Photoplethysmography and Its Clinical Application

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REVIEW ARTICLE

Photoplethysmography and Its Clinical Application

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ABSTRACT

Photoplethysmography (PPG), introduced in 1937, is routinely used for monitoring heart rate, blood perfusion and oxygen saturation of the blood in the intensive care units for the past several decades. It is also being used for the assessment of peripheral blood flow and venous filling time in noninvasive vascular laboratories. It works on the principle of light/infrared absorption in the body segment and detection and processing of transmitted light/infrared radiation.

In the past few decades, there has been more emphasis on the pulse morphology. Analysis of higher harmonic components and derivation of cardiovascular indices have emerged as powerful tools for the assessment of arterial aging, endothelial function, and vascular compliance. The ease of operating and extreme low cost of PPG system has made it ideal for objective assessment of autonomic nervous system (ANS). This technique is presently being explored for the personal monitoring of blood glucose noninvasively.

Keywords: Digital blood flow, Endothelial function, Heart rate variability, Photoplethysmography, Stiffness index, Venous filling time.

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INTRODUCTION

Literal meaning of plethysmography is the recording of instantaneous volume of an object. Due to irregular shape of different body parts, it is routinely used for volume assessment in the field of medicine. There are several plethysmographic methods for recording volume changes in any part of the body, such as volume displacement plethysmography, strain gauge plethysmography, impