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Cuffless Continuous Blood Pressure Estimation From Pulse Morphology of Photoplethysmograms

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\textbf{ABSTRACT} Cuffless blood pressure monitoring is critical for the prevention and early diagnosis of a wide variety of cardiovascular diseases. However, cuffless blood pressure estimation devices suitable for home healthcare applications still suffer from numerous technological limitations. In this paper, we propose a novel method to continuously estimate blood pressure from the pulse morphology of the photoplethysmographic signals, acquired by a commercial oximeter. We conducted cold-pressor tests for 70 healthy subjects, simultaneously acquiring the photoplethysmograms from the oximeter and the continuous blood pressure from a commercial sphygmomanometer as a reference. The shape of each pulse was extracted, normalized, and regressed with the reference blood pressure using support vector machines. The performance of the regression model for each subject was evaluated using 10-fold cross-validation. Results showed that the predicted values from the regression model were highly correlated with the reference measurements from the commercial device. The mean correlation coefficients were 0.748, 0.754, and 0.775 for systolic, diastolic, and mean blood pressures, respectively. The mean errors were 0.043 mmHg, 0.011 mmHg, and 0.008 mmHg, with standard deviations of 5.001 mmHg, 3.689 mmHg, and 4.140 mmHg for systolic, diastolic, and mean blood pressures, respectively. These results suggest high feasibility of the proposed method to be employed in wearable medical and home healthcare devices.

\textbf{INDEX TERMS} Blood pressure, cold pressor test, oximeter, photoplethysmogram, support vector machine.

\section{I. INTRODUCTION}
Cardiovascular diseases are the largest cause of death throughout the world as reported by the World Health Organization [1]. In 2015, 17.7 million people died from cardiovascular diseases, representing 31\% of all global deaths. As high blood pressure is one of the most serious risk factors, blood pressure monitoring becomes an indispensable tool for the prevention and early diagnosis of cardiovascular diseases. However, current devices for hospital blood pressure measurements are based on the occlusion of arteries with mechanical auxiliary of an inflatable cuff, which is typically cumbersome and uncomfortable to the users. Therefore, developing a portable, user-friendly, and low-cost device without a cuff suitable for home healthcare blood pressure monitoring is in high demand.

Although numerous studies have been conducted on cuffless blood pressure estimation, most of them are methods based on the pulse transit time (PTT) or pulse wave velocity (PWV). PTT is defined as the time for the pulse to travel from one site of the body to another site, and PWV is the distance that the pulse travels divided by the PTT. For simplicity, both techniques are often referred to as “PTT-based”. PTT-based methods are effective in blood pressure estimation because PTT is strongly correlated with blood pressure, with a relationship that can be linear [2] or nonlinear [3]. PTT-based methods can be divided into three categories: (1) photoplethysmogram (PPG) combined with other cardiovascular signals (e.g., electrocardiogram [2]–[7], ballistocardiogram [8]–[12], seismocardiogram [13], [14] phonocardiogram [15]–[17] or impedance
plethysmography [18], [19]), where the PTT is measured as the temporal distance from a characteristic point of the other signal to a characteristic point of the PPG; (2) dual-channel PPG at different peripheral sites, where the PTT is measured as the temporal distance between the corresponding characteristic points of the two PPG signals [20]–[22]; and (3) single-channel PPG, where the PTT is calculated as the temporal difference between the forward and the reflected waves, which are extracted from the second derivative of the PPG [23], [24].

There have also been several studies on cuffless blood pressure estimation based on non-PTT methods. As the pulse morphology of the PPG is associated with blood pressure, some studies tried to estimate blood pressure by establishing the correlation between blood pressure and PPG features such as pulse amplitude [25], signal steepness [26], alternating current component [27], peak-to-onset interval [28], pressure index [29], heart rate and modified normalized pulse volume [30], amplitude and phase features in Fourier transform [31], and many other features in time domain and frequency domain [32]. These features were sometimes combined with PTT-based methods to improve accuracy [33]–[37]. Non-PTT methods do not require the ‘auxiliary’ signal but only one PPG channel, which greatly increases user comfort in comparison with the first and second categories of PTT-based methods. However, they have the same difficulty in feature extraction as the third category of PTT-based methods, because the morphology of PPG is highly susceptible to noise or artifacts. Therefore, certain characteristic points may be erroneously detected, or worse, entirely missed for certain individuals (see Fig. 1b Class 3 and Class 4).

