Model-Based Mean Arterial Pressure Estimation Using Simultaneous Electrocardiogram and Oscillometric Blood Pressure Measurements

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***Abstract*— An accurate noninvasive estimation of mean arterial pressure (MAP) is of great importance in the evaluation of circulatory function and prognosis of some cardiovascular diseases. This paper proposes a novel oscillometric MAP estimation method based on the dependence of pulse transit time (PTT) on cuff pressure (CP). The PTT computed as the time interval between the electrocardiogram (ECG) R-peaks and the maximum slope points on the oscillometric pulses is mathematically modeled by considering the cuff-arm-artery system and the blood flow dynamics. It is then analytically shown that MAP can be approximated as the CP at which the PTT is maximum. Based on our theoretical findings, a new method of MAP estimation from simultaneous ECG and oscillometric blood pressure measurements is proposed. Our proposed method is validated with a pilot study in which 150 recordings from 10 subjects are analyzed. The reference MAP is computed from the systolic and diastolic pressures measured by the Food and Drug Administration-approved Omron HEM-790IT monitor using three different formulas given in the literature. The performance of our proposed method is compared with the maximum amplitude and zero-crossing methods in terms of mean error (ME), mean absolute error, and standard deviation of error (SDE). It is found that our proposed method achieves improvements of more than 20% in SDE compared with the maximum amplitude method and more than 50% in ME compared with the zero-crossing method.**

***Index Terms*— Blood pressure (BP), electrocardiogram (ECG), estimation, mathematical modeling, mean arterial pressure (MAP), oscillometry, pulse transit time (PTT).**

I. Introduction

MEAN arterial pressure (MAP) is of physiological and clinical importance, as it is an indicator of the pressure at which blood is supplied to critical organs. MAP is also used as a predictor of cardiovascular risk and as a parameter for estimating central blood pressure (BP) [1]–[3].

Oscillometry is the most common measurement method used in electronic BP monitors [4]. An occluding cuff is usually placed around the subject's arm and deflated from a suprasystolic to a subdiastolic pressure. The cuff is connected to a pressure sensor that detects the pressure variations within the cuff known as oscillometric pulses [5]–[13].

In oscillometry, MAP is conventionally estimated as the cuff pressure (CP) at which the oscillometric pulses attain maximum amplitude [14]. However, detecting the true maximum-amplitude oscillometric pulse is not always trivial since movement, muscle contractions, and other artifacts could distort the oscillometric pulses [15]–[17]. Moreover, the amplitude of the oscillometric pulses do not show a clear maximum in some health conditions and age groups [18]. For example, in the elderly, the amplitude of the oscillometric pulses may exhibit a plateau, making it difficult to find the exact location of the MAP. In [18] and [19], different techniques of detecting the maximum-amplitude oscillometric pulse were compared and it was found that having good-quality oscillometric pulses is important for improving the MAP estimation results. As an alternative, a few oscillometric pulse morphology-based methods have been proposed for estimation of MAP [20], [21]. These methods are based on extracting various features of the individual pulses and studying their changes as a function of CP. However, these methods are without physiological and theoretical basis and have not been adequately validated. There is, therefore, a need to develop robust methods to accurately measure MAP.

A relatively new method that goes beyond oscillometry involves the estimation of BP from pulse transit time (PTT) [22]–[25]. PTT is defined as the time it takes by a pressure pulse to travel between the heart and a peripheral arterial site [26]. In practice, for ease of measurement, PTT is often measured as the time interval between the electrocardiogram (ECG) R-peaks and certain points on the arterial pulses recorded from a peripheral site. It has been observed that there is a correlation between the PTT and BP that could be used to estimate BP [27]. In [28], a wireless medical device was designed to continuously monitor the ECG, BP, and blood oxygen of a patient and deliver pertinent information to first responders. In [29], synchronized ECG signals were acquired for removing motion artifacts from oscillometric signals to increase the

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accuracy of BP measurements. However, these devices required pressure and ECG sensors auxiliary to the cuff, defeating the simplicity of the oscillometric BP estimation method.

Recently, our research group has proposed an integration of ECG and BP monitoring into a single device that enables the measurement of PTT in oscillometry [22]. The PTT was measured as the time interval between the ECG R-peaks and the oscillometric pulses recorded using a pressure sensor within the cuff. This alleviated the need for any auxiliary pressure sensors placed at other arterial sites. It was empirically found that the PTT measured as the time interval between the ECG R-peaks and the maximum slope points of the oscillometric pulses exhibits a maximum at a CP close to MAP. However, no theoretical foundation for the behavior of PTT as a function of CP was established. Moreover, the sensitivity of the PTT to cardiovascular system parameters was not studied. In [24] and [30], it was shown through theoretical modeling that systolic pressure, diastolic pressure, and MAP can be determined directly from the maxima of PTT signals measured as the time interval between the ECG R-peaks and the oscillometric pulse peaks, troughs, and zero-crossings, respectively. The proposed method provided robust estimates of the systolic and diastolic pressures as the peaks and troughs of the oscillometric pulses can be easily detected. However, detection of the zero-crossings is very sensitive to the filtering technique used to extract the oscillometric pulses from the CP waveform, making this technique somewhat unreliable for the estimation of MAP.

In this paper, we propose a new model and method for the estimation of MAP from the PTT measured from maximum slope points on the oscillometric pulses. This paper is novel in the following ways.

