} and subtracting from the ALA model to extract the oscillating component, as shown in (4.4). Eventually OMW_{sim} is obtained by multiplying the oscillating component with the proportional factor φ equal to 40 in this research. The peaks and troughs of the OMW_{sim} in (4.5) are employed and compared to the corresponding

actual oscillometric waveforms (OMW_{act}) to estimate BP. BP is influenced considerably by the elastic property of the brachial vessel, so compliance parameter ‘ c ’ of the model is determined prior to estimation of the BP. To this end, procedure P1 is developed to compare the successive peak ratios of the simulated and corresponding actual pulses in the diastolic region and evaluate parameter ‘ c ’ of the model by minimizing the sum of the squared differences of the actual and simulated peak ratio of oscillometric pulses in (4.12). Peak ratios are estimated in order to eliminate A_0 and A_m , as demonstrated in (4.6–4.10), and to reduce the number of the unknown parameters in the optimization process.

Procedure P2 employs the estimated parameter ‘ c ’ and optimizes A_0 , A_m , and $P_a(t)$ in (4.13) by minimizing the sum of the squared differences between the actual and simulated peak amplitudes. The arterial pressure $P_a(t)$ is denoted as P_{a_pk} in Fig. 4.3 because it is the arterial pressure at peaks of the OMW_{sim} . As a result, the optimized P_{a_pk} is considered as the SBP.

Procedure P3 employs the estimated parameter ‘ c ’, and the optimized A_0 and A_m from P2 to optimize $P_a(t)$ at troughs of the OMW_{sim} in the diastolic region. Similarly, $P_a(t)$ at troughs are denoted by P_{a_tr} , and the optimized value is considered as the DBP. The optimized P_{a_tr} is the pressure at which the sum of the squared values of the simulated and actual troughs in (4.14) is minimized. The optimized peaks and troughs of the OMW_{sim} for one sample recording in the diastolic region are illustrated in Fig. 4.14.

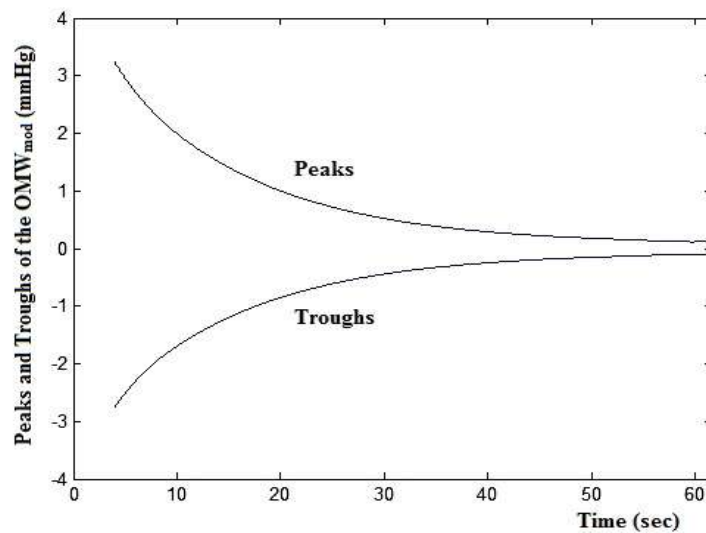


Fig. 4.14. Optimized peaks and troughs of the OMW_{sim} in the diastolic region for one recording.

The P1 optimizes the compliance parameter ' c ' accurately, but the optimization process is time consuming. To this end, a linear regression model between parameter ' c ' of the model and the amplitude ratio of the actual oscillometric pulses at the MAP (R_{act}) was derived to simplify the ALA-based method and estimate parameter ' c ' with the same accuracy. In order to derive the linear regression model, the lumen area model in (4.18) was employed from the literature [20] to construct the simulated version of a given recording and to determine parameter ' c ' of the model by minimizing the squared difference between R_{act} and R_{sim} (4.24). The optimization process is accomplished only once to derive the linear regression model. Parameters ' a ', ' b ', and ' d ' in (4.18) are the simulated cuff constants and are known for the optimization process. Cuff pressure $P_c(t)$ is also known and replaced with the deflating CP of the given recording. In order to provide the arterial pressure $P_a(t)$, the BP simulator in (4.15) is employed from the literature [104] and customized to construct the simulated version of the subject's arterial pressure by replacing the MAP with the MAP_{DTA} , HR with the heart rate of the subjects, and optimizing the amplitudes of the fundamental and the second harmonic (C_0 , C_1) through an optimization process shown in Fig. 4.12. The amplitudes C_0 , C_1 are optimized in (4.22) by minimizing the sum of the squared differences between the actual and simulated systolic and diastolic pressures.

Each optimized parameter ' c ' corresponds to one R_{act} , so the correlation between R_{act} and ' c ' is investigated over DS1, and a linear regression line is fitted accordingly. Correlations for all datasets were encouraging and about the same value. For example, a correlation of 98% has been observed between R_{act} and the corresponding compliance parameter ' c ' over DS1.

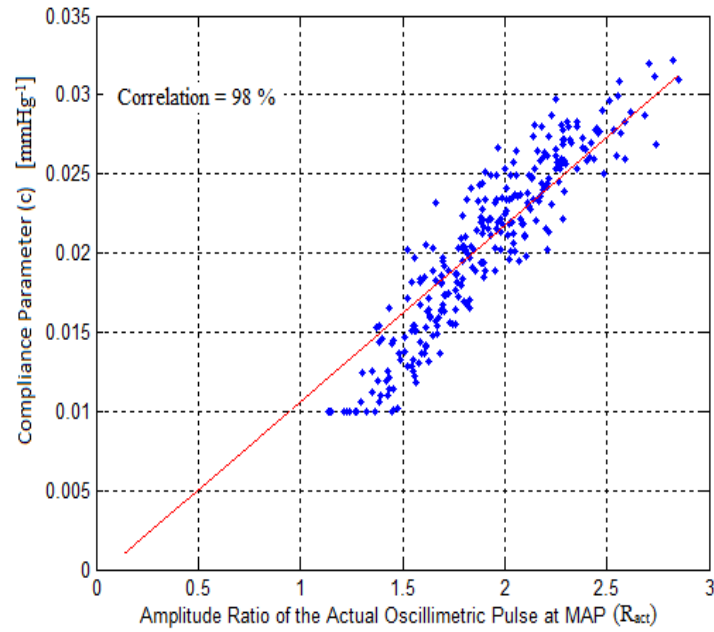


Fig. 4.15. Linear regression between amplitude ratio of the actual oscillometric pulse at MAP (R_{act}) and corresponding compliance parameter ' c ' in the diastolic region over 425 recordings for the dataset DS1.

The linear regression model in (4.25) is derived between R_{act} and compliance parameter ' c ' by using the polynomial method and fitting a curve over 425 recordings of DS1.

$$c = 0.01101R_{act} - 0.0003981 \quad 4.25$$

The number of outliers are shown in Table 4.8 for all datasets, after application of the DTA over estimated BP by MAA, MMSA, and ALA-based method.

Table 4.8: Outliers detected by DTA for MAA, MMSA, ALA-based method over all datasets.

Number of outliers	BP estimation algorithms					
	MAA		MMSA		ALA-based	
	SBP	DBP	SBP	DBP	SBP	DBP
From DS1	129	49	213	75	120	54
From DS2	6	0	4	9	1	0
From DS3	38	0	27	0	17	0

4.5 Conclusion

The proposed ALA-based method was applied to DS1, comprised of 425 recordings obtained from 85 healthy subjects, and the corresponding results are shown in Table 4.2. According to these results, the MAE of the BP estimated by the MAA was improved by 21% and 47%, and the STDE was improved by 25% and 47% for SBP and DBP, respectively. Similarly, the MAE of the estimated BP by the MMSA was improved by 57% and 57%, and the STDE was improved by 50% and 59% for SBP and DBP, respectively.

For the next step, the DTA was applied to the estimated results by the ALA-based method and trusted BP readings were validated against corresponding nurse references. The improved accuracies were shown in Table 4.5 after removing the outliers from DS1. The MAE of the estimated BP by the MAA was improved by 21% and 47%, and the STDE was improved by 32% and 51% for SBP and DBP, respectively. Similarly, the MAE of the estimated BP by the MMSA was improved by 57% and 57%, and the STDE was improved by 55% 62% for SBP and DBP, respectively.

Also, the ALA-based method was applied on DS2, comprised of 150 recordings obtained from 10 healthy subjects, and corresponding results were shown in Table 4.3. According to the observations, the MAE of the estimated BP by the MAA was improved by 9.5% and 5.2%, and the STDE was improved by 22% and 6.2% for SBP and DBP, respectively. Similarly, the MAE of the estimated BP by the MMSA was improved by 17% and 31%, and the STDE was improved by 30% and 46% for SBP and DBP, respectively.

For the next step, the DTA was applied to the estimated results by the ALA-based method, and trusted BP readings are validated against Omron. The improved accuracies are shown in Table 4.6 after removing the outliers from DS2. The MAE of the estimated BP by the MAA was improved by 9.8% and 5.9%, and the STDE was improved by 22% and 6.6% for SBP and DBP, respectively. Similarly, the MAE of the estimated BP by the MMSA was improved by 17% and 31%, and the STDE was improved by 30% and 46% for SBP and DBP, respectively.

Finally, the ALA-based method was applied to DS3, comprised of 78 recordings obtained from 13 sick subjects some with chronic cardiovascular diseases, and corresponding were shown in Table 4.4. According to the observations, the MAE of the estimated BP by the MAA was improved by 39% and 26%, and the STDE was improved by 26% and 3.3% for SBP and DBP,

respectively. Similarly, the MAE of the estimated BP by the MMSA was improved by 17% and 21%, and the STDE was improved by 31% and 4.0% for SBP and DBP, respectively.

For the next step, the DTA was applied to the estimated results by the ALA-based method, and trusted BP readings were validated against BpTru. The improved accuracies were shown in Table 4.7 after removing the outliers from DS3. The MAE of the estimated BP by the MAA was improved by 40% and 29%, and the STDE was improved by 36% and 20% for SBP and DBP, respectively. Similarly, the MAE of the estimated BP by the MMSA was improved by 19% and 24%, and the STDE was improved by 40% and 21% for SBP and DBP, respectively.

In conclusion, the proposed estimation algorithm is more accurate than the popular MAA and MMSA estimation algorithms and can improve accuracy of the measurements considerably. The ALA-based method provides trusted BP readings when complemented by the DTA. Moreover, both the proposed ALA-based method and DTA are applicable on healthy and sick subjects, even those with severe chronic cardiovascular diseases.

Chapter 5

Improvement of PTT-based BP Estimation Algorithm

In terms of the accurate BP estimation algorithm, I have proposed an improvement to another coefficient-free algorithm that estimates BP from the PTT-CP dependency [26]. The pulse transit time (PTT) is the time-distance between the R_peak of the electrocardiogram (ECG) signal and some specific point of the corresponding pressure pulse. The specific point is generally the zero-crossing of the oscillometric pulse where the oscillometric waveform (OMW) crosses from a negative to positive value, and the PTT from the corresponding R_peak to this point is defined as the zero-crossing PTT (PTT_{zc}). Similarly, the PTT can be measured from R_peak to the peak (PTT_{pk}) or to the trough (PTT_{tr}) of the OMW pulses. The advantage of this method is that it is coefficient-free, and it estimates BP without employing empirical constants; still, the method is very sensitive to noises that affect PTTs. One of the unavoidable sources of noise is the breathing effect that affects the PTT through the expanding and shrinking of chest space at each respiratory cycle, which results in undesired variations in BP and PTTs accordingly. One of the solutions is to remove the noise from the PTTs prior to analyzing them. Noise removal procedures from biological signals such as BP are very complex. Recently, in [26], noises were minimized by detecting and removing the outliers from transit times and smoothing the remaining signal for further analysis. The method is still complex, because detecting outliers requires statistical analysis of the PTT, and more importantly, it should be repeated for PTT_{pk} , PTT_{zc} , and PTT_{tr} at each cardiac cycle. Moreover, PTT should be smoothed by moving average filter prior to any analysis, which is time consuming and, more importantly, shifts the transit times a bit, which is undesired and affects the accuracy of the method.

