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NON-INVASIVE CUFFLESS BLOOD PRESSURE MEASUREMENT

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Abstract - To overcome the drawbacks in cuff based bp monitors, a new method for measuring BP has been proposed, which does not require a cuff. By using this approach, individuals can avoid the potential inaccuracies associated with cuff-based BP monitors and obtain more reliable. BP readings. The important principle used in this device is PhotoPlethysmoGram (PPG) and electrocardiogram (EKG). PPG is a simple and affordable optical measuring technique that is frequently used for heart rate monitoring. Thus measures the volumetric fluctuations of blood circulation and we obtain our PPG signal data. This device is also integrated with Clinicalgrade ECG sensor(AFE) which provide highly accurate data. This device algorithm is designed to analyse the PPG and ECG signal and by comparing the peaks of both the waves and using our model the systole and diastole values are obtained. Uniqueness in this device is we can get our results just with our fingertips neither cuff is placed to measure BP nor electrodes are placed in chest to detect ECG.

Keywords: PhotoPlethysmoGram(PPG), Electrocardiogram (ECG), Pulse transit time.

I. INTRODUCTION

Blood pressure (BP) is a primary concern when it comes to heart health. Monitoring BP readings and fluctuations is crucial in identifying potential health problems. The World Health Organization suggests that individuals should check their BP at least once a day to detect any spikes and reduce the risk of developing cardiovascular disease. Currently, cuff-based BP monitoring systems, including mercury-based sphygmomanometers, aneroid pressure monitors, and automatic BP monitors, are commonly used in clinical settings. However, using such cuff based BP monitors has some drawbacks, such as the potential for inaccurate readings due to slight movements, high chances of observer error, difficulty in monitoring infants or small children, noise interference resulting in inaccurate readings, calculation of systolic and diastolic blood pressure based on mean arterial pressure, and variations in machines based on the manufacturer. The regular adult cuff size is too short for individuals with an arm circumference of 32 cm or larger and will lead to overestimation of BP. Incorrect placement of the cuff can also result in inaccuracies when using cuff-based BP monitors. To overcome this issue, a new method for measuring BP has been proposed, which does not require a cuff. This novel method involves comparing the photoplethysmogram (PPG) and electrocardiogram (ECG) waves to obtain accurate measurements of blood pressure. By using this approach, individuals can avoid the potential inaccuracies associated with cuffbased BP monitors and obtain more reliable BP readings.

The field of invention for non-invasive cuffless blood pressure measurement is classified as medical devices and healthcare technology. It entails the development of novel methods and equipment for monitoring blood pressure



without the use of typical inflatable cuffs. It combines various technologies, including digital signal processing, biosensors, and wearable devices to provide a convenient and comfortable way to monitor blood pressure. The Biosensor detects physiological signals related to blood pressure, such as arterial waveforms, pulse transit time, and pulse wave velocity. Biosensors can be integrated into wearable devices or embedded in other health monitoring equipment. These devices are and equipped with sensors processing capabilities to continuously monitor blood pressure.

The background of the invention for noninvasive blood pressure measurement stems from the longstanding clinical necessity to accurately and continuously monitor an individual's blood pressure without the discomfort and inconvenience associated with traditional cuff-based methods. Traditional sphygmomanometers, while reliable, are often impractical for continuous monitoring and can lead to patient discomfort and compliance issues. As a response to these challenges, the field of non-invasive blood pressure measurement has evolved. integrating advancements in biosensors, digital signal processing, wearable technology, and artificial intelligence to develop innovative solutions capable of providing accurate and real-time blood pressure data in various settings, from home health monitoring to clinical and telemedicine applications, ultimately enhancing healthcare outcomes and patient convenience. The concept of blood pressure dates measurement back to ancient civilizations. Early physicians recognized the importance of pulse as a vital sign, with Hippocrates describing the pulse as a key indicator of health. However, systematic measurement of blood pressure didn't occur until much later. The 19th century saw significant advancements in blood pressure measurement techniques. The sphygmograph, a

