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A review of machine learning techniques in photoplethysmography for the non-invasive cuff-less measurement of blood pressure

C. El-Hajj*, P.A. Kyriacou

Research Centre for Biomedical Engineering, City, University of London, Northampton Square, EC1V 0HB, London, United Kingdom

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ABSTRACT

Hypertension or high blood pressure is a leading cause of death throughout the world and a critical factor for increasing the risk of serious diseases, including cardiovascular diseases such as stroke and heart failure. Blood pressure is a primary vital sign that must be monitored regularly for the early detection, prevention and treatment of cardiovascular diseases. Traditional blood pressure measurement techniques are either invasive or cuff-based, which are impractical, intermittent, and uncomfortable for patients. Over the past few decades, several indirect approaches using photoplethysmogram (PPG) have been investigated, namely, pulse transit time, pulse wave velocity, pulse arrival time and pulse wave analysis, in an effort to utilise PPG for estimating blood pressure. Recent advancements in signal processing techniques, including machine learning and artificial intelligence, have also opened up exciting new horizons for PPG-based cuff less and continuous monitoring of blood pressure. Such a device will have a significant and transformative impact in monitoring patients' vital signs, especially those at risk of cardiovascular disease. This paper provides a comprehensive review for non-invasive cuff-less blood pressure estimation using the PPG approach along with their challenges and limitations.

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1. Introduction

Hypertension or high blood pressure (BP) is a leading cause of death throughout the world and a critical factor for increasing the risk of serious diseases, including cardiovascular diseases such as stroke and heart failure, as well as kidney diseases [1]. Hence, BP is a vital sign that must be monitored regularly for early detection, prevention and treatment of cardiovascular diseases in order to avoid further serious complications. However, only one-third of the hypertensive population have their BP under control [2]. This is due to the lack of availability and accessibility for reliable and continuous BP monitoring systems. When systolic BP is above 140 mmHg or diastolic BP is above 90 mmHg, it is called hypertension, and such undesirable blood pressures can damage internal body organs when left untreated [3].

In current clinical practice, BP is measured either invasively using catheterisation or non-invasively using cuff-based methods. The invasive method works by inserting a catheter incorporating a blood pressure sensor directly into the blood vessel or heart to measure the arterial pressure. BP measured invasively is continuous in nature and the most accurate, hence it is recognised as

* Corresponding author.
E-mail address: chadi.el-hajj@city.ac.uk (C. El-Hajj).

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the gold standard for blood pressure measurement internationally [4]. However, this method is severely invasive, carries multiple risks such as infection, bleeding and only applicable for critically ill patients in hospitals, primarily used during surgical procedures and in intensive care units [4,5]. The standard BP measurements in clinical practice are non-invasive cuff-based using either oscillometric or auscultatory techniques [6,7]. Cuff-based methods provide BP measurements without any major side effects as opposed to BP measured invasively. However, these devices use a cuff attached to the arm which can only measure BP intermittently with intervals between measurements greater than at least two minutes. These devices are too cumbersome to wear during measurements. Patients will feel uncomfortable with long term monitoring due to the painful cuff inflation which interrupts the regular blood flow. Consequently, current clinical BP measurement techniques are not suitable for continuous ambulatory BP monitoring.

Recently, BP measurements using the photoplethysmogram (PPG) has shown a lot of promise. The PPG approach allows for the estimation of BP non-invasively by observing two waveforms obtained from signals such as two PPG signals from two anatomical locations or a combination between a PPG signal and the electrocardiogram (ECG). Previous studies have reported an inverse correlation between BP and pulse transit time (PTT) [8–10]. PTT based approach has been studied extensively in the past decades with mounting evidence that it can provide cuff-less non-invasive BP measurements. PTT is the time delay for the pressure waveform to travel between two arterial sites [10]. Pulse arrival time (PAT) is another popular approach, PAT can be defined as the time difference between the R-peak of the ECG signal and the peak of the PPG signal when measured within the same cardiac cycle [11]. Another approach for estimating BP is pulse wave velocity (PWV) [12]. PWV calculates the velocity of the pulse wave using two PPG sensors located on the same arterial branch with a known distance apart. Once PTT, PAT or PWV parameters are estimated, BP can be derived through mathematical models. While these models represent well-known approaches for cuff-less non-invasive BP monitoring, their implementations pose several challenges, and hence none of these techniques has been established as a reliable clinical tool for measuring BP. These methods require two measurements from two (synchronised) sensors which can be inconvenient and not practical for patients. Also, these sensors might have different sampling rates in real-time, plus their operability depends on rather complicated arterial wave propagation models. More importantly, for continuous measurement of BP, these methods need constant calibration - due to different physiological parameters for individuals or patient/probe movement- which make it undesirable. Even with per-person calibration, these models can only provide BP estimation for a short period of time and are still not reliable indicators for beat-to-beat BP.

Given the recent technological advancements in signal processing techniques, and the rise of machine learning, numerous research groups around the world have recognised the remarkable potential that these algorithms can bring to the healthcare industry for improving patient's wellbeing. As such, there have been a lot of interest, evident in the literature, for utilising machine learning and neural networks algorithms for providing non-invasive cuff-less and continuous BP measurements. Many different BP estimation models have been established using machine learning techniques instead of deriving BP mathematically. Specifically, these machine learning BP models are based on PTT, PAT and PWV parameters, however, in this case BP estimation is data driven. The purpose of all these efforts is to enhance BP estimation accuracy. Even though some progress has been made, more work is surely needed to best realise these approaches.

One innovative approach that has recently emerged for cuff-less, continuous and calibration-free BP measurement is pulse wave analysis (PWA). In PWA, temporal features are extracted from the PPG waveform. Many temporal features show good correlation with the BP of an individual [13]. This approach provides optical BP with only one PPG sensor, hence it has significant advantages over the previous approaches. Firstly, the PPG technology used for such applications is relatively simple and inexpensive, plus the acquisition of the PPG signals is straight forward, assuming that the sensor is placed on a vascular tissue. Secondly, the BP pulse waveform has resemblance to PPG blood volume pulse. BP estimation using this approach is also data driven. Linear and non-linear machine learning algorithms have been employed over recent years. There are increasing evidence in the literature that PPG-based models can provide cuff-less and continuous BP measurement. The objective of this paper is to review PPG based models for cuff-less BP measurement utilising machine learning. The paper is structured as follows. We first begin by providing a brief description for existing non-invasive cuff-less BP measurement techniques. We then provide a summary for most of the BP machine learning based models available in the literature and their limitations. This is followed by a discussion of the work done so far and their challenges. We conclude by providing some suggestions for future research directions in this field.

2. Existing non-invasive cuff-less BP methods

Over the past several decays, many research groups across the world have devoted a lot of time and considerable effort to provide non-invasive cuff-less and continuous BP monitoring. The motivation behind this work is to replace the current cuff-based BP devices. Cuff-based devices often need a trained personal, and they can cause irritation and inconvenience for patients due to cuff inflation and deflation. Cuff-based methods do not provide continuous BP measurements and are sometimes inaccurate. Consequently, current clinical cuff-based BP devices are not suitable for providing continuous BP monitoring which could play a significant role in the early detection of cardiovascular diseases amongst many other applications.

One way to overcome these difficulties is the photoplethysmography approach. PPG is a non-invasive optical technique for measuring the blood volume changes per pulse [14]. PPG has a widespread application in health care used for making predictions for vital health related parameters. For instance, PPG has been used for determining heart rate, atrial stiffness, blood oxygen saturation, and blood glucose levels [14] as well as measuring BP [27,32,43]. There are two different modes for recording the PPG signal namely transmission and reflectance. The PPG sensor consists of two components: a Light Emitting Diode (LED) to illuminate the skin surface and a photodetector for measuring the changes in light absorption over a period of time. The high frequency part of the PPG signal, also known as 'AC' component, contain information regarding heart pulsation. The 'AC' component is superimposed onto a large non-pulsating lower frequency part known as 'DC' components affect by various factors such as respiration, absorption from non-vascular tissue, and sympathetic nervous system activity [14]. As mentioned previously, the PPG is employed to extract several parameters that are used for the estimation of BP. The remainder of this section will explore these parameters and the sensors needed for measurements along with their implementation challenges and limitations.