In this chapter, the mathematical model of the PTT is reviewed to understand the theory behind the method and see how we can estimate BP from the PTT-CP dependency without removing the noise. According to the mathematical model of the PTT-CP dependency, each transit time has a maximum over cuff deflation period. The maximas are critical points that correspond to BP. The problem with the previous method is that the maximum point of each transit time signal is searched over the whole cuff deflation period that increases the risk of

locating false maxima. The proposed solution is to narrow down the search domain of each transit time signal over the cuff deflation period. To this end, I have used trusted boundaries of the DTA to determine the search domain of each transit time and to search the maximas inside the trusted boundaries of each transit time. Therefore, the searching domains are around the maximum points, and we have reduced locating the false maximas considerably. Results are validated against references and compared with corresponding validated results from the old method in [26]. The improved results were encouraging because I could eliminate the noise removal procedure and estimate BP directly from noisy transit times even more accurately.

Based on the mathematical model of the PTT, which is derived from the Bramwell and Hill equation [8, pp 64], the PTTs against cuff deflating pressure have a maximum point. This maximum point is critical, because it reflects important information needed to estimate BP. Each of the three PTT_{pk} , PTT_{tr} , and PTT_{zc} are PTTs measured from the onset of the R_peaks to the peak, trough, and zero-crossing of the oscillating pulses at each cardiac cycle. The maximum point PTT_{pk} corresponds to SBP, while the maximum points PTT_{tr} and PTT_{zc} correspond to DBP and the MAP respectively. It is important to consider that this is in theory and is based on the mathematical model of PTTs where there is not any noise involved in equations, but in practice we are dealing with noisy signals that result in huge fluctuations in PTTs. Fluctuations exhibit false maximas in transit times over the cuff deflation period and wrong BP readings accordingly.

5.1 Pulse Transit Time Model

The PTT is the time delay needed by the BP waveform to travel from heart to arm, in addition to time needed to travel underneath the cuff; so PTT is the sum of two transit times: PTT_a , that accounts for transit time from heart to the arm, and PTT_c that accounts for the time that the BP pulse travels underneath the cuff [97, 107]. Similarly, the pulse wave velocity from heart to the arm (PWV_a) is different from the velocity with which the BP pulse travels underneath the cuff (PWV_c). Velocities PWV_a and PWV_c are actually the average pulse wave velocities over arm length (L_a) and cuff length (L_c), respectively (5.1-5.3).

$$PTT(t) = PTT_a(t) + PTT_c(t) \quad 5.1$$

$$PWV_a(t) = L_a / PTT_a(t) \quad 5.2$$

$$PWV_c(t) = L_c / PTT_c(t) \quad 5.3$$

The pre-ejection period (PEP), which is the time delay from the onset of the R_peak to the aorta, is a small time constant, and, as such, it is not considered in the mathematical model because its effect is negligible when analyzing the PTT-CP dependency [107].

As stated before, the PTT model is based on the Bramwell and Hill equation [8] that estimates the pulse wave velocities from the average of the lumen areas along the arterial segments between heart and the arm and underneath the cuff separately (5.4, 5.5)

$$PWV_a(t) = \sqrt{\frac{A_a(t)}{\rho}} \sqrt{\frac{\partial P_a(t)}{\partial A_a(t)}} \quad 5.4$$

$$PWV_c(t) = \sqrt{\frac{A_c(t)}{\rho}} \sqrt{\frac{\partial (P_a(t) - P_c(t))}{\partial A_c(t)}} \quad 5.5$$

where ρ is the blood density, and $P_a(t)$ and $P_c(t)$ represent arterial BP (ABP) and CP respectively. $A_a(t)$ and $A_c(t)$ are the average arterial lumen areas along the arterial segments from heart to arm and underneath the cuff, respectively. PTTs can be modeled according to the Bramwell and Hill equation (5.6).

$$PTT(t) = L_a \sqrt{\frac{\rho \partial A_a(t)}{A_a(t) \partial P_a(t)}} + L_c \sqrt{\frac{\rho \partial A_c(t)}{A_c(t) \partial P_t(t)}} \quad 5.6$$

According to the model proposed in [50], the arterial lumen area (ALA) increases exponentially with the cuff deflation if transmural pressure is negative, and it continues to expand with further deflation if transmural pressure is positive [109, 26]. Both models have the same value (A_0) when transmural pressure is equal to zero ($P_a = P_c$). The two models are combined to model the ALA behavior during the cuff deflation period from SSBP to SDBP (5.7)

$$\begin{cases} A(t) = A_0 e^{aP_t(t)} & \text{for } P_t(t) \leq 0 \\ A(t) = A_m - (A_m - A_0) e^{-cP_t(t)} & \text{for } P_t(t) \geq 0 \end{cases} \quad 5.7$$

where $A(t)$ is the ALA underneath the cuff, ‘a’ and ‘c’ are compliance indices of the brachial artery at the systolic and diastolic regions respectively, A_0 represents the lumen area at zero transmural pressure, and A_m is the fully expanded lumen area.

The average lumen area underneath the cuff when the cuff is fully inflated (A_{cst}) is considered to be zero in (5.7), but for our calculations we have considered a non-zero value for A_{cst} in (5.8), because in oscillometry the measured CP is a reflection of the entire ALA change underneath the cuff rather than one section. The ALA increases from the center to the edge of the cuff, so the average area underneath the cuff is non-zero, even when the artery is completely closed at the center of the cuff bladder [110-112], So (5.7) should be modified to the model in (5.8)

$$\begin{cases} A_c(t) = A_{cst} + A_0 e^{aP_t(t)} & \text{for } P_t(t) \leq 0 \\ A_c(t) = A_{cst} + A_m - (A_m - A_0) e^{-cP_t(t)} & \text{for } P_t(t) \geq 0 \end{cases} \quad 5.8$$

where $A_c(t)$ is the average ALA underneath the cuff, and A_{cst} represents the constant non-zero lumen area over the whole cuff bladder when the artery under the cuff is collapsed and the lumen area at the center of the cuff bladder is zero.

Since there is no cuff over the arterial branch from heart to arm, transmural pressure is always positive, and therefore only the second term of (5.7) is used to model the lumen area from heart to arm (5.9)

$$A_a(t) = A_{a,m} - (A_{a,m} - A_{a,0}) e^{-cP_a(t)} \quad 5.9$$

where subscript ‘a’ is used to distinguish between the ALA model parameters of the arterial segment between the heart and arm from those of the arterial segment underneath the cuff.

After the lumen area is modeled for both the arm and cuff segments, required derivatives are taken and replaced in (5.6) to obtain the PTT model from heart to cuff (5.10–5.17).

$$\frac{\partial A_a(t)}{\partial P_a(t)} = c(A_{a,m} - A_{a,0}) e^{-cP_a(t)} \quad 5.10$$

$$\frac{\partial A_c(t)}{\partial P_t(t)} = \begin{cases} aA_0 e^{aP_t(t)} & \text{for } P_t(t) \leq 0 \\ b(A_m - A_0) e^{-cP_t(t)} & \text{for } P_t(t) \geq 0 \end{cases} \quad 5.11$$

$$PTT_a(t) = L_a \sqrt{\rho c \left(\frac{1}{1 - \frac{A_{a,m} - A_{a,0}}{A_{a,m}} e^{-cP_a(t)}} - 1 \right)} \quad 5.12$$

$$PTT_{c1}(t) = L_c \sqrt{\rho a \left(1 - \frac{1}{1 + \frac{A_0}{A_{cst}} e^{aP_t(t)}}\right)} \quad 5.13$$

$$PTT_{c2}(t) = L_c \sqrt{\rho c \left(\frac{1}{1 - \frac{A_m - A_0}{A_m + A_{cst}} e^{-cP_t(t)}} \right) - 1} \quad 5.14$$

$$PTT(t) = PTT_a(t) + \begin{cases} PTT_{c1}(t) & \text{for } P_t(t) \leq 0 \\ PTT_{c2}(t) & \text{for } P_t(t) \geq 0 \end{cases} \quad 5.15$$

It can be observed from (5.16) and (5.17) that PTTs are a function of transmural pressure $P_t(t)$. Moreover, parameters ‘a’ and ‘c’ are compliance parameters in systolic and diastolic regions and are always positive, so $PTT_{c1}(t)$ will increase and $PTT_{c2}(t)$ will decrease monotonically as the transmural pressure increases. This brings us to the conclusion that $PTT_c(t)$, which is the PTT of the cuff segment, has a maximum of $P_t(t)=0$. It can be observed from (5.12) that $PTT_a(t)$, which is the PTT of the arm segment, is a function of $P_a(t)$ and has no dependency with CP and oscillates during each heartbeat. Furthermore, since transit times are estimated from R_{peak} to a specific point of the corresponding pulse at each heartbeat, $PTT_a(t)$ will be a constant value added to $PTT_c(t)$ to estimate $PTT(t)$. For example, $PTT_a(t)$ would be a constant if $P_a(t)$ in (5.12) is replaced with a fixed value, such as SBP, DBP, or the MAP. Therefore, $PTT_a(t)$ is treated as a constant over the cuff deflation period.

$$PTT(t) = L_a \sqrt{\rho c \left(\frac{1}{1 - \frac{A_{a_m} - A_{a_0}}{A_{a_m}} e^{-cP_a(t)}} \right) - 1} + L_c \sqrt{\rho a \left(1 - \frac{1}{1 + \frac{A_0}{A_{cst}} e^{aP_t(t)}}\right)} \quad \text{for } P_t(t) \leq 0 \quad 5.16$$

$$PTT(t) = L_a \sqrt{\rho c \left(\frac{1}{1 - \frac{A_{a_m} - A_{a_0}}{A_{a_m}} e^{-cP_a(t)}} \right) - 1} + L_c \sqrt{\rho c \left(\frac{1}{1 - \frac{A_m - A_0}{A_m + A_{cst}} e^{-cP_t(t)}} \right) - 1} \quad \text{for } P_t(t) \geq 0 \quad 5.17$$

PTT from the heart to the brachial measuring site is modeled and shown in (5.16) and (5.17). The model in (5.16) accounts for the systolic region where transmural pressure is negative, while (5.17) accounts for the diastolic region where transmural pressure is positive. The first parts of both equations are equal, of constant value, and are independent of the CP deflation. The second part of both equations will change over the cuff deflation period, so PTTs will change according to the change in $P_c(t)$ for the whole deflating range.

5.2 DTA Augmented PTT-based BP Estimation Algorithm

Trusted boundaries of the estimated BP are determined by the DTA (Fig. 5.1) and are utilized to narrow down the searching domains of PTTs for maximum points instead of searching the whole range of the noisy data from SSBP to SDBP. The noisy data was employed and BP was estimated directly from the noisy transit times with the contribution of the DTA. The risk of finding false maximas is reduced considerably, and maximum points are located directly from the noisy transit times. The maximum point of PTT_{pk} , PTT_{tr} , and PTT_{zc} transit times are searched from SBP2 to MAP2, MAP2 to DBP2, and SBP2 to DBP2 boundaries, respectively.