device that recorded pulse waveforms. However, this device didn't directly measure blood pressure. The early 20th century marked the development of the sphygmomanometer, the most common device used for blood pressure measurement today. The auscultatory method of blood pressure measurement involves a cuff and a stethoscope to listen for sounds indicating blood flow changes in the arteries during cuff inflation and deflation. With advancements in technology, electronic and automated blood pressure monitors became prevalent in the latter half of the 20th century. These devices provided more accurate and convenient measurements compared to traditional mercury-based Additionally, sphygmomanometers. the integration of digital displays and memory functions facilitated easier recording and tracking of blood pressure readings. The 21st century has witnessed further innovations in blood pressure measurement techniques, particularly the exploration of non-invasive cuffless methods. These methods leverage wearable sensors, signal processing algorithms, and machine learning to estimate blood pressure parameters without the need for cuffs, offering potential improvements in patient comfort and convenience. From ancient observations modern to technological innovations, the history of blood pressure measurement is a testament to humanity's relentless pursuit of understanding and monitoring cardiovascular health. As we continue to advance, the quest for more accurate, convenient, and non-invasive blood pressure measurement methods remains ongoing, promising better healthcare outcomes for individuals worldwide.

II. LITERATURE SURVEY

Tung-Li, Hsieh. (2023) have studied "A Hemodynamic Pulse Wave Simulator Designed for Calibration of Local Pulse Wave Velocities Measurement for Cuffless Techniques" The



paper proposes a device to simulate human pulse wave signals for the calibration of cuffless blood pressure measurement devices. The simulator consists of an electromechanical system to simulate the circulatory system and an arm model-embedded arterial phantom. The cuffless device measures the local pulse wave velocity (PWV) of the simulator, and a hemodynamic model is used to calibrate the cuffless device's measurement performance. The study demonstrates that using a multiple linear regression (MLR) model for calibration significantly improves the accuracy of the cuffless device, reducing the mean absolute error and measurement error. The proposed pulse wave simulator provides a standardized method for assessing the performance of cuffless blood pressure monitors and can be used for mass production and verification of these devices. The simulator simulates PWV by incorporating elastic tubes embedded in the pulse simulator model to simulate the physiological phenomenon of pulse wave transit during human circulation. The simulator also generates pulse wave signals that represent systolic blood pressure (SBP) and diastolic blood pressure (DBP) using an electric pump and pressure sensors. The difference between SBP and DBP is the pulse pressure (PP), and the mean arterial pressure (MAP) is calculated as the sum of 1/3 of SBP and 2/3 of DBP[1]

Carolin et al., (2023) studied "Cuffless Beat-to-Blood from Beat Pressure Estimation Photoplethysmogram Signals" Many studies have been published on blood pressure (BP) estimation from photoplethysmogram (PPG) signals in recent years, aiming to overcome limitations of current BP devices. However, most of these studies suffer from methodological drawbacks regarding data handling, leading to overly positive evaluation of such methods. The paper addresses these limitations and presents a new approach for cuffless beat-to-beat BP estimation from raw PPG signals. The proposed method achieves a

mean absolute error of 8.07 ± 6.86 mmHg for diastolic BP and 8.73 ± 7.36 mmHg for systolic BP when evaluated on unseen test subjects. The use of a convolutional neural network (CNN) enables beat-to-beat BP estimation from PPG signals, providing a novel contribution to the field. The paper also explores the transparency of the model's decision-making through layer activation analysis and investigates the impact of fine-tuning for personalization of the model.[2]

H. Samimi et al., (2023) reviewed "A PPG-Based Calibration-Free Cuffless Blood Pressure Estimation Method Using Cardiovascular Dynamics" The paper proposes a calibration-free method for blood pressure estimation using dynamic changes in the pulse waveform and information from photoplethysmogram (PPG) morphology. The method shows a high correlation between blood pressure estimated with PPG morphology features and the calibration method. The authors suggest that PPG morphology features could replace the calibration stage for a calibration-free method with similar accuracy. The proposed methodology was tested on 200 patients and resulted in a mean error of -0.31 mmHg for diastolic blood pressure (DBP) and -4.02 mmHg for systolic blood pressure (SBP). The study supports the potential for using PPG signals for calibration-free cuffless blood pressure estimation and improving accuracy by incorporating information from cardiovascular dynamics. The paper also mentions the use of deep learning and mathematical models for blood pressure estimation based on PPG morphology features. The authors highlight the for improving blood pressure potential estimation accuracy of other methods, such as those based on pulse transit time, by incorporating information from cardiovascular dynamics [3]