2.1. Pulse transit time

One approach for cuff-less non-invasive BP measurement is PTT. PTT is defined as the time that takes the pressure wave to travel between two arterial sites [10]. There is an inverse proportional

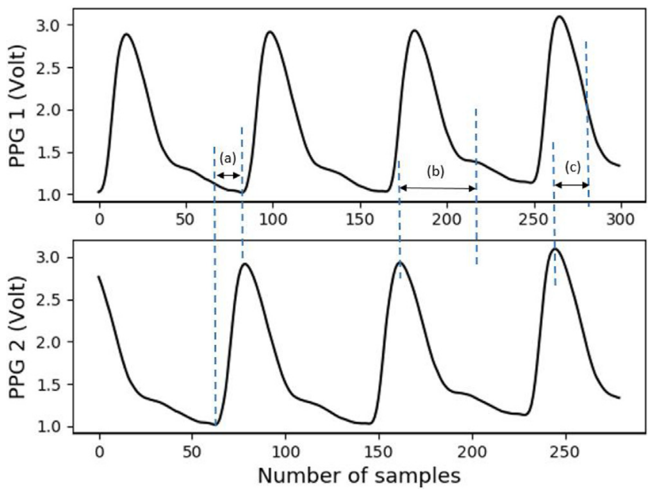

Fig. 1. Different PTT measurement points between two PPGs. (a) foot-to-foot time delay, (b) peak-to-dicrotic notch time delay, and (c) peak to mid-point of the falling edge time delay.

relationship often found between PTT and BP. PTT can be measured using two PPG sensors located on two distant sites in the body. The parameter is estimated as the time delay between the proximal and distal PPG waveforms. It should be noted that many papers in the literature refer to pulse arrival time as PTT, however, PTT is hardly investigated [11,15]. The most common sites for PTT measurements are fingers, ears and toes [16]. Different measurement points have been investigated in the literature. For example, Chen et al. [17] found that there is a strong relationship between PTT measured as foot-to-foot time delay and invasive Diastolic Blood Pressure (DBP), however, another study suggested that is not always the case [18]. PTT can also be measured as the time difference from mid-point of the falling edge of the proximal PPG to the peak of the peripheral PPG or as the time difference from dicrotic notch of the proximal PPG and the peak of the peripheral PPG [19], as shown in Fig. 1.

BP measurements using the PTT based approach typically involves three steps: two PPG sensors for measuring proximal and distal PPG waveforms, calculation of the PTT parameter, and calibration. Hence, there are several obvious disadvantages when using the PTT approach for estimating BP. Firstly, two sensors are needed for the estimation. PPG sensors are very sensitive to patient/probe movement which results in motion artefacts in the waveforms [14]. Consequently, signal processing needs to be done on both waveforms for smoothing and motion artefacts removal etc., whilst keeping the recordings in sync. Additionally, it is affected by physiological parameters of individuals and thus requires per person calibration [10].

2.2. Pulse arrival time

Pulse arrival time (PAT) is defined as the time interval between the electrical activation of the heart and arrival of the pulse wave at a location on the body like the finger, toe, and forehead. In other words, PAT is the sum of PTT in addition to the ventricular electromechanical delay and isovolumic contraction period, commonly known as Pre-ejection Period (PEP) delay [10]. PEP can be influenced by stress, age, emotion, and movement. PAT is measured using two sensors, an ECG and a PPG sensor. PAT parameter is estimated as the time difference between the R peak of the ECG and a point on the PPG rising edge [10]. Three characteristic points on the PPG waveform have been considered to calculate the time delay such as the foot of the PPG [20], mid-point on the rising edge [21] and peak of the PPG [22], as shown in Fig. 2. Although it was found that PAT can reduce the diastolic pressure accuracy [23], it is still used in the literature for its simplicity. Some studies show that PAT is an inadequate surrogate for PTT for systolic and diastolic blood pressure [24], however, others suggest that PAT improves Systolic Blood Pressure (SBP) [25]. This method shares the same disadvantages mentioned in the PTT section. For instance, PAT is measured using two different sensors, ECG and PPG with different sampling rate. Both sensors are prone to motion artefacts and require signal processing which is not straight forward especially if the continuous monitoring of blood pressure, and the intermittent measurement is desirable. PAT also requires calibration for different individuals.

2.3. Pulse wave velocity

Another cuff-less method for BP estimation is pulse wave velocity. PWV is the speed of the pressure wave propagation in the blood vessels which is based on the theory of wave propagation for fluids in elastic pipes. The motivation behind this approach is that BP can be determined from the velocity of the heartbeat pulse. The heart initiates the pressure pulse, in turn the blood is pushed or propagates through central arteries down to smaller distal arteries by expanding and contracting during systole and diastole respectively [26]. This phenomena results in the changes of the vessels wall elasticity and highly affects the velocity of the pressure pulse. Particularly, the elasticity of the arteries determines the speed at which the pulse wave travels [11]. This relationship can be illustrated using Moens-Kortweg equation [12].

PWV is measured using two PPG sensors located on the same arterial branch with a known distance apart. PWV can be obtained by dividing the artery length (D) between the two references by pulse transit time (PTT) as follows:

$$PWV = \frac{D}{PTT}$$

For example, McCombie et al. [12] took advantage of the relationship between BP and vessels elasticity to derive BP through PWV approach using two PPG signals. The artery length is measured as a distance, while the PTT is measured as the time difference for the pressure wave to travel from the previous PPG sensor to the leading PPG sensor. This method is difficult to perform non-invasively as several challenges occur during the calculation of PWV. It requires two measurements from two sensors. The arterial elasticity varies between individuals and is highly dependent on factors such as age, diet, etc. The length of the artery mandatory for the equation above also varies from one person to another. Therefore, it requires frequent calibration due to different physiological parameters between individuals as well as the expiration of the calibration in a short period of time [37]. This concern is the bottleneck preventing PWV from being used in health care. Calibration procedures are not permitted by health care standards [44]. Hence, PWV is not a practical nor suitable replacement for cuff-based BP devices.

2.4. Pulse wave analysis

Pulse Wave Analysis (PWA) refers to signal processing and extractions for certain characteristic features from the PPG waveform. This method requires only one measurement sensor, the PPG. Development in computing and data analysis tools have made it easier to pre- and post-process physiological signals such as the PPG and ECG. Signal processing like filtering and feature extraction have been employed in PPG pulse wave analysis. These features are typically used for creating models using machine learning and deep neural networks for estimation of blood pressure. Several studies have investigated the feasibility of cuff-less and continuous BP predictions using only one PPG sensor [27,30–32,43]. This

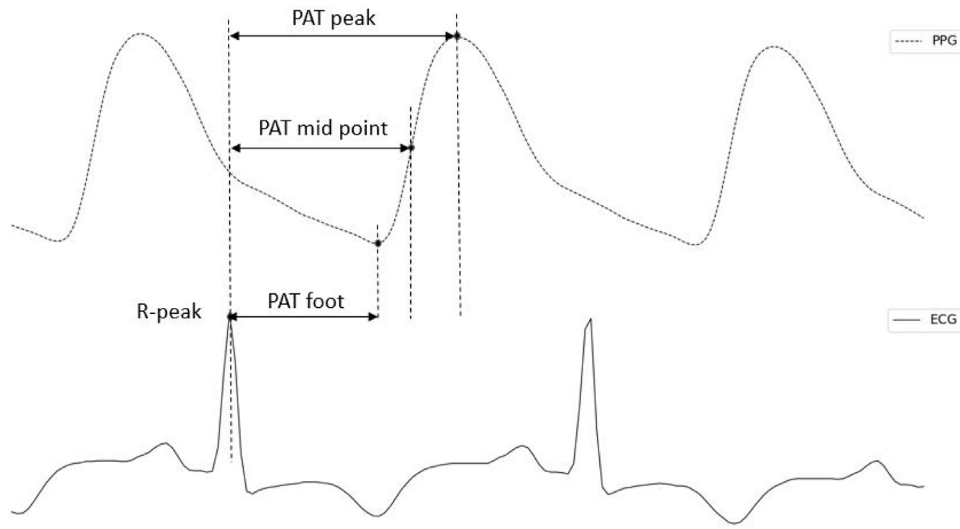

Fig. 2. PAT measurement points, from R-peak of the ECG to foot, mid-point on the rising edge and peak of the PPG.

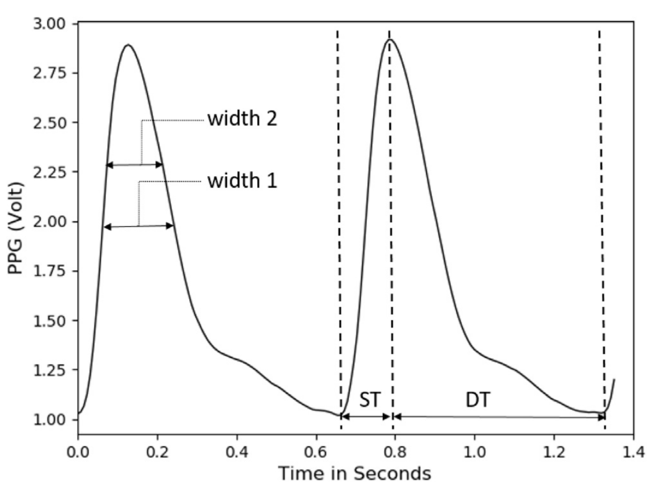

Fig. 3. Four PPG features: Systolic upstroke Time (ST), Diastolic Time (DT), width 1 refers to width at ½ amplitude and width 2 refers to width at 2/3 amplitude.

approach is very promising and appealing as it offers simple and accurate cuff-less BP estimation. The main disadvantages attached to this approach is that, the PPG is prone to motion artefacts due to movements, and the relationship between the BP and the PPG waveform is not fully understood [13]. Hence, more research is certainly needed to better understand this approach.