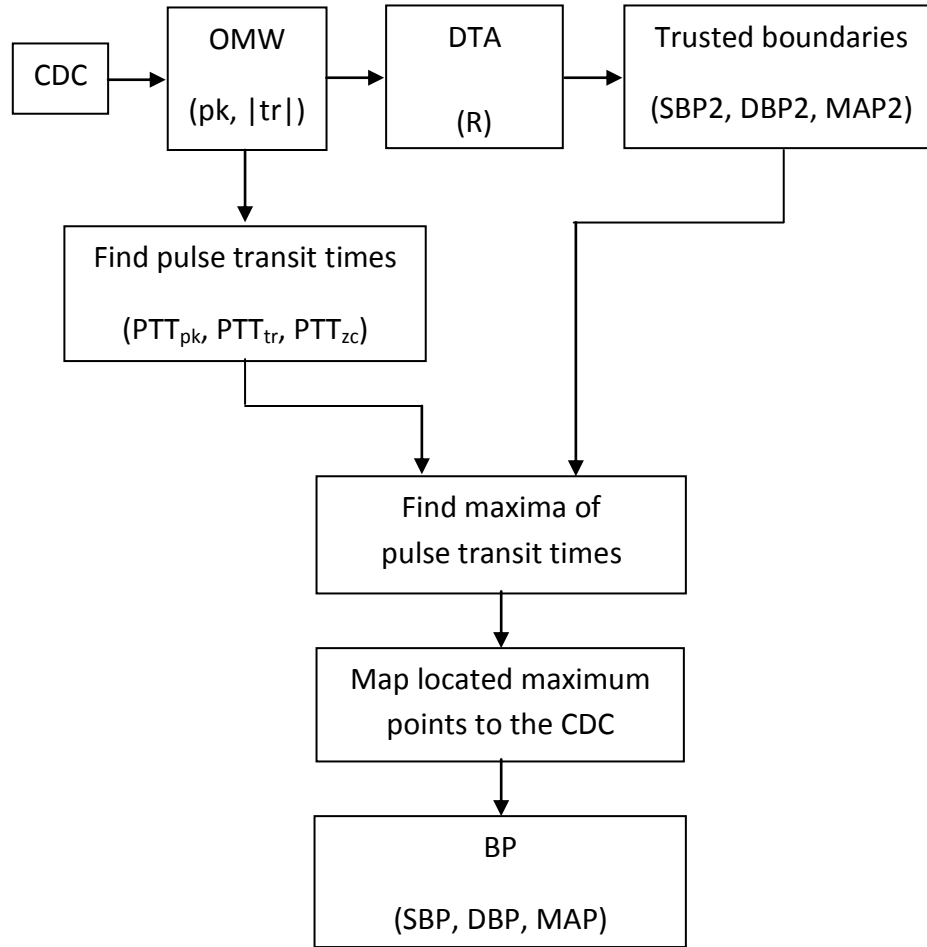


Fig. 5.1. Blood pressure estimation algorithm from pulse transit times using DTA.

As stated before, SBP, DBP, and the MAP are determined from the PTT_{pk} , PTT_{tr} , and PTT_{zc} PTTs, respectively. According to the PTT model, PTT_{pk} has a maximum at $P_c(t)=SBP$, PTT_{tr} has

a maximum at $P_c(t)=\text{DBP}$, and PTT_{zc} has a maximum at $P_c(t)=\text{MAP}$. Therefore, each of the PTT_{pk} , PTT_{tr} , and PTT_{zc} transit times has one maximum point that corresponds to SBP, DBP, and the MAP respectively.

According to the proposed improvement, the oscillometric waveform is extracted from the input CDC recording, and the DTA is applied to locate the oscillometric pulse at the MAP and to determine the trusted boundaries. The PTT of each heartbeat is calculated as the time difference between the R_{peak} of the ECG pulse and the peak, trough, and zero-crossing of each corresponding oscillometric pulse [26]. Trusted boundaries are applied to the PTTs to narrow down the searching domains of the maximum point of each transit time. The maximum point of PTT_{pk} , PTT_{tr} , and PTT_{zc} correspond to SBP, DBP, and the MAP respectively, so the located maximums are mapped to the CDC, and BP is estimated subsequently.

In theoretical PTT models, noise was not considered, and it was easy to find the maximum point of transit times. In practice, noise is present with a big contribution, and it is hard to find the true maximum points because noise affects the transit times and generates false maximums. That's why we need to remove the noise prior to PTT analysis. Removing the noise from the recorded signal makes the method complex, time consuming, and expensive to manufacture. The proposed method limits the searching domains of the maximum points and reduces the risk of finding false maximums, so BP can be estimated even from the noisy transit times, and we do not need to include noise removal procedures to clean PTTs prior to locating maximum points.

5.3 Results and Discussion

In order to test the PTT-based methods, we need a dataset with an ECG recorded simultaneously with BP, so DS2 is employed to test the proposed improvement and compare the validated results with the old method. In order to compare the searching domains in old and improved methods, one sample recording from DS2 is analyzed and illustrated in Fig. 5.2. According to the observations, Omron references for this specific recording were 121 mmHg, 89 mmHg, and 73 mmHg for SBP, the MAP, and DBP, respectively, and the trusted boundaries SBP2, MAP2, and DBP2 were estimated at 155 mmHg, 96 mmHg, and 61 mmHg, respectively. PTTs are estimated and plotted against the oscillometric pulse numbers and illustrated in Fig. 5.2. As illustrated, PTTs are noisy and exhibit lots of fluctuations. The maximum point of each

transit time is expected to be around the corresponding Omron reference while they are buried under the huge fluctuations. For example, the PTT_{pk} that determines SBP has a maximum pulse number around $PN=80$, while it should be around $PN=28$. The false maximum will provide a false SBP accordingly, because CP at $PN=80$ is greater than the value at $PN=28$ and, subsequently, SBP will be underestimated because the temporal position of the maximum points are mapped to the CP to estimate BP. Similarly, the PTT_{tr} that will determine the DBP is expected to exhibit a maximum around $PN=73$, while the observation is around $PN=40$. This will overestimate the DBP enormously. Finally, the PTT_{zc} that will determine the MAP is expected to have a maximum at $PN=54$, while the observed pulse number is around $PN=118$, so the MAP will be underestimated in this case. The proposed improvement is employed here to narrow down the searching domains and get closer to the expected pulse numbers to estimate the BP more accurately. Trusted boundaries are employed to look for the maximum points of PTT_{pk} from $PN=1$ to $PN=50$, PTT_{tr} from $PN=50$ to $PN=87$, and PTT_{zc} from $PN=1$ to $PN=87$. By limiting the searching domains, the maximum points became closer to the expected locations, and BP is estimated more accurately from the noisy PTTs.

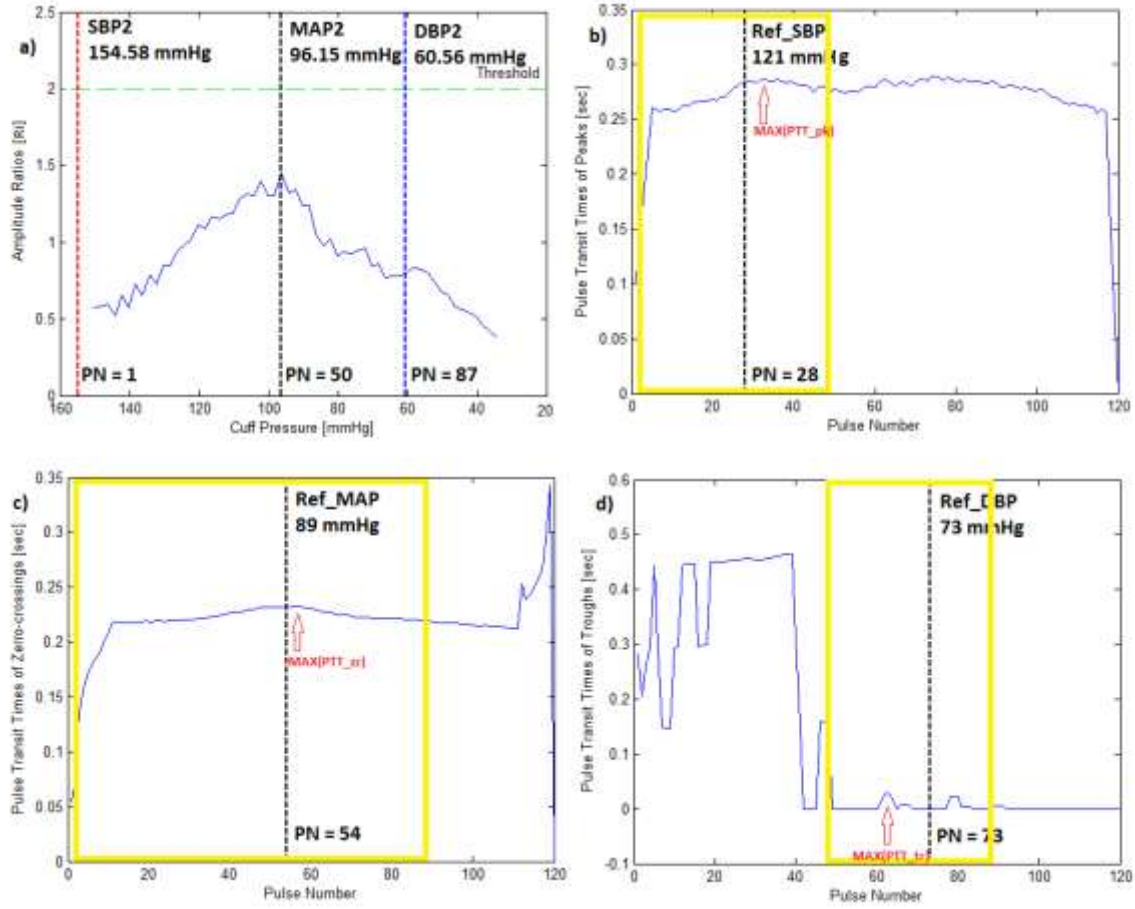


Fig. 5.2. Pulse transit times of one recording. (a) Amplitude ratio versus cuff pressure. (b) Pulse transit times of peaks (PTT_{pk}). (c) Pulse transit times of zero-crossings (PTT_{zc}). (d) Pulse transit times of troughs (PTT_{tr}).

According to the measurements, the Omron references for this specific recording were 121 mmHg, 89 mmHg, and 73 mmHg for SBP, the MAP, and DBP, respectively, while the trusted boundaries SBP2, MAP2, and DBP2 were estimated at 154.58 mmHg, 96.15 mmHg, and 60.56 mmHg, respectively. The PTTs are estimated and plotted against the oscillometric pulse numbers and illustrated in Fig. 5.2. As shown in Fig 5.2b, 5.2c, and 5.2d, the PTTs are noisy and exhibit numerous fluctuations. The maximum point of each transit time is expected to be around the corresponding Omron reference while they are buried under large fluctuations. For example, PTT_{pk} that determines SBP has a maximum pulse number around PN= 80, while it should be around PN=28. This false maximum will provide a false SBP accordingly, because the CP at PN=80 is greater than the value at PN=28 and, subsequently, SBP will be underestimated because the temporal position of the maximum point is mapped to the CP to estimate the BP.

Similarly, PTT_{tr} that determines the DBP is expected to exhibit a maximum around $PN=73$, while it is observed around $PN=40$. This will overestimate the DBP enormously. Finally, PTT_{zc} that determines the MAP is expected to have a maximum at $PN=54$, while the observed pulse number is around $PN=118$, so the MAP will be underestimated in this case. The proposed improvement is employed here to narrow down the searching domains and get closer to the expected pulse numbers to estimate the BP more accurately. The trusted boundaries are employed to search for the maximum points of PTT_{pk} from $PN=1$ to $PN=50$, PTT_{tr} from $PN=50$ to $PN=87$, and PTT_{zc} from $PN=1$ to $PN=87$.

