Photoplethysmography: Towards a Non-Invasive Pressure Measurement Technique

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***Abstract*— There is a need for a non-invasive and continuous blood pressure monitor. Photoplethysmography (PPG) is one of the techniques that were investigated for this purpose in an *in vitro* model where the relationship between the PPG and pressure-volume (P-V) changes was investigated. Pressure and red (R) infrared (IR) PPG signals were recorded continuously in an arterial model that simulates fluid flow utilizing a pulsatile pump. Flow rates were controlled through three set-points of pumping frequencies at low and high stroke volumes. Normalized Pulse Volume (NPV) is defined as the light intensity ratio at each wavelength, R (NPV_R) and IR (NPV_{IR}). Adjusted Pulse Volume (APV) was determined for both wavelengths. It was found that the optimum method for estimation of the pulsatile volume is through APV, which has a remarkable correlation (r^2=0.99, p<0.001) with the assumed exponential P-V model. APV obtained significantly better fit when compared to NPV_{IR} (r^2=0.73, z=25.85, p<0.001) and NPV_R (r^2=0.95, z=12.26, p<0.001). Our preliminary findings emphasize the potential of APV as a non-invasive continuous method of blood pressure measurement.**

I. Introduction

Blood pressure is a vital measurement of hemodynamic status and is a marker of adequate organ perfusion. Non-invasive continuous measurement of blood pressure is desirable in monitoring patients during a surgical operation or in intensive care units and for home health care. Some of the currently used methods such as the auscultatory method have limitations (i.e. can only provide intermittent measurements). Photoplethysmography (PPG) is one of the methods investigated for the estimation of continuous blood pressure measurements or blood pressure change. The vascular unloading method widely used in commercial blood pressure devices produces inaccuracies during hypotension [1] and hemodynamic instabilities [2]. The suitability of the pulse wave velocity (PWV) or pulse arrival time (PAT) method was also investigated [3],[4]. However, some question the reliability of this approach as a clinical device [5], [6]. The main difficulty of the PWV method is because the elasticity of the vessel is not constant and differs from one individual to another and is affected by neurohormonal factors. In fact, the change in pressure is a factor that alters PWV. To investigate the potential of PPG as a technique for non-invasive pressure measurement, a fundamental understanding of the PPG is to be established.

PPG is an optical technique mainly applied in pulse oximetry for estimating blood oxygen saturation. The sensor commonly uses red (R) and infrared (IR) light sources and a photodetector and is attached to a skin surface. The signal provides an oscillatory component (PPG_{AC}) synchronized with the heartbeat and another steady component (PPG_{DC}). Despite the simplicity of the technique, the origin of both components is not well-understood. The latter is believed to generate from the low frequency varying functions, such as respiratory and thermoregulation and the former is assumed to reflect blood volume changes[7].

Recent studies explored the potential of the amplitude of the PPG_{AC} in providing a direct measurement of blood pressure. It was reported that the magnitude of the PPG_{AC} is considerably more reliable in providing a measure of arterial blood pressure when compared to PWV. However, such findings encountered inaccuracies in standing positions when compared to supine positions or weekend correlations during REM sleep phases [8], [9].

To achieve a reliable and robust method for the measurement of blood pressure utilizing optical techniques such as PPG, an understanding of light interaction with pulsatile flow should be established. This study presents an investigation of the relationship between the PPG and pressure signals in an *in-vitro* setup assuming an exponential pressure-volume relationship. From a mechanical point of view, the optical interaction of the PPG components at distinct wavelengths is investigated at varied flow rates, through changing pumping frequencies and stroke volumes.

From a fluid dynamics point of view, the pulsatile flow consists of an oscillatory component and another steady component [10]. In conjunction with the Lambert-Beer law, this concept is utilized to define the normalized pulse volume (NPV) for R (NPV_R) and IR (NPV_{IR}). Relying on previous studies that report on the depth of penetration of R and IR wavelengths [11], the adjusted pulse volume (APV) is determined using both wavelengths.

II. Principle

Pressure-Volume (P-V) relationship is known to follow an exponential behavior in the human circulation [12], [13] as noted in (1). Our assumption is that this practice is valid in the developed *in vitro* model which mimics the mechanics of the human circulation.

$$P = b\exp(nV) \tag{1}$$

Here b and n are parameters of the model.