2.5. BP-PPG based estimation using machine learning

The idea to measure BP using only PPG signals was investigated by Teng and Zhang [27]. In their study, the relationship between arterial BP and four PPG features were evaluated using a linear regression model. The authors collected their own PPG and BP signals from 15 healthy male subjects aged 24-30. The features selected from the PPG signals were: width at 1/2 and 2/3 amplitude, systolic upstroke time and diastolic time, shown in Fig. 3. Two challenges were reported in the process of extracting these features. In some PPG signals, they have experienced a shift in the foot position and in other signals the foot position was not clear due to poor signal recording. It is crucial for the position of the peak and foot to be clear and consistent for extracting the correct feature values. Consequently, Continuous Wavelet Tranform (CWT) was employed to overcome the two aforementioned challenges. Additionally, the correlation between the extracted features and BP values were evaluated, and only features with the highest correlation to BP were selected for regression analysis. It was found that the diastolic time has a higher correlation with Systolic blood pressure (SBP) and diastolic blood pressure (DBP) than other features. The mean error and standard deviation between the estimated BP values and the reference BP values were 0.21 ± 7.32 mmHg and 0.02 ± 4.39 mmHg for SBP and DBP respectively. According to the American National Standards of the Association for the Advancement of Medical Instrumentation (AAMI), the mean difference and standard deviation of non-invasive BP should not exceed 5 ± 8 mmHg from a reference BP evaluated on no less than 85 patients. However, the relationship between BP and PPG is not always linear [32,47], and this study was conducted on 15 young healthy all male volunteers. This suggests that there is a low variability in terms of BP range between volunteers which may explain the reason behind the low estimation error using a linear model. Moreover, estimating SBP and DBP using classical machine learning methods requires two different models, one for each objective. In this case, DBP and SBP were strongly correlated [50], thus learning both objectives using one model structure would further improve the estimation by learning shared data representations. This can be achieved using neural network for estimating both SBP and DBP simultaneously using one model. In 2008, Hassan et al. [28] derived a regression model for estimating only SBP based on PTT method without the need for calibration for every individual subject. In their study, PPG and ECG signals were collected from 10 healthy subjects with BP reference values measured by a sphygmomanometer with a cuff attached to the subject's right arm. The peripheral pressure pulses were measured at the fingertip using a PPG sensor. Both PPG and ECG were recorded simultaneously for 45 s sampled at 1 kHz using AD instruments followed by the calculation of the PTT values. Regression models were then established for each subject then combined together to get a new regression estimation model that fits all subjects. Subsequently, the average of the slope values from all individual regression models becomes the new reference slope for the new regression model. The results were below 5 ± 8 mmHg error rate set by the AAMI but evaluated on a very small dataset of 10 all male subjects while the AAMI requires at least 85. Having a diverse range of BP values that truly represent the population (males and females from different age range) would increase model generalisation for accurate BP monitoring. PPG features have also been proved to correlate favourably with BP [13,27], thus including PPG features would improve the model's generalisation. The linear model performed relatively well given the linear relationship between PTT and BP when evaluated on this dataset. However, this model does not account for the temporal variation in the extracted features which should be modelled for continuous, accurate, and well generalised BP prediction. A simple non-recurrent model only considers the relevant features and with no feedback loop from previous cycles. This can be attained using recurrent neural network represented by a recurrent link passing information learnt from previous time steps along with the present input features for estimating BP values.

Wong et al. [29] investigated the correlation between BP and PTT under different circumstances i.e. pre-exercise, post-exercise etc. In this study, the model was evaluated on 14 normotensive subjects with no history of cardiovascular disease using least-square regression. The authors designed an in-house circuitry to detect the derivative of the ECG (dECG) and PPG. The dECG and PPG were sampled by an analogue to digital converter (ADC) at 1 kHz and brachial BP was recorded intermittently on the subject's right arm with an automatic BP monitor. Beat-to-beat PTT parameter was calculated from the peak of the dECG to the peak of the PPG derivative. Two tests were carried out using the same model coefficient six months apart. The least square model from their first experiment was applied with the same coefficient half a year later to predict BP of a different pressure baseline. The results show that arterial BP increased and PTT decreased sharply after exercise and there is a high correlation between SBP and PTT. However, the regression coefficient obtained from the first study (6 months before) failed to predict BP well in all subjects when the blood pressure values changed in the second experiment. The mean error and standard deviation resulted from the aforementioned experiment were 1.4 $\pm$ 10.2 mmHg for SBP and 2.1 $\pm$ 7.3 mmHg for DBP. This drawback is due to the fact that PTT requires calibration when the blood pressure baseline changes between different subjects. Additionally, the least-square regression cannot estimate both SBP and DBP simultaneously and requires implementing two different models to learn each objective separately. As mentioned previously, these two objectives are correlated and thus should be estimated using one model to improve the estimation precision. Also, this technique requires two sensors for measuring the PTT parameters. It has been shown in the literature that the PTT parameters expire one day after the initial calibration which in turn would increase the estimation error [45]. For all these reasons, this technique is not reliable for long term continuous BP monitoring. Suzuki and Oguri (2009) [30] presented a technique for measuring SBP using only a PPG sensor. In their study, SBP was estimated using error-correcting output coding method based on an aggregation of AdaBoost as a binary classifier machine. This method was evaluated on 368 volunteers. Individual information and characteristic features from their PPG waveform were used to calculate BP. The reference BP values were measured every minute with a cuff placed on the right brachial using a commercial BP device and the PPG signals were measured at the left finger by a commercial sensor. The PPG features selected in this study were percussion wave, tidal wave, dicrotic notch and dicrotic wave. The mean error and standard deviation were 1.2 $\pm$ 11.7 mmHg. Hence, the results were highly variable, did not satisfy the AAMI requirements and could only provide intermittent SBP measurement. Moreover, although AdaBoost is a non-linear function, it is not appropriate for time domain analysis and for handling the complexity of the task, therefore, its accuracy will decrease for multiday BP estimation. Additionally, the feature set is relatively small and should be enhanced further for effectively modelling the relationship between PPG features and BP.

Ruiz-Rodriguez et al. [31] introduced a continuous cuff-less BP monitoring using a deep neural network, namely, Deep Belief Network- Restricted Boltzmann Machine (DBN-RBM). The authors collected their PPG signals through pulse oximetry with reference to invasive BP values. PPG and BP measurement devices were attached to a processing module connected to a General Electric (GE) Datex Ohmeda device. The signals were recorded for a period of 30 min. PPG and BP signals that exhibited anomalies such as overdamping or underdamping phenomena, motion artefacts (due to unexpected patient movement, cough etc.) or extrasystole, were excluted during signal analysis and therefore signal quality were optimal. Each 30 min signals were then segmented into 10 s frames. The neural network model applied in this study, DBN-RBM, belongs to a family of networks that build probabilistic generative models. Values of SBP, MAP, and DBP were obtained through a mathematical algorithm that detects the maximum amplitude of the PPG oscillations. This promising method estimates BP continuously without a cuff and does not necessitate calibration. The advantages of this study is that it can model SBP, MAP and DBP using one structure, thus allowing the model to capture the strong correlation between the three objectives. However, the results of SBP, DBP and mean arterial pressure (MAP) predictions were highly variable which in turn causes the standard deviation to exceed 8 mmHg limit imposed by standards of the AAMI. It was stated that the high variability might be influenced by the respiratory variability in the PPG signals. Also, the PPG processing module significantly affected the results since it changes the shape of the obtained PPG pulse. The results of this study might be improved by providing a feedback link from previous cycles to the input layer to account for the temporal dependencies in the PPG features. In Kurylyak et al. [32], another type of neural network was employed for estimating SBP and DBP using just PPG signals. More than 15,000 heartbeats were analysed from PPG signals extracted from the MIMIC database [33]. This study improves on Teng and Zhang [27] by using 21 temporal features instead four features extracted from a much bigger and more representative dataset (patients under treatments, drugs, elderly etc). A feedforward neural network with 21 input vector was applied to estimate SBP and DBP, these features are shown in Fig. 4. The SBP and DBP results from the neural network outperformed the linear regression method tested on the MIMIC dataset and satisfies the AAMI standards. The results of this study can be enhanced by adding information about the peripheral resistance, arterial stiffness, cardiac output and blood volume that strongly affect BP [13]. Additionally, similar to the previous method used in [31], the feedforward model is not suited for time domain tasks as it is not equipped with a feedback link and a memory to carry information from previous time steps for more accurate predictions. Recurrent neural networks (RNN) are built specifically to handle time domain data by providing a better control for the flow of information much more efficiently for this task and hence is a more appropriate choice for reliable continuous BP monitoring.