Hemalatha K, Suganthi L, and Manivannan M (2010) have studied "Hybrid Cardiopulmonary



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Model for Analysis of Valsalva Maneuver with Radial Artery Pulse." The primary aim of this research was to examine how respiratory influences impact the pressure pulse of the concept radial artery; а akin to photoplethysmography. The study employed a comprehensive model that combined features from both lumped parameter and distributed parameter (PPG) systems. This hybrid model merged the transmission line arterial tree model, spanning from the aorta to the radial artery, with a cardiopulmonary (CP) model using lumped parameters. By introducing variations in intrapleural pressure (Ppl) due to respiration into the circulatory system, the study enabled a thorough exploration of cardiopulmonary interactions. The resultant correlation coefficients derived from the model's output closely aligned with experimental results. This integrated model holds potential for assessing the clinical implications of the radial artery pulse in diagnosing cardiac and respiratory conditions, as it constitutes a vital element in both conventional medical practices and complementary medicine systems. The model's PPG signal is interpreted as a representation of the radial signal [4].

Tarifi, Aaron Fainman, Adam Basheq Pantanowitz, David M. Rubin have studied "A Machine Learning Approach to the Non-Invasive Estimation of Continuous Blood Pressure Using Photoplethysmography".Blood pressure is an important vital sign that sometimes requires continuous measurement. The current methods include cuff measurements (manual auscultation and oscillometric techniques) for non-continuous measurement and invasive arterial cannulation for continuous measurement. The use of photoplethysmography as a cuffless, noninvasive, and continuous blood pressure measurement system is investigated through the use of four neural networks. These predict the systolic blood pressure, diastolic blood pressure, mean arterial blood pressure, and waveform shape. The models are trained on 890 h of data from 1669 patients in the MIMIC-III Featuretrained artificial database. neural networks predict the systolic blood pressure to 5.26 ± 6.53 mmHg (mean error \pm standard deviation), the diastolic blood pressure to 2.96 \pm 3.31 mmHg, and the mean arterial pressure to 3.27 ± 3.55 mmHg. These are used to shift and scale the predicted waveform, allowing the waveform prediction neural network to optimise for the wave shape rather than the amplitude. The waveform prediction has 86.4% correlation with the actual arterial blood waveform. results pressure A11 meet clinical blood international pressure measurement standards and could potentially change how blood pressure is measured in both clinical and research settings. However, more data from healthy individuals and analysis of the models' biases based on clinical features is required[5].

III. PROPOSED METHODOLOGY



Fig 1. Flow chart for working procedure

Blood pressure (BP) is a primary concern when it comes to heart health. Monitoring BP readings and fluctuations is crucial in



identifying potential health problems. The World Health Organization suggests that individuals should check their BP at least once a day to detect any spikes and reduce the risk of developing cardiovascular disease. Currently, cuff-based BP monitoring systems, including mercury-based sphygmomanometers, aneroid pressure monitors, and automatic BP monitors, are commonly used in clinical settings. However, using such cuff-based BP monitors has some drawbacks, such as the potential for inaccurate readings due to slight movements, high chances of observer error, difficulty in monitoring infants or small children, noise interference resulting in inaccurate readings, calculation of systolic and diastolic blood pressure based on mean arterial pressure, and variations in machines based on the manufacturer [6]. The regular adult cuff size is too short for individuals with an arm circumference of 32 cm or larger and will lead to overestimation of BP. Incorrect placement of the cuff can also result in inaccuracies when using cuff-based BP monitors. To overcome this issue, a new method for measuring BP has been proposed, which does not require a cuff. This novel method involves comparing the photoplethysmogram (PPG) and electrocardiogram (ECG) waves to obtain accurate measurements of blood pressure[7]. By using this approach, individuals can avoid the potential inaccuracies associated with cuffbased BP monitors and obtain more reliable BP readings. This project involves a combination of software and hardware components to achieve its objectives.

MATLAB:

MATLAB serves as the primary software tool for this project. It plays a pivotal role in processing and analysing the digital signals acquired from the ECG and PPG sensors. It provides powerful tools for visualizing ECG and PPG signals in graph format. Algorithms implemented in MATLAB allow precise removal of artifacts (such as DC offset and baseline wander) from the acquired signals. Techniques like high-pass filtering enhance signal quality[8].