When we apply PPG to an arterial model, total light intensity can be written as a function of fluid volume, given that the distance between the light sources and the photodetector is constant. The pulsatile volume is a combination of an oscillatory component $(\tilde{V}_o)$ and a steady component $(\bar{V}_s)$. Assuming that Lambert-Beer's Law holds the following equation can express the relation between the total incident (I_0) and total transmitted light (I):

$$I = \exp(-\varepsilon_s c_s \bar{V}_s)\exp(-\varepsilon_o c_o \tilde{V}_o) I_0 \tag{2}$$

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Where, c is the concentration of the light-absorbing substance in each component and ε is the absorbance coefficient. The subscripts, o and s, denote oscillatory and steady components respectively. Given that $(\bar{V}_s)$ is constant at the same pressure and wall elasticity, the following equation holds for the steady volume component:

$$\bar{I} = \exp(-\varepsilon_s c_s \bar{V}_s) I_0 \quad (3)$$

Where, $(\bar{I})$ is constant light intensity obtained from the steady volume layer.

Hence, from (2) and (3), the following can be derived

$$\tilde{V}_o = (-\varepsilon_o c_o)^{-1}.\ln(\Delta I_{\lambda 1}/\bar{I}_{\lambda 1}) \quad (4)$$

Where $\Delta I_{\lambda 1}$ is the amplitude of the oscillatory optical signal, and $\bar{I}_{\lambda 1}$ is the level of the steady optical signal, at a particular wavelength $\lambda 1$.It is noted that $\ln(I_{\lambda 1}/\bar{I}_{\lambda 1})$ is in direct proportion to the oscillatory component of the total fluid volume $(\tilde{V}_o)$, via the unknown constant term $(\varepsilon_o c_o)$, presuming that both are constant. Hereafter, normalized pulse volume (NPV) is given by:

$$NVP = -\ln(\Delta I_{\lambda 1}/\bar{I}_{\lambda 1}) \quad (5)$$

The reliance of the penetration depth on light wavelength is well documented [11], and this concept is used in deriving the adjusted pulse volume APV. The volume of steady flow layer is known to develop in the center of the tube, where light with higher wavelength provides a better estimation, and the oscillatory flow occurs in layers closer to the wall, where shorter wavelengths provide a more accurate estimate, therefore:

$$\bar{I}_{\lambda 2} = \exp(-\varepsilon_s c_s \bar{V}_s) I_0 \quad (6)$$

Given that $\lambda_2 > \lambda_1$, (2) and (6) lead to

$$\tilde{V}_o = (-\varepsilon_o c_o)^{-1}.\ln(\Delta I_{\lambda 1}/\bar{I}_{\lambda 2}) \quad (7)$$

Given that $(\varepsilon_o c_o)$ is constant. Hereafter, the adjusted pulse volume (APV) is referred to as

$$APV = -\ln(\Delta I_R/\bar{I}_{IR}) \quad (8)$$

Equation (1) is rewritten as:

$$\ln(P_s) = n\tilde{V}_o + \ln(b) \quad (9)$$

Where, P_s is the systolic pressure signal that drives the oscillatory fluid volume. It was previously noted that NPV and APV are in direct proportion to the oscillatory component of the fluid volume $(\tilde{V}_o)$ via the unknown constant term $(\varepsilon_o c_o)$. In this study, both parameters are kept constant in a controlled setup to validate the derived relationship. Therefore, (9) can be finally rewritten to give the following:

$$\ln(P_S) = -n.NPV_R + \ln(b) \quad (10)$$

$$\ln(P_S) = -n.NPV_{IR} + \ln(b) \quad (11)$$

$$\ln(P_S) = -n.APV + \ln(b) \quad (12)$$

III. Materials and Methods

An *in-vitro* study was carried out to determine the optical response of PPG_{AC} and PPG_{DC} of R and IR signals at different flow rates. The *in-vitro* setup, described in the following subsections was designed to simulate the flow conditions observed in the healthy and diseased human circulation in the range of 45-150 mmHg mean pressure values.

