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TOPICAL REVIEW

Photoplethysmography and its application in clinical physiological measurement

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Abstract

Photoplethysmography (PPG) is a simple and low-cost optical technique that can be used to detect blood volume changes in the microvascular bed of tissue. It is often used non-invasively to make measurements at the skin surface. The PPG waveform comprises a pulsatile ('AC') physiological waveform attributed to cardiac synchronous changes in the blood volume with each heart beat, and is superimposed on a slowly varying ('DC') baseline with various lower frequency components attributed to respiration, sympathetic nervous system activity and thermoregulation. Although the origins of the components of the PPG signal are not fully understood, it is generally accepted that they can provide valuable information about the cardiovascular system. There has been a resurgence of interest in the technique in recent years, driven by the demand for low cost, simple and portable technology for the primary care and community based clinical settings, the wide availability of low cost and small semiconductor components, and the advancement of computer-based pulse wave analysis techniques. The PPG technology has been used in a wide range of commercially available medical devices for measuring oxygen saturation, blood pressure and cardiac output, assessing autonomic function and also detecting peripheral vascular disease. The introductory sections of the topical review describe the basic principle of operation and interaction of light with tissue, early and recent history of PPG, instrumentation, measurement protocol, and pulse wave analysis. The review then focuses on the applications of PPG in clinical physiological measurements, including clinical physiological monitoring, vascular assessment and autonomic function.

Keywords: ageing, artery, autonomic function, blood pressure, cardiac output, cardiovascular, diabetes, endothelial function, heart rate, infrared, microcirculation, photoplethysmography (PPG), pulse wave analysis, Raynaud's phenomenon, vascular disease, vein

1. Background to the topical review

Photoplethysmography (PPG) is an optical measurement technique that can be used to detect blood volume changes in the microvascular bed of tissue (Challoner 1979). It has widespread clinical application, with the technology utilized in commercially available medical devices, for example in pulse oximeters, vascular diagnostics and digital beat-to-beat blood pressure measurement systems. The basic form of PPG technology requires only a few opto-electronic components: a light source to illuminate the tissue (e.g. skin), and a photodetector to measure the small variations in light intensity associated with changes in perfusion in the catchment volume. PPG is most often employed non-invasively and operates at a red or a near infrared wavelength. The most recognized waveform feature is the peripheral pulse, and it is synchronized to each heartbeat. Despite its simplicity the origins of the different components of the PPG signal are still not fully understood. It is generally accepted, however, that they can provide valuable information about the cardiovascular system (Kamal *et al* 1989).

This review has two parts. An introductory section describes the basic principle of PPG operation, light interaction with tissue, early and recent history of PPG, instrumentation, measurement protocol, and pulse wave analysis. The second section reviews current and potential clinical applications in physiological measurement under the categories of clinical physiological monitoring, vascular assessment and autonomic function.

2. Photoplethysmography

2.1. The photoplethysmography waveform

The pulsatile component of the PPG waveform is often called the 'AC' component and usually has its fundamental frequency, typically around 1 Hz, depending on heart rate (figure 1). This AC component is superimposed onto a large quasi-DC component that relates to the tissues and to the average blood volume. This DC component varies slowly due to respiration, vasomotor activity and vasoconstrictor waves, Traube Hering Mayer (THM) waves and also thermoregulation (Burton 1939, Burton and Taylor 1940, Hertzman and Dillon 1940b, Hertzman and Roth 1942a, 1942b, 1942c, Hertzman and Flath 1963, Hyndman *et al* 1971, Peñáz 1978, Ahmed *et al* 1982, Harness and Marjanovic 1989, Nitzan *et al* 1996b, 1996a, general thermoregulatory pulse changes in Shusterman *et al* (1997), Schultz-Ehrenburg and Blazek (2001), Nitzan *et al* (2001)). These characteristics are also body site dependent (Allen and Murray 2000b). With suitable electronic filtering and amplification both the AC and DC can be extracted for subsequent pulse wave analysis.