In this paper, we propose a novel method using support vector machine (SVM) to estimate blood pressure from single-channel PPG waveforms acquired by a low-cost, commercially available medical oximeter. The use of SVM renders it feasible to directly obtain the relationship between the PPG morphology and blood pressure, without the need for detecting complicated characteristic points and extracting PPG features. This method has the advantages of simple implementation, and is capable of continuously estimating the systolic, diastolic, and mean blood pressure for each heartbeat.

II. METHODS

A. RELATIONSHIP BETWEEN THE MORPHOLOGY OF PPG AND BLOOD PRESSURE

PPG is typically obtained by a pulse oximeter, a device commonly used in the clinic that clips onto a finger for monitoring the heart rate and blood oxygen levels. The device works on the following principle: Light of certain wavelengths transmitted by an LED in the pulse oximeter penetrates into the tissue of the finger and is sensed by a photoelectric detector. As the light absorbed by the tissue is associated with the blood perfusion, the PPG signals collected by the detector reflect the changes of blood volume in each heartbeat, which contain cardiovascular information such as heart rate, heart rate variability, cardiac output, arterial stiffness, and blood pressure [38].

Fig. 1a shows a typical morphology of the PPG, which contains a valley, a peak, a tidal wave, a dicrotic notch and a dicrotic peak. The morphology is affected by blood pressure, systemic vascular resistance, stroke volume, peripheral perfusion, and fluid responsiveness [39]. It may change in different cardiovascular conditions in different individuals. Dawber et al. divided various morphologies of PPG into four classes [40] (shown in Fig. 1b): Class 1, a distinct notch is evident on the downward slope of the pulse wave; Class 2, no notch develops but the line of descent becomes horizontal; Class 3, no notch develops but there is a well-defined change in the angle of descent; and Class 4, no evidence of a notch is seen. In general, a higher class is more prevalent in elder people [40], [41], and a higher class usually suggests higher blood pressure, higher arterial stiffness, and higher vascular resistance [42].

Despite the complexity, the predominant contributor to PPG morphology is the blood pressure [39]. It is well-known that the aortic pulse is influenced by the Windkessel effects of the aorta and large elastic arteries. When the pressure increases in the aorta during systole, more blood is infused to the peripheral arterioles, resulting in a peak of the PPG signal. When the pressure travels forward to the capillaries and reflects back due to higher vascular resistance, the blood volume fluctuates and forms a dicrotic notch and a dicrotic peak. As a consequence, the PPG morphology is similar to the blood pressure waveform. Millasseau et al. demonstrated that the relationship between the PPG morphology and the radial pressure pulse can be represented by a single transfer function [43]. Others made efforts to empirically correlate certain PPG features to the blood pressure by linear regression [25]–[28], [30]–[32]. In our previous experiments [44], we also observed that the morphology of PPG changed (e.g., the peak blunted, the dicrotic notch disappeared, shown in Fig. 2) when the blood pressure was elevated by cold stimulus. Although no explicit formulas were found, it is certain that the morphology of PPG and blood pressure are closely related. Therefore, it is possible to use advanced machine learning techniques to determine their relationship and then

![Figure 1. Morphology of photoplethysmograms. (a) Characteristic points. (b) Classification according to Dawber et al. [40].]
use it to estimate blood pressure from the morphology of the PPG signal.

**B. DATA ACQUISITION**

A total of 70 healthy subjects (49 males and 21 females, age 21–32 years, height 150–185 cm, weight 40–90 kg) were recruited and all subjects were asked to refrain from caffeine, alcohol, cigarettes or strenuous exercise for at least 2 hours before the experiment. The study was conducted in Shenzhen Institutes of Advanced Technology. All the experiments were approved by the Institutional Review Board of Shenzhen Institutes of Advanced Technology (registration number: SIAT-IRB-120515-H0009).