Suzuki and Ryu [34] proposed a PPG feature selection method for estimating SBP. The data were acquired using a cuff-based BP device attached to the left upper arm and PPG recording acquired from the index of the right arm from 80 healthy subjects aged between 20–60 years old. Their method uses an orthogonal array and the signal to noise ratio (SNR) obtained from the Taguchi method for selecting PPG features that are robust against noise for multiple regression analysis. After calculating the SNR and an orthogonal array, seven features were selected – from the first and second order derivative of the normalised PPG signal – all with a positive SNR and influence for estimation of BP. It was found that the Taguchi method improved the effectiveness of the feature selection method for estimating SBP at the presence of large individual variability. However, the linear predictive model utilised here shares the same limitation mentioned before, which is not ideal for time series tasks for long term monitoring. Furthermore, this study only estimates SBP from data collected from healthy volunteers which is not optimal for detecting cardiovascular diseases. Therefore, this model is not clinically reliable for continuous BP measurements.

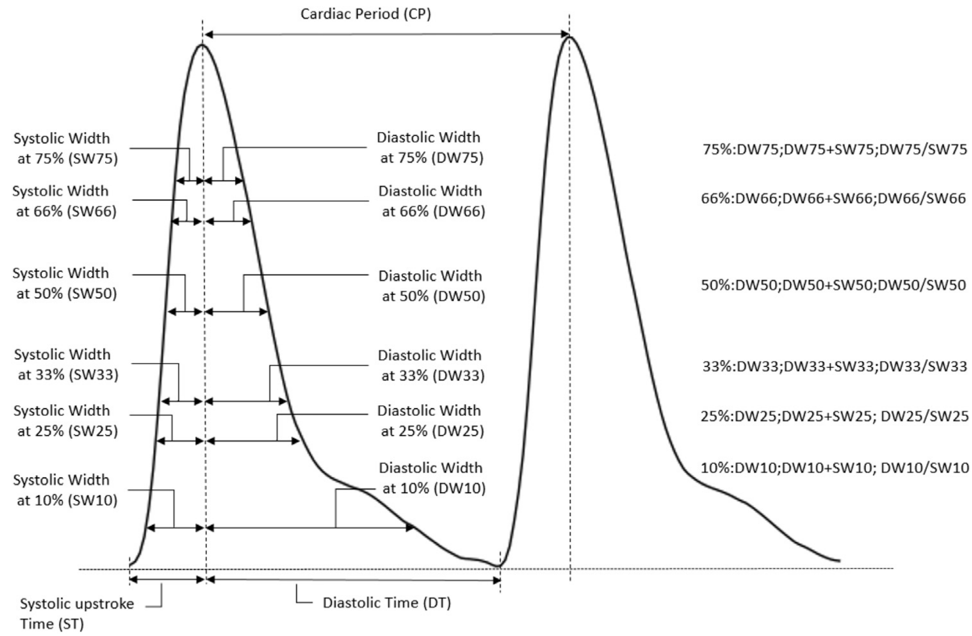

Fig. 4. Potential 21 temporal PPG features for BP estimation.

Choudhury et al. [35] introduced a method that maps PPG features with intermediate patient specific latent parameters which are then used to derive the SBP and DBP values. For this study, PPG and BP signals were extracted from The University of Queensland Vital Signs Dataset. The PPG signals were filtered using a band-pass filter with a cut-off frequency of 0.7 Hz and 3 Hz. Maximal Information Coefficient has been used as feature selection method to reduce the number of feature extracted from each PPG cycle. The final PPG features selected for the regression analysis were: systolic upstroke time, diastolic time, sum of systolic and diastolic width at 33 % and at 75 % amplitude. After feature extraction, outliers were removed from the dataset using a threshold based approach. The Windkessel model has been applied to estimate total peripheral resistance and arterial compliance for individuals followed by a linear regression model for estimating BP values. This method provides non-invasive cuff-less BP values. The estimated error values were below 0.8 for both SBP and DBP, however, their model predictions were highly variable. This caused the standard deviation to be high ± 13.1 mmHg for SBP and ± 10.23 mmHg for DBP. Moreover, this technique could not predict very high or very low BP values and was not validated on a multiday BP dataset for continuous monitoring.

Shen et al. [36] proposed a stepwise regression BP model based on 5 features extracted from ECG and PPG signals for estimating SBP, DBP, and MAP. The PPG, ECG and continuous BP were collected from 10 healthy subjects. The ECG and PPG were collected using a multi-channel physiological instrument sampled at 1 kHz and the BP references were recorded using Finapres (Finapres Medical Systems B.V., Netherlands). All the recordings were done simultaneously for a period of 10 min. Given the high sampling frequency and the recording instrument utilised in the data collection, filtering was not necessary. The feature vector consisted of PTT values, systolic time, diastolic time, PPG area, and ECG time interval of a single cardiac cycle. The mean error and standard deviation were less than 6 ± 6.5 mmHg for all the BP values, evaluated on a very small dataset of 10 healthy volunteers, and thus does not satisfy the AAMI standards. Also, stepwise regression is not the best option for sequential time domain data, especially when continuous BP monitoring is desired since it does not store knowledge learnt from previous cycles. Besides, it requires three different models for predicting SBP, DBP and MAP separately, meaning that it does not capture the strong correlation between them for increasing the BP prediction accuracy. The three objectives, SBP, DBP and MAP, can be estimated in parallel using more advanced models such as neural networks. In 2015, Kachuee et al. [37] proposed a calibration free BP estimation using the PTT approach. The data was acquired from the MIMIC online database. Signal pre-processing was applied to the PPG signals from which several whole base PPG features were extracted and combined with PTT parameters. Signal pre-processing includes: simple averaging filter to smooth the signals, removing signal block with irregular and unacceptable BP and heartrate values, removing signal block exhibiting motion artefacts and calculating PPG signal autocorrelation. In total, ten features were used as input for a regularised linear regression model as well as two non-linear models, namely feedforward neural network and a support vector machine (SVM). Although these methods provide cuff-less, continuous and calibration free BP measurements, it still bears many disadvantages mentioned earlier. It requires two sensors, and their neural network and SVM model do not explicitly model the temporal dependencies in the data resulting in long-term inaccuracy. Moreover, the results for SBP, DBP, and MAP did not meet the AAMI standards. Therefore, further improvement in terms of choices of models and features are surely needed for accurate BP estimation.

Datta et al. [38], used a combination of machine learning and mathematical modelling for calculating SBP and DBP from PPG signals. The authors acquired their own data in an effort to include a wide range of BP values and proof the effectiveness of their noise cleaning techniques. PPG signals were measured from the right hand index finger using a fingertip pulse oximeter sampled at 60 Hz. BP signals on the other hand were recorded using a digital BP monitoring device directly after the PPG signal acquisition. Their proposed method introduces noise cleaning techniques to reduce the noise of the PPG signals. The following processing steps were applied to help reduce the noise in the PPG signals: mean subtraction normalising the PPG signals, band-pass filter to remove low and high frequency respiratory movement and jitters respectively, baseline correction to bring the end cycles to same level, topline correction for removing random fluctuations in the signal amplitudes and finally cycle selection. After processing, the most relevant PPG features were selected, namely: age, weight, systolic upstroke time, systolic area, time between cycle onset to dicrotic notch, width at 50 % and 75 % amplitude. Subsequently, the latent parameters of the Windkessel were modified based on those PPG features. A linear regression model was applied for estimating the latent parameters. This study claims that the overall BP estimation error is within 10 % of commercially available digital BP monitoring device. Nonetheless, the relationship between some of the used features and the BP is not always linear, hence the results can be improved further with non-linear recurrent functions such as recurrent neural networks. Sideris et al. [39] introduced a cuff-less continuous BP measurement for remote health monitoring systems. The data was collected from ICU patients from the MIMIC database with PPG measured by pulse oximetry and reference to invasive BP. A Long Short Term Memory (LSTM) network was applied on the PPG signals to estimate SBP, DBP, and arterial blood pressure. LSTM is the state of the art recurrent neural network that takes into consideration previous states or events in the prediction process, and therefore, leverage long-term pattern to deliver more accurate BP estimations. Unlike most studies that utilise domain knowledge for extracting features from each PPG cycle, in this study the input data for the LSTM network were overlapping PPG windows/frames. However, the evaluation metric used in for the evaluation is root mean squared error and the model was only tested on 42 patients. As such, their model evaluation did not follow the conventional standard set by the AAMI or British Hypertension Society, hence the results are not comparable with other studies that mostly use mean absolute error. Moreover, the authors stated that the model optimisation i.e. number of cells, hidden layers, window size etc. was beyond the scope of their study. Duan et al. [40] proposed a feature exploration method for cuff-less BP estimation using PPG sensor only. The University of Queensland Vital Signs Dataset was adopted for evaluation. For improving the PPG signals quality over noise, wavelet transform and average filtering were applied first to remove the noise. Subsequently, several analytical techniques were utilised, such as random error elimination, adaptive outlier removal and maximum information coefficient and Pearson's correlation for features selection. Three separate sets with eleven features, each was proposed to predict SBP, DBP and MAP out of fifty-seven possible feature candidates. A support vector machine was used as an estimator model. The results of this study satisfy the AAMI standards in terms of error rate, however, this dataset contains only 32 cases and SVM is not suitable for long term continuous BP measurements the accuracy will decrease over time. As mentioned earlier, non-recurrent models cannot estimate BP efficiently since it does not provide feedback from previous events, as it is the case for regulating the arterial pressure in the human body that involves multiple feedback control loops. Therefore, history of the BP events affects future values.

