Exploration and Validation of Alternate Sensing Methods for Wearable Continuous Pulse Transit Time Measurement Using Optical and Bioimpedance Modalities

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***Abstract*— In this work we explore the viability of a multi-modal sensing device that can be integrated in a wearable form factor for daily, non-invasive ambulatory blood pressure (BP) monitoring. A common approach in previous research has been to rely on measuring the pulse transit time (PTT), which has been shown to be correlated with the BP. In this work, we look into the feasibility of measuring PTT using sensors separated by a small distance on one arm so that any eventual realization of the system is convenient to wear and use over long periods of time. Moreover, we investigate the combined use of two different modalities for cardiovascular measurement: the optical photoplethysmogram (PPG) as well as the bio-potential based impedance (Bio-Z) measurement. These two modalities have been previously only studied on their own or in conjunction with the electrocardiogram (ECG) for the purpose of estimating PTT. We measure the PTT from the wrist to the finger using Bio-Z and PPG sensors, and compare it to the conventional PTT measured from the ECG to PPG at the finger, in order to prove that it can be an effective replacement for existing PTT measurement strategies. Moreover, successful measurement of PTT with two different modalities of sensors at close proximity will allow designs with multiple heterogeneous sensors on a more versatile wearable sensing platform that is optimized for power and is more robust to environmental or skin contact changes. This will enable the next generation of smart watches that capture PTT and BP. Experiments were conducted *in vivo* with simultaneous ECG, Bio-Z and PPG sensors, and results indicate that the PTT calculated from the Bio-Z and PPG sensors placed at a close distance correlates well with the more established PTT measurement using the ECG in conjunction with PPG, with correlation coefficient as high as 0.92.**

I. Introduction

Hypertension is one of the most important cardiac ailments affecting a significant portion of the world's population. In order to diagnose a patient for the first time, as well as monitor the progress of a patient taking medication, it is important to measure blood pressure (BP) regularly and reliably. For repeated measurements in the long term, it is ideal for the method of measurement to be non-invasive. Moreover, the measurement device should be easy to use for a non-expert, and allow for in-home measurement which means more frequent measurement without the need for hospital visits, and also provides the most natural context for the patient; this approach minimizes any external environmental influences on the reading, such as the 'white coat syndrome' wherein patients experience an artificially increased blood pressure merely due to the presence of a practitioner taking the measurement for them.

Currently, the most convenient method is the use of the sphygmomanometer with its inflatable cuff that allows users to autonomously measure blood pressure at home. However, even this device can be considered invasive, given the inflated pressure that affects the blood flow and causes discomfort. This could lead to reluctance on the part of the patients to take readings, which in turn leads to less data for the doctor to use and an increased likelihood of missed diagnoses of critical conditions. Furthermore, this solution provides only a one-time measurement while the user is seated expressly for the purpose of measuring blood pressure. In other words, we are lacking a continuous stream that is paired with contextual information such as the activity being performed at the time of informative BP trends; for example it would be insightful to know if the daily commute by car is causing the user's BP to spike up significantly.

A prominent solution for continuous monitoring in the literature is the measurement of pulse transit time (PTT) instead. It has previously been shown that PTT is correlated with BP, so PTT could be translated to BP given effective calibration techniques [1, 2]. However, most existing solutions do not represent a single integrated PTT measurement device in a wearable form factor that is easy to use. Moreover, to the best of the authors' knowledge, a combination of bio-impedance (denoted Bio-Z) and photoplethysmography (PPG) has not previously been tested as a viable alternative to existing PTT measurement methods.

In this work, we study the three most commonly used signal modalities for PTT measurement: ECG, Bio-Z and PPG. Using a unified system to compare the PTT from Bio-Z and PPG, to the traditional ECG and PPG approach, will definitively prove the validity of alternative solutions that are more wearable. Moreover, proving that a multi-modal measurement (Bio-Z and PPG) can work will open the door for optimizing according to various design trade-offs for any given system. For instance, a watch could include several Bio-Z and PPG sensors, and the designer can always choose the best pair of sensors for PTT measurements based on criteria such as contact quality, signal fidelity and power consumption. Thus, we present experimental results that would lay the

Human subject testing was conducted at Texas A&M University under IRB approval IRB2017-0086D and informed consent was provided to all participants.

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platform for the development of a wearable BP monitoring system, while also proving the viability of combining Bio-Z and PPG sensors at small distances to measure PTT.