In the experiment, the subject was instructed to lie in the supine position on a mattress. The PPG signal was collected on the right index finger by a medical pulse oximeter (CMS50FW Pulse Oximeter, Contec, Qinhuangdao, China) with sampling frequency of 60 Hz. At the same time, the blood pressure was continuously monitored by a commercial medical device - the Finometer® MIDI (Model II, Finapres Medical Systems B.V., Amsterdam, The Netherlands) with a finger cuff around the right middle finger. The Finometer, through automatically inflating and deflating the cuff, is capable of measuring beat-to-beat systolic, diastolic, and mean blood pressure. The collected data from the two systems (pulse oximeter and Finometer) were synchronized using the local time of the data acquisition computer.

The experimental procedure was adopted from published work [44], in which each subject underwent a 13-min process that included three stages (shown in Fig. 3). In the first stage, the subject was resting on a mattress for 5 min, with the room temperature conditioned at 26 °C. In the second stage, the subject was instructed to immerse his/her left hand into 10 °C cold water for 3 min, in order to produce vasoconstriction and to elevate the blood pressure. In the third stage, the subject took his/her hand out of the water and rested for another 5 min. During the experiment, the subject was asked to keep as still as possible to reduce random noise and motion artifacts.

The total collected data include PPG signals and beat-to-beat blood pressures of 70 subjects, 676–1297 heartbeats for each subject, with systolic, diastolic, and mean blood pressure in the range of 85–175 mmHg, 48–117 mmHg, and 64–147 mmHg, respectively. The average change occurred by the cold pressor among all subjects were 48 mmHg, 37 mmHg, and 42 mmHg for systolic, diastolic, and mean blood pressure, respectively.

**C. NORMALIZATION OF PPG WAVEFORM**

All data were processed offline in Matlab (The Mathworks Inc., Natick, MA, USA). The PPG signals were first filtered by a Butterworth low-pass filter with a cutoff frequency of 15 Hz to reduce high-frequency noise, and then were filtered by a Butterworth high-pass filter with a cutoff frequency of 0.45 Hz to remove the low-frequency wandering. The filtered signals are shown in Fig. 4a.

A coarse to fine algorithm were applied to detect the peaks and valleys in the PPG signals [45]. We first found coarse peaks and valleys in the distorted PPG signals that were filtered by a band-pass filter of 0.45 - 2 Hz, in which the dicrotic notches and dicrotic peaks were removed (shown in Fig. 4b). Next, we found the maxima or minima in the neighborhood of the coarse peaks or valleys in the filtered signals to refine the locations (shown in Fig. 4c). The PPG signals were then split by the valleys and the pulse waveform for each heartbeat was obtained. The pulse waveform was then normalized both with respect to time and to amplitude so that all waveforms had the same length and the same amplitude. As most machine learning algorithms
required the input vector of the same length, normalization in time uniformed original waveforms of different temporal lengths, thus suitable as machine learning inputs. Also, as the amplitude was mainly affected by the amplifiers of the data acquisition system, normalization of amplitude reduced the effect of the amplifiers and uniformed all the data. Both normalization in time and amplitude were linear stretching transformation, which kept the main morphology of PPG waveforms unchanged.

The normalization procedure is shown in Fig. 5. A starting point was defined as 10% the height of the upslope above the preceding valley. An end point was defined as 10% the height of the downslope above the following valley. The pulse wave of interest was selected as the signals between the starting point and the end point to avoid the long tail effects near the valley points, and it was then re-sampled to 50 points using spline interpolation. Next, the baseline, which was defined as the straight line from the starting point to the end point, was subtracted and the amplitude was normalized to [0, 1]. Finally, all the normalized pulse waveforms had 50 sample points with amplitudes in [0, 1].

During the normalization, some outliers must be removed. We treated a pulse waveform as an outlier if it met one of the following criteria: (1) The temporal length of the pulse waveform was more than 1.5 times the heart period or less than half of the heart period, where the heart period was estimated as the total duration of the PPG signal for each subject divided by the number of total detected valleys; (2) the height difference between the starting point and the end point was larger than 1/3 the height of the upslope or downslope, as too large variation in the baseline was deemed to be non-stationary; and (3) the pulse waveform was apparently corrupted by artifacts or large noise amplitude, for example, when the subject spoke or coughed, in which case the part of the pulse waveform that was obviously affected was manually removed.