As another sample, the pulse transit times of another randomly selected subject is illustrated in Fig. 5.3.

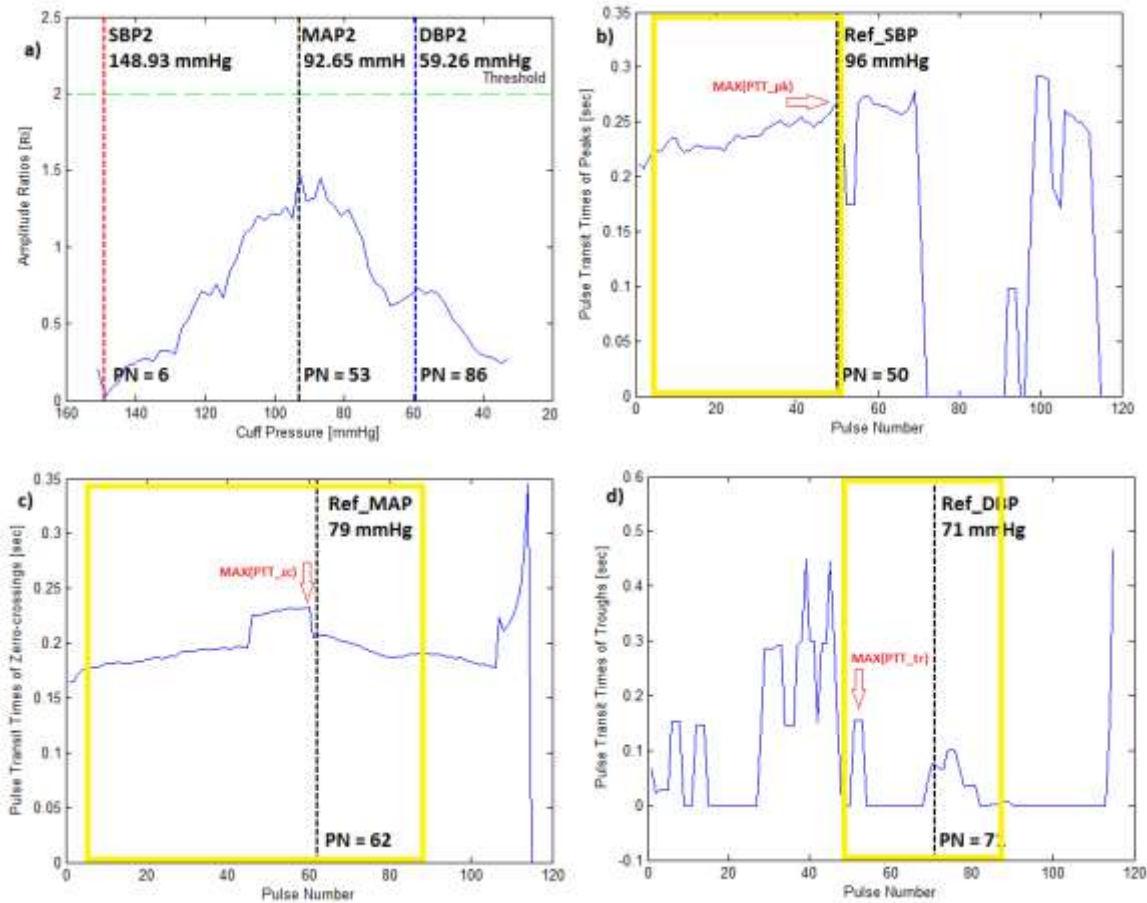


Fig. 5.3. Pulse transit times of another recording. (a) Amplitude ratio versus cuff pressure. (b) Pulse transit times of peaks (PTT_{pk}). (c) Pulse transit times of zero-crossings (PTT_{zc}). (d) Pulse transit times of troughs (PTT_{tr}).

The reference SBP, MAP, and DBP are 96 mmHg, 79 mmHg, and 71 mmHg, respectively for the specific measurement illustrated in Fig. 5.3. After applying the DTA to the noisy transit times, the maximas are expected from PN=6 to PN=53 for PTT_{pk} , PN=6 to PN=86 for PTT_{zc} , and PN=53 to PN=86 for PTT_{tr} . According to the observations, the maximas are closer to the reference pressures after application of the DTA.

By limiting the searching domains, the maximum points became closer to the expected locations, and BP was estimated more accurately from the noisy PTTs. Experiments were conducted to estimate BP from PTTs utilizing both the old and improved methods. The old method in [26] removes outliers from the noisy signal and smoothes the cleaned signal for each transit time, while the proposed improvement can estimate BP from the noisy transit times. I tested the PTT-based method on DS3, but I could not get good results over sick subjects even with the improved method. Therefore the proposed improvement is applicable on healthy subjects.

The MAE and STDE are estimated over 150 recordings for both the old and improved methods. The validated results in Table 5.1 were encouraging, since the proposed improved method is superior to the old one due to being less complex and more accurate.

Table 5.1: Accuracy of the PTT-based algorithm for both old and improved methods.

DS2 150 Rec's	Old method (after removing noise) [mmHg]			Improved method (without removing noise) [mmHg]			Reduced error % relative to old method		
	SBP	MAP	DBP	SBP	MAP	DBP	SBP	MAP	DBP
MAE	5.3	5.7	4.5	5.3	5.7	3.9	0.8	0.9	14
STDE	5.8	4.3	5.8	3.9	4.1	5.7	35	5.0	2.2

5.4 Conclusion

Automated oscillometric methods are the most commonly used in BP monitors in the market. Several manufacturers have their own devices with specific embedded algorithms that estimate BP based on empirical parameters. BP estimation methods based on empirical parameters are simple and easy to develop but suffer when it comes to accuracy. Accuracy of the oscillometric BP monitors is a big challenging issue. Researchers are working on coefficient-free algorithms to eliminate the empirical parameters and improve the accuracy of the measurements. Coefficient-free algorithms are often complex and expensive to develop. The trade-off between accuracy and cost is where we can propose an accurate coefficient-free algorithm with less complexity. BP can be estimated from pulse PTT-CP dependency non-invasively. The method is coefficient-free but very sensitive to noise. Therefore, estimated PTTs (Fig. 5.2.) are noisy and cannot be used for accurate BP estimation unless noises are removed. Recently, an accurate method was proposed to clean the PTTs by removing the outliers and smoothing the remaining PTTs [26]. The method is accurate, but it is still complex to develop. It is complex because removing outliers is a procedure based on the statistical analysis of the recordings, and the procedure is applied three times for each PTT of a single recording. Moreover, smoothing the remaining clean transit times is an additional process that increases the complexity of the method itself.

The proposed improvement eliminates the noise removal procedure from PTTs and estimates the BP directly from the noisy transit times. Trusted boundaries are estimated by applying the DTA on a given recording to identify the searching domains of the maximum point of each transit time. For example, the maximum of PTT_{pk} in Fig. 5.2 is searched for from $PN=1$ to $PN=50$, and it is found around $PN=28$, which is much closer to the Omron SBP=121 mmHg. Otherwise, it would be found at around $PN=73$ with the SBP=73 mmHg, which is inaccurate. Similarly, PTT_{tr} , and PTT_{zc} transit times are limited by trusted boundaries prior to finding the minimum points.

Accuracy of the old and improved method is validated against Omron and compared to show the level of the improvements for the estimated SBP, DBP, and MAP. Results of the improved method shown in Table 5.1 with the eliminated noise removal procedure were even more accurate compared to the old method. The improved method solves the complexity issue of the

old method by eliminating the noise removal method, and it estimates BP directly from the PTTs with even better accuracy.

According to the validated results shown in Table 5.1, the proposed method has improved the MAE by 0.8%, 0.9%, and 14%, and has improved the STDE by 35%, 5.0%, and 2.2% for SBP and DBP, respectively.

Chapter 6

Discussion

The objective of this research is to increase the accuracy of the oscillometric BP monitors. Measurement conditions are an important source of inaccuracy in oscillometry, and they affect BP measurements. In this research, a novel algorithm is proposed to determine the trusted boundaries of the measurements from the peak and trough information of the oscillometric pulse at the MAP. Trusted boundaries are the upper and lower pressure limits of the estimated SBP and DBP, respectively. In other words, the estimated BP should be inside the trusted boundaries to be considered a trusted measurement. Otherwise, the measurement is incorrect or untrusted, and the estimated BP is inaccurate and should be ignored by the examiner accordingly. The examiner has the option to repeat the measurements until a trusted measurement is observed or see the doctor if unsuccessful after a couple of attempts.

The accuracy of the implemented BP estimation algorithm is also very important and can convert the trusted recordings to accurate BP readings. Good measurement conditions and accurate estimation algorithms can provide trusted BP measurements. Coefficient-free methods are the most accurate BP estimation methods, because they do not adopt any fixed empirical parameters to estimate BP. For example, the MMSA is a popular coefficient-free method that estimates BP from the slopes of the OMWE in systolic and diastolic regions, which is described in the literature review. As another example, BP can be estimated from the PTT-CP dependency and is applicable when an ECG signal is available. The method is called the PTT-based method, and is discussed in chapter 5. In this research, a novel method called the ALA-based method is proposed, which is coefficient-free and more accurate than the other existing methods. The proposed method employs the arterial lumen area oscillations model in the diastolic region to estimate SBP and DBP. The employed ALA model requires compliance parameter ' c ' to estimate BP. At the first attempt, the compliance parameter was estimated through an optimization process that was accurate, but time consuming. To this end, another method was proposed to determine ' c ' directly from a linear regression model derived between the amplitude ratio of the actual oscillometric pulse at the MAP (R_{act}) and corresponding parameter ' c '.

In addition, the trusted boundaries of the recordings are employed to improve the existing PTT-based method. The PTT-based method requires ECG to determine PTTs. PTTs are delays from the R_peak of the ECG to the peaks, zero-crossings, and troughs of the oscillometric pulses. Each PTT has a maximum during the cuff deflation period. These maximums from the R_peak of the ECG to the peaks, zero-crossings, and troughs of the oscillometric pulses correspond to SBP, the MAP, and DBP, respectively. The method is very sensitive to noise and requires clean transit times prior to estimation of BP. Removing the noise from small biological signals is a big issue and increases the complexity of the method considerably. Trusted boundaries determined by the Dynamic Threshold Algorithm (DTA) narrow down the searching domains of the maximums and make it possible to find the true maximum points from the noisy transit times.

6.1 Trustworthiness Evaluation of the BP Readings

Even with the most accurate automated oscillometric monitors, one may get inaccurate results if do not consider the proper measurement conditions. On the other hand, most of the patients do not have the required expertise to measure BP themselves. They may get different results if they measure BP repeatedly and do not know how to trust the measurements. One solution is to average the results and trust the average. Repeating the measurements is time consuming and untrusted, because untrusted BP readings also contribute to an average. In chapter 2, DTA is proposed to determine the trustworthiness of the measured BP to help the examiners determine whether trust the measurement or not. The method determines a specific threshold for each subject and compares the amplitude ratio of all oscillometric pulses with the determined threshold to find the oscillometric pulse at the MAP and estimate the trusted boundaries from the peak and trough amplitudes of the located pulse. SBP and DBP are proportional to the pk and |tr| of the oscillometric pulse at the MAP by proportional constants χ_s, χ_d respectively. It means that SBP and DBP can be estimated directly from the oscillometric pulse at the MAP if we have χ_s, χ_d . Estimating BP is not the objective of the DTA, but estimating the trusted boundaries. The maximum trusted value for the SBP is known as SBP2, and it should be more than the SBP. Conversely, the minimum trusted value for the DBP is known as DBP2 that should be less than the DBP. Therefore, χ_s should increase and χ_d should decrease at the same time to their optimized values. According to the observation before and after removing the outliers, optimized

constants should be equal to find the optimum outliers. The optimization process was based on maximizing the accuracy of the measurements after removing the outliers from the datasets. The simplified flowchart of the DTA is shown in Fig. 6.1.