II. Related Works

One of the most common methods for PTT measurement in the literature is the measurement of the time delay between the R-peak of the ECG and a characteristic point on the PPG waveform [3]. Since the R-peak constitutes a clear feature on the ECG, this technique provides a reasonable approximation of the time it takes for the pulse to travel from the heart to the point of measurement of the PPG on each heartbeat.

However, there are two issues with this type of measurement relying on ECG. Firstly, there is a pre-ejection period (PEP) between the onset of the R-peak and the actual pumping out of blood from the heart. So in effect, this method is measuring not just PTT, but PEP + PTT. This is problematic because the PEP can vary over time unpredictably, thus confounding the attempts to measure PTT [4]. Furthermore, because of the nature of the potential difference measurement for ECG, it is challenging to use a device with a small form factor that is also easily wearable. Most typical ECG lead configurations require significant separation between the differential electrodes to elicit useful signals. One solution that allows relatively close proximity of electrodes is to place them on the chest [5], but it would be challenging to build a device that can unobtrusively attach there while still being capable of transmitting the signals, and also being convenient to repeatedly recharge and reattach. Another of our previous works built a platform that can sense both ECG and PPG in a wrist watch form factor but this requires a touch on an electrode from the finger of the other arm in order to complete a circuit with electrodes either side of the heart [6]; so this again constitutes a distinct action for the purpose of occasional measurement, and is obviously not feasible during certain activities such as driving and running.

There has also been research showing that PTT measured between the ECG R-peak and a Bio-Z sensor correlated well with PTT measured between ECG and a PPG sensor [7]. However, this work did not look into the PTT from the Bio-Z sensor to the PPG sensor, which would be necessary for a wearable system that did not rely on ECG.

One previous work explored the possibility of excluding ECG by using two different PPG sensors, one on the finger and one on the wrist, to measure PTT [8]. However, their results were not validated with any existing established measures of PTT. Another work also showed dual PPG on the carotid artery on the neck [9]. Apart from the relative inconvenience of a sensor on the neck, the measurements from this work were also not compared with other established PTT measures or a continuous measurement of BP. Similarly, another work explored the use of a pair of Bio-Z channels, but the results were not validated for correlation and consistency against existing measures [10]. We believe it is important to validate any new proposed metrics against existing ones so that they can be easily incorporated with established clinical metrics.

III. Theory

This section will describe briefly the various signals of interest, as well as how the PTT is derived from these.

A. Electrocardiogram

The electrocardiogram (ECG) is a representation of the electrical activity of the heart, as measured by bio-potential electrodes placed on the surface of the skin. Features such as the P, Q, R, S and T waveforms map out the different phases of a single heartbeat. Of particular interest to us is the R-peak, which signifies the onset of the ventricular depolarization of the heart; this is a clear marker that provides a good approximation for the start of the heartbeat and the pumping out of blood.

B. Photoplethysmogram

The photoplethysmogram (PPG) is an optical measurement that characterizes the volume flow of blood through the measurement site. A PPG sensor consists of an LED paired with a photodiode placed externally on the surface of the skin. The LED emits light of suitable wavelength – typically red, infrared or green – into the skin, and the photodiode transduces the reflected light into a proportionate amount of current. As the blood rushes into the blood vessels beneath the measurement site during each cardiac cycle, it absorbs a certain amount of the incident light which in turn means there is a sharp decrease in the light reflected back to the photodiode. The amount of reflection then gradually increases before falling again at the time of the next pulse. Thus, the amount of blood flow at the measurement site over time can be inferred.

C. Bioimpedance

The bioimpedance (Bio-Z) is the electrical impedance of body tissues to an applied current which can be used to measure the amounts of body fluids such as blood volume in blood vessels. The Bio-Z variations (ΔZ) correspond to variations of blood volume due to the heart's activity in each cardiac cycle [11]. The Bio-Z can be modeled as in Figure 1, where R_I, R_E and C_m represent the resistance of intra-cellular fluid (ICF), the resistance of extra-cellular fluid (ECF) and the capacitance of the cell membrane respectively, and ΔR_I, ΔR_E and ΔC_m represent the impedance variation due to blood flow at the measurement site. The Bio-Z can be measured by applying an AC sinusoidal current through a pair of electrodes and sensing the voltage with two different electrodes near the excitation electrode (Kelvin connection). The measured voltage is a sinusoidal voltage at the same frequency as the applied current and its amplitude is modulated by the Bio-Z. Demodulation is used to extract Bio-Z by multiplying the sensed signal by the excitation signal.