It computes the first derivative of the PPG signal. This derivative reveals dynamic changes in blood volume over time, providing valuable insights into cardiovascular dynamics.

The algorithms detect peaks in both the ECG and the first derivative of the PPG signal. These peaks play a crucial role in calculating Pulse Transit Time (PTT), which serves as an indicator of blood pressure.

Processing 4.3:

Processing 4.3 is utilized as the platform for acquiring ECG and PPG signals in analog format and converting them into digital signals. Processing 4.3 facilitates the conversion of analog signals into digital format, ensuring compatibility with MATLAB for further processing. After analog-to-digital conversion, the signals are stored in CSV files for subsequent processing in MATLAB. Processing 4.3 manages the acquired signal data, organizing it in a structured format suitable for analysis in MATLAB



Fig 2. ECG and PPG analog output

HARDWARE COMPONENTS

MAX86150 Breakout Board:

The MAX86150 breakout board is a critical component for acquiring both ECG (Electrocardiogram) and PPG (Photoplethysmogram) signals simultaneously.





It offers biopotential sensing capabilities, allowing precise sampling of physiological signals. By integrating ECG and PPG functionalities, it streamlines the data acquisition process.

The MAX86150 captures electrical signals generated by the heart (ECG). These signals provide insights into cardiac activity. The same board also measures blood volume changes using optical sensors (PPG). PPG signals reveal pulsatile changes in blood flow, aiding in heart rate estimation and SpO2 monitoring.



Fig 3. Breakout Board

Arduino UNO Microcontroller:

The Arduino UNO serves as the central processing unit for interfacing with the MAX86150 breakout board. It facilitates communication between the sensors and the processing software (such as MATLAB). The microcontroller manages data transmission, synchronization, and control. The Arduino UNO reads raw ECG and PPG data from the MAX86150. It preprocesses the signals, performs necessary calculations, and prepares them for further analysis. The processed data can then be transmitted to a computer or other devices for visualization and interpretation.

Development Methodology



Fig 4. Signal Acquisition

OWIIC Connectors:

QWIIC connectors are specifically chosen for their compatibility and ease of use. They simplify the wiring process, ensuring reliable signal transmission. These connectors typically have a four-pin design, making it straightforward to connect the MAX86150 breakout board to the Arduino UNO. QWIIC connectors eliminate the need for complex wiring configurations, reducing the risk of errors during setup.

Signal Acquisition:

The MAX86150 breakout board and Arduino UNO capture ECG and PPG signals, which provide vital physiological data related to heart activity and blood flow. The proper setup of hardware components establishes connections using QWIIC connectors to facilitate reliable signal transmission.

Analog to Digital Conversion:

The analog signals obtained from the sensors are converted into digital format, for preserving signal integrity and enabling further processing. Appropriate analog-to-digital conversion techniques are employed to accurately represent the analog signals in a



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digital domain, ensuring fidelity in subsequent analysis.

Signal Preprocessing:

Perform signal preprocessing enhance the quality and usability of the acquired data. Removal of DC offset from the signals using high pass filtering methods to center the signals around zero and eliminate unwanted bias is performed. Filters are applied to mitigate baseline wander and other artifacts present in the signals, ensuring a cleaner signal for subsequent analysis.

First Derivative Calculation:

The first derivative of the PPG signal is calculated to capture its rate of change over time. This derivative provides insights into the dynamics of the PPG waveform, including the steepness of its incline and decline, which can be indicative of physiological phenomena such as arterial stiffness and vascular tone.

Peak Detection:

Peaks are identified in both the ECG and first derivative PPG signals using peak detection algorithms. Peaks in the ECG signal correspond to specific events in the cardiac cycle, such as the depolarization and repolarization of the heart's chambers. Peaks in the first derivative PPG signal represent significant changes in blood volume and pressure within the arterial system, which can be used as reference points for subsequent analysis.

PTT Estimation:

The Pulse Transit Time (PTT) between corresponding peaks in the ECG and PPG signals is calculated. PTT is a measure of the time it takes for a pulse pressure wave to travel between two arterial sites and is influenced by factors such as arterial compliance and stiffness. Estimating PTT provides valuable information about vascular health and can serve as a surrogate marker for cardiovascular function.