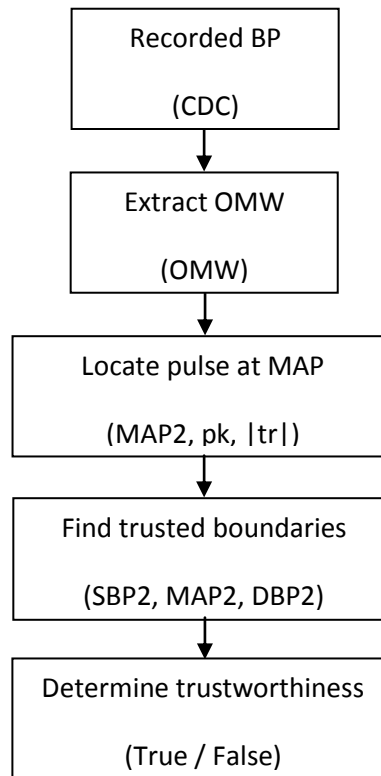


Fig. 6.1. Simplified flowchart for the trustworthiness evaluation of the BP readings.

Two popular BP estimation algorithms MAA and MMSA are employed to estimate BP of the subjects over healthy and sick datasets. The DTA is applied to the OMW of all recordings, and outliers are detected and removed from entire datasets. The estimated SBP and DBP are validated against corresponding references before and after removing the outliers, and levels of improvements are determined for each estimation algorithm over all dataset. The improvements are illustrated in Tables 3.1–3.3. According to the observations, accuracy of the measurements improved considerably after removing the outliers from either healthy or sick datasets.

6.2 ALA-based BP Estimation Method

The accuracy of automated oscillometric BP monitors is the main challenge among researchers. Many studies have been carried out to increase accuracy without increasing the complexity of the design. The MAA estimates BP from the OMWE with the least complexity in design, which makes it popular among producers. The major problem is the systolic and diastolic ratios that are determined empirically over specific recordings to derive SBP and DBP directly from the maximum amplitude of the OMWE. The empirical ratios may estimate SBP and DBP for a broader range of the healthy subjects, but there is no guarantee that it extends to all subjects, that's why coefficient-free methods are in focus as the most accurate BP estimation methods. Coefficient-free methods do not adopt empirical ratios, so they can be extended to wider ranges of subjects.

In chapter 4, a novel coefficient-free method is proposed that estimates BP accurately. This method estimates BP from the mathematical model of the ALA in the diastolic region. The mathematical model is adopted from [108, 109], and the diastolic region is the region at which the arterial pressure is greater than or equal to the CP, so with almost half the data obtained from the OMW, the proposed method can estimate BP accurately. The proposed method estimates BP by optimizing the unknown parameters of the ALA model denoted by ' c ', A_0 , A_m , P_{a_pk} , and P_{a_tr} where parameter ' c ' is the compliance parameter of the ALA model in the diastolic region, and A_0 and A_m represent lumen areas at transmural pressure equal to zero and fully expanded vessel, respectively. Parameters P_{a_pk} , P_{a_tr} are the arterial pressure at the peak and trough of the oscillometric pulses and are optimized to provide SBP and DBP, respectively. The unknown parameters are optimized in three procedures (P1–P3). In P1, unknown parameters are reduced to parameter ' c ', which is optimized to evaluate the compliance parameter. In P2, the optimized ' c ' is used to optimize three unknown parameters: A_0 , A_m , and P_{a_pk} . In P3, the optimized ' c ', A_0 , and A_m are used to optimize the unknown parameter P_{a_tr} . As stated before, P_{a_pk} and P_{a_tr} are the arterial pressures at the peak and the trough of the oscillometric pulses, so the optimized values are known as the SBP and DBP, respectively.

The P1 evaluates parameter ' c ' of the model by minimizing the sum of the squared differences between the actual and simulated peak ratio of successive oscillometric pulses in the diastolic region. Estimated parameter ' c ' is accurate, but P1 is time consuming. In order to simplify the method, the DTA is employed to derive a linear regression model between the

amplitude ratio of the actual oscillometric pulse at the MAP (R_{act}) and the corresponding parameter ' c '. Therefore, parameter ' c ' is simply estimated from the corresponding R_{act} for all measurements.

In order to derive the linear regression model, the ALA model in (4.18) is employed to construct the simulated oscillometric waveforms. The constructed simulated oscillometric waveforms are customized to simulate the actual oscillometric waveforms. In order to customize the constructed simulated oscillometric waveform, the arterial pressure model in (4.15) is employed and customized to simulate the arterial pressure of corresponding recordings by replacing the MAP with MAP_{DTA} , and HR with the heart rate of the subjects. Moreover, parameters C_0 and C_1 are optimized by minimizing the sum of the squared differences between the actual and simulated SBP and DBP. The customized arterial pressure and deflating CP are used in (4.19) to construct transmural pressure. The customized transmural pressure is then used in (4.18) to construct the customized ALA model over all recordings. The customized ALA model include constants ' a ', ' b ', and ' d ' that are the simulated cuff parameters. The parameter ' c ' is different for each recording and estimated through an optimization process. The DTA is employed to locate the oscillometric pulse at the MAP for both the actual and corresponding simulated waveforms and optimize parameter ' c ' of the ALA model by minimizing the squared difference between the R_{act} and the corresponding R_{sim} . The simplified flowchart of the compliance parameter evaluation is illustrated in Fig. 6.2. Finally, a linear regression model is derived between ' c ' and the corresponding R_{act} . The whole process is done only one time in order to derive the linear regression model. The linear regression model is used later by the ALA-based method to estimate ' c ' from the corresponding R_{act} of a given recording.

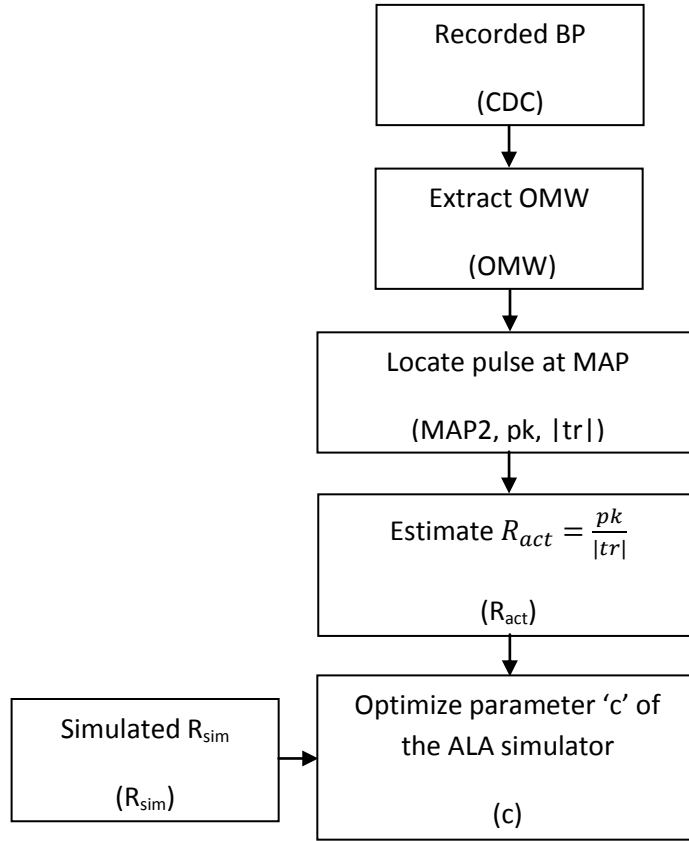


Fig. 6.2. Simplified flowchart for the compliance parameter evaluation.

In order to compare the accuracy of the simplified ALA-based method with the two popular MAA and MMSA estimation algorithms, the estimated SBP and DBP of all estimation techniques are validated against corresponding references for all datasets and level of improvements achieved by ALA-based method are estimated and shown in Tables 4.2-4.4.

Furthermore, DTA is applied to the results of ALA-based method, outliers are detected and removed from datasets, and results are validated again after removing the outliers from datasets. The validated results after application of the DTA and removing the outliers are compared to corresponding results before removing the outliers, and levels of improvement achieved by the DTA are estimated for all datasets and are shown in Tables 4.5–4.7.

In order to obtain the most accurate BP readings, an invasive approach is unavoidable, though such an approach is associated with potential adverse effects and is not recommended unless in urgent cases that are examined in intensive care units of hospitals. Alternatively, non-invasive approaches are available to approximate the invasive BP. Generally, the accuracy of the newly developed methods is validated against another non-invasive monitoring device like Omron as the reference that uses different methods to estimate the BP more accurately. We cannot be

certain that either method gives us an unequivocally correct measurement. Based on this problem, Bland and Altman developed a graphical statistical approach to assess the degree of agreement between two methods [121, 122]. The reference monitoring device is sometimes known as the “golden standard,” but this does not imply that measurements are 100% accurate and without error [123]. Bland and Altman applied their assessment approach on BP data in [123,124]. The Bland and Altman results are illustrated as a Bland-Altman plot that presents the averages of the two methods (x-axis) against the differences between them (y-axis). The agreement of the methods is quantified by the bias (ME) and the limits of agreement ($ME \pm 1.96 \times STDE$) that are shown by horizontal dotted lines on the plots. The Bland-Altman plot illustrates how the error between two methods or devices is distributed over the range of the average values. Generally, a smaller bias and narrower limits of agreements show a better agreement between two devices. The Bland-Altman plots between estimated SBP and DBP by the proposed ALA-based method and corresponding reference pressures over all datasets are illustrated in Fig. 6.3 to Fig. 6.5 to study the agreement between reference values and the estimated blood pressures.

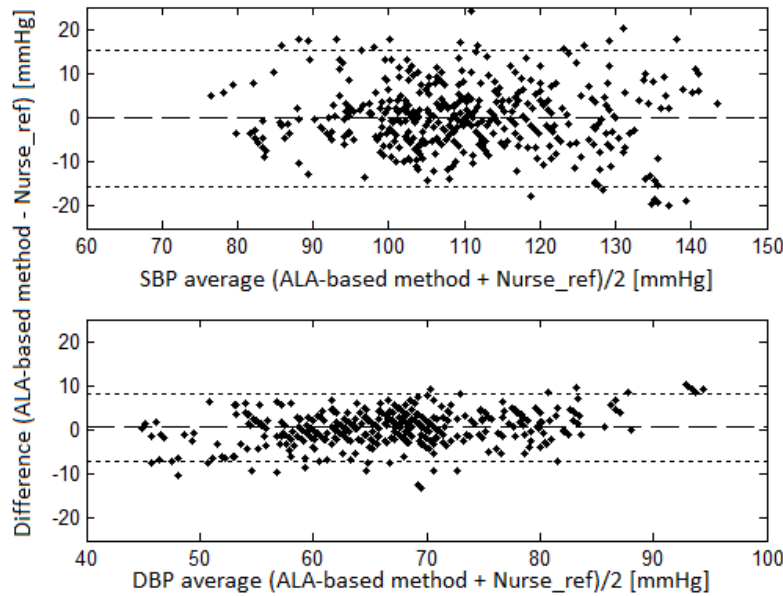


Fig. 6.3. Bland-Altman plot of the ALA-based method versus Nurse references for DS1. The horizontal dotted lines for SBP, and DBP plots show the degree of agreement with the ME bias in the middle.