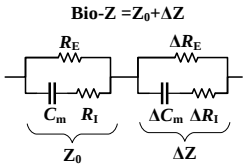

Figure 1 - The Bio-Z electrical circuit model

D. Pulse Transit Time

The PTT represents the time it takes for a pulse wave to

travel between two points on the body. Since the two points can vary in distance depending on the sensors used, a simple method to normalize and produce a unified metric is to divide the PTT by the distance between the two points which gives the pulse wave velocity (PWV). This PWV can then be converted to BP with appropriate calibration. As mentioned in Section II, a common way to measure the PTT is to measure the time between the R-peak of the ECG and a characteristic point on the PPG, as shown in Figure 2 below, and this is denoted ECG-to-PPG PTT. However, the time difference between the point of maximum negative inclination on the Bio-Z waveform and the characteristic point of the PPG waveform could also represent PTT (Bio-Z-to-PPG PTT); without the restrictions of ECG measurement, this form of PTT could allow an easily wearable solution that is convenient to use, so in this work we explore if the PTT measured this way correlates well with previously established methods of PTT measurement.

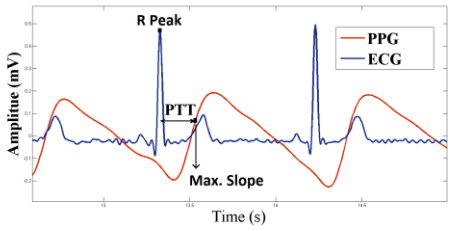

Figure 2 - PTT estimation using ECG and PPG waveforms

In order to bring the measurements closer to a 'wearable sensor' scenario, we made efforts to reduce the distance between Bio-Z electrodes as much as possible, and also made the measurement close to the wrist to mimic a sensor placed underneath a watch.

IV. Methods

A. Measurement Circuits

The measurement of Bio-Z, PPG and ECG are done by the circuits shown in Figure 3. The circuits consist of an analog front-end which captures accurately the signals from the three sets of sensors placed on body. The three physiological signals are sampled simultaneously by the ADC ADS1274 from Texas Instruments to ensure timing synchronization between them. The ADC has 24-bit resolution with a sampling rate of 128 kSPS to enable accurate measurement of PTT with error less than 7.8µs or 0.026% of an average PTT.

The ECG is measured by the SparkFun Single Lead Heart Rate Monitor, which is based on the AD8232 analog front end developed by Analog Devices. The leads were attached to Covidien pre-gelled ECG patches, and placed one on each arm to provide a single channel of ECG as shown previously in Figure 3. The analog output of the SparkFun board was connected to one of the channels of the ADC.

The circuits of the Bio-Z sensor are implemented using discrete components in order to measure accurately the small variations of Bio-Z due to blood flow through a small area on the arm. A current source is used to generate a sinusoidal current signal with programmable amplitude and frequency, which is injected into the arm. The programmable current source consists of an MCU that controls a DAC to generate a sinusoidal voltage signal (V_{DAC}), which is converted to a current signal by a voltage-to-current converter. The amplitude of V_{DAC} is adjusted to ensure a fixed current amplitude of 500 µA to be compliant with safety standards [12]. Any residual DC voltage at the DAC output is removed by a series capacitor to avoid injecting DC current into the subject. After some experimental testing, the frequency of the AC current is chosen to be 8 kHz for the best detection of Bio-Z variations due to blood flow.

The sense path of Bio-Z consists of an instrumentation amplifier (IA) which amplifies the signal from the sense electrodes in order to be sampled by the ADC. In order to accurately detect Bio-Z variations less than 0.1 Ω from the arm due to blood flow, the Analog Devices AD8421 IA is selected for its low noise spectral density of 3.5 nV/√Hz at 1 kHz, and high input impedance compared to the electrode-tissue impedance. The IA has programmable gain set by an external resistor (R_G) which is adjusted to provide gain of 40 dB to measure Bio-Z up to 70 Ω. In addition, the IA has high CMRR of 126 dB to cancel out the DC offset voltage before the ADC to ensure full utilization of ADC dynamic range.