D. SUPPORT VECTOR REGRESSION

The normalized pulse waveforms were then regressed with the systolic, diastolic, and mean blood pressure using an SVM. The SVM is a popular machine learning method for classification and regression. It can solve the convex optimization problem of regression, which is defined below [46]:

\[
\text{minimize} \quad \frac{1}{2} \|w\|^2 \\
\text{subject to} \quad \begin{cases} 
\gamma_i - \langle w, x_i \rangle - b \leq \epsilon \\
\langle w, x_i \rangle + b - \gamma_i \leq \epsilon 
\end{cases}
\]

where in this case \(x_i\) is the feature vector of the normalized pulse waveform, \(y_i\) is the target value of systolic, diastolic or mean blood pressure, \(w\) is the weight vector, \(b\) is the intercept, \(\langle w, x_i \rangle + b\) is the prediction value for the feature vector \(x_i\), and \(\epsilon\) is a threshold of the deviation.

The SVM is based on the inductive principle of structural risk minimization. It can efficiently perform a nonlinear classification or regression by implicitly mapping their input feature vectors into higher dimensional spaces using a kernel function, such as the linear function, the polynomial function, the radial basis function (RBF), and the sigmoid function:

- linear: \(K(x_i, x_j) = x_i^T x_j\)
- polynomial: \(K(x_i, x_j) = (\gamma x_i^T x_j + r)^d, \gamma > 0\)
- RBF: \(K(x_i, x_j) = \exp(-\gamma \|x_i - x_j\|^2), \gamma > 0\)
- sigmoid: \(K(x_i, x_j) = \tanh(\gamma x_i^T x_j + r)\)

where \(\gamma, r, d\) are kernel parameters. Compared to other machine learning algorithms, SVM has solid mathematics foundation and good generalization performance [47]. It runs faster by using the kernel function and does not require a very large dataset for training, rendering it especially suitable for biomedical applications of small sample sizes.

The LIBSVM package developed by C.-C. Chang and C.-J. Lin [48] was employed for SVM training and testing. The RBF kernel was chosen for the regression of the normalized pulse waveforms and the blood pressure, because it is widely used and has good performance for a variety of data characteristics. The penalty parameter \(C\) and the RBF parameter \(\gamma\) for each subject were optimized through grid searching. As there were no test data, the 10-fold cross-validation was used to test the accuracy of the regression model. For each subject, the data were divided into 10 subsets of equal size, in which nine subsets were used for training the regression model and the remaining one was used for testing the accuracy of the model, and then this process was repeated 10 times so that each instance in the whole dataset was tested exactly once.

E. STATISTICAL ANALYSIS

For each subject, the predicted values using the SVM regression were compared with the reference values measured by the Finometer device. Pearson correlation coefficient (CC), root-mean-square error (RMSE), mean error (ME) and standard deviation (SD) of errors were calculated as:

\[
CC = \frac{\sum_{i=1}^{n} (x_i - \bar{x})(y_i - \bar{y})}{\sqrt{\sum_{i=1}^{n} (x_i - \bar{x})^2 \sqrt{\sum_{i=1}^{n} (y_i - \bar{y})^2}}
\]

FIGURE 5. Normalization of the pulse waveform for each heartbeat. (a) Definition of the starting point, the end point and the baseline. (b) Normalized pulse waveform of 50 sample points with amplitudes in [0, 1].
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FIGURE 6. Morphological changes of photoplethysmograms when the blood pressure was elevated by cold stimulus. (a and c) Normalized pulse waveforms with systolic blood pressure increasing in two different subjects. At each x-point of blood pressure, the corresponding y-axis column presents the pulse waveform whose amplitude was indicated by color. (b and d) Normalized pulse waveforms at different blood pressure levels in the corresponding subject in a and c.

RMSE = \sqrt{\frac{1}{n-1} \sum_{i=1}^{n} (y_i - x_i)^2} \tag{7}

ME = \frac{1}{n} \sum_{i=1}^{n} (y_i - x_i) \tag{8}

SD = \sqrt{\frac{1}{n-1} \sum_{i=1}^{n} (y_i - x_i - ME)^2} \tag{9}

where \( y \) is the predicted value, \( x \) is the reference value and \( n \) is the number of samples.