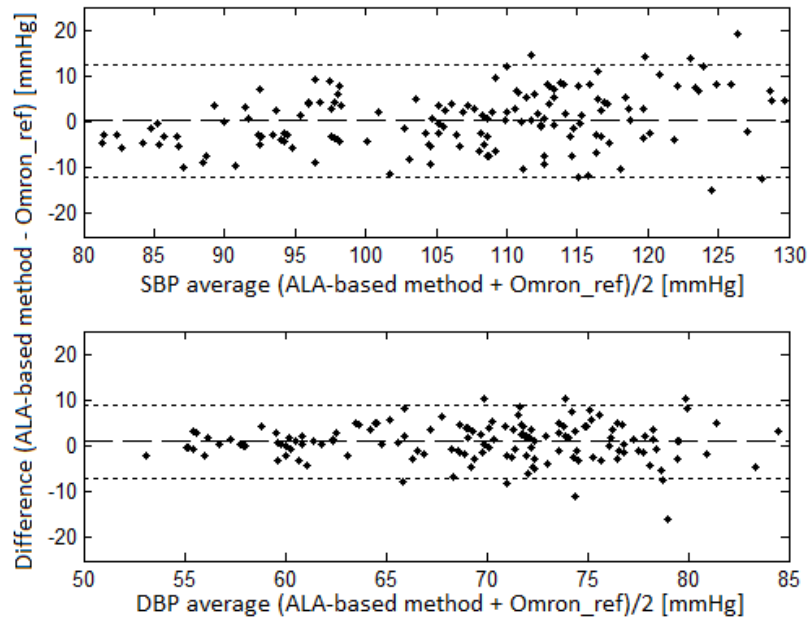


Fig. 6.4. Bland-Altman plot of the ALA-based method versus Omron references for DS2. The horizontal dotted lines for SBP, and DBP plots show the degree of agreement with the ME bias in the middle.

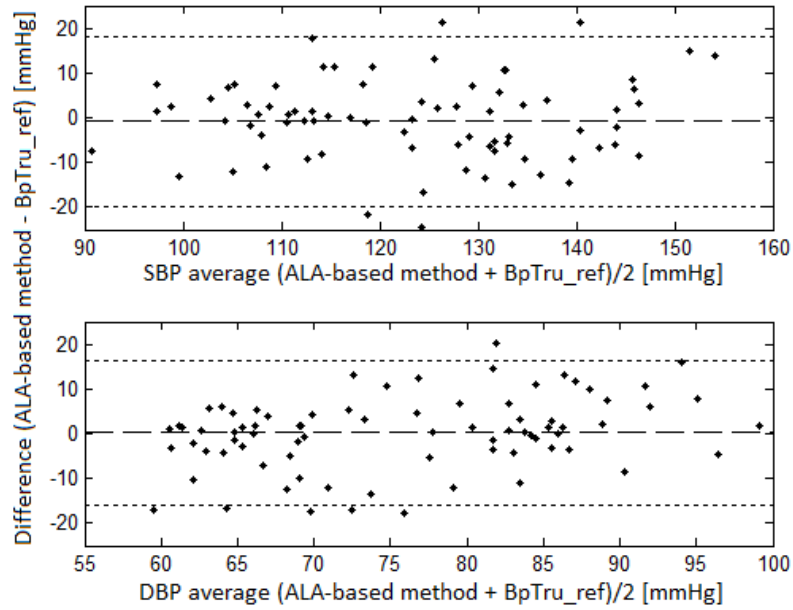


Fig. 6.5. Bland-Altman plot of the ALA-based method versus BpTru references for DS3. The horizontal dotted lines for SBP, and DBP plots show the degree of agreement with the ME bias in the middle.

6.3 Improvements for PTT-based BP Estimation Method

BP can be estimated from PTTs, where PTTs are the delays from the R_{peaks} of the ECG signal to the peaks, zero-crossings, and troughs of the corresponding oscillometric pulses [26]. Pulse transit times are measured for each oscillometric pulse and recorded as trains of PTTs. In theory, each train of PTTs has a maximum corresponding to the BP (4.41, 4.42). The SBP, the MAP, and DBP are the CP corresponding to maximums of the transit times from the R_{peaks} to the peaks, zero-crossings, and the trough of the oscillometric pulses, respectively. In practice, noise is present, and it affects the transit times such that the maximums deviate considerably and result in inaccurate estimation of the BP accordingly. Recently, a method was proposed in literature to detect the outliers and remove them from transit times. Next, the cleaned transit times were smoothed and the maximums were located thereafter. The outliers are transit times that are considerably different from the neighborhoods. Several thresholds are set empirically to statistically detect the outliers from the noisy transit times, which are best fit to the employed dataset and are not extendable to new recordings. This is the main problem of the method, since the expected accuracy completely lost when I changed the dataset. Another problem is the complexity of the method, which increases with further statistical analysis of the transit times, because detecting and smoothing the outliers are repeated for each transit time of a given recording. Another disadvantage of the method is that requires an ECG to perform. The only advantage of the method is that it is coefficient-free and estimates BP without adopting the empirical ratios.

In order to stay with the advantage of the method and avoid disadvantages and the complexity as the main problem, trusted boundaries of the measurements are employed to find the maximum points directly from the noisy transit times. Trusted boundaries narrow down the searching domains of the maximum points and reduce findings of false maximums. The maximum points of PTT_{pk} , PTT_{zc} , and PTT_{tr} are located from SBP2 to MAP2, SBP2 to DBP2, and MAP2 to DBP2, respectively (Fig. 5.2). This improvement considerably simplifies the method and provides even more accurate BP readings. The simplified flowchart illustrated in Fig. 6.6 estimates trusted boundaries SBP2, MAP2, and DBP2 of a given recording, employs the PTT-based algorithm to construct PTTs, locates the maximum amplitude of each PTT inside the trusted boundaries, and estimates BP from mapping the CP to temporal positions of the located maximum points.

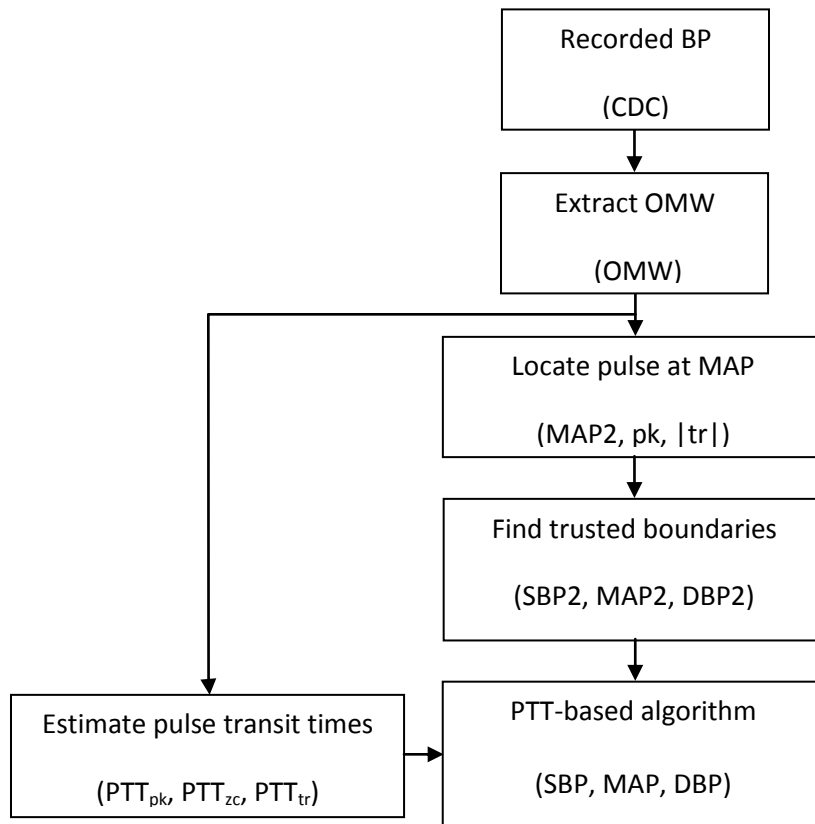


Fig. 6.6. Simplified flowchart for the improved PTT-based BP estimation algorithm.

The proposed improvement is applied to DS2, including ECG recordings, and validated against Omron. Validated results for both the old and proposed methods are compared and shown in Table 5.1.

Chapter 7

Conclusions and Future Work

BP is one of the important vital signs that carry important information about the physiological state of the human body [125]. It is an important hemodynamic parameter that is routinely monitored to diagnose and manage conditions such as hypertension and hypotension [15, 126]. Invasive methods are the most accurate approach for arterial BP measurements. However, due to the difficulty and risk associated with invasive methods, non-invasive methods are used to approximate the invasive measurements. Among the non-invasive methods, oscillometry is more popular and is the focus of this research. In this research, issues of oscillometry are investigated from measurement conditions and BP estimation method perspectives, and solutions are proposed accordingly.

In terms of the measurement conditions, several factors must be taken into account. For example, a large cuff will underestimate BP readings, while an overly small cuff will provide BP readings that are overestimated. The cuff size, which is a function of subject's arm, should be selected according to the American Heart Association (AHA) guidelines for BP measurement [127]. We use a single device for different subjects with different arms, so the BP readings are susceptible to error, and the trustworthiness of the readings is unknown, which is one of the challenging issues of oscillometry. The second most common error in BP measurement is incorrect limb position. To accurately assess blood flow in an extremity, influences of gravity must be eliminated. The subject's arm should be level with the heart during BP measurement. Higher or lower elevation of the arm will underestimate or overestimate the BP by approximately 2 mmHg per inch of the elevation, respectively. Although it is easy to follow the proper measurement conditions, most of the patients, especially those with no expertise at home, fail to consider that, and estimated pressures become inaccurate. The white coat hypertension is another source of the error. In many patients, BP is always higher when measured by doctors or nurses because of the defense reaction that causes a rise in BP that is associated with patient anxiety during doctor visits. Also, BP varies in individuals according to the time of day, meals, smoking, anxiety, temperature, and season. To sum up, there are many factors that should be taken into

account prior to BP measurements in order to get accurate BP readings. In clinical practice, accuracy of BP readings is very important, because even small errors in measurement can lead to inaccurate diagnoses and potentially life-threatening conditions such as stroke and myocardial infarction [128-130]. Despite the advances in technology and increase in clinical use, automated NIBP monitoring still faces challenges in accuracy and trustworthiness of the measurements. Chronic patient conditions, like atrial fibrillation (AF) and heart failure, and noise such as motion artifacts tend to render NIBP estimations somewhat inaccurate and untrusted [10-12]. Current NIBP monitoring technology provides no self-contained method to evaluate the fidelity and trustworthiness of BP measurements. To address this problem, the DTA is proposed to evaluate the trustworthiness of the estimated BP and assist the examiners to know whether they should repeat the measurements or not. The DTA is independent of the estimation algorithms, so the DTA was applied on all datasets, and trusted boundaries were estimated for each estimated BP by MAA, and MMSA estimation algorithms and outliers was determined and removed from the datasets. Next, the validated results of the cleaned dataset were compared to corresponding results before removing the outliers, and level of improvements achieved by DTA was shown in Tables 3.1–3.3. According to the observations, accuracy of the results increases considerably when the outliers are removed from datasets for both healthy and sick subjects.

