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Investigation of finger reflectance photoplethysmography in volunteers undergoing a local sympathetic stimulation

H. Njoum, P.A. Kyriacou

Abstract— Optical sensors used in clinical applications have gained great popularity over the last few decades, especially the photoplethysmographic (PPG) technique used in estimating arterial blood oxygen saturation in the well-known medical devices called pulse oximeters. In this study we investigate the photoplethysmogram further in an effort to understand its origin better, as there is a significant void in the current knowledge on the PPG quantitative measurement. The photoplethysmographic signal provides a heart rhythm pulsating AC component, and a non-pulsating DC component. The signal is commonly believed to originate from tissue volume changes only and hasn't been investigated intensively. This *in vivo* study examines the source of the PPG signal in relation to pulse amplitude and pulse rhythm while volunteers undergo a right hand ice immersion. It was found that the PPG signal is sensitive in detecting the sympathetic stimulation which corresponds to volumetric and heart rate changes. During the immersion, AC pulse amplitudes (PA) from both hands decreased significantly, while DC levels increased significantly in the right hand and non-significantly in the left hand. Also, a significant decrease in the pulse repetition time (PRT) was observed. Using blood pressure-flow theories, these results suggest that there are possibly other factors in the blood flow regulation that alter the blood optical density which contributes to the detected signal. Further studies need to investigate PPGs in relation to blood optical density and the dynamics of the pulsatile flow effects besides volumetric changes. Such investigations might explore more applications of the PPG in medicine.

I. BACKGROUND

Since the 1930's, the non-invasive optical technique named 'photoplethysmography' has gained broad interest. A photoplethysmographic signal can be obtained at any vascular location on the skin surface using optical probes operating in either reflection or transmission mode [1-2]. During these measurements, light is directed to the tissue, where it travels in complex pathways facing multiple stages of reflection, absorption and scattering. Photoplethysmography is extensively used for the estimation of arterial blood oxygen saturation, a technique known as pulse oximetry. Pulse oximeter sensors use red and infrared optical wavelengths that are sensitive to changes in arterial oxygen saturation because of differences in the light absorption of oxygenated and deoxygenated haemoglobin at these two wavelengths. After the light is transversed or reflected through the vascular tissue, it reaches the photodetector and the current variations are electronically amplified and recorded to provide the photoplethysmographic signal. The detected signal comprises of two PPG components; the pulsatile AC component and the non-pulsating DC component [3-4].

A. The origin of the PPG signal

The validity of the PPG quantitative measurement is questioned because most investigators in the field rely on the assumption that the detected light has a linear relationship with the intravascular volume, therefore considering the red cell density to be directly proportional to that space. However, other factors of blood flow behaviour are also believed to contribute to the signal. Findings from some studies on the origin of photoplethysmography have demonstrated that light travelling through blood can diffuse preferentially in the direction of the motion of blood. This pattern of diffusion was suggested to emerge from a combination of the plasma skimming, which occurs at the vessel wall and from the orientation effects of the erythrocytes when in motion [5-7]. In addition, studies have related haematocrit concentration to the PPG pulse amplitude, and attempts to estimate haemoglobin concentration using PPGs have also been initiated [8-9]. The role of such factors and their contribution to the origin of the PPG signals has not been investigated rigorously yet. The dynamics of the pulsatile flow in the blood circulation needs to be considered in relation to the PPG signal and is discussed briefly below.

B. The pulsatile flow and the pressure propagation wave

Blood flow distribution controls are initiated by neural, cardiac and respiratory interactions. These maintain a balance between tissue perfusion and heart mechanics in a complex relationship of bioelectrical signals, biochemical reactions and a variety of mechanical forces [10]. The heart impulse is generated at the sinoatrial (SA) and atrioventricular (AV) nodes in the heart, causing a synchronized rhythmic frequency which can be clearly observed in the smaller vascular bed when using the PPG technique. These electrical impulses caused by the SA and AVR nodes result in the contraction of the heart muscle. Therefore, circumferential stresses are generated in the heart, a force normal to the cardiac wall is applied to the fluid, and the intracardiac pressure increases shortly and then falls during the heart relaxation period. The detailed study of biological tissue conductivity in relation to blood flow motion and tissue perfusion is still under investigation [11]. Nevertheless,

these forces result in the pressure-flow relationship that has been studied for many years [12-13]. The well-known Hagen-Poiseuille law considers a steady, laminar, viscous and non-compressible fluid in a straight smooth walled tube. The classical approach of haemodynamic points at arterial distensibility and volume change as the primer determinants of pulse pressure. In the presence of the pulsatile blood flow and the complexity of the geometry and elasticity of vessel networks, there are additional forces to be considered. These are inertia and viscosity, which are related to distensibility in a complex manner. These forces are more significant in small capillaries where the blood is thought to obtain shear thinning and viscoelastic properties. This suggestion has been debated, considering the flow to be continuous in a laminar flow. Blood is really a suspension of proteins and cells in an aqueous medium and its dynamics are more complicated than classically assumed. A discussion of non-Newtonian fluid dynamics and its relation to heart forces is beyond the scope of this study [14]. However, the approach adopted considers the complex relationship of pressure and flow dynamics. An attempt to explain PPG signal behaviour in relation to this consideration is discussed later.

Consequently, the volume contained within the arteries is a function of the pressure difference across their wall, called the transmural pressure. Transmural pressure is seen as a haemodynamic signal that exerts a force on the vessel wall. It depends on the intracardial fluid dynamics and the heart morphology. The blood pressure exerted against the walls of an artery and the energy required to move blood at a certain velocity is interrelated by the Bernoulli's principle, where the total energy of blood flow (potential and kinetic energy) at any given point in a system is constant [13]. This approach will be adopted later to explain the change in the pulse repetition time.

C. Sympathetic System stimulation

The immersion of one hand in an ice-water bath, the so-called cold pressor test, is a standard autonomic function test to assess the sympathetic activity. Neural and hormonal reactions will allow cutaneous vasoconstriction in the dermis, a rise in both systolic and diastolic blood pressure and therefore, increased heart rates are also associated with the immersion [15-17]. This study was conducted in healthy subjects, who underwent ice immersion of the right hand for 30s, while recording PPG signals and temperature measurements from both hands. Electrocardiogram signals were also recorded.

This in vivo investigation was designed to allow local sympathetic nervous stimulation and observe changes in the PPG signal in relation to the following effects; (a) the volumetric changes in the vessels in both hands due to vasoconstriction, followed by vasodilation response, (b) the pulsating wave speed changes due to the heart rate immediate increase during the immersion.

II. MATERIALS AND METHODS

The experimental set-up for this in vivo study is described in Figure 1.