A. The in-vitro prototype

A pulsatile flow loop illustrated in Figure 1 was designed to contain an elastic tube model that produces a range of patterns of mechanical forces at the inner surface of the flexible tubing. A pulsatile pump (1423 PBP, Harvard Apparatus, US) was used to generate the pulsatile flow. The pump permitted flow regulation by two means: (1) controlling the stroke volume, (2) and the pumping rate. A custom-made Plexiglas fluid reservoir (volume: 8 L) contained the fluid within the circulation was also constructed.

A flexible polyvinyl chloride (PVC) tubing (length: 20 cm, outside diameter (OD): 22 mm, and an inner diameter

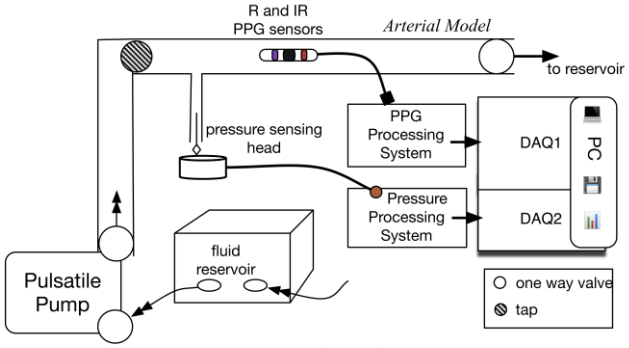

Figure 1. A schematic diagram of the flow loop used to impose mechanical stress at variable flow patterns.

(ID): 16 mm) was connected to the input of the system to enable a fully developed flow before entering the model. The model consisted of a PVC tube (Elastic Modulus~ 28 MPa, ID: 16 mm, OD: 1.8 mm) which simulates a large artery.

The model was mounted onto a specially designed support system which incorporated rubber clamps to hold the tubes at a constant length without interfering with their movement. An initial axial stretch of 1-2% was used to ensure that the flexible tubes remained in a straight position during the pumping phase. One-way check valves with preset opening pressure (50 mmHg) were introduced at both ends of the model which provided the control over the resistance and backward flow. Valves were also added at the entrance of the design to allow control of flow paths and switch to bypassing tube to eliminate any bubbles in the system. The room temperature during all in vitro experiments was maintained at 23 ± 0.5 ℃

B. Sensors and instrumentation

1) Sensors

The Reflectance Photoplethysmography sensor used was designed and fabricated. Two LEDs, Red (R) and Infrared (IR), at a peak wavelength of 640 nm and 860 nm respectively, were aligned in a reflectance mode at a three mm distance from the photodiode (PD) (Vishay, UK). A 3D

printed (Makerbot, US) encasing was designed and produced to fix the probe at one mm contact gap with the pulsating tube without interfering with its motion. A 3D model of the designed PPG probe and encasing is illustrated in Figure 3.

The pressure was measured at the entrance of the model using a catheter-tip transducer (Harvard Apparatus, U.S.) inserted through the lumen of the model.

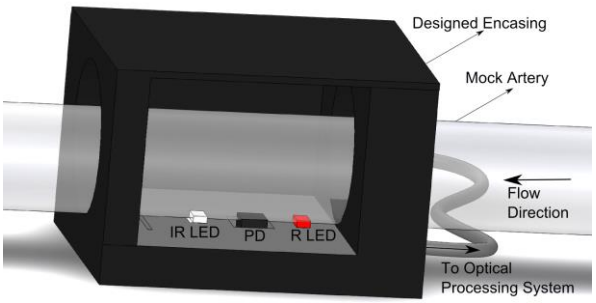

Figure 3. 3D illustration of the custom-made PPG optical sensor enclosing a tube section, showing Infrared (IR) and Red (R) LEDs, photodiode (PD), mock artery and the designed encasing

2) Optical Processing System

For the acquisition of PPG signals, a custom-made two-channel dual wavelength PPG instrumentation system was designed. The PPG processing system was constructed on printed circuit boards to pre-process and convert the detected current into voltages for later acquisition. The processing system used multiplexed current sources (set to 25 mA) to drive both red and infrared LEDs consecutively. The micro controller generates the digital switching clock so that the photo detector captures both at a frequency of 900 Hz. The mixed signals were fed into the demultiplexer and were then split into their respective red and infrared PPG signals. Pressure signals were digitized using the 9172-c Data-Acquisition card (DAQ2) (National Instruments, UK). R and IR PPG signals were digitized using the PCIe-6321 16-bit (DAQ1)16-bit (DAQ1) (National Instruments, UK). All signals were digitized at a sampling rate of one kHz.