1) We derive a new mathematical model for the PTT computed as the time interval between the ECG R-peaks and the maximum slope points on the oscillometric pulses by considering the cuff-arm-artery system and the blood flow dynamics. To the best of the authors' knowledge, no mathematical model that explains the behavior of PTT measured from the maximum slope points on the oscillometric pulses exists in the literature.
2) Based on our developed model, we propose a new method of estimating MAP using simultaneous ECG and oscillometric BP measurements. Our proposed method relies on the analysis of PTT measured from maximum slope points on the oscillometric pulses. The advantage of using the oscillometric maximum slope points instead of the zero crossings [24], [30] in the computation of PTT is that the maximum slope points can be detected more accurately, directly from the CP waveform using a simple differential operator.
3) We compare our proposed method to the oscillometric maximum amplitude [14] and the zero-crossing [24], [30] methods in a pilot study undertaken on 150 recordings from 10 subjects. The reference MAP is obtained from the measured systolic and diastolic pressures using three different formulas given in the literature. The comparison is made in terms of mean error (ME), mean absolute error (MAE), and standard deviation of error (SDE). The Bland–Altman analysis is performed to study the agreement between our estimates and the reference readings.

This paper is organized as follows. In Section II, our simultaneous ECG and oscillometric BP measurement system is introduced, a mathematical model for PTT is derived, the theory of MAP estimation from PTT is developed, and the validation setup is described. In Section III, our theoretical findings are validated by analyzing actual ECG and oscillometric BP recordings. In Section IV, this paper is concluded.

II. Methodology

A. Measurement System

To measure PTT in oscillometry, the oscillometric BP and the ECG signals should be recorded simultaneously [26]. In this paper, the oscillometric BP and the ECG signals were acquired simultaneously using a prototype designed in our research laboratory [22], as shown in Fig. 1. Our measurement system consists of eight main components: 1) a brachial cuff with a flexible dry ECG electrode; 2) a wristband with a flexible dry ECG electrode; 3) a manual air pump with a screw-controlled pressure-release valve; 4) a mini dc automatic air pump; 5) an analog pressure transducer; 6) an analog ECG amplifier; 7) the National Instruments C Series 9239 data acquisition module; and 8) the National Instruments LabVIEW system design software.

The brachial BP cuff is placed around the subject's upper left arm and controlled by an automatic 6 V dc mini air pump. The pump operates with a push-button mounted on the prototype. Once the push-button is pressed, it turns the pump on and the brachial cuff is gradually inflated and then deflated to conduct the oscillometric measurement. A screw-controlled manual pressure release valve is connected inline with the brachial cuff. The screw on the valve can be rotated manually to control the deflation rate of the cuff.

Dry flexible ECG electrodes are embedded both inside the brachial cuff that is wrapped around the subject's arm and inside a wristband that the subject wears on the other hand's wrist. The two ECG leads, one from the brachial cuff and one from the wristband, form the input to the ECG amplifier. This is equivalent to an ECG lead 1 configuration. The ECG amplifier has an input impedance of 20 MΩ and a voltage gain of 1000. The ECG amplifier includes circuitry for stabilizing the supply voltage and for signal conditioning.

A Vernier pressure transducer is connected to the brachial cuff through an air hose to convert the CP oscillations into an analog voltage signal. The Vernier pressure transducer operates on a dc supply voltage of 5 V.

The analog voltage outputs from the ECG amplifier and the Vernier pressure transducer are fed to two of the four simultaneously sampled analog input channels of the National Instruments C Series 9239 module mounted on a CompactDAQ data acquisition board. The National

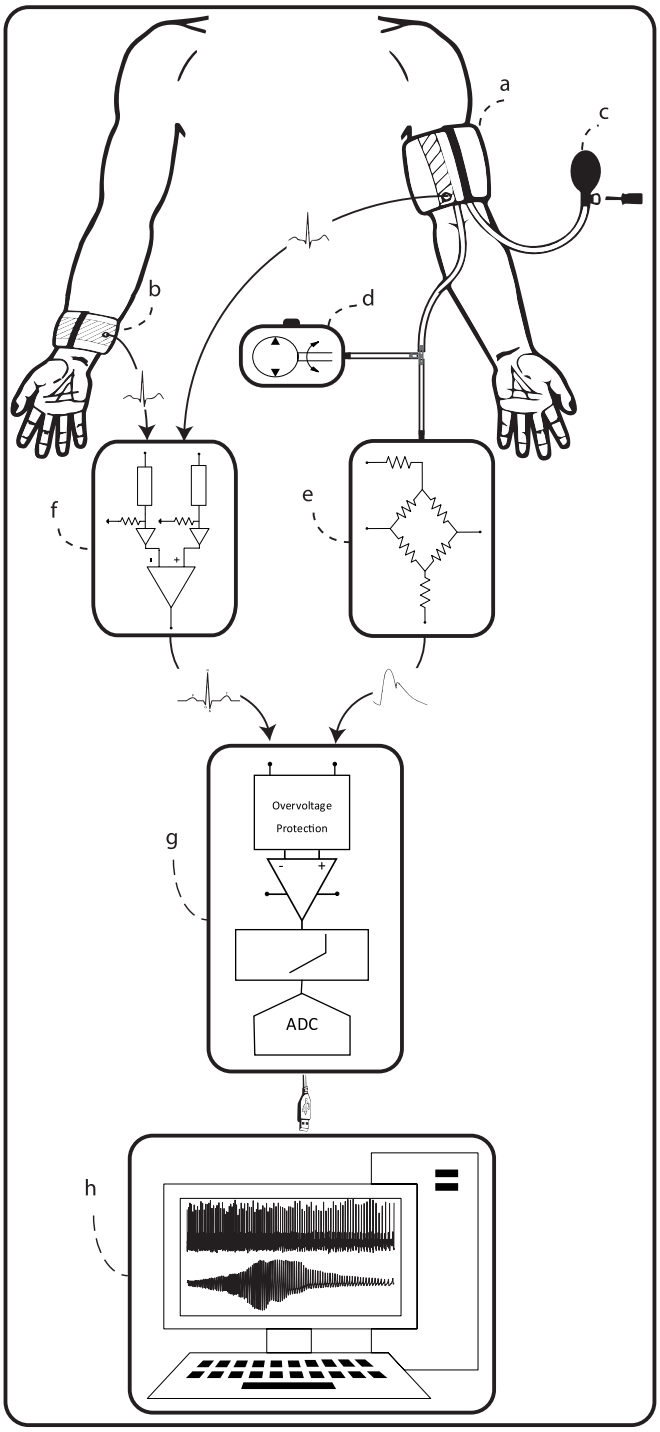

Fig. 1. Functional block diagram of our measurement system. (a) Brachial cuff with conductive fabric. (b) Wristband with a conductive fabric. (c) Manual air pump and screw-controlled pressure-release valve. (d) Automatic dc mini air pump. (e) Vernier pressure transducer. (f) ECG amplifier. (g) National Instruments C Series 9239 data acquisition module. (h) Personal computer with National Instruments LabVIEW system design software.

Instruments module operates on a dc supply voltage of 10 V. These analog signals are conditioned, buffered, and then sampled at a frequency 1.613 kHz by a 24-bit delta-sigma analog-to-digital converter. The quantized signals are transmitted to a personal computer via a universal serial bus cable.

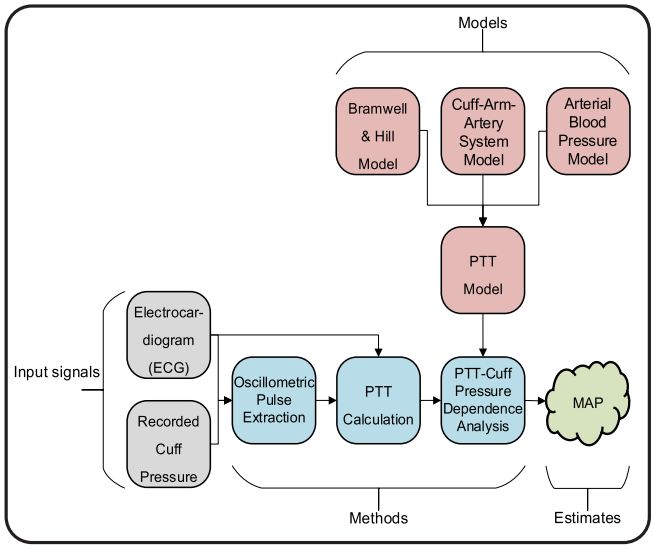

Fig. 2. Block diagram representation of our proposed PTT model and MAP estimation method.

The National Instruments LabVIEW system design software is used for data acquisition of the ECG and the oscillometric BP signals. A customized LabVIEW user interface is developed that displays the acquired ECG and oscillometric BP signals in real time. Signal processing and statistical analysis are performed offline using MATLAB.

This configuration provides an ergonomic integration of ECG and oscillometric BP monitoring that enables the robust measurement of PTT.

B. Pulse Transit Time Model

In [24] and [30], we developed a model for the PTT measured as the time interval between the ECG R-peaks and peaks, troughs, and zero-crossings of the oscillometric pulses. The model derivation for PTT was straightforward as the peaks, troughs, and zero-crossings of the oscillometric pulses always occur at the time points at which the arterial pressure is equal to systolic pressure, diastolic pressure, and MAP, respectively, independent of the CP value. However, the proposed model in [24] and [30] does not explain the behavior of the PTT measured from maximum slope points on the oscillometric pulses, as the maximum slope of the oscillometric pulses occur at different arterial pressures depending on the CP value.

In this section, a new mathematical model for the PTT computed as the time interval between the ECG R-peaks and the maximum slope points on the oscillometric pulses is derived out of cardiovascular system parameters. The necessary components of the model proposed in [24] and [30] will first be introduced in (1)–(6). Equations (7)–(16) correspond to the new model that is developed in this paper. A block diagram representation of our proposed PTT model and MAP estimation method is shown in Fig. 2.

When estimated as part of an oscillometric measurement, PTT is modeled with two main components: the time it takes for the pulse to arrive from the heart to the brachial artery $\tau_0(t)$ and the time it takes for the pulse to travel along the brachial

artery underneath the cuff $\tau_c(t)$ [22], [24], [31]

$$\tau(t) = \tau_0(t) + \tau_c(t) \tag{1}$$

where $\tau_0(t) = L_0/v_0(t)$ and $\tau_c(t) = L_c/v_c(t)$. L_0 and L_c are the lengths of the arterial segments between the heart and the arm and underneath the cuff, respectively, and $v_0(t)$ and $v_c(t)$ are the average pulse wave velocities over L_0 and L_c, respectively. As our goal is to analyze the changes in PTT as a function of applied CP, we do not take into account the preejection period in our model. Since the PEP can be treated as a constant at rest and is not sensitive to CP variations, this is a reasonable assumption [31].

Using the Bramwell and Hill equation [32], $v_c(t)$ and $v_0(t)$ can be written, respectively, as follows:

$$v_c(t) = \sqrt{\frac{A_c(t)}{\rho}} \times \sqrt{\frac{\partial(p_a(t) - p_c(t))}{\partial A_c(t)}} \tag{2}$$

$$v_0(t) = \sqrt{\frac{A_0(t)}{\rho}} \times \sqrt{\frac{\partial p_a(t)}{\partial A_0(t)}} \tag{3}$$

where ρ is the blood density, $p_a(t)$ and $p_c(t)$ represent the arterial and CPs, respectively, and $A_c(t)$ and $A_0(t)$ are the average arterial lumen areas (ALA) along the arterial segments underneath the cuff and between the heart and the arm, respectively.