III. RESULTS
A. TYPICAL EXAMPLES

The morphological changes of PPG signals during the cold pressor test are shown in Fig. 6. In Fig. 6a and 6c, when the blood pressure was increasing, the peak of the normalized pulse waveform was becoming wider (the red part) and the dicrotic peak was moving higher (from blue to green in Fig. 6a and from green to yellow in Fig. 6c). In Fig. 6b and 6d, when the blood pressure was elevated by the cold stimulus, the peak was broadened and the dicrotic peak was raised. According to Dawber et al.'s classification mentioned above [40], in Fig. 6b, the pulse wave at 120 mmHg was graded in Class 1 with a distinct notch clearly seen, and it shifted to Class 2 with a horizontal line on the downslope when the blood pressure was increased to 150 mmHg. In Fig. 6d, the pulse wave at 110 mmHg was graded in Class 2 with a horizontal line, and it shifted to Class 3 with only a changed angle of descent when the blood pressure was increased to 140 mmHg. These results showed that it was feasible to estimate blood pressure directly from the morphology of PPG signals.

B. STATISTICAL ANALYSIS FOR ALL SUBJECTS

The CC, RMSE, ME and SD parameters for each subject were presented in Fig. 9. As shown in Fig. 9a, most of the CCs were larger than 0.5, which means that the predicted values and reference values had close correlations for most subjects. In Fig. 9b, all the RMSEs were less than 8 mmHg except for 3 subjects, indicating that the predicted values were very close to the reference values. In Fig. 9c, the MEs were less than 1 mmHg and approximately zero, which means that the predicted values were almost unbiased to the reference values. In Fig. 9d, most of the SDs were less than 8 mmHg except for the systolic blood pressure in 3 subjects, which indicates that the variations of the errors were sufficiently small.

A typical example of the blood pressure estimation was given in Fig. 7 and Fig. 8. It is shown in Fig. 7 that during the cold pressor test, the predicted values of the systolic, diastolic, and mean blood pressure using the SVM regression well followed the corresponding reference values measured by the Finometer, which indicated that they had close correlations. The correlations were more clearly seen in Fig. 8, where the scatter data were very close to the regression line and the correlation coefficients between the predicted values and the reference values were 0.910, 0.886, and 0.921 for systolic, diastolic, and mean blood pressure, respectively.

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FIGURE 9. Comparison of predicted values and reference values across 70 subjects. (a) Correlation coefficients (CC). The presented data were all statistically significant ($p < 0.05$). (b) Root-mean-square error (RMSE). (c) Mean error (ME). (d) Standard deviation (SD) of errors. SBP, systolic blood pressure; DBP, diastolic blood pressure; MBP, mean blood pressure.

TABLE 1. Distributions of the statistical parameters among all the subjects.

| Parameter        | Maximum | Median | Minimum | Mean |
|------------------|---------|--------|---------|------|
| CC$_{cor}$       | 0.999   | 0.794  | 0.316   | 0.748|
| CC$_{con}$       | 0.952   | 0.780  | 0.291   | 0.754|
| CC$_{cmp}$       | 0.956   | 0.816  | 0.354   | 0.775|
| RMSE$_{corr}$(mmHg) | 9.662  | 4.758  | 2.522   | 5.001|
| RMSE$_{corr}$(mmHg) | 7.302  | 3.441  | 2.457   | 3.688|
| RMSE$_{corr}$(mmHg) | 7.737  | 3.964  | 2.355   | 4.139|
| ME$_{corr}$(mmHg) | 0.426   | 0.026  | -0.334  | 0.043|
| ME$_{corr}$(mmHg) | 0.367   | -0.007 | -0.234  | 0.011|
| SD$_{corr}$(mmHg) | 9.664   | 4.758  | 2.523   | 5.001|
| SD$_{corr}$(mmHg) | 7.306   | 3.442  | 2.458   | 3.689|
| SD$_{corr}$(mmHg) | 7.743   | 3.961  | 2.356   | 4.140|

CC, Pearson correlation coefficient; RMSE, root-mean-square error; ME, mean error; SD, standard deviation. SBP, systolic blood pressure; DBP, diastolic blood pressure; MBP, mean blood pressure.

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IV. DISCUSSIONS

We demonstrated the estimation of blood pressure directly from the morphology of PPG. The proposed method requires only a commercial oximeter for PPG acquisition, thus eliminating (1) the requirement of the inflatable cuff in traditional sphygmomanometers and (2) the assistance from other cardiovascular signals such as the ECG. These simplifications bring user convenience, enabling long-term monitoring of blood pressure out of the hospital. Furthermore, this method can be easily extended to wearable medical devices such as armbands [49], earphones [12] and mattresses [50], where the oximeter can be embedded thus does not interfere with user activities.