3) Measurement Protocol

Two liters of hexahydrate cobalt nitrates in saline solution (concentration = 0.6 M) were prepared. The reservoir was filled, and the fluid was circulated in the model for 10 minutes before data collection in order to allow the system to stabilize and eliminate any bubbles. Data collection continued for one minute at each pumping frequency (0.67 Hz, 1 Hz, and 1.8 Hz) at a stroke volume of 30 ml. Stroke volumes were increased to 70 ml and data recording continued for one minute at the three frequency set-points.

4) Data and statistical analysis

The recorded signals were analyzed in a customized Matlab script (Mathworks, US). PPG_{AC} was extracted using a band-pass filter with a cut-off frequency in the range (0.15-30 Hz). PPG_{DC} levels were obtained using a low-pass filter at a cut-off frequency of 0.05 Hz. Root Mean Square Error (RMSE) and R-square (r) values indicate the goodness of curve fitting. Comparison of correlation coefficients was stated as a z-value, obtained via the Fisher r-to-z transformation.

IV. Results

The collected signals were of high quality. Figure 2 presents a five-second sample obtained with a stroke volume of 30 ml and a pumping frequency of 0.67 Hz. Panel (a) shows the PPG_{AC} signals at R and IR wavelengths. Panel (b) shows the PPG_{DC} levels at R and IR wavelengths. Pressure signals are presented in panel(c).

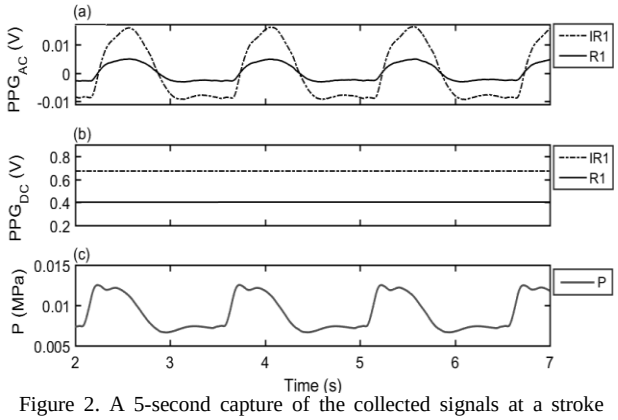

Figure 2. A 5-second capture of the collected signals at a stroke volume of 30 ml and a frequency of 0.67 Hz. Panel (a) presents PPG_{AC} components for Red (R) and infrared (IR) signals. Panel (b) presents PPG_{DC} levels for R and IR signals, and panel (c) shows pressure signals (P).

Typical scattergrams and curve fits applying (10), (11) and (12) are shown in Figure 4. The three different methods of *dV* estimation are shown. Points include cycle-to-cycle data of 60 seconds at each pumping frequency (0.67 Hz, 1 Hz, and 1.8 Hz) and both stroke volumes (30 ml and 70 ml). Panel (a) presents ln(P)-APV function. Panel (b) exhibits ln(P)-NPV_{IR} function and panel(c) presents ln(NPV_R)-P. Values of the goodness of fit (r^2 and RMSE) are also listed for each function.

V. Discussion

The primary contribution of this study is to validate the relationship between the components of the PPG signal at both wavelengths and pressure, based on the exponential model for the finger arterial P-V function in an *in-vitro* controlled setup at varying flow rates.

The observed closeness of fit is seen in Figure 4 confirms the validity of the descriptive model function in the *in vitro* model. The APV correlation was highly significant (r=0.99, RMSE=0.002, n=420, p<0.0001) and showed a remarkably better fit than the NPV method. NPV also obtained consequential correlations (r^2=0.73, RMSE=0.292, n=420, p<0.0001) and (r^2=0.95, RMSE=0.108, n=420, p<0.0001) for NPV_R and NPV_{IR} respectively. In fact, correlation comparisons showed that *APV* fit was significantly better than that obtained from NPV_R (z=12.26, p<0.0001) and NPV_{IR} (z=25.85, p<0.0001).