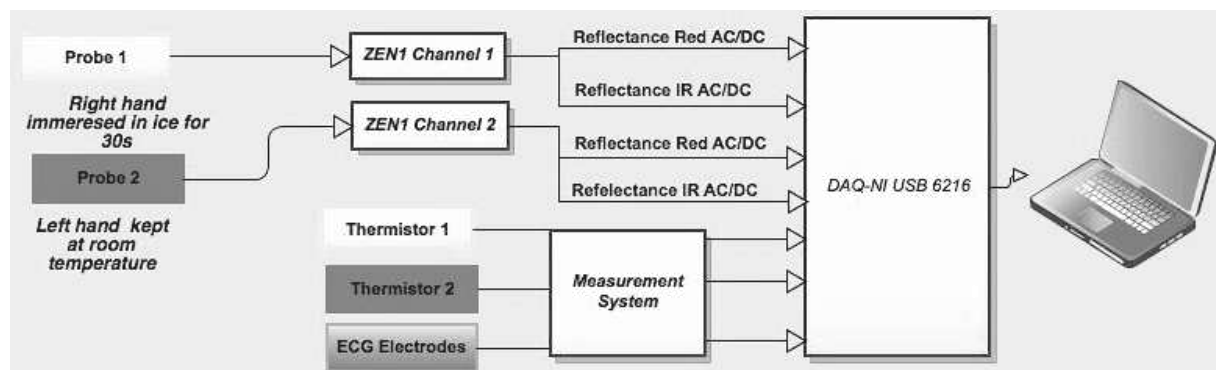


Figure 1: Block diagram of the experimental set up

A. Reflectance PPG Probes

A pair of identical custom-built reflectance PPG finger probes (Probe 1 and Probe 2) were developed. Each probe comprises of two surface mount ceramic type infrared LEDs with peak emission wavelength of 880 nm, two red LEDs with peak emission wavelength of 660 nm and a photodiode. The LEDs are arranged to maintain a separation distance of 5 mm from the centre of the photodiode. The LED driving current (20 mA) is controlled digitally in the PPG processing system switching the LEDs on and off asynchronously. The duty cycle of the switching pulses is 33.3%.

B. Instrumentation

The PPG processing system (ZEN1) was developed by the Biomedical Engineering Research Group (BERG) [18]. The circuits were constructed on printed circuit boards to pre-process, record and display raw PPG signals from two channels and two wavelengths on a laptop personal computer. The detected currents from the photodiodes are converted into voltage using a differential transimpedance amplifier. The micro-controller, acts as the master clock to generate digital switching signals at a frequency of 500 Hz. These digital signals directly correspond to the LED switching. The mixed PPG signals at the output of the transimpedance amplifier are split into their respective red and infrared PPG signals using a demultiplexer.

The temperature measurement system was developed to contain all necessary temperature linearization circuits. The measurements were obtained utilising two (one for each hand) water resistant rapid response (0.6 s) thermistors (thermistor 1, thermistor2).

The Electrocardiogram (ECG) signals were also recorded as a gold standard measurement for heart rate rhythms. The ECG measurement system was developed using an instrumentation amplifier and a sallen-key bandpass filter. Electrodes (Ag/AgCl) were placed using standard limb leads (Lead I).

A 16-bit data acquisition card (6212 DAQ, National Instruments Inc.) was used to acquire the raw analogue signals. All digitized signals were further processed (digital filtering, amplification, etc.) using a virtual instrument implemented in LabView.

C. Methods

The experimental protocol for this study was approved by the Senate Research Committee at City University London. Twelve healthy subjects were recruited, 5 females, 7 males, aged 18-45 years (mean age \pm SD, 26.9 ± 4.6 years; range, 19-33 years). All subjects gave informed written consents for their participation. The subjects were asked to abstain from smoking and exercising for at least two hours before the experiment. All testing was conducted in a temperature control room with the temperature was maintained at $21 \pm 2^\circ\text{C}$. Subjects were required to acclimatize to the testing room temperature upon arrival for a few minutes. The developed reflectance PPG probes were clipped on both index fingers. Skin thermistors were tightly attached on the tip of the middle fingers. The recording started once the volunteer was comfortable and continued for two minutes as baseline monitoring. The volunteer was then asked to slowly immerse their right hand until the wrist was fully in the ice-water bath (maintained at $2 \pm 2^\circ\text{C}$). After 30 s, the volunteer was asked to rest their hand back at room temperature on a dry surface. The recording continued for an average of 9 min as a rewarming period.

III. RESULTS

Good quality PPG signals were obtained from all participants. Changes in infrared PPG components and temperature values for a recording of nine minutes for both index fingers from one of the volunteers is shown in figure 2.