Unlike the previous PPG time domain approaches, Xing and Sun [2] introduced a frequency domain methodology for extracting certain features from the PPG signals. Fast Fourier transformation (FFT) was applied on the PPG to extract fundamental features such as amplitude and shape information. FFT uses a small number of parameters to keep most of the information about the PPG waveform. This method applied a feedforward neural network to estimate the BP and was evaluated on 69 patients collected from the MIMIC database and 23 volunteers. Signals were first preprocessed as follows: PPG and BP signals were aligned to remove their phase lag. Only good quality signals were selected based on predefined criteria. PPG signals were then normalised and analysed in the frequency domain. This was followed by extraction of both amplitude and phase features from the waveform using FFT. The authors reported that this method performed well for BP estimation. However, they also suggested that FFT features are not sufficient markers for building BP estimation model, and hence, a more efficient model is required to take into consideration the essential PPG waveform characteristics. Moreover, their feature extraction method has some limitations. When rapid changes occur in BP values, the features will be influenced by adjacent beat, which will lead to a decrease in the accuracy of BP estimation. Additionally, a feedforward neural network is not suitable for continuous long term BP monitoring as the estimation error will increase for longer estimation period. Gaurav et al. [41] used only PPG signals to estimate SBP and DBP. Their work combines PPG based features with Heart Rate Variability (HRV) related features in an effort to enhance the input feature vector for a more accurate BP estimation. The data was derived from the MIMIC online database from which 3000 PPG and BP signals were extracted. Signals were then pre-processed to remove inconsistent windows, and irregular BP and heartrate values. The BP and PPG are also aligned for feature extraction. PPG windows obtained from the previous step were normalised using min-max scaler. Afterwards, 8 PPG features were extracted from the magnitude and temporal information of each PPG window. Furthermore, 19 features were extracted from the filtered second derivate PPG signals. Additionally, 8 non-linear cardiac cycle time ratio based features were also extracted along with 11 HRV features from 10 consecutive peak interval of the PPG. All these features combined together constitute the input vector for three feedforward neural networks for each systolic and diastolic BP. The mean error for the DBP and SBP reported were 0.03 ± 6.85 mmHg and 0.16 ± 4.72 mmHg respectively. Hence, as a results this method met the AAMI and presented significant improvement on previous methods published in the literature tested on large datasets. Nonetheless, this method is computationally expensive given the fact that 46 features were derived from PPG and its second derivative along with HRV features which was then fed into 6 neural networks. Tuning model's parameter is time consuming, consequently, finding the best parameters and architectures for 6 models is very complex. Selecting the right model such as recurrent networks can further reduce the variability and enhance estimation precision. Gao et al. [42] developed a method for estimating SBP using only PPG signals. Their method uses a non-linear SVM with discrete wavelet transformation. It was found to be robust against small irregularities in the PPG waveform which enabled them to use PPG signals obtained from a pulse oximeter and phone. The PPG signals were collected using an Android application and Discrete Wavelet Transform was used for extracting temporal characteristics. The feature set includes: systolic upstroke time, diastolic time, age, gender along with thousands of features extracted from the obtained DWT coefficients. Afterwards, forward feature selection technique was utilised to include only those features that have an effect on the BP estimation. Test results from PPG obtained from both pulse oximeter and phone were on the limits imposed by the AAMI. The error estimation can be enhanced by estimating not only SBP but DBP as well, given the strong correlation between the two. This could be done by providing a feedback from the DBP model to the SBP model or simply using neural networks allowing for SBP and DBP estimating using one model. Furthermore, refining the feature set would also improve the prediction by taking into account information such as peripheral resistance and vessel elasticity from first and second derivative of the PPG [13]. Also, this technique was evaluated on 65 subjects with no history of cardiovascular disease, hence, a larger and more diverse dataset will enhance model generalisation for early detection of cardiovascular diseases.

Liu et al. [43] proposed a cuff-less BP measurement based on PPG and its second derivative. This work attempts to enhance the SBP and DBP prediction by combining the 21 features used in Kurylyak et al. [32] along with 14 features from the second derivative of the PPG (SDPPG), shown in Fig. 5. SDPPG contain information about the aortic compliance and stiffness which is highly related to BP. A support vector machine was applied as a BP estimator. This study reported a 40 % accuracy improvement in BP estimation when tak-

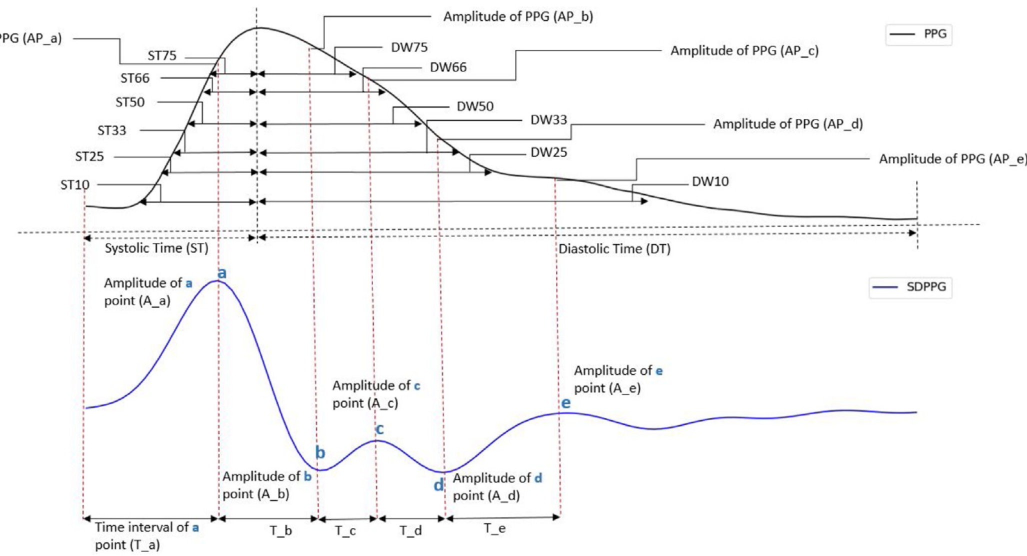

Fig. 5. Temporal PPG features and potential Second Derivative PPG (SDPPG) features.

ing the SDPPG features into account -using the 35 features- as opposed to 21 features and a neural network applied in Kurylyak et al. Experimental results for 35 features evaluated using an SVM were 8.54 ± 10.9 for SBP and 4.34 ± 5.8 for DBP compared to 13.4 ± 11.6 and 6.9 ± 5.9 for SBP and DBP respectively, evaluated on a neural network. The major challenge in this technique is extracting the correct SDPPG features values which are entirely dependent on the visibility of the five peaks a,b,c,d and e in Fig. 5. These five peaks, which mark the 'W' shape in the SDPPG signal, were not visible for all patients, and hence, the models were evaluated on a very small dataset consisting of 910 PPG cycles. The overall performance of the model on this dataset is poor in terms of accuracy and the study did not stratify the AAMI requirements for a reliable cuff-less BP estimation. Kachuee et al. [44] proposed methods to estimate BP using PAT for continuous, cuff-less and calibration-free estimation for SBP, DBP and MAP. PPG, ECG and BP signals were collected from the MIMIC database. The ECG and PPG signal processing consisted of motion artefacts removal and de-noising using discrete wavelet composition. In this study, the proposed method is based mainly on PAT features along with other whole-based PPG features. Two types of features were extracted, namely, physiological parameters (e.g. heartrate, arterial stiffness index, augmentation index) and other features that describe the shape of the PPG waveform. For reducing the effect of collinearity between the features and reducing the dimensionality of 190 extracted features, PCA has been utilised to reduce the dimension down to 15 new features while preserving 98 % variance in the data. Several traditional machine learning techniques, such as linear regression, SVM, Random Forest, and Adaboost, have been used to achieve better accuracy model. The results show that there exists a considerable non-linearity in this task which can be inferred from the superior performance displayed by the non-linear functions such as SVM and ensemble learning methods. Their techniques met the standards of the AAMI for DBP and MAP. However, it suffers from several disadvantages, such as the need for two sensors, the SBP prediction did not satisfy the AAMI standards and their DBP and MAP accuracy were just on the acceptable limit of the AAMI standards, which will eventually deteriorate for longer continuous BP monitoring using the applied models.