Another advantage of the proposed method is that it avoids the detection of complicated characteristic points of the dicrotic peak and the dicrotic notch as compared to the aforementioned non-PTT methods. The difficulty of non-PTT methods are that (1) characteristic points may be wrongly detected when the PPG signals are corrupted by noise or artifacts, and (2) they are barely detectable when the dicrotic notch is indistinguishable from the peak [51]. Instead, the proposed method directly uses the morphology of the PPG, and the blood pressure was determined by all the 50 points of the normalized pulse waveform. Therefore, the proposed method is more robust to noise, hence providing improved accuracy.

Several limitations and technical concerns should be taken into account. (1) Training. In the current experimental design, the training phase involves the use of cold stimulus to elevate the blood pressure, which is not suitable for cardiovascular patients, due to the potential risk of strokes or heart attacks. Cold stimulus can be replaced by a safer and more convenient procedure such as hand elevation [52]. However, as is reported that various activities such as isometric exercise and isotonic exercise caused different patterns in blood pressure change [53], whether the proposed method is applicable to other physiological procedures would require further investigation. (2) Individual variations. We built an SVM model for each subject and there were 70 models in total for all the subjects. Therefore, the model for one subject cannot be applied to another. We have also tried to build a generalized model for all the subjects but the results are not good. We attributed the difficulty to the large individual variations. As different subjects may have different hemodynamic responses during the cold pressor test [54], it is almost impossible to describe all the subjects using only one model. An alternative is to build a group of models for specific ages, genders, and blood pressure levels, which might minimize the influence of individual characteristics. (3) Drawbacks of normalization. Normalization in time and amplitude preserves the PPG morphology but reduced the influence of the amplitude and the heart rate, which may contain useful information of the cardiovascular system. This information was eliminated when the PPG waveform was normalized. Additionally, the filters in the normalization process may affect the PPG morphology, and those filters we used were empirical ones that would lead to the shown performance. (4) Application conditions. In PTT-based method, it is reported that the regression models obtained half a year ago could not predict blood pressure well with reasonable accuracy in all subjects [55]. The proposed method may have the same problem, because the PPG morphology is not only affected by the blood pressure but also the arterial stiffness and the vascular resistance. In the short term, the arterial stiffness and the vascular resistance can be regarded as constant. Therefore, it is sufficient to assume that the PPG morphology is closely correlated with systolic, diastolic, and mean blood pressure, respectively. These results are very close to the specifications defined by the American Association for the Advancement of Medical Instrumentation (AAMI) that the ME should be within ±5 mmHg and the SD should be less than 8 mmHg. These results suggested that the proposed method has great potential to provide accurate blood pressure estimation.
the blood pressure. The proposed method indeed provides an accurate estimation. In the long term, the arterial stiffness and the vascular resistance may vary and should be taken into consideration. Therefore, the proposed method cannot be extended to long-term monitoring of blood pressure, which intermittent calibration can be a solution. (5) Computational load. In the current implementation, the SVM algorithm is processed offline on a personal computer. It may be difficult to implement them on a portable or wearable device for real-time prediction, where the computing power and internal memories are limited. However, this is not envisioned to be an issue as smart devices advances in computational power.

V. CONCLUSION
In this paper, we propose a new method to estimate blood pressure directly from the morphology of the PPG signals, avoiding detection of complicated characteristic points and extraction of PPG features. This method is capable of continuously estimating blood pressure using a commercial pulse oximeter, without an inflatable cuff or other auxiliary signals. A 70-healthy-subject experiment shows that the estimated blood pressures were highly correlated with the reference from the commercial device. The mean correlation coefficients were 0.748, 0.754, and 0.775 for systolic, diastolic, and mean blood pressures, respectively. The mean errors were 0.043 mmHg, 0.011 mmHg, and 0.008 mmHg, with standard deviations of 5.001 mmHg, 3.689 mmHg, and 4.140 mmHg for systolic, diastolic, and mean blood pressures, respectively. Since the proposed design is inexpensive and simultaneously comfortable to the user, it provides a highly desirable approach to the implementation of wearable devices for home healthcare blood pressure monitoring applications.

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