The arterial pressure pulse $p_a(t)$ is modeled using a Fourier series representation [14], [33]–[35]

$$p_a(t) = \text{MAP} + \alpha_1 \cos(2\pi f_c t) + \alpha_2 \cos(4\pi f_c t + \phi) \tag{4}$$

where two harmonics of the cardiac signal were considered to be adequate as they carry most of the signal power [14]. In this model, f_c is the cardiac rate, α_1 and α_2 represent the amplitude of the first and second harmonics of the cardiac signal, respectively, and ϕ is the phase difference between the two harmonics.

The average ALA underneath the cuff $A_c(t)$ is modeled as [24], [25], [36]

$$A_c(t) = \begin{cases} E_c + C_c e^{a_c(p_a(t) - p_c(t)} & \text{for } p_a(t) \le p_c(t) \\ (E_c + D_c) + (C_c - D_c)e^{-b_c(p_a(t) - p_c(t))} & \text{for } p_a(t) > p_c(t) \end{cases} \tag{5}$$

where a_c and b_c are the average compliance indices, C_c is the average ALA at zero transmural pressure, and D_c is the average fully expanded ALA, over the arterial segment underneath the cuff. E_c represents the average nonzero ALA over the whole cuff bladder width when the arterial area at the center of the cuff is zero.

The average ALA between the heart and the arm $A_0(t)$ is modeled as [24], [25], [36]

$$A_0(t) = D_0 + (C_0 - D_0)e^{-b_0 p_a(t)} \tag{6}$$

where b_0 is the average arterial compliance index, C_0 is the average ALA at zero transmural pressure, and D_0 is the average fully expanded ALA, over the arterial segment between the heart and the arm.

Equation (1) represents the general PTT model for any point on the arterial pressure pulse. Using our device, PTT is experimentally measured as the time interval between the ECG R-peak and maximum slope points of the oscillometric pulses. Therefore, to find the PTT model corresponding to the maximum slope points of the oscillometric pulses, the general arterial pressure model $p_a(t)$ in (2) and (3) should be replaced by the arterial pressure values (represented by $p_{\text{am}}(t)$ hereafter) at which the oscillometric pulses exhibit the maximum slope. It has been shown that the oscillometric pulses are proportional to the oscillations of the ALA segment underneath the cuff [14]. Therefore, the arterial pressure values $p_{\text{am}}(t)$ corresponding to the maximum slope points of the oscillometric pulses can be found as the solution to

$$\partial^2 A_c(t)/\partial t^2 = 0 \tag{7}$$

where $A_c(t)$ is given in (5). By substitution of (5) in (7) and simplification, $p_{\text{am}}(t)$ can be formulated as follows:

$$p_{\text{am}}(t) = \begin{cases} P_{a1} & \text{for } p_c(t) \le P_{a1} \\ p_c(t) & \text{for } P_{a1} < p_c(t) \le P_{a2} \\ P_{a2} & \text{for } p_c(t) > P_{a2} \end{cases} \tag{8}$$

where P_{a1} and P_{a2} are obtained as the solutions to the following:

$$-b_c \left(\frac{\partial p_a(t)}{\partial t}\right)^2 + \frac{\partial^2 p_a(t)}{\partial t^2} = 0 \tag{9}$$

$$a_c \left(\frac{\partial p_a(t)}{\partial t}\right)^2 + \frac{\partial^2 p_a(t)}{\partial t^2} = 0 \tag{10}$$

with $p_a(t)$ given in (4).

Now, by the substitution of (5)–(8) in (1)–(3) and simplification, the PTT computed from the maximum slope points on the oscillometric pulses $\tau_m(t)$ is obtained as follows:

$$\tau_m(t) = \tau_{m0}(t) + \tau_{mc}(t) \tag{11}$$

where

$$\tau_{m0}(t) = \begin{cases} T_0(P_{a1}) & \text{for } p_c(t) \le P_{a1} \\ T_0(p_c(t)) & \text{for } P_{a1} < p_c(t) \le P_{a2} \\ T_0(P_{a2}) & \text{for } p_c(t) > P_{a2} \end{cases} \tag{12}$$

$$\tau_{mc}(t) = \begin{cases} T_{c1}(P_{a1} - p_c(t)) & \text{for } p_c(t) \le P_{a1} \\ T_{c1}(0) & \text{for } P_{a1} < p_c(t) \le P_{a2} \\ T_{c2}(P_{a2} - p_c(t)) & \text{for } p_c(t) > P_{a2} \end{cases} \tag{13}$$

$$T_0(x) = L_0 \sqrt{\rho b_0 \left(\frac{1}{1 - \frac{D_0 - C_0}{D_0} e^{-b_0 x}} - 1\right)} \tag{14}$$

$$T_{c1}(x) = L_c \sqrt{\rho b_c \left(\frac{1}{1 - \frac{D_c - C_c}{D_c + E_c} e^{-b_c x}} - 1\right)} \tag{15}$$

$$T_{c2}(x) = L_c \sqrt{\rho a_c \left(1 - \frac{1}{1 + \frac{C_c}{E_c} e^{a_c x}}\right)} \tag{16}$$