Miao et al. [45] proposed a beat-to-beat BP estimation method using a combination of data mining techniques and a mechanism-driven model. For this study, the data was collected from 73 healthy subjects for a static BP estimation experiment, 35 healthy subjects for dynamic BP estimation where the subjects had to exercise for 5 min and 10 subjects for a follow up to test the robustness of their models. The PPG signals were collected from the left index finger and the BP reference was collected using Finpres. Fourteen features were first extracted from (the first and second derivative) PPG and ECG signals followed by a genetic algorithm-based feature selection method for selecting the most influential features for BP estimation for each subject. As a result, features with the highest effect on SBP and DBP estimation were selected. A multivariate linear regression (MLR) and support vector regression were established to evaluate the effectiveness of the genetic algorithm. A reported 2 mmHg reduction in standard deviation for different calibration time intervals, compared to PTT-based model, was achieved by their approach. The results from their experiments show that the SVR outperformed the MLR model signifying the non-linear relationship between the features and BP. Furthermore, it was found that the error of the proposed models deteriorates significantly one day after model construction (with initial calibration) but stabilises afterwards for longer calibration periods, as opposed to the PTT-based approach where the error continuous to increase 1–3 days after the initial calibration. Moreover, their proposed approach still requires two sensors, and their models are not suitable for handling time series data for continuous BP estimation.

In 2018, Wang et al. [46] proposed a BP estimation based on features extracted from PPG signal using the multitaper method (MTM). PPG and ECG signals were acquired from MIMIC database and a total of 58,795 valid PPG interval were extracted from 72 subjects. MTM was employed to extract the spectral components that were combined with two features from the PPG waveform to constitute the input feature vector for a feedforward neural network. The advantages of this approach is that it can provide cuff-less continuous BP measurements with acceptable results using one sensor, mean error of 4.02 ± 2.79 mmHg for SBP and 2.27 ± 1.82 mmHg for DBP. This level of accuracy is achieved while the feedforward neural network does not incorporate temporal dependencies in its estimation which prevents long term accurate predictions. The incorporation of such features, using recurrent neural networks may further improve the accuracy of predictions. Shimazaki et al. [47], introduced a BP estimation model from PPG features extracted using an autoencoder. For this study, the data was collected from 687 healthy male subjects and 676 healthy female subjects. The PPG signals were measured from the left index finger, while the BP reference was measured every minute using a sphygmomanometer with a cuff attached to the right upper arm. An autoencoder was applied as an alternative for conventional feature engineering. An autoencoder is a neural network algorithm that can reconstruct a better version of its input vector by extracting complex features and adding new ones. The resulting features obtain from the autoencoder were then passed into a feedforward neural network for estimating SBP. It was found that the features learnt by the autoencoder are effective for BP estimation and the non-linear learner outperformed the linear regression model. However, the standard deviation of the error for this method was 11.86 mmHg, exceeding the ±8 mmHg standard deviation set by the AAMI, and therefore the results were highly variable and is not deemed reliable for clinical BP measurements. This suggests that the new constructed features obtained from the autoencoder are not optimal for BP estimation, since the autoencoder alters the original PPG waveform which might have caused the high variability in the BP estimation. In a comparison study between different machine learning approaches, khalid et al. [48] extracted three features from the PPG waveform. The University of Queensland vital sign dataset (contains 32 cases) has been acquired for evaluating their proposed technique. The PPG signals were filtered using Savitzky-Golay filter and the baseline wandering was also removed. This was followed by a 2-dimentional normalisation for both amplitude and width. The PPG signals were also segmented into 5 s frame and manual check was performed for removing bad quality segments or segments with no reference to BP values. Pulse area, pulse rising time and width at 25 % were used as features for three traditional machine learning models. Regression tree, multiple linear regression and support vector machine were established for prediction SBP and DBP. The models were analysed for three BP categories: normotensive, hypertensive and hypotensive. The decision tree outperformed both SVR and the linear regression models for both SBP and DBP. The mean error difference only for the regression tree for normotensive people were within AAMI standard and the rest of the models had standard deviation above 8 mmHg. Additionally, since only intermittent non-invasive BP references were available for this study, the BP estimation was implemented on the basis of each PPG segments. Hence, this method does not allow continuous beat-to-beat BP estimation.

In 2018, Dey et al. [49], developed an ensemble of BP estimation models based on demographical and physiological features. A unique set of PPG features were also incorporated in the models for estimating SBP and DBP using lasso regression model. The authors collected their own PPG signals from 205 volunteers of diverse demographical and physiological profiles. PPG signals were recorded for 15 min using a phone Heart Rate sensor sampled at 125 Hz. Each PPG waveform was segmented into 15 s window where each window is interpolated to a fixed length (using cubic spline interpolation) and normalised using min-max normalisation before the correlation coefficients were determined. BP values were collected before and after each PPG recording using a mercury cuff-based device. A total of 233 time and frequency domain features were extracted from a single heartbeat (one PPG pulse). The first four derivatives of the PPG signals were considered for feature extraction. Features from each individual cycle were averaged over the 15 s window. Other features, demographic and physiological information (age, height, weight, gender) were also used as independent features. Lasso regression model was applied to first estimate DBP value which were then used as input along with other features for estimating SBP values. In an effort to take full advantage of the demographic and physiological feature, the dataset was partitioned separately based on age (young < 40 and old > = 40), gender (female and male), and BMI (underweight BMI < 24 kg/m^2 and overweight BMI > = 24 kg/m^2). Afterwards, the regression models were applied on each individual partition. The results show that the addition of multiple independent partitions on the basis of demographic and physiological features can further improve the BP estimation values. The systolic and diastolic values of the combined model were 6.9 ± 9 mmHg and 5.0 ± 6.1 mmHg respectively. This study demonstrates that it is possible to utilise PPG signals collected from a phone for the estimation of BP values and incorporating demographic and physiological information can further enhance estimation accuracy. However, in terms of model precision, the results did not satisfy the AAMI standards for SBP and further improvements are needed such as the use of more advanced models and particularly recurrent neural network which are capable of processing more data, specifically time domain data. Additionally, evident from the results, the feature extraction process is somewhat overcomplicating the task. Optimising the input feature set is crucial for improving model performance in terms of accuracy and time complexity.