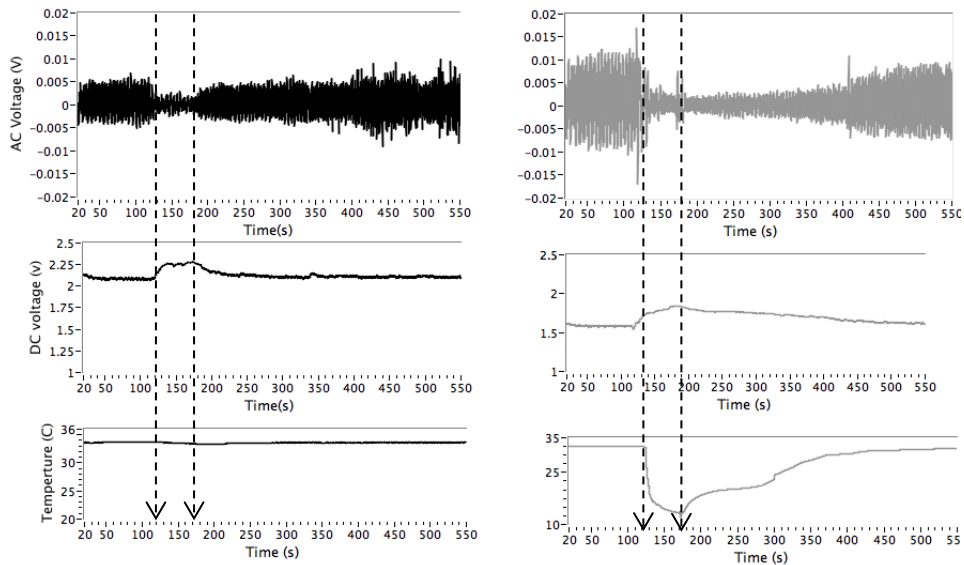


Figure 2: Infrared reflectance AC and DC PPG signals and skin temperatures from one volunteer. Left hand signals, resting at room temperature are in black and right hand signals, undergoing ice-water immersion in grey. Ice immersion period is marked between arrows.

The increase in the sympathetic tone was apparent once the immersion had started. Temperature values dropped significantly in the right hand and DC PPG levels increased in both hands. The pulse amplitude (AC signal) decreased in both hands. Once the immersion had ended, PPG values gradually returned to baseline in the right hand, while the PPG signals instantly returned to baseline in the left hand (see Fig. 2). Generally, PPG recordings were still useful for cardio assessment in most volunteers during the immersion as can be seen in figure 3.

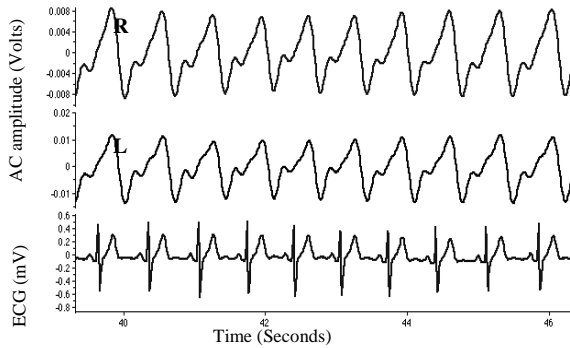


Figure 3A: Baseline ECG and infrared AC PPG recordings from both hands.

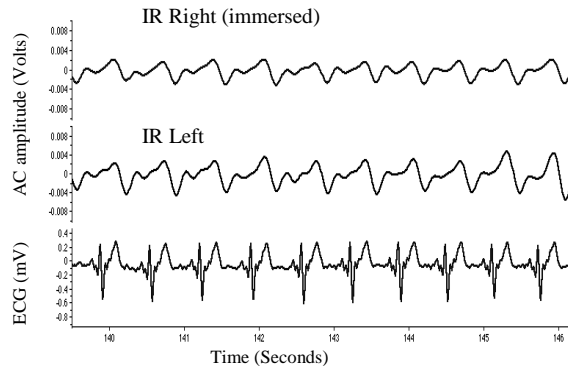


Figure 3B: ECG and infrared AC PPG recordings from both hands during the immersion.

Occasionally, volunteers had a drop in PA sufficient to diminish the signal quality and others experienced discomfort at the end of the immersion, which resulted in some movement artefacts. On average, the temperature values decreased statistically significant in the right hand ($P < 0.005$) for the duration of the immersion. The average decrease in temperature was $20^{\circ}\text{C} (\pm 5^{\circ}\text{C})$ at the end of the 30 s of immersion. Thereafter, temperature values increased gradually until the end of the study. The average temperature increase was $12^{\circ}\text{C} (\pm 2^{\circ}\text{C})$ after 5 minutes of the immersion. Left hand temperatures had different patterns of response in volunteers, and can be averaged to $\pm 1^{\circ}\text{C} (\pm 0.5^{\circ}\text{C})$.