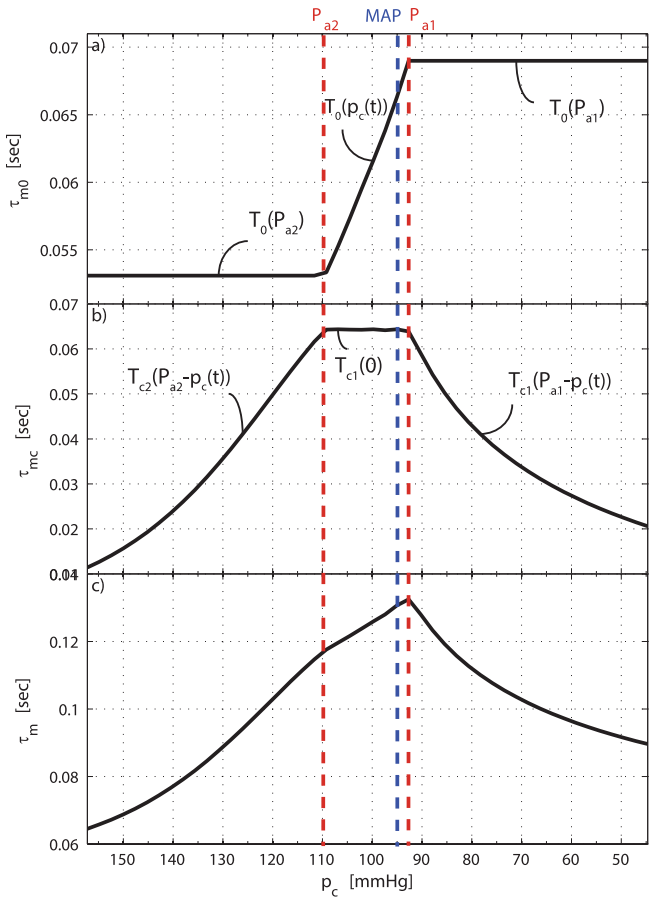

Fig. 3. Simulated PTT computed from maximum slope points on the oscillometric pulses. (a) PTT from the heart to the brachial artery (τ_{m0}). (b) PTT along the brachial artery underneath the cuff (τ_{mc}). (c) Total PTT (τ_m). The vertical dashed lines from left to right show the points at which CPs are equal to P_{a2}, MAP, and P_{a1}, respectively. Note that the x-axis goes from high to low CP values to reflect cuff deflation.

where $\tau_{m0}(t)$ and $\tau_{mc}(t)$ represent the time it takes for the pulse to arrive from the heart to the brachial artery and the time it takes for the pulse to travel along the brachial artery underneath the cuff, respectively, measured from the maximum slope points on the oscillometric pulses. The $\tau_{m0}(t)$ and $\tau_{mc}(t)$ components at different CPs are represented by T_0, T_{c1}, and T_{c2}, as shown in Fig. 3.

From (12) and (14), it is observed that $\tau_{m0}(t)$ has a flat maximum for CPs less than P_{a1}, as shown in Fig. 3(a). From (13), (15), and (16), it is observed that $\tau_{mc}(t)$ exhibits a flat maximum for CPs between P_{a1} and P_{a2}, as shown in Fig. 3(b). Therefore, according to (11), $\tau_m(t)$ attains a maximum at CP equal to P_{a1}, as is shown in Fig. 3(c). From Fig. 3, it is observed that $\tau_m(t)$ maximum occurs at a CP very close to MAP (2.30-mmHg difference). Therefore, MAP can be approximated as the CP at which $\tau_m(t)$ attains a maximum or, in other words, at CP equal to P_{a1}. Typical values of the cardiovascular parameters in the human artery were used in this simulation [14], [37], [38]; where $a_c = 0.09$ mmHg^{-1}, $b_0 = 0.03$ mmHg^{-1}, $b_c = 0.03$ mmHg^{-1}, $C_0 = 0.1$ cm^2, $C_c = 0.1$ cm^2, $D_0 = 0.4$ cm^2, $D_c = 0.4$ cm^2, $E_c = 0.018$ cm^2, MAP $= 95$ mmHg, $f_c = 75$ beats/min, $\alpha_1 = 10$ mmHg, $\alpha_2 = 9$ mmHg, and $\phi = -1.2$ radians. It should be noted that the exact location of MAP depends on the model parameters.

According to (4) and (9), P_{a1} is a function of arterial compliance index b_c and arterial pressure pulse parameters α_1, α_2, and ϕ. As a result, MAP estimation results could be affected as these parameters vary between different health conditions, age groups, and so on. A parametric sensitivity analysis was performed to examine the accuracy of MAP estimation results as parameters b_c, α_1, α_2, and ϕ change by $\pm 50\%$ around their typical values in the human brachial artery with α_2 set to 0.7 of α_1 [14], [37], [38]. It was observed that the MAP estimation error gradually increases as the parameter values increase from their typical values. However, the absolute error is always less than 5 mmHg, which meets the international standard requirement for automatic noninvasive BP devices [39]. Therefore, the CP at which $\tau_m(t)$ attains a maximum could be used as an accurate approximation of the MAP.

It should be pointed out that the PEP could alter Fig. 3(c) by shifting it upward by a small constant. However, the PEP does not alter the shape of the PTT curves and location of their maxima as it can be assumed to be constant at rest during the measurement interval [31].

C. MAP Estimation Method

Based on the model of the PTT developed in Section II-B, our proposed MAP estimation method is summarized as follows.

1) Detect the R-Peaks of the ECG Signal: For this purpose, the MIT/PhysioNET MATLAB QRS onset detector software is utilized [40].

2) Detecting the Peaks of the Oscillometric Pulses: The oscillometric peaks are detected as the maxima of the oscillometric pulses that lie between every two consecutive ECG R-peaks.

3) Detecting the Troughs of the Oscillometric Pulses: The oscillometric troughs are detected as the minima of the oscillometric pulses that lie between every two consecutive oscillometric peaks.

4) Detecting the Maximum Slope Points on the Oscillometric Pulses: The oscillometric maximum slope points are detected as the maxima of the derivative of the oscillometric pulses that lie between every consecutive oscillometric trough and peak.

5) Calculating the PTT: The PTT is calculated as the time interval between the detected the ECG R-peaks and the maximum slope points on the oscillometric pulses.

6) Removing Outliers: Since the calculated PTT signal is noisy, an outlier removal technique is applied to remove the samples that appear to be inconsistent with the remainder of the signal. The adopted outlier removal technique is based on fitting a quadratic polynomial function to the PTT signal [41]. An outlier is defined as a value that is more than three standard deviations away from the quadratic polynomial fit. The outliers are then removed and this procedure is repeated until no more outliers are detected.