Tanveer and Hasan [50] proposed a two hierarchy levels model to estimate BP using ECG and PPG signals. The lower level is an artificial neural network (ANN) used to extract morphological features. The ANN is connected with upper level which consists of two stacked long short term memory (LSTM) layers to take into consideration the temporal variation for the features extracted by the ANN in the lower level. This method, similar to the one proposed by Shimazaki et al. [47], uses a neural network to extract features instead of using traditional feature engineering techniques used by most researches. This paper argues that it is hard to obtain correct features from the ECG and PPG signals since the waveform contour changes from one subject to another, and hence the position of these features varies or maybe not be visible for all patients. Therefore, it is not certain that all these features can be extracted from all patients for a complete and reliable dataset. To overcome this challenge, the author applied an ANN on a small set of PPG and ECG signals that were collected from 39 subjects acquired from the MIMIC database. Both PPG and ECG signals were pre-processed for removing the baseline wandering and high frequency noise. This was achieved by a bandpass filter using Tunable-Q wavelet transform. Both signals are segmented into a fixed length of three consecutive peaks to avoid varying number of cycles per fixed number of seconds between subjects. This was followed by normalisation and resampling for both signals to a length of 256 samples per segment. The concatenated PPG and ECG segments constitute the input feature vector for the ANN model. The results suggest that, compared to traditional feature engineering-based model, this automatic feature extraction technique combined with an LSTM model provides a much better accuracy. The SBP and DBP mean absolute error values were 1.1 mmHg and 0.85 mmHg respectively, however, the AAMI requires at least 85 patients. Moreover, this method requires two signals sampled at two different sampling rate and involves fine tuning two models which can be difficult, time consuming and varies depending of the data size. In Su et al. [51], a four-layer LSTM network was employed to estimate SBP and DBP from ECG and PPG signals. This method built an LSTM model with (1) a bidirectional structure to access larger scale context information of input sequence and (2) residual connections to allow the gradient in the LSTM network to propagate efficiently. The ECG and PPG signals were recorded with a Biopac system while the BP signals were recorded with a Finapres at the same time. All these signals were sampled at 1000 Hz for a period of 10 min from 84 healthy subjects at rest position. Another dataset was also collected from 12 subjects for a multi-day continuous BP consisting of 8 min recording for each signal. Since the main focus of the paper was to demonstrate the importance of modelling the time variation of the input features, the authors simply selected seven features from the PPG and ECG signals, such as PTT values, Heart Rate, systolic upstroke time, etc. It was reported that the results of this method outperformed all previous models with significant improvement for multi-day BP datasets and root mean squared error of 3.9 mmHg and 2.66 mmHg for SBP and DBP respectively, on the static 84 subject BP dataset. Therefore, suggesting that modelling the temporal dependencies leads to a much accurate prediction for long-term BP measurements compared to classical models. Optimising the feature set, which was not the focus of this paper, would increase the precision and performance of the model. However, it is difficult to compare the results with other methods since this study did not follow the conventional metric, mean absolute error and standard deviation set by the AAMI.

Fujita et al. [52] proposed a cuff-less SBP estimation method using partial least-square (PLS) regression. Their multivariate estimation method used Level Crossing Features (LCF) extracted from the contour lines randomly drawn on the PPG's second derivative. The authors collected their own signals from 265 subjects with SBP 133.1 ± 18.4 mmHg and aged 62.8 ± 16.8 years participated in the study. The SBP reference values were acquired from the left upper arm using an automatic BP monitor at rest position and the PPG signals were recorded immediately after the BP recording for a period of 20 s. The PPG signals were pre-processed by a first order low-pass filter and a finite impulse response filter to remove high frequency noise. The LCF features were extracted from the second order derivative PPG of which two types of features were obtained, namely, the number of crossing and the length of the curve line. This paper attempted to simplify the SBP estimation by using a very small set of input data comprising six LCF features evaluated on PLS regression. Only 38 % of the subjects had their SBP estimation below 5 mmHg. Consequently, this method received grade D using the British Hypertension Society BP metric, suggesting that this technique is not fit for clinical trial. Additionally, it also shows that PLS is not appropriate for long-term BP measurements and the LCF features are not ideal for BP estimation. Besides, their dataset comprised only healthy subjects in a resting position, hence the dataset does not contain diverse BP values that represent the population. Chen et al. [53] proposed SBP and DBP estimation models based on PTT approach in addition to PPG waveform characteristics. The impact value for each feature was investigated and a genetic algorithm was also used for fine tuning model parameters. SVM and multivariate linear regression models were established to predict BP values evaluated on MIMIC dataset. A total of 772 sets of waveforms were extracted from the MIMIC database containing ECG, PPG and BP signals. The PPG and ECG signals were first cleaned from motion artefacts, irregular segments and missing waveforms. Furthermore, both ECG and PPG signals were denoised using wavelet threshold denoising method and cubic spline interpolation respectively. Fourteen features were extracted such as PTT, heart rate, and other features describing the shape of the PPG waveform. All these features were normalised using min-max scaler and the importance of each feature was investigated using mean impact value (MIV) for removing redundant features and reducing the input dimension. The results from their proposed SMV method were 3.27 ± 5.52 mmHg for SBP and 1.16 ± 1.97 for DBP, hence it satisfies the AAMI requirement for non-invasive cuff-less BP estimation. The results can be further improved by taking into account demographical features such as age, gender, weight etc. Additionally, evaluation for long term BP prediction i.e. one week, one month or six months should be conducted to test the model's performance for long term measurement. The experimental results from [45] shows that the performance of PTT based models decrease for long term monitoring due to the expiration of the PTT parameter and the inability of the SVM to perform well for multiday estimation. In Ripoll and Vellido [54], a Restricted Boltzmann Machine (RBM) was established as a proof of concept for estimating SBP and DBP values. The RBM-BP estimation model was based on the PTT approach. The data used from 250 patients collected from the MIMIC database. All biomedical signals were segmented into a 5 s window. Motion artefacts and noisy waveforms were also removed from the dataset. Three different RBMs were established for estimating SBP and DBP using one input feature each, namely, PTT, 1/PTT and log (PTT). The performance of this method decreased as the measurement parts from the calibration point. The overall results from this experiment were acceptable and received grades A and B according to the BHS metric. However, there are several limitations to this method, such as the need for two sensors, the accuracy of the model decreases after 6 min of the initial calibration and therefore, as a result it necessitates calibration. Also, the RBM is not capable for estimating continuous BP since it will suffer from vanishing or exploding gradient in long term continuous BP prediction. Consequently, utilising a recurrent model should further increase the accuracy for longer tracking capabilities for BP values. Estimation accuracy can be further increased by including demographical features and whole-base PPG features.

A breakdown for all the BP machine learning based models listed in this review paper are presented in Table 1.

3. Discussion & conclusion

Currently, cuff-less non-invasive BP measurements can be divided into techniques that use only a PPG sensor and techniques that use a hybrid approach namely a PPG sensor and the ECG. The hybrid approach is mainly based on PTT or PAT. PTT is the time that takes the blood pressure wave to travel between two points on the body and is inversely correlated with BP. PAT is defined as the time interval between the electrical activation of the heart and arrival of the pulse wave at a location on the body peripheral. PAT is PTT in addition to Pre-ejection Period. PAT can be measured using two sensors, an ECG sensor and a PPG sensor. It is based on the time difference between the R peak of the ECG and a point on the PPG rising edge. Although both PTT and PAT can achieve accurate and acceptable results, these methods are not easy to implement and have several practical challenges. PTT and PAT parameters expires after a short period causing the estimation accuracy to deteriorate as it parts away from the initial calibration. Moreover, both methods require two measurement sensors that need to be synchronised, and placed on fixed positions on the body which is hard and inconvenient for patients to maintain during measurements. Additionally, both sensors have different sampling rates in real time. Furthermore, PPG and ECG sensors are very sensitive to motion artefacts due to movements during the recording which in turn require rigorous signal processing before the signals can be used in a BP study.

To overcome some of these challenges, researchers introduced pulse wave analysis method. Pulse wave analysis approach can be used to estimate BP using only one PPG sensor without an ECG. Even though the origin of the PPG components is not fully understood, it is acceptable that PPG can provide information about the cardiovascular system. This approach is simple, inexpensive and more convenient for patients during measurement since it only uses one light sensor. In this approach several temporal features are extracted from the PPG and used as input data for machine learning and neural network models for BP estimation. The main obstacle for BP monitoring using PPG is accuracy. Different guidelines were created for researchers to follow in order to compare their methods to reference invasive BP values. These guidelines were set by the British Hypertension Society (BHS) and AAMI. According to AAMI, the mean error difference between estimated and reference should not exceed 5 mmHg, and the standard error deviation should not exceed 8 mmHg for 85 patients.

In conclusion, linear and non-linear models for estimating BP have been employed over the past 15 years. In some cases, where the dataset belongs to healthy individuals, some of the linear models were able to achieve reasonable and acceptable results.

Table 1
Summary for all the BP estimation methods presented in this paper.