Averaged values for all signals can be seen in figure 4, average right finger pulse amplitude decreased from baseline by 51% ($\text{SD} \pm 0.077$) for the red wavelength and 73% ($\text{SD} \pm 0.312$) for the infrared wavelength. While, the average PA of the left finger decreased from baseline by 55% ($\text{SD} \pm 0.138$) for the red wavelength and 62%

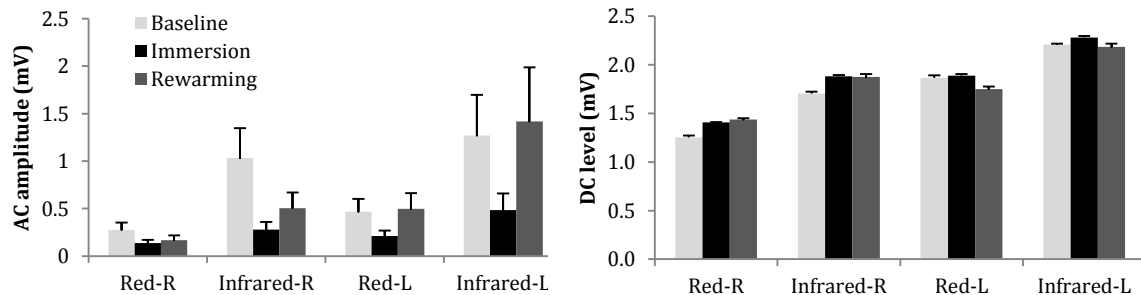


Figure 4: Averaged values for AC and DC amplitudes for the periods; baseline (2 mins), immersion (30 secs) and rewarming (5 mins).

($\text{SD} \pm 0.427$) for the infrared wavelength. All PA values decreased significantly ($P < 0.005$). An immediate increase also occurred in the DC component of the PPG signal in the right hand. The average right finger DC levels increased significantly ($P < 0.005$) from baseline by 13% ($\text{SD} \pm 0.005$) and 11% ($\text{SD} \pm 0.011$) for the red and infrared wavelengths respectively. The average left hand DC PPG levels increased only by 2% ($\text{SD} \pm 0.018$) in the red PPG segment and by 3% ($\text{SD} \pm 0.016$) in the infrared PPG segment.

There was an immediate increase in heart rates in all volunteers at the moment of skin-ice bath contact averaged to 10 beats per minute (BPM) as seen in figure 5. Thus, a significant drop ($P < 0.005$) in the PRT was observed (see Fig.6). These values returned to baseline once the immersion had ended.

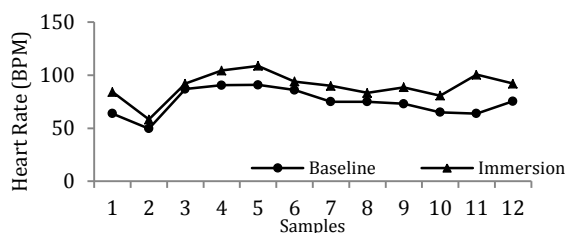


Figure.5 Averaged heart rate (BPM) for all volunteers for baseline period and during immersion. Calculated from PPG signals.

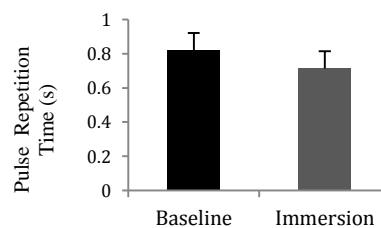


Figure.6 Averaged PPG pulse repetition time for all volunteers.

IV. DISCUSSION

This study found that while the right hand temperature values decreased during the immersion in ice water, PPG recordings from both hands have shown that there was an increase in the DC PPG levels, and a decrease in the pulse amplitude of the PPG signal. In addition, there was a decrease in pulse repetition time.

The PPG has been used as a tool to measure vasomotor tone under various experimental conditions. The peripheral vasoconstriction and vasodilation affect both the AC and DC components of the PPG signal. Most previous studies have been limited by the inability or lack of interest to access the complete PPG signal. A significant feature of our study is that we recorded the PPG continuously throughout and we analysed both components for different locations under local sympathetic stimulation.