7) Smoothing the PTT Signal: The PTT signal is smoothed using a seven-point moving average filter. Afterward, a cubic

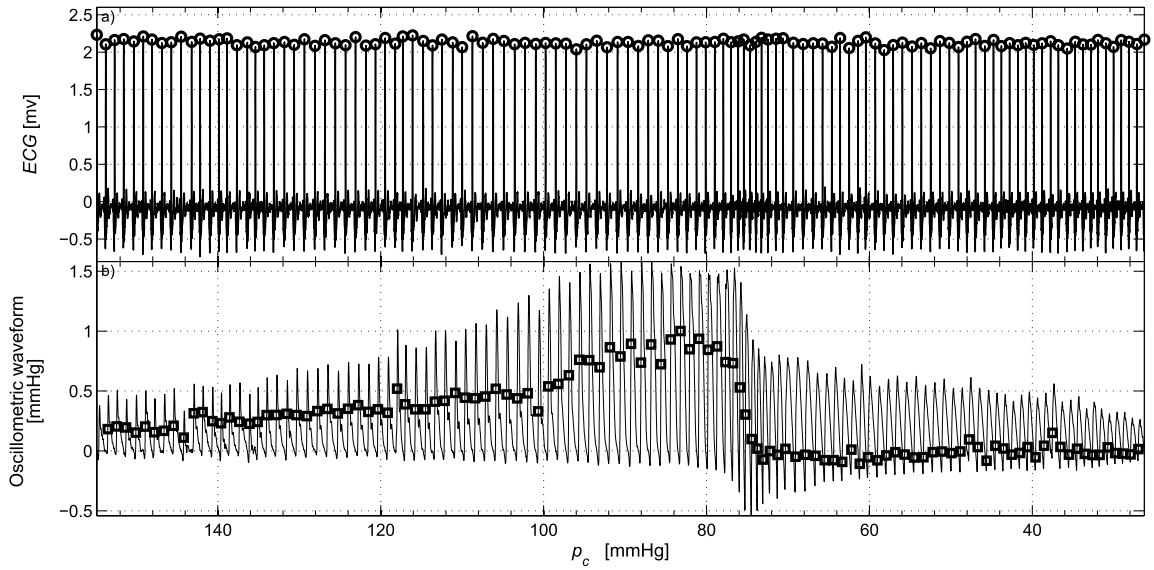

Fig. 4. Example of the (a) simultaneously recorded ECG and (b) oscillometric BP signals. The ECG R-peaks and maximum slope points on the oscillometric pulses are shown in circles and squares, respectively. Note that the x-axis goes from high to low CP values to reflect cuff deflation.

smoothing spline function is fitted to the smoothed signal to remove any remaining artifacts.

8) Estimating the MAP: The CP at which the smoothed PTT signal has a maximum is determined as the MAP.

D. Validation Setup

Our proposed method was initially validated with a pilot investigation on 150 oscillometric BP recordings acquired from 10 healthy subjects. The dataset consisted of six males and four females aged from 24 to 63 years. Recordings from each subject were obtained on three separate days with five sets of recordings on each day. Each set of recordings started with the Food and Drug Administration (FDA)-approved Omron HEM-790IT monitor measurement on the right arm. As soon as the Omron measurement ended, our device prototype measurement started on the left arm. Although there may be differences in BP measured from right and left arms, studies have shown that the mean interarm difference is not significant in healthy subjects [42]–[47] such as the ones tested in this pilot investigation. To validate our method in a patient population where there are substantial mean interarm differences, all measurements should be taken from the same arm. This paper was approved by the University of Ottawa Research Ethics Board and written informed consent was obtained from all subjects.

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

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

For more details regarding the data collection protocol, the reader is referred to [22].

The reference MAP was calculated from the systolic BP (SBP) and diastolic BP (DBP) measured by the FDA-approved Omron monitor using three different formulas.

1) Thirty-Three Percent Formula: The conventional formula for calculating MAP from the measured SBP and DBP is based on adding 33% of the pulse pressure (PP) to DBP [1] as follows:

$$\text{MAP} = \text{DBP} + 0.33 \times \text{PP} \tag{17}$$

where

$$\text{PP} = \text{SBP} - \text{DBP}. \tag{18}$$

2) Fourty Percent Formula: It has been shown that the conventional formula for calculating MAP in (17) underestimates the MAP [48]. In [49], this formula was corrected by replacing the 33% coefficient by a coefficient of 40% as follows:

$$\text{MAP} = \text{DBP} + 0.40 \times \text{PP}. \tag{19}$$

3) Heart Rate-Dependent Formula: Both (17) and (19) fail to take into account the effect of heart rate on the shape of the arterial pressure pulse and as a result on the MAP calculated from the measured SBP and DBP. In [50], a new formula for calculation of MAP that incorporates the heart rate was proposed and shown to obtain more accurate results. The heart rate dependent formula can be written as follows:

$$\text{MAP} = \text{DBP} + (0.33 + 0.0012\ \text{HR}) \times \text{PP} \tag{20}$$

where HR represents the heart rate.

A repeated-measures analysis of variance [51] was also conducted on the reference MAP readings that were performed

over three different days. It was found that the three-day measurement procedure had no statistically significant effect on BP levels with $F(2, 18) = 3.29$ and $p > 0.05$, where $F(df_{\text{time}}, df_{\text{errpr}})$ is the F-statistic, df_{time} is the degree of freedom of time $(\#days - 1)$, and df_{errpr} is the degree of freedom of the error $[(\#days - 1) \times (\#subjects - 1)]$ and p is the p-value.