2.2. Optical considerations of the origins of the photoplethysmography waveform

The interaction of light with biological tissue is complex and includes the optical processes of (multiple) scattering, absorption, reflection, transmission and fluorescence (Anderson and Parrish 1981). Several researchers have investigated the optical processes in relation to PPG measurements (Hertzman and Randall 1948, Brown *et al* 1965, D'Agrosa and Hertzman 1967, Weinman 1967, Zweifler *et al* 1967, Challoner 1979, Ochoa and Ohara 1980, Nijboer *et al* 1981, Roberts 1982, Lindberg and Öberg 1993, de Trafford and Lafferty 1984, Kamal *et al* 1989). They have highlighted the key factors that can affect the amount of light received by the photodetector: the blood volume, blood vessel wall movement and the orientation of red blood cells (RBC). The orientation effect has been demonstrated by recording pulsatile waveforms from dental pulp and in a glass tube where volumetric changes should not be

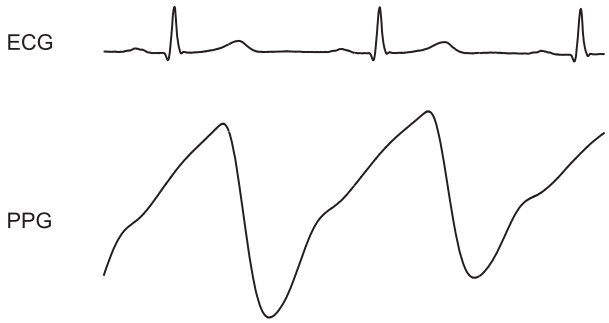

Figure 1. The pulsatile (AC) component of the PPG signal and corresponding electrocardiogram (ECG). The AC component is actually superimposed on a much larger quasi-DC component that relates to the tissues and to the average blood volume within the sample. It represents the increased light attenuation associated with the increase in microvascular blood volume with each heartbeat. In practice, the PPG waveform is often inverted.

possible, and more recently by Näslund *et al* (2006) who detected pulsatile waveforms in bone. The recorded pulses do bear a direct relationship with perfusion, and the greater the blood volume the more the light source is attenuated. However, attempts at pulse amplitude quantification ('calibration') have been largely unsuccessful (Hertzman 1938, Challoner and Ramsay 1974, Jespersen and Pedersen 1986, Cejnar *et al* 1993).

The wavelength of optical radiation is also important in light–tissue interactions (Cui *et al* 1990), and for three main reasons: (1) *The optical water window*: the main constituent of tissue is water that absorbs light very strongly in the ultraviolet and the longer infrared wavelengths. The shorter wavelengths of light are also strongly absorbed by melanin. There is, however, a window in the absorption spectra of water that allows visible (red) and near infrared light to pass more easily, thereby facilitating the measurement of blood flow or volume at these wavelengths. Thus, the red or near infrared wavelengths are often chosen for the PPG light source (Jones 1987), (2) *Isobestic wavelength*: significant differences exist in absorption between oxyhaemoglobin (HbO_2) and reduced haemoglobin (Hb) except at the isobestic wavelengths (Gordy and Drabkin 1957). For measurements performed at an isobestic wavelength (i.e. close to 805 nm, for near infrared range) the signal should be largely unaffected by changes in blood oxygen saturation, and (3) *Tissue penetration depth*: the depth to which light penetrates the tissue for a given intensity of optical radiation depends on the operating wavelength (Murray and Marjanovic 1997). In PPG the catchment (study) volume, depending on the probe design, can be of the order of 1 cm^3 for transmission mode systems. PPG can provide information about capillary nutritional blood flow and the thermoregulatory blood flow through arterio-venous anastomosis shunt vessels.

2.3. Early and recent history of photoplethysmography

This paragraph gives a brief summary of the early history of PPG and is taken from the excellent review article by Challoner (1979). In 1936 two research groups (Molitor and Kniazuk of the Merck Institute of Therapeutic Research, New Jersey, and Hanzlik *et al* of Stanford University School of Medicine) described similar instruments used to monitor the blood volume changes in the rabbit ear following venous occlusion and with administration of vasoactive drugs. Molitor and Kniazuk also described recordings made with a reflection mode PPG system from human fingers. A pioneer who helped establish the PPG technique was Alrick Hertzman from the Department of Physiology at St. Louis University School of

Medicine, St. Louis, MO. In 1937, Hertzman and his colleagues published their first paper on PPG describing the use of a reflection mode system to measure blood volume changes in the fingers induced by the Valsalva manoeuvre, exercise and with exposure to cold. This excellent contribution to the field demonstrated the potential clinical utility of the technique. In 1938, Hertzman undertook a validation of the PPG technique by comparing blood volume changes with those measured simultaneously by mechanical plethysmography. Preliminary observations on the PPG technique were also reported in the same year by Matthes and Hauss. Hertzman and Dillon (1940a) split the AC and DC components with separate electronic amplifiers and monitored vasomotor activity. Potential sources of error with the technique have been identified by Hertzman (1938), who emphasized that good contact with skin was needed, but without excessive pressure that would result in blanching. He advised that movement of the measurement probe against the skin should be avoided. These observations led to the development of elaborate positioning devices. Illumination was identified as another important design consideration. Hertzman also used a battery powered torch bulb which was less than ideal because of its relatively wide spectrum, particularly in the infrared because of local tissue heating, errors due to the effects of oxygen saturation, and the widespread illumination which can mix skin microvascular blood flow with larger vessel signals. Furthermore, constant light intensity could not be guaranteed.

In more recent decades the desire for small, reliable, low-cost and simple-to-use non-invasive (cardiovascular) assessment techniques are key factors that have helped re-establish photoplethysmography. Advances in opto-electronics and clinical instrumentation have also significantly contributed to its advancement. The developments in semiconductor technology, i.e. light emitting diodes (LED), photodiodes and phototransistors, have made considerable improvements in the size, sensitivity, reliability and reproducibility of PPG probe design. A major advance in the clinical use of a PPG-based technology came with the introduction of the pulse oximeter as a non-invasive method for monitoring patients' arterial oxygen saturation (Aoyagi *et al* 1974, Yoshiya *et al* 1980). There have also been considerable developments in computer-based digital signal processing and pulse wave analysis.

2.4. Photoplethysmography instrumentation

Modern PPG sensors often utilize low cost semiconductor technology with LED and matched photodetector devices working at the red and/or near infrared wavelengths (*CIE* IR-A near infrared band 0.8 to 1 μm, Duck (1990)). An excellent review of optical sensor technology for PPG and pulse oximetry applications is written by Webster (1997).

The choice of light source is important (Burke and Whelan 1986, Lindberg and Őberg 1991, Ugnell and Öberg 1995). LEDs convert electrical energy into light energy and have a narrow single bandwidth (typically 50 nm). They are compact, have a very long operating life ($>10^5$ h), operate over a wide temperature range with small shifts in the peak-emitted wavelength, and are mechanically robust and reliable. The averaged intensity of the LED should be constant and preferably be sufficiently low to minimize excessive local tissue heating and also reduce the risk of a non-ionizing radiation hazard. The choice of photodetector is also important (Weinman and Fine 1972, Fine and Weinman 1973). Its spectral characteristics are chosen to match that of the light source. A photodetector converts light energy into an electrical current. They are compact, low-cost, sensitive, and have fast response times. Near infrared devices can be encased with daylight filters. The photodetector connects to low noise electronic circuitry that includes a transimpedance amplifier and filtering circuitry.