Blood Pressure Estimation:

Developed algorithms estimate Diastolic Blood Pressure (DBP) and Systolic Blood Pressure (SBP) based on PTT measurements. The established relationships between PTT and blood pressure are used to derive accurate estimations of DBP and SBP, which are essential indicators of cardiovascular health.

Optimization and Iteration:

Iteratively optimize the methodology based on testing results and feedback from stakeholders. Fine-tune algorithms and signal processing techniques to improve accuracy, efficiency, and robustness, ensuring the reliability of the final system.

IV. RESULT AND DISCUSSION

<u>Ecg signal load</u>

Once acquiring digital signal of PPG and ECG waveform from the processing software next inserting those signals to MATLAB. Frist the ECG signal is loaded as in .txt format, and the loaded signal is doubled. In the provided code snippet, the variable 'y' is loaded from a file using 'load('ecgm.txt')'. However, it seems the data type of ,y, is initially set as duration, which may not be appropriate for further signal processing tasks. Duration data type is typically used to represent time intervals, not signal values. By converting the data type from duration to double ('y = double(y)'), you're essentially converting the ECG signal values from their original data type (duration) to a numerical format (double precision floating point numbers). This allows you to perform mathematical operations and signal processing tasks on the ECG signal data effectively. The implemented MATLAB algorithms effectively removed DC offset and baseline wander from



the ECG resulting in improved signal quality and specifying how the graph of ECG should be displayed.

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Fig 5. ECG Signal load

Ppg signal load

The same procedure is repeated for the PPG signal too, where the digital signal is loaded in MATLAB in .txt format, to convert the original data type to numeric format again the PPG signal is doubled. This allows you to perform mathematical operations and signal processing tasks on the PPG signal data effectively. The implemented MATLAB algorithms effectively removed DC offset and baseline wander from the PPG resulting in improved signal quality and specifying how the graph of PPG should be displayed.

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Fig 6. PPG Signal load

Ecg peak detection

Next comes the peak detection part of the generated ECG waves,

Initialization: 'j = 1': Initializes a variable 'j' to 1. This variable is used to index the 'val' and 'pos' arrays, which store the values and positions of the detected peaks, respectively. 'n = length(y)': Retrieves the length of the ECG signal stored in the variable 'y'.

Peak Detection Loop: The loop iterates through the ECG signal starting from the second sample ('for i = 2: n-1'). 'if' statement checks if the current sample y(i) is greater than the previous sample 'y(i-1)', greater than or equal to the next sample 'y(i+1)', and greater than 45% of the maximum value of the ECG signal $(0.45*\max(y))$. If all conditions are met, it indicates a potential peak in the ECG signal. If a peak is detected, its value 'y(i)' is stored in the 'val' array, and its position 'i' is stored in the 'pos' array. The index 'j' is then incremented ('j = j + j1') to prepare for the next potential peak.

Normalization: ecg peaks = j - 1: Calculates the total number of detected peaks by subtracting '1' from the final value of 'j'. This adjustment is necessary because 'j' was incremented after the last peak detection loop iteration. ecg pos = pos ./ 1000: Normalizes the peak positions ('pos') by dividing them by 1000. This normalization is likely performed to convert the positions from sample indices to seconds, assuming a sampling frequency of 1000 Hz (which might be the case considering comment regarding the passband the frequency).

Plotting: 'plot (pos, val, '*r')': Plots the detected peaks on the ECG signal plot. Peaks are marked with red asterisks ('*r'). The x-axis represents the positions of the detected peaks ('pos'), and the y-axis represents the corresponding peak values ('val'). title ('ECG peak'): Sets the title of the plot to 'ECG peak'.

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Fig 7. ECG peak detection



Ppg peak detection

Peak Detection Using Built-in Function:

[peaks,locs]=findpeaks(z,'MinPeakHeight', threshold peak,'MinPeakDistance',

window_size_peak); This line uses the findpeaks function to detect peaks in the PPG signal z.

MinPeakHeight: Specifies the minimum height of peaks to be detected. Peaks below this threshold will be ignored.

MinPeakDistance: Specifies the minimum distance between consecutive peaks. This prevents detecting multiple peaks within a short time span, which can occur due to noise or artifacts.