No	Title	Authors	Pub. year	Conclusions	Algorithms
1	Continuous and noninvasive estimation of arterial blood pressure using a photoplethysmographic approach.	Teng and Zhang [27]	2003	Estimated SBP and DBP using 4 features vector extracted from PPG signals. It was found that the diastolic time has higher correlation with SBP and DBP than other features.	Linear regression
2	Measuring blood pressure using a photoplethysmography approach	Hassan et al. [28]	2008	Estimated SBP calibration free based on the PTT approach. The slope of the linear model for each individual subject are averaged out to constitute the slope of the new linear regression model that can be used for every person.	Linear regression
3	An evaluation of the cuffless blood pressure estimation based on pulse transit time technique: a half year study on normotensive subjects	Wong et al. [29]	2009	Studied the correlation between BP and PTT under different circumstances. The results show that arterial BP increased and PTT decreased sharply after exercise, and SBP and PTT are highly correlated. Estimated SBP and DBP.	Least square regression
4	Cuffless blood pressure estimation by error-correcting output coding method based on an aggregation of adaboost with a photoplethysmograph sensor	Suzuki and Oguri [30]	2009	SBP was estimated from PPG signals using error-correcting output coding method based on an aggregation of binary classifiers. The SBP values were first classified according to random thresholds then learning models were used to estimate SBP.	AdaBoost classifier
5	Innovative continuous non-invasive cuffless blood pressure monitoring based on photoplethysmography technology	Ruiz-Rodríguez et al. [31]	2013	Built a probabilistic generative models to estimate SBP, DBP and MAP.	Deep Belief Network Restricted Boltzmann Machine
6	A Neural Network-based method for continuous blood pressure estimation from a PPG signal.	Kurylyak et al. [32]	2013	Estimated SBP and DBP using only PPG signals. Extracted 21 features from the PPG waveform and used a non-linear function to account for the non-linear relationship between BP and PPG.	Feedforward neural network
7	Feature selection method for estimating systolic blood pressure using the taguchi method.	Suzuki and Ryu [34]	2014	Proposed a PPG features selection methodology for estimating SBP. Selected PPG features that are robust against noise.	Taguchi feature extraction method and multiple regression
8	Estimating blood pressure using Windkessel model on photoplethysmogram.	Choudhury et al. [35]	2014	Estimated SBP and DBP using PPG signals only. Maps PPG features with intermediate person specific latent parameters which are then used to derive the SBP and DBP values.	Windkessel model followed by linear regression
9	Cuffless and continuous blood pressure estimation based on multiple regression analysis.	Shen et al. [36]	2015	Proposed BP model based on 5 features extracted from ECG and PPG signals for estimating SBP, DBP and MAP.	Stepwise regression
10	Cuff-less high-accuracy calibration-free blood pressure estimation using pulse transit time.	Kachuee et al. [37]	2015	Introduced a calibration free BP estimation model using PTT method. Applied signal processing techniques and extracted PPG features combined with PTT values. Several linear and non-linear models were tested to obtain SBP, DBP and MAP.	Regularised linear regression, artificial neural network, and support vector machine
11	Blood pressure estimation from photoplethysmogram using latent parameters.	Datta et al. [38]	2016	This study have applied noise reduction techniques to clean the PPG signals from noise. A combination of machine learning and mathematical modelling have been used to estimate SBP and DBP from PPG signals only.	Linear regression for latent parameter estimation followed by mathematical BP models

Table 1 (*Continued*)

No	Title	Authors	Pub. year	Conclusions	Algorithms
12	Building continuous arterial blood pressure prediction models using recurrent networks.	Sideris et al. [39]	2016	Introduced a BP measurement system for remote health monitoring. Estimate SBP, DBP and MAP from PPG signals.	Recurrent neural network
13	A feature exploration methodology for learning based cuffless blood pressure measurement using photoplethysmography.	Duan et al. [40]	2016	Proposed a PPG feature exploration methodology for estimating SBP, DBP and MAP from PPG signals only. Several analytical techniques were utilised, such as random error elimination, adaptive outlier removal and maximum information coefficient.	Support vector machine
14	Optical blood pressure estimation with photoplethysmography and FFT-based neural networks	Xing and Sun [2]	2016	Introduced a frequency domain methodology for extracting certain features from the PPG signals for SBP and DBP estimation. This research applied Fast Fourier Transformation on PPG to features selection.	Feedforward neural network
15	Cuff-less PPG based continuous blood pressure monitoring—A smartphone based approach.	Gaurav et al. [41]	2016	Estimated SBP and DBP using PPG-only features combined with Heart Rate Variability features for improving the input feature vector.	Artificial neural network
16	Data-driven estimation of blood pressure using photoplethysmographic signals	Gao et al. [42]	2016	Developed a model for estimating SBP using only PPG signals. This study introduced a technique that is robust against small PPG waveform irregularities enabling researchers to use PPG signals obtained from pulse oximetry and phones.	Support vector machine with discrete wavelet transformation
17	Cuffless Blood Pressure Estimation Based on Photoplethysmography Signal and Its Second Derivative.	Liu et al. [43]	2017	Estimated SBP and DBP using 21 PPG features and 14 features from its second derivative.	Support vector machine
18	Cuffless blood pressure estimation algorithms for continuous health-care monitoring.	Kachuee et al. [44]	2017	Proposed methods for estimating BP calibration free using PAT approach. Combined PAT features with PPG whole-base features. Estimated SBP, DBP and MAP using several machine learning techniques.	Linear regression, random forest, decision tree, SVM and Adaboost.
19	A novel continuous blood pressure estimation approach based on data mining techniques.	Miao et al. [45]	2017	Proposed a beat-to-beat BP estimation method using a combination of data mining techniques and a mechanism-driven model. Fourteen features were first extracted from the PPG and ECG signals followed by a genetic algorithm-based feature selection method.	Linear regression and SVM models
20	A novel neural network model for blood pressure estimation using photoplethesmography without electrocardiogram.	Wang et al. [46]	2018	Proposed a BP estimation model for SBP and DBP based on features extracted from PPG signal using multitaper method.	Feedforward neural network
21	Features Extraction for Cuffless Blood Pressure Estimation by Autoencoder from Photoplethysmography.	Shimazaki et al. [47]	2018	Introduced a BP estimation model from PPG features extracted using an autoencoder neural network followed by another model for estimating SBP values.	Autoencoder followed feedforward neural network
22	Blood Pressure Estimation Using Photoplethysmography Only: Comparison between Different Machine Learning Approaches.	khalid et al. [48]	2018	Extracted 3 features from the PPG waveform for predicting SBP and DBP. Three traditional machine learning techniques were applied, namely. The models were analysed for three BP categories: normotensive, hypertensive and hypotensive.	Multiple linear regression, SVM and regression tree.

Table 1 (*Continued*)

No	Title	Authors	Pub. year	Conclusions	Algorithms
23	InstaBP: Cuff-less Blood Pressure Monitoring on Smartphone using Single PPG Sensor.	Dey et al. [49]	2018	Developed an ensemble of BP estimation models based on demographical and physiological features. A unique set of PPG features were incorporated in the models for estimating SBP and DBP.	Lasso regression
24	Cuffless Blood Pressure Estimation from Electrocardiogram and Photoplethysmogram Using Waveform Based ANN-LSTM Network.	Tanveer and Hasan [50]	2018	Proposed a two hierarchy levels model to estimate BP using ECG and PPG signals.	Lower level is an artificial neural network followed a two stacked LSTM layers in the upper level
25	Long-term blood pressure prediction with deep recurrent neural networks.	Su et al. [51]	2018	Estimate SBP and DBP from ECG and PPG signals. This method built an LSTM model with (1) a bidirectional structure to access larger scale context information of input sequence and (2) residual connections to allow the gradient in the LSTM network to propagate efficiently.	Four layers LSTM
26	PPG-Based Systolic Blood Pressure Estimation Method Using PLS and Level-Crossing Feature.	Fujita et al. [52]	2019	Proposed a SBP estimation method using regression. Multivariate estimation method used level crossing features extracted from the PPG second derivative.	Partial least-square regression
27	A Non-Invasive Continuous Blood Pressure Estimation Approach Based on Machine Learning.	Chen et al. [53]	2019	Introduced SBP and DBP estimation models based on PTT approach in addition to pulse waveform characteristics. Used genetic algorithm to study the impact of each feature.	SVM and linear regression
28	Blood pressure assessment with differential pulse transit time and deep learning: a proof of concept.	Ripoll and Vellido [54]	2019	Established as a proof of concept neural network model for estimating SBP and DBP values. The BP estimation model was based on the PTT approach.	Restricted Boltzmann Machine

However, other studies show that when these models are evaluated on different individuals they fail to estimate BP values acceptable by AAMI standard requirements. In this case, the model coefficients need to be recalibrated. As a results, many non-linear models have also been employed such as, support vector machine, random forest, feedforward neural network, etc. In many cases, the non-linear models outperformed the linear models but again depending on the dataset and approach used i.e. PTT, PAT or PWA (PPG only). More advanced methods have also been proposed such as recurrent neural networks and LSTM which have a huge advantage over the previously mentioned models. These models are equipped with the ability to model the variation of the extracted features with respect to time. Tests reported an improvement in the BP estimation using these models and the possibility to employ recurrent models for long term continuous measurements.

Overall, the PPG is a most promising technique with a great potential on offering BP measurements in a non-invasive, continuous and cuff-less manner. Such a device will have significant and transformative impact in the monitoring of patients, especially those who at risk of cardiovascular disease. It is encouraging to see so much global interest by researches and industry alike in this field. There are still challenges to be resolved, however if the momentum of this research topic continuous in the same trajectory as it is now it is very hopeful that a PPG based non-invasive, cuff-less and continuous BP monitoring device could be commercialised in the near future.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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