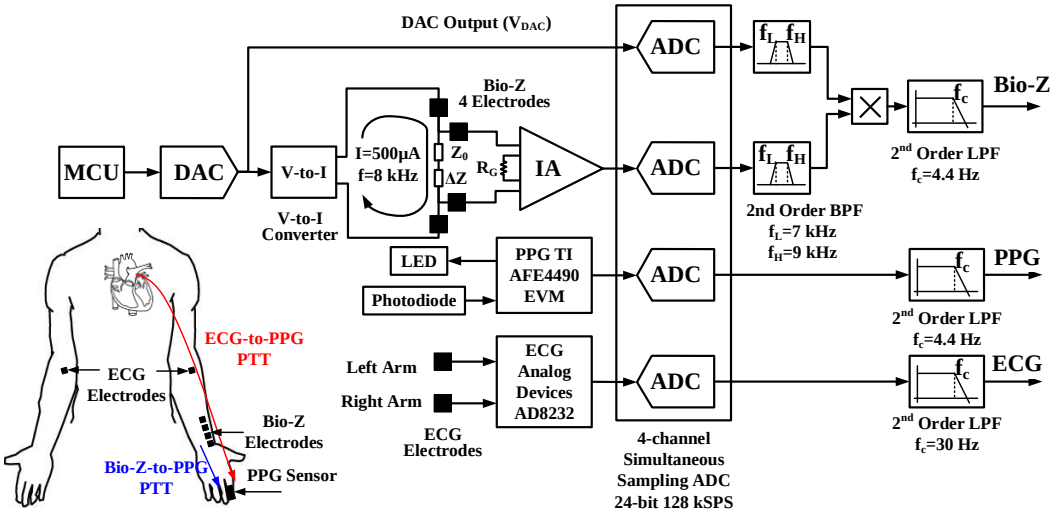

Figure 3 - Overall measurement circuit schematic and the different PTT measurements using ECG, Bio-Z and PPG sensors

The PPG was measured using the AFE4490 EVM by Texas Instruments. The sensor itself is a finger-clip based transmitting type PPG device, *i.e.*, the LED emits light onto the top of the finger, and the photodiode receives the light via the bottom of the finger. The EVM was configured such that the on-board ADC was bypassed, and the photodiode output was directly routed to one of the channels of our own ADC just like the ECG and Bio-Z channels. The EVM was also configured to continuously emit light at the infra-red wavelength. This wavelength was chosen due to its high penetration into the skin for better sensing of the activity of the larger arteries underneath the surface [13].

B. *Signal Processing*

The Bio-Z is extracted by demodulation in the digital domain by multiplying the IA output by the excitation signal, which is the DAC output. The IA and DAC outputs are sampled simultaneously by the ADC, then filtered by a bandpass filter centered on the excitation frequency. The same filter is used for the IA and DAC signals to avoid introducing any phase error between the two signals before demodulation. The demodulated output is filtered by a second order low pass filter with a cut-off frequency of 4.4 Hz to remove the image frequency and out of band noise, and measure heart rates up to 180 beats per minute.

The PPG and ECG signals are filtered by a low pass filter with f_c=4.4 Hz and 30 Hz respectively to remove 60 Hz power line interference and other high frequency spurs and noise. The ECG filter has a higher cut-off frequency in order to retain the higher frequency components of the R peak.

After filtering, the ECG, Bio-Z and PPG signals are analyzed to determine the points of R peaks in ECG, the points of maximum negative slope of the Bio-Z and maximum positive slope of the PPG in order to calculate the corresponding PTT values.

An example of all three signals as measured by our circuit, and after digital filtering on MATLAB, is shown below in Figure 4.

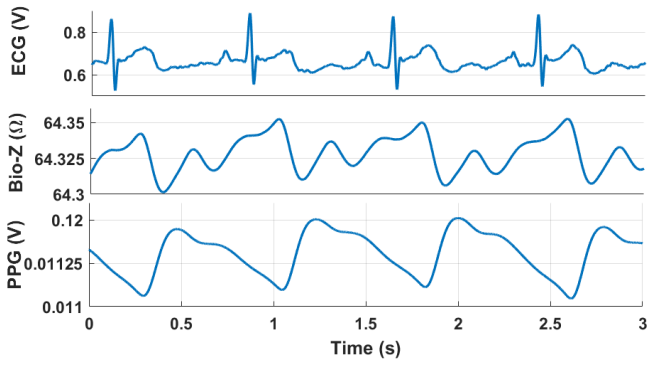

Figure 4 - (From top to bottom) ECG, Bio-Z and PPG signals as measured by our circuit, after digital filtering

B. *Experiment Description*

Human subject data collection was done with all three sets of sensors attached simultaneously. For the Bio-Z measurement, the electrodes were attached to the Covidien pre-gelled patches and placed along the left forearm of the subject, such that the impedance was measured near the wrist. The separation between the two voltage sensing electrodes was 2.5 cm, and the current injection electrodes were immediately bracketing these. The PPG finger clip was placed on the left index finger. The ECG leads were attached a little further up on each arm.