Custom Peak Detection Loop: This loop iterates through the PPG signal starting from the second sample (for i = 2: n-1). It checks if the current sample z(i) is greater than the previous sample z(i-1), greater than or equal to the next sample z(i+1), and greater than 43% of the maximum value of the PPG signal (0.43*max(z)). If all conditions are met, it indicates a potential peak in the PPG signal. If a peak is detected, its value z(i) is stored in the val array, and its position i is stored in the pos1 array. The index m is then incremented (m = m + 1) to prepare for the next potential peak.

Normalization: $ppg_peaks = m - 1$: Calculates the total number of detected peaks by subtracting 1 from the final value of m. This adjustment is necessary because m was incremented after the last peak detection loop iteration.

ppg_pos = pos1. / 1000: Normalizes the peak positions (pos1) by dividing them by 1000. This normalization is likely performed to convert the positions from sample indices to seconds, assuming a sampling frequency of 1000 Hz.

ppg_val = val;: Copies the values of detected peaks into ppg_val.

Plotting: plot (pos1, val,'*g'): Plots the detected PPG peaks on a separate plot. Peaks are marked with green asterisks ('*g'). The x-axis represents the positions of the detected peaks (pos1), and the y-axis represents the corresponding peak values (val). title ('ECG & PPG signal'); Sets the title of the plot to 'ECG & PPG signal'. Legend ('ECG signal','PPG signal'): Adds a legend to the plot indicating the signals being plotted.



Fig 8. ECG and PPG detected peak graph

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Fig 9. PPG peak detection

PTT detection

ptt = (ppg_pos - ecg_pos): Calculates the PTT by subtracting the corresponding ECG peak positions (ecg_pos) from the PPG peak positions (ppg_pos). This calculation results in an array ptt containing the time intervals between each PPG peak and its corresponding ECG peak. The PTT represents the time taken for the pulse wave to travel from the heart (ECG peak) to a peripheral location (PPG peak).



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Fig 10. PTT detection





BP calculation

Input Height: 'Height = input ('Please specify Height');': This line prompts the user to input their height. The height is needed for the calculation of pulse wave velocity (PWV) in the subsequent steps.

Calculate Pulse Time: 'pulsetime = mean2(ptt);': Calculates the mean pulse transit time ('pulsetime') from the array of PTT values ('ptt'). This value represents the average time taken for the pulse wave to travel from the heart to a peripheral location. 'pulsetime1 = pulsetime * 1000;': Converts the pulse transit time from seconds to milliseconds. This conversion is likely because the input height (Height) might be in meters, and other constants in the calculations are in SI units.

Calculate Pulse Wave Velocity (PWV): 'PWV = ((0.5 * Height) / pulsetime1);': Computes the pulse wave velocity using the formula: PWV = (0.5 * Height) / PulseTime. Pulse wave velocity represents the speed at which the pulse wave

travels along a blood vessel. It's proportional to the stiffness of the vessel and inversely proportional to its compliance.

Calculate Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP): 'SBP = ((-1.28) * (PWV^2)) + (1156.3 * PWV);': Computes the systolic blood pressure (SBP) using the formula provided. The formula appears to be derived from empirical data and theoretical models that relate PWV to blood pressure. DBP = ((-0.61) * (PWV^2)) + (854.5 * PWV);': Computes the diastolic blood pressure (DBP) using a similar formula based on PWV.

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Fig 12. SBP and DBP results

V. CONCLUSION

The provided MATLAB code segments collectively aim to estimate blood pressure using signals derived from both ECG (Electrocardiogram) and PPG (Photoplethysmogram) measurements. Initially, peak detection algorithms are applied both signals to identifv the peaks to corresponding to individual heartbeats. Subsequently, the pulse transit time (PTT) between the peaks of the two signals is calculated, representing the time taken for the pulse wave to travel from the heart (ECG peak) to a peripheral location (PPG peak). Leveraging the user's height as an input parameter, the code computes the pulse wave velocity (PWV), a key metric influenced by arterial stiffness and compliance. Employing empirically derived formulas, the code then estimates both systolic and diastolic blood pressure based on the



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calculated PWV. These steps outline a technical approach utilizing signal processing techniques and physiological principles to derive blood pressure estimates from ECG and PPG signals, thereby offering a non-invasive method for cardiovascular assessment. However, it's essential to acknowledge that the accuracy of these estimates may be influenced by factors such as individual variability, signal quality, and the assumptions inherent in the employed models. Further validation and refinement of these methods may be warranted to enhance their reliability in clinical practice.

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