Accuracy of the estimation algorithms is another issue that considerably contributes to the trustworthiness of the BP readings. To address this problem, different coefficient-free methods were proposed in the literature. For example, BP can be estimated from the CP and PTT dependency. It has been shown in (5.16) and (5.17) that PTTs have maximums over the cuff deflation period. The maximum points of transit times correspond to SBP, the MAP, and DBP, where transit times are measured from the R_{peak} of the ECG signal to the corresponding peaks, zero-crossings, and troughs of the oscillometric pulses, respectively. The problem is that the method is very sensitive to noise, and even the breathing effect, which is always present, can deviate the transit times considerably and result in inaccurate BP readings. The noise can be removed from either input recoded signal or PTTs. In a recent study [26], noise was removed from PTTs acquired from a noisy input signal. In order to remove false maximums, the mean and standard deviation of the transit times were estimated, and transit times greater than the mean+STDE were detected and removed from existing transit times. Next, the remaining data was smoothed and interpolated with the sampling frequency in order to get the same number of

the samples that we had before removing the false transit times. This could reduce the risk of finding false maximums from all three PTT_{pk} , PTT_{zc} , and PTT_{tr} transit times. Moreover, empirical parameters are set to detect outliers that are best fit to the employed dataset, which may be less accurate for new recordings. The method requires more hardware and software to function properly, which is also a challenge, especially when it is adjusted with the empirical parameters that best fit to the employed dataset. In this research, an improvement is proposed to reduce the complexity of the design and simplify the method without adopting any empirical parameters. The trusted boundaries determined by the DTA are used to narrow down the searching domains of the maximum points. The maximum points for PTT_{pk} , PTT_{zc} , and PTT_{tr} are located from SBP2 to MAP2, SBP2 to DBP2, and MAP2 to DBP2, respectively, so the risk of finding false maximums is reduced considerably. The old and improved methods are tested on DS2, which includes simultaneous ECG recordings, and results are validated against Omron over 150 recordings obtained from 10 healthy subjects aged from 24 to 63 years old.

The PTT-based methods require an ECG signal to be recorded simultaneously with the BP signal, so electrodes need to be attached to the patient's body during the BP measurement. Even with the improved method we need to measure three transit times for each recording, which increases the complexity of the method.

In this research, a novel method called the ALA-based method is proposed that estimates BP accurately. The proposed method is based on the ALA model in the diastolic region (4.2). The simulated oscillometric waveforms in the diastolic region are constructed and customized according to the corresponding actual waveforms. The peaks and troughs of the actual and corresponding simulated oscillometric pulses in the diastolic region are used to optimize the arterial pressure at peaks and troughs of the oscillometric pulses and estimate SBP and DBP, respectively. The proposed method was tested on healthy and sick subjects, and validated results of the MAA, MMSA, and ALA-based methods were shown in Tables 4.1-3.3.

The compliance parameter ' c ' required by the ALA-based method was estimated by a time consuming optimization procedure (P1). To simplify the method with the same accuracy, a linear regression model is derived and replaced with the P1. The vessel compliance is an important biomarker for cardiovascular health and function [131, 132], and it influences patients' arterial BP. Researchers have proposed various methods for non-invasive assessment of arterial stiffness

based on arterial pulse wave morphology analysis and pulse wave velocity (PWV) analysis [16–18], [133–136]. However, these methods suffer from certain limitations, since both pulse wave morphology and PWV are intricately linked to a number of other factors like physical activity, BP, and blood glucose level [137, 138]. Therefore, the estimated vessel compliance based on the pulse morphology and PWV may not be consistently accurate. Additionally, PWV measurement requires a reference heartbeat signal that needs to be acquired using auxiliary ECG electrodes, because we need to estimate PTTs from the R_{peak} of the ECG pulses to specific points of the corresponding OMW pulses, such as peaks, zero-crossings, or troughs. This requires procedures to analyze pulse wave velocities obtained from the PTTs to estimate vessel compliance accordingly. To provide compliance parameter ‘ c ’ of the ALA-based method, a simplified method is proposed that estimates ‘ c ’ from the amplitude ratio of the oscillometric pulse at the MAP (R_{act}).

In conclusion, the proposed DTA and ALA-based BP estimation method increase accuracy of the estimated BP by rejecting untrusted measurements and estimating accurate BP from trusted measurements if implemented together in oscillometric monitors. According to the validated results in Tables 4.5–4.7, important improvements have been observed by trusted results from the proposed ALA-based method compared to the MAA and MMSA estimation algorithms.

The following are several relevant directions that can be explored in future works:

- Although the auscultation method and calibrated FDA-approved BP monitors were utilized to provide the reference pressures at each step of the work, it is recommended to validate the proposed methods with invasive measurements as future work.
- In chapter 3, χ_s and χ_d were used to determine the trusted boundaries, while, as future work, we can approximate these two proportional constants for healthy subjects and estimate SBP, and DBP directly from pk and $|tr|$ of the oscillometric pulse at MAP by minimizing the differences between simulated blood pressures and corresponding reference values.
- The arterial pressure simulator employed in chapter 4 was composed of two harmonics, while, as future work, we can increase the number of harmonics and get better results.

Appendix A - Pilot Study

Our proposed methods are tested and validated on three oscillometric waveform datasets:

1) The first dataset (DS1) was provided by Biosign Technologies Inc. The dataset comprised 425 oscillometric BP recordings acquired from 85 healthy subjects composed of 48 males and 37 females aged from 12 to 80 years old using an automated wrist BP monitor (UFIT TEN-10) in accord with the recommendations of the ANSI/AMMI/ISO standard [96]. Following each wrist oscillometric measurement, and after a one-minute delay, two independent simultaneous reference readings were also recorded at the arm level by two nurses using the auscultatory method and a double stethoscope. The average value of the two measurements was used as the reference pressure of each subject for the corresponding trial. The dataset is fully described in Appendix B.1.

2) The second dataset (DS2) was provided by our research group in University of Ottawa [97]. This dataset comprised 150 oscillometric BP recordings acquired with a prototype called InBeam designed in our research laboratory from 10 healthy subjects composed of 6 males and 4 females aged from 24 to 63 years old. Analogous Food and Drug Administration (FDA)-approved Omron HEM-790IT arm monitor readings were used as the reference. Furthermore, an ECG signal was recorded simultaneously utilizing a wristband wrapped around the right wrist of the subjects and employed to detect the peaks, troughs, and zero-crossings of each oscillometric waveform pulses [97]. InBeam prototype setup is illustrated in Fig. A.1. Regarding the FDA-approved Omron HEM-790IT as a reference to validate the results, it should be noted that the device has gone through rigorous clinical validations according to protocols set forth by the European Society of Hypertension (ESH), Association for the Advancement of Medical Instruments (AAMI), and British Hypertension Society (BHS) [98-101]. Therefore, for this pilot study, the successful validation of the proposed methods against the Omron monitor is sufficient to support its potential significance and efficacy. Main components of the prototype (A) are analog pressure transducer, analog ECG amplifier, mini dc air pump, and a screw-controlled manual pressure release valve. Lead II configuration is employed to record ECG data. A strip of thin flexible conductive fabric (D) is used as the cuff pressure sensor placed underneath the cuff wrapped around the subject's left hand, and incorporating as the ECG first electrode at the same time.

Another conductive strip (E) is placed under an ordinary wristband wrapped around the subject's right wrist incorporating as the second ECG electrode. More details about the design of the cuff and the wristband can be found in [103]. Electrodes are connected to the prototype with two separate wires. Moreover, two hoses are used to connect the cuff to the prototype, one for deflating the cuff and another for recording the pressure vibrations inside the cuff which is converted to the corresponding pressure signal by the transducer predicted inside the prototype. A pressure transducer (BPS-BTA from Vernier Software & Technology, Beaverton, OR) is used to convert the mechanical pressure vibrations of the brachial cuff received from the first hose to the corresponding electrical BP signal during the cuff deflation period. The transducer operates on a dc supply voltage of 5V to produce an output BP signal of 0-5V corresponding to an input pressure range of 0-250 mmHg. The ECG amplifier is to amplify the ECG signal received from the two electrodes. The core of the ECG amplifier consists of an instrumentation amplifier (INA-129, Texas Instruments, Dallas, TX) operating on another separate dc supply voltage of $\pm 5V$ to produce an output ECG signal of 20-2000 μV . The 6 volts dc mini air pump is to inflate the cuff through the second hose connected to the brachial cuff. The screw-controlled manual pressure release valve which is connected in-line with the brachial cuff, the analog pressure transducer, and the mini dc air pump is to control the deflation rate of the cuff by manually adjusting the pressure release valve with a small screw.

National Instruments LabVIEW development environment is used for acquiring and controlling the both ECG and CP signals and using a personal computer (PC). Both ECG (B) and CP (C) signals are acquired simultaneously at a sampling rate of 1000 Hz and are monitored in real-time. To validate the calibration of the prototype periodically, a medical grade mechanical pressure gauge (Android sphygmomanometer, Mexico) (F) is employed and connected to the first hose from the brachial cuff through a T-connector. Matlab (The Math Works Inc., Natick, MA) is used for further reading, processing, and analysis of the acquired ECG and CP signals in this research. The dataset is fully described in Appendix B.2.

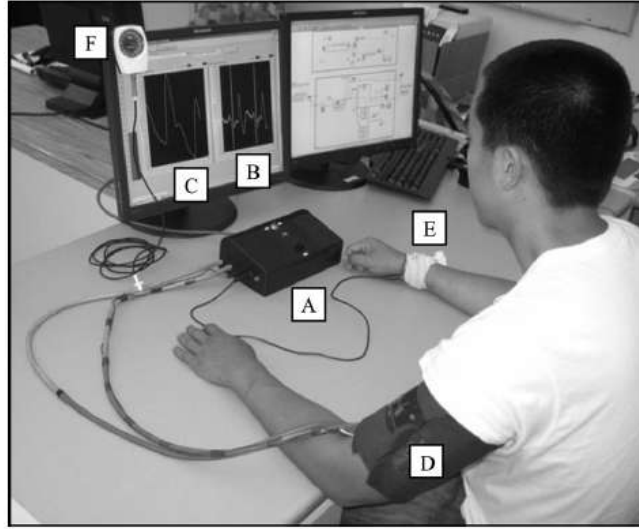


Fig. A.1. InBeam prototype setup. (A) InBeam prototype device. (B) ECG signal. (C) CDC signal. (D) Brachial cuff with the first embedded flexible ECG electrode wrapped around the subject's left arm. (E) Wristband with the second embedded flexible ECG electrode wrapped around the subject's right wrist. (F) Sphygmomanometer for periodically validating the calibration of the InBeam prototype. Air hoses and electrical leads connect the cuff and the wristband to the prototype. Adapted from published paper of Saif Ahmad, "Electrocardiogram-assisted blood pressure estimation", IEEE Transactions on Biomedical Engineering, vol. BM-59, pp. 608–618, 2012. Used with permission.

3) The third dataset (DS3) was provided by Health Parametrics Incorporation. The dataset comprised 78 oscillometric BP recordings acquired with a prototype called HPI EABPM-01 from 13 sick patients with various chronic conditions including atrial fibrillation, hypertension, and obesity. Patients are composed of 5 males and 8 females aged from 46 to 85 years old. Each recording started on the right arm with the clinically popular device - BpTru BPM-100 approved by the Food and Drug Administration. As soon as the BpTru measurement ended, HPI measurement started on the left arm. Furthermore, an ECG signal was recorded simultaneously utilizing the two dry flexible electrodes made of conductive fabric inside the cuff along with a handle with two rigid chrome plated electrodes on the HPI prototype device. The patients grip the handle on the HPI device with the left hand during the measurement. The dataset is fully described in Appendix B.3.

Appendix B - Datasets

The three datasets that were used to evaluate the performance of the proposed methods in this thesis are described in this Appendix.

B.1 Dataset 1 (DS1)

The first oscillometric waveform dataset was provided by Biosign Technologies Inc. This dataset was acquired using an automated wrist BP monitor (UFIT TEN-10) in accord with the recommendations of the ANSI/AMMI/ISO standard [96]. The dataset includes 85 subjects, 48 males and 37 females, aged from 12 to 80. Five sets of oscillometric wrist BP measurements were obtained from each subject resulting in a total of 425 measurements. Following each wrist oscillometric measurement, and after a one-minute delay, two independent simultaneous reference readings were also recorded at the arm level by two nurses using the auscultatory method. A double stethoscope was used for this purpose, as shown in Fig. B.1. The average value of these two measurements was used as the reference pressure of each subject for the corresponding trial. The measurement conditions stipulated by the ANSI/AMMI/ISO standard aim to minimize the intrinsic physiological variability of the BP over time, but still the SBP and DBP may change from the moment of the wrist measurement until the reference measurements are performed. The ranges of the recorded SBPs and DBPs were 78-147 mmHg and 42-99 mmHg, respectively. The nurse references are provided only for SBP and DBP.