Four trials of data were collected from each of 3 human subjects with their informed consent. Each subject was seated with the arm outstretched on a table in some trials as shown in Figure 5 below and the arm raised up in other trials to cause variation in PTT. Each trial of data collection was restricted to 16 seconds of data at a sampling rate of 128kHz due to limitations of the data acquisition software tool.

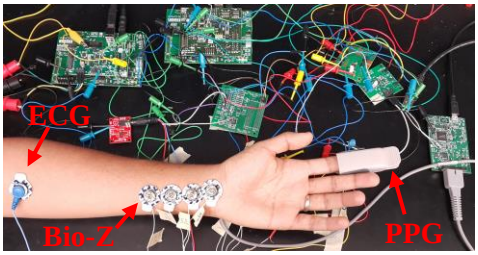

Figure 5 - Data collection setup

V. Experimental Results

Firstly, we confirmed that none of the signals were compromised for any of the trials by calculating the beat to beat heart rate for all three sets of signals and ensuring that they matched. Figure 6 below aggregates the respective PTT values for the three subjects from all the trials and shows the correlation between the Bio-Z-to-PPG PTT and the ECG-to-PPG PTT. This shows a high correlation, with a correlation coefficient ranging from 0.73 to 0.92. This indicates that PTT from Bio-Z-to-PPG over a small distance from wrist to finger carries a similar amount of information compared to the PTT from ECG-to-PPG, and thus it could represent a viable alternative.

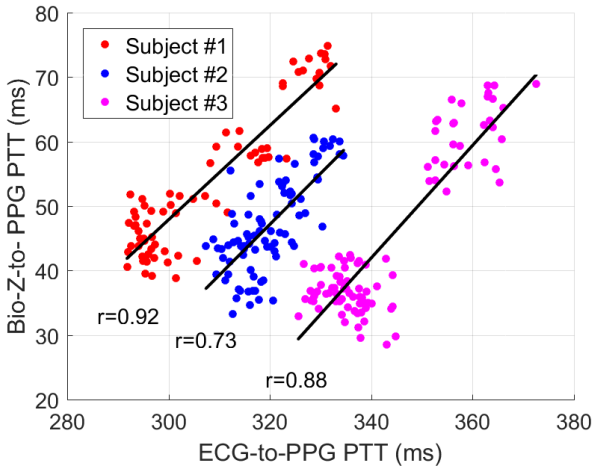

Figure 6 - Correlation between Bio-Z-to-PPG PTT and ECG-to-PPG PTT for 3 subjects

Figure 7 below shows the beat-to-beat PTT for one trial on Subject #1 over time; we can see how the PTT from Bio-Z to PPG tracks very well the variations and trends observed in the other PTT from ECG to PPG over a wide range of values.

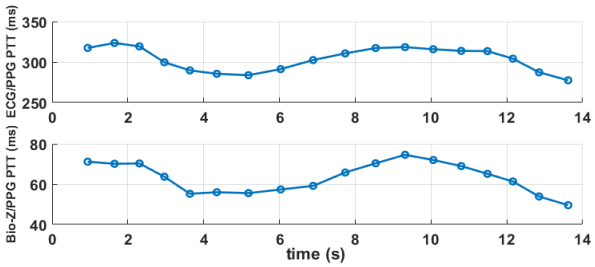

Figure 7 – Beat-to-beat PTT for ECG/PPG and Bio-Z/PPG for Subject #1.

Table 1 – The correlation coefficient of Bio-Z-to-PPG PTT and the average measured PWV from wrist to finger for the 3 subjects

Subject	***Correlation Coefficient of Bio-Z-to-PPG PTT***	***Average measured PWV from wrist to finger (m/s)***
Subject #1	0.92	5.5
Subject #2	0.73	5
Subject #3	0.88	6.25

Finally, the average measured PWV between the Bio-Z sensor at the wrist and PPG sensor at the finger was from 5 to 6.25 m/s as shown in Table 1, which is within the expected physiological limits for humans [14].

VI. Conclusion

In this work we showed how Bio-Z and PPG sensors placed close together can be a viable alternative to estimating PTT rather than using ECG. This would enable the development of wearable devices, in the form factor of a watch for example, that could continuously monitor PTT which would then be converted to BP after sufficient calibration. This would reduce the burden on the user, make it more convenient to generate a larger amount of data and also increase the chances of diagnosing a cardiac illness sooner. The new measure of PTT was shown to correlate well with the existing measure using ECG and PPG, and this also opens the door for the optimal design of multi-modal systems based on specific trade-offs for each modality.

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