III. Experimental Results

The MAP estimates obtained using our proposed method were compared with those obtained using oscillometric maximum amplitude [14] and the zero-crossing [24] methods in terms of ME, MAE, and SDE [39], [52], [53] on the whole dataset of 150 simultaneous ECG and BP recordings.

Fig. 4(a) and (b) shows examples of simultaneous ECG and oscillometric BP signals recorded using the measurement system described in Section II. The ECG R-peaks and maximum slope points on the oscillometric pulses are shown in circles and squares, respectively.

Fig. 5(a) shows the oscillometric waveform envelope (OMWE) computed as the magnitude difference between the peaks and troughs of the oscillometric pulses shown in Fig. 4(b). Fig. 5(b) shows the PTT computed as the time interval between the ECG R-peaks and zero crossings of the oscillometric pulses shown in Fig. 4. Fig. 5(c) shows the PTT computed as the time interval between the ECG R-peaks and maximum slope points on the oscillometric pulses shown in Fig. 4. In Fig. 5, the original and the smoothed waveforms are plotted in dashed gray lines and solid black lines, respectively. It is observed that while the OMWE exhibits a plateau at CPs around the MAP [Fig. 5(a)], the PTTs have sharper maxima at CPs close to the MAP [Fig. 5(b) and (c)]. The mean and standard deviation of the maximum of PTT measured as the time interval between the ECG R-peaks and the maximum slope points on the oscillometric pulses were 213.03 ms and 16.15 ms, respectively, on the whole dataset of 150 recordings.

Table I shows the estimation errors in terms of ME, MAE, and SDE over the whole dataset of 150 simultaneous ECG and BP recordings. The reference MAP was calculated using three different formulas introduced in Section II-D. The rows 2–4 in Table I list the estimation errors using the 33% formula in (17) to compute the reference MAP. The rows 5–7 in Table I list the estimation errors using the 40% formula in (19) to compute the reference MAP. The rows 8–10 in Table I list the estimation errors using the heart rate-dependent formula in (20) to compute the reference MAP.

It is observed that the maximum amplitude method suffers from high SDE in all the three cases (SDE $\geq$ 7.32 mmHg). Moreover, the maximum amplitude method shows relatively high ME ($\geq$3.72 mmHg) and MAE ($\geq$5.65 mmHg) when using the more accurate 40% and heart rate-dependent formulas for the computation of the reference MAP.

It is also observed that the zero-crossing method suffers from high ME in all the three cases (ME $\geq$ 5.31 mmHg). Moreover, the zero-crossing method shows high MAE ($\geq$7.82 mmHg) when using the more accurate 40% and heart rate-dependent formulas for the computation of the reference MAP.

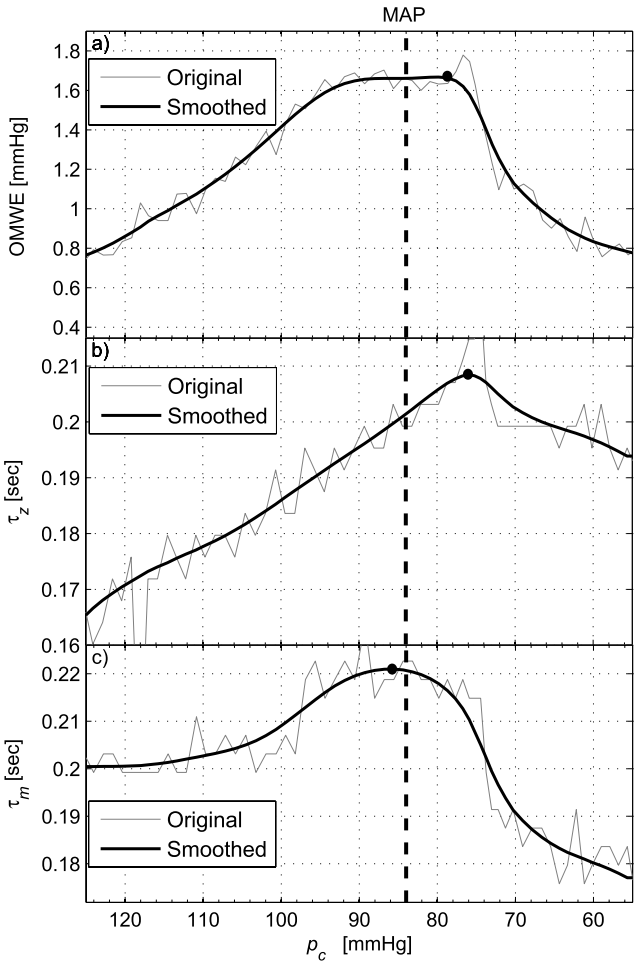

Fig. 5. Example of the (a) OMWE, (b) PTT computed as the time interval between the ECG R-peaks and zero-crossings of the oscillometric pulses (τ_z), and (c) PTT computed as the time interval between the ECG R-peaks and the maximum slope points on the oscillometric pulses (τ_m). The bold vertical dashed line shows the MAP location in all figures. Note that the x-axis goes from high to low CP values to reflect cuff deflation.