A high pass filter reduces the size of the dominant DC component and enables the pulsatile AC component to be boosted to a nominal 1 V peak-to-peak level. Carefully

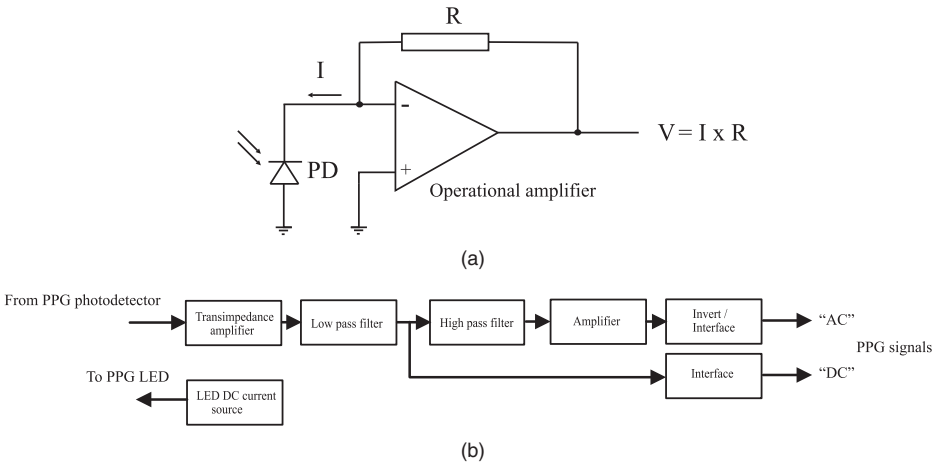

Figure 2. Electronic building blocks used in a typical PPG measurement system. (a) A transimpedance (current-to-voltage) amplifier stage that converts light intensity at the photodiode (PD) to an amplifier output voltage ($V = I \times R$, transimpedance gain proportional to feedback resistor value R). (b) The signal conditioning stages surrounding the transimpedance amplifier which include low pass filtering, high pass filtering and further amplification, inversion and signal interfaces. The AC component and a measure of the DC component are available for pulse wave analysis. A constant current driver stage for the PPG LED is also shown.

chosen filtering circuitry is also needed to remove the unwanted higher frequency noise such as electrical pick up from (50 Hz) mains electricity frequency interference. Figure 2(a) shows a transimpedance amplifier design and figure 2(b) shows the signal conditioning stages surrounding this, including low pass filtering, high pass filtering and further amplification, signal inversion and signal interface. The choice of high pass filter cut-off frequency is particularly important and is often a design compromise; excessive filtering can distort the pulse shape but too little filtering can result in the quasi-DC component dominating over the AC pulse (Allen and Murray 2003, 2004). This example system shows a constant current driver stage for the PPG probe LED.

There are two main PPG operational configurations: transmission ('trans-illumination') mode operation where the tissue sample (e.g. fingertip) is placed between the source and detector, and reflection ('adjacent') mode operation where the LED and detector are placed side-by-side. Clearly, transmission mode PPG imposes more restrictions than the reflection mode PPG on the body locations available for study. The PPG probe should be held securely in place to minimize probe-tissue movement artefact. There are other sources of artefact that need to be considered in the measurement technology. For example, artefact can arise from ambient light interference but can be reduced in several ways: by suitable probe attachment to the skin (e.g. using a dark Velcro wrap-around cuff), by further shading of the study site area and performing measurements in subdued lighting, and by electronic filtering (e.g. light modulation filtering, Webster (1997)). Ambient light interference in PPG-based systems has also been discussed by Hanowell *et al* (1987).

Many of the studies reported in the PPG literature are for a single site, often the ear, finger or toe, where pulses can easily be detected (including Stern (1974), Barnes *et al* (1977a, 1977b), Sherebrin and Sherebrin (1990), Allen and Murray (1993), Chowienczyk *et al* (1999), Hahn *et al* (1999), Bortolotto *et al* (2000), Foo *et al* (2006), Millasseau *et al* (2006)). Many other skin measurement sites are available for vascular assessment (Tur *et al* 1983). The supraorbital

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