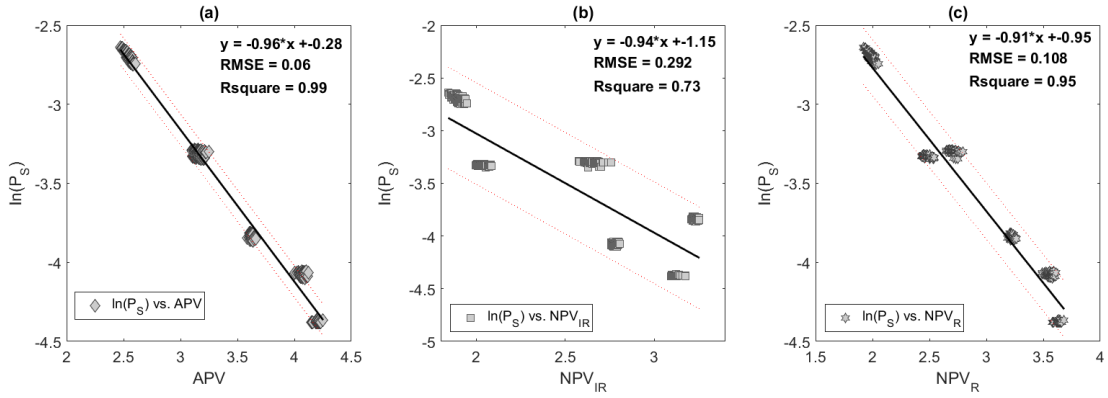

Figure 4 Typical scattergrams and curve fits for ln(P)-V functions using the different methods are presented. Panel (a) shows the natural logarithmic systolic pressure ln(Ps)- adjusted pulse volume (APV) function. Panel (b) shows ln(Ps)-infrared normalized pulse volume (NPVIR)-function. Panel(c) shows ln(Ps)-red normalized pulse volume (NPVR) function. Values of the goodness of fit are presented in R-square(r) and Root Mean Square Error (RMSE). Points include cycle-to-cycle data of 60 seconds at each experimental stage, i.e. pumping frequencies (0.67 Hz, 1 Hz, and 1.8 Hz) at both stroke volumes (30 ml and 70 ml). Dotted lines are 90% prediction bounds.

Steady flow is known to develop in the center of a circular tube where fluid movement obtains the maximum possible velocity in a straight line. Whereas, PPG_{AC} relates to oscillatory flow volume and is directly affected by the pressure signal and the elastic properties of the wall. The presence of oscillatory and steady flow highlights the important role of the penetration depth of IR and R signals. Though it was unfeasible in this study to quantify this depth, previous studies have confirmed that IR signals penetrate deeper into tissues, which would suggest satisfactory measurement of the steady flow [11]. However, due to the different absorption characteristics of the steady flow region, this might contribute to an error in the AC signal obtained at higher wavelengths. The R signal is known to reach a shallower layer, an on that ground, it can be used for a better representation of pulsatile flow. Therefore, APV, as calculated from (8), provides a more realistic measurement of the pulsatile flow considering both oscillatory and steady components.

Previous investigations of the relationship between pressure and the magnitude of PPG_{AC} in human studies reported the inverse of the relationship observed in this study (i.e. light attenuation was observed at increasing pressure) [7]. The mechanism of the endothelial activation controls the vascular tone through the vessel diameter is known to contribute to this inverse behavior. At high pressures, the vascular resistance increases by the effect of vasoconstriction and, therefore, the expected drop in total volume. A recent study reported on the dependency of chemical control on the mechanical stimuli in endothelial cells [15], and, therefore, it is expected that the derived relationship would still be valid in a human study.

VI. Conclusion

This study explored the relationship between PPG_{AC} and PPG_{DC} of R and IR signals with pressure signals at different flow rates in an *in-vitro* setup that mimics the human circulation. While oscillatory fluid volumes estimated using NPV_R and NPV_{IR} showed significant correlation fitting with the exponential P-V relationship, the optimum fit was obtained using APV, derived from both wavelengths. The presented relationship is validated at different pulse frequencies and stroke volumes with mean pressure values range of 45-180 mmHg. The validity of the derived relationship over this wide range of mean pressures at varying pumping rates and stroke volumes indicates that the method has a potential for *in-vivo* applications even during hemodynamic instabilities. Future *in-vivo* investigations are required for further validation.

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