TABLE I
ME, MAE, and SDE of Our Proposed Method (PTT-MaxS) Versus the Oscillometric Maximum Amplitude (OSC-MA) [14] and the Zero-Crossing (PTT-Zero) [24] Algorithms Based on 150 Recordings From 10 Subjects

MAP Formula	Error [mmHg]	MA-OSC	Zero-PTT	MaxS-PTT
33% Formula	ME	1.25	5.31	-2.80
	MAE	4.63	4.30	4.09
	SDE	7.32	5.74	4.79
40% Formula	ME	3.72	7.82	-0.79
	MAE	5.65	7.92	3.32
	SDE	7.51	4.54	4.71
Heart Rate-Dependent Formula	ME	4.09	8.19	-0.42
	MAE	6.00	8.29	3.42
	SDE	7.65	4.74	4.78

On the other hand, our proposed method achieves relatively low MAE ($\leq$4.09 mmHg) and SDE ($\leq$4.79 mmHg) in all

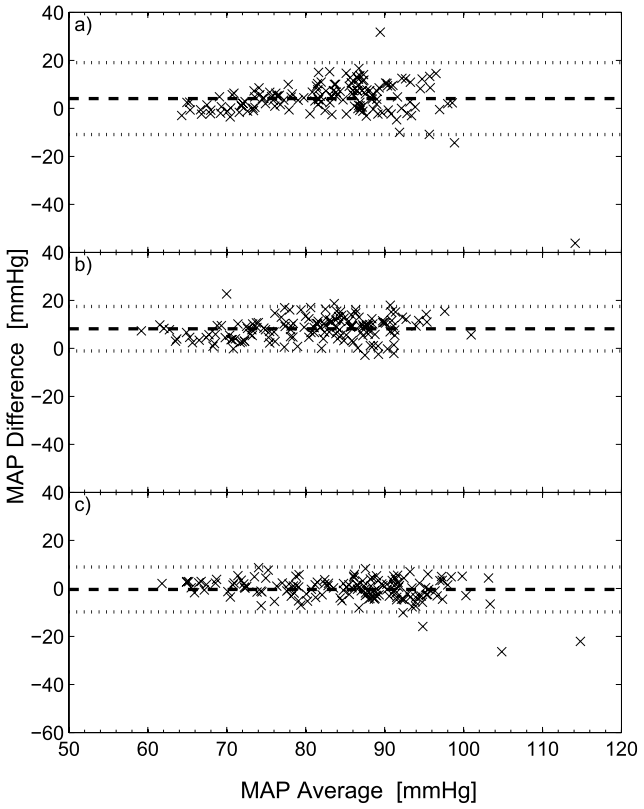

Fig. 6. Bland–Altman plots of the MAP estimates for (a) maximum amplitude method, (b) zero-crossing method, and (c) our proposed method versus the reference MAP obtained using the heart rate-dependent formula in (20). The horizontal dotted lines show the limits of agreement, while the horizontal dashed line shows the bias.

the three cases. The improvements with our proposed method are even more obvious when using the more accurate 40% and heart rate-dependent formulas for the computation of the reference MAP, where the ME is significantly reduced in magnitude (ME ≤ 0.79 mmHg).

These improvements are associated with the facts that our proposed method:

1) uses the maximum slope points on the oscillometric pulses to calculate the PTT that can be more accurately detected compared with the zero crossings of the oscillometric pulses;
2) does not rely on the OMWE that could exhibit no distinguishable maximum.

It should be noted that errors reported in this paper include the error of the estimation methods and the interarm BP difference. However, since the interarm BP difference is independent of the error of the estimation methods, the variance of the interarm BP difference would be added to the variance of the estimation error in the same way for all the methods [54]. Therefore, our method would still give the best accuracy in terms of SDE. In addition, since the mean interarm BP difference is very small for normal subjects (about 1 mmHg) [42]–[47], it would not affect the MEs reported in this paper.

To analyze the agreement between different MAP estimation methods and the reference MAP, the Bland–Altman analysis was performed [55]. Fig. 6(a)–(c) shows the Bland–Altman plots of the MAP estimates of our proposed method, the zero-crossing method, and the maximum amplitude method, respectively, versus the reference MAP obtained using the heart rate-dependent formula in (20). The x-axis of the plots shows the average estimates of different methods and the reference MAP, while the y-axis shows the difference of the estimates and the reference MAP. The bias (ME) and the limits of agreement (ME $\pm$ 1.96 $\times$ SDE) are shown in dashed and dotted lines, respectively. It is observed that while the errors of all the methods are almost evenly distributed over the measured pressure range, the bias and the limits of agreement for our proposed method are relatively smaller. The bias of our proposed method is -0.42 mmHg, while the bias of the zero-crossing and maximum amplitude methods are 8.19 and 4.09 mmHg, respectively. Moreover the limits of agreement of our proposed method are 5.70 mmHg smaller than those of the maximum amplitude algorithm. That is, the MAP estimates made by our proposed method are in close agreement with the reference values.

IV. Conclusion

The main contributions of this paper are the development of a new mathematical model that describes the behavior of PTT computed as the time interval between the ECG R-peaks and the maximum slope points on the oscillometric pulses, and the formulation of a novel method for estimating MAP from the computed PTT. The successful validation with empirical data confirmed the accuracy of our proposed theoretical model and MAP estimation method. Three different formulas were used to compute the reference MAP from the measured systolic and diastolic pressures. It was found that our proposed method outperforms the zero crossing and maximum amplitude methods regardless of the formula used in calculating the reference MAP.

Noninvasive BP monitors typically rely on an initial estimation of MAP. The initial MAP estimate is used to derive the SBP and DBP from the envelope of the oscillometric pulses using some estimation ratios. Therefore, the results of this paper may be used to improve the accuracy of noninvasive BP monitors.

We assumed that our model parameters do not change with cuff deflation during a measurement. We understand that for certain patient populations and disease states, such as atrial fibrillation, the PTT model parameters may well change during a measurement, which may be as short as 30 s. Therefore, future work will focus on models that incorporate the time variability of these parameters.

Future work will also involve undertaking clinical testing on a larger number of healthy subjects as well as patients, where the method will be compared against auscultatory measurements by trained observers and, if possible, against invasive intraarterial measurements.

Acknowledgment

The authors declare that they have founded a company called Health Parametrics Inc. to commercialize the ECG-assisted blood pressure monitoring technology, and they have submitted patent applications in the USA, U.K., and Canada with regards to this technology.

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