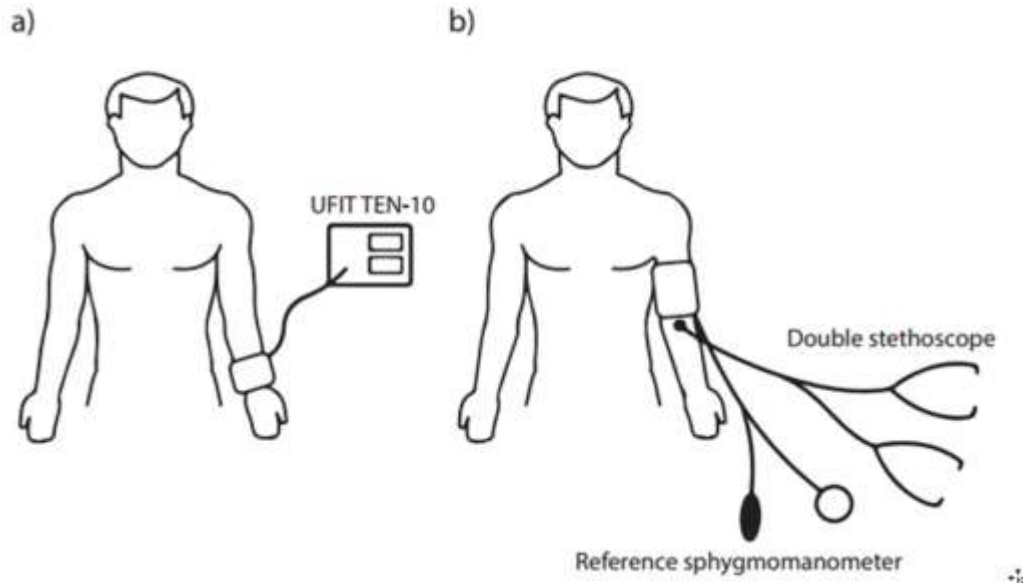


Fig B.1. Biosign setup to collect 425 wrist measurements from 85 healthy subjects. (a) UFIT TEN-10 measurement from left wrist. (b) After a one-minute delay, two independent simultaneous reference readings are recorded at the arm level by two nurses using the auscultatory method. Adapted from Mohamad Forouzanfar [Ph.D. thesis, “A Modeling Approach for Coefficient-Free Oscillometric Blood Pressure Estimation”, University of Ottawa, 2014]

The data collection protocol for each subject can be summarized as follows:

- 1) Invite the subject to the trial area and inform him/her of the measurement steps.
- 2) Sit the subject comfortably and apply the arm cuff appropriately to left arm and the UFIT cuff to the left wrist at heart level.
- 3) Start the UFIT recording from left wrist.
- 4) Wait one minute.
- 5) Start the two simultaneous auscultatory readings from the left arm.
- 6) Wait one minute.
- 7) Repeat steps 3-6 four times.
- 8) End session.

B.2 Dataset 2 (DS2)

The second dataset was collected by our research group in University of Ottawa. This dataset comprised 150 simultaneous oscillometric BP and ECG recordings acquired with a prototype designed in our research laboratory [97]. The data was collected from 10 healthy subjects, 6 male and 4 females, aged from 24 to 63 years. This study was approved by the University of Ottawa Research Ethics Board, and written informed consent was obtained from all subjects. Recordings

from each subject were obtained on three separate days with five sets of recordings in each day. Each set of recordings started with the Food and Drug Administration (FDA)-approved Omron monitor (HEM-790IT) measurement on the right arm. As soon as the Omron measurement ended, our prototype measurement started on the left arm. The subject also wore the wristband of the prototype on the right wrist for simultaneous ECG recording as shown in Fig. B.2. Since the American Heart Association recommends at least a 1 min gap between two consecutive BP measurements [6], the five sets of measurements were performed with three-minute gaps. Although there may be differences in BP measured from right and left arms, studies have shown that such differences are not statistically important in healthy subjects [98] such as the ones tested in this pilot investigation.

The data collection protocol for each subject can be summarized as follows:

- 1) Invite the subject to the trial area and inform him/her of the measurement steps.
- 2) Sit the subject comfortably and apply the prototype arm cuff appropriately to left arm at heart level, the prototype wristband to the right wrist, and the Omron cuff to the right arm at heart level.
- 3) Start Omron recording from right arm.
- 4) Start the prototype recording from left arm, as soon as Omron recording ends.
- 5) Wait three minutes.
- 6) Repeat steps 3-5 four times.
- 7) End session.
- 8) Wait for at least 24 hours.
- 9) Repeat steps 1-8 two times.

Our prototype recordings comprised inflating the prototype cuff to a pressure of 160 mmHg and then deflating it slowly to a pressure of 20 mmHg. The deflation rate was 1.5-3.5 mmHg/sec. Following the measurement, the oscillometric and ECG signals corresponding to a cuff pressure range of 25-155 mmHg were chosen for further analysis. The ranges of the reference recorded SBPs and DBPs were 79-136 mmHg and 52-86 mmHg, respectively. The Omron device only provides the SBP and DBP as references.

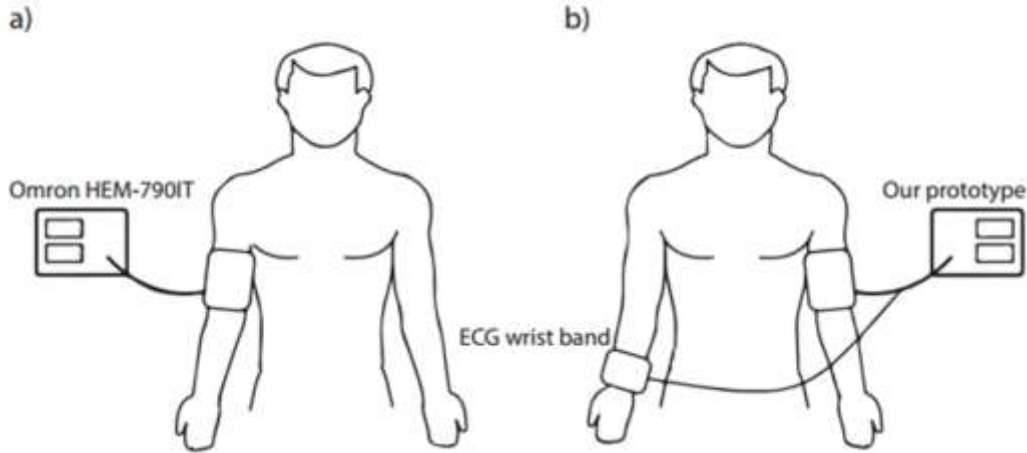


Fig. B.2 InBeam setup to collect 150 arm measurements from 10 healthy subjects. (a) Omron HEM-790IT measurement from right arm. (b) As soon as the Omron measurement ends, our prototype measurement starts on the left arm. The subject also wears the wristband of the prototype on the right wrist for simultaneous ECG recording. Adapted from Ph.D. thesis of Mohamad Forouzanfar, “A Modeling Approach for Coefficient-Free Oscillometric Blood Pressure Estimation”, University of Ottawa, 2014. Used with permission.

B.3 Dataset 3 (DS3)

The third dataset was collected by Health Parametrics Inc. (HPI). This dataset comprised 78 simultaneous oscillometric BP and ECG recordings acquired with a prototype device Wi-Fi Prototype HPI EABPM-01. The data was collected from 13 sick patients with various chronic conditions including atrial fibrillation, hypertension, and obesity. Patients were composed of, 5 male and 8 females, aged from 46 to 85 years. Six recordings were obtained from each patient in a day. Each recording started on the right arm with the clinically popular device - BpTru BPM-100 approved by the Food and Drug Administration, as shown in Fig. B.3. As soon as the BpTru measurement ended, HPI measurement started on the left arm. Two dry flexible electrodes made of conductive fabric inside the cuff along with a handle with two rigid chrome plated electrodes on the HPI prototype device are used for simultaneous ECG recording. The patients grip the handle on the HPI device with the left hand during the measurement. The ranges of the reference recorded SBPs and DBPs were 87-161 mmHg and 51-102 mmHg, respectively.

The data collection protocol for each subject can be summarized as follows:

- 1) Invite the subject to the trial area and inform him/her of the measurement steps.
- 2) Sit the subject comfortably and apply the HPI arm cuff appropriately to left arm at heart level, and the BpTru cuff to the right arm at heart level.

- 3) Start BpTru recording from right arm.
- 4) Start the HPI recording from left arm, as soon as BpTru recording ends.
- 5) Wait three minutes.
- 6) Repeat steps 3-5 five times.
- 7) End session.

HPI prototype recordings comprised inflating the prototype cuff to a pressure of 180 mmHg and then deflating it slowly to a pressure of 20 mmHg. The deflation rate was 1.5-3.5 mmHg/sec. Following the measurement, the oscillometric and ECG signals corresponding to a cuff pressure range of 25-175 mmHg were chosen for further analysis. The ranges of the reference recorded SBPs and DBPs were 87-161 mmHg and 51-102 mmHg, respectively. The BpTru device only provides the SBP and DBP as references.

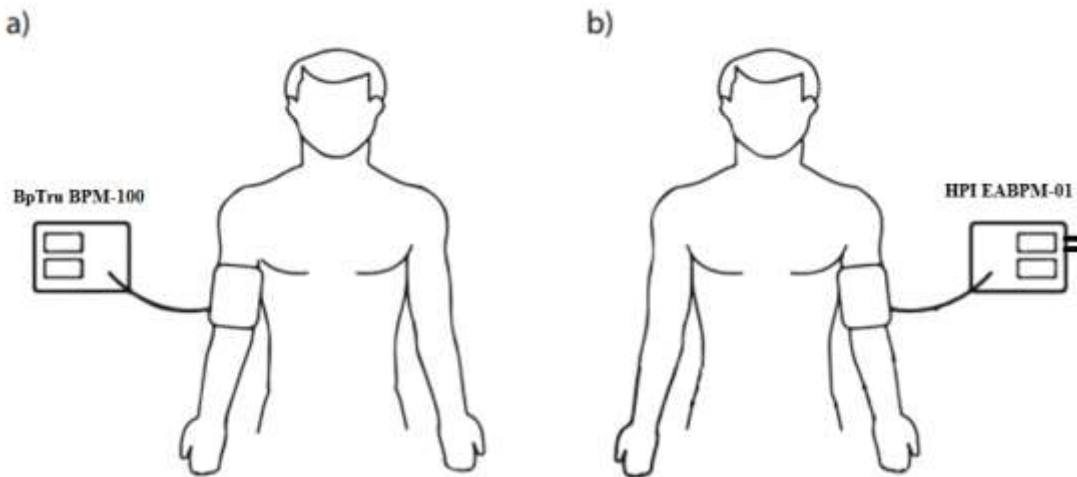


Fig. B.3. HPI setup to collect 78 arm measurements from 13 sick subjects. (a) BpTru BPM-100 measurement from right arm. (b) As soon as the BpTru measurement ends, HPI prototype measurement starts on the left arm. Two dry flexible electrodes made of conductive fabric inside the cuff along with a handle with two rigid chrome plated electrodes on the HPI prototype device are used for simultaneous ECG recording.

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