An increase in DC levels was accompanied with a drop in PA in a separate pattern in both hands. This is not completely surprising, because sympathetic stimulation will cause a vasoconstriction in the vascular bed. The vasoconstriction can be seen in the increase of the DC component of the PPG, which perhaps is correspondent to the changes in venous blood fraction. This behaviour is also expected because of the thickening of the dermis layer during the sympathetic response. The dermis is consistent of collagen fibres, which contributes to events of multiple scattering and can be viewed as a turbid media [19]. The different changes in DC levels in both hands confirm that the right hand (undergoing the immersion) is more constricted than that resting at room temperature. This is also expected, due to α -adrenoceptors distribution in the endothelial cells. Endothelial cells release locally acting chemical messengers in response to various changes in their environment, such as changes in oxygen (O_2) or physical stretching of the wall. These local vasoactive mediators act on the underlying smooth muscle to alter its state of contraction. The relative contributions of these various chemical changes in the local metabolic control of blood flow in systemic arterioles are still being investigated [20].

Pulse amplitude decreased significantly in both hands, this can be referred to vasoconstriction effects and the expected drop in the arterial blood volume as described above. Whether PA and DC changes are due to volumetric changes solely is undetermined. The drop in PRT is another observed change to be discussed. The pulsating wave speed is a strong function of pressure as mentioned earlier, due to the elastic properties of the red blood cells and the nonlinear elastic properties of the arterial wall. Previous studies have confirmed that an increase in blood pressure is accompanied with the heart rate increase during the cold pressor test [16]. Others have also observed the gradual drop in PA PPG signals, while volunteers underwent controlled artificially induced hypoperfusion using a blood pressure cuff [21].

Theories admitting the complexity of pressure-flow relationship consider three forces, the friction force, the kinetic force and the force exerted on the wall vessels in relation to its distensibility. These parameters affect each other and the pressure wave is an instantaneous sum of these applied forces. The observed change in the heart rate during the immersion is known to be associated with reduced arterial distensibility [22]. Relying on the Bernoulli's principle, any increase in one form of the energy has to come at the expense of the other; hence the reduced distensibility should be correlated with increased transmural pressure (tension on wall) and therefore, lateral pressure between the red blood cells is expected to decrease. Bernoulli's equation overlooks the viscosity of the fluid so relying on Poiseuille considerations of a viscous fluid, the change in total pressure is expected to result in an increase in their frictional forces. Those forces are affected by the red blood cells count or their phenomenal reversible mechanical properties. These properties are also believed to allow changes in cells' membrane structure, shape and size in order to maintain the required balance. Therefore, an increase in blood viscosity is expected during the increased sympathetic tone and the elevated heart rate [23-24]. These changes are plausibly related to changes in the optical density of blood in terms of concentration, molecules' structure or size. This might explain the similar pulse amplitude behaviour in both hands regardless of the different change in the DC levels. We estimate that blood optical density may vary in relation to pressure and metabolic conditions, which might affect the detected light and will be of direct interest to all investigators in the field of photoplethysmography and its applications. Further *in vivo* and *in vitro* investigations need to explore the pulsatile dynamics in relation to PPG, highlighting blood viscosity and possibly rheology. Potentially, a standardized PPG technique might allow applications related to a variety of blood pathologies (sepsis, sickle cells, anaemia and others) where the blood optical density is altered from the norm.

V. CONCLUSION

In this experiment, we found that changes in the AC and DC components of the PPG and finger temperature characterize the change in the sympathetic tone during the immersion of the hand in ice (vasoconstriction and increased heart activity) and the parasympathetic tone after the immersion (vasodilation and baseline heart activity). The increased sympathetic tone includes both effects of vasoconstriction and elevated heart rate. Clearly they both contributed to changes in PPG DC levels, pulse amplitude and repetition time. Theories of blood pressure and flow indicate that such effects not only allow changes in the optical path length but might

also affect the biological tissues' absorption coefficients during blood circulation. The path to quantify a standardized PPG waveform suggest further exploration of tissue optical properties in relation to the molecular and cellular mechanisms of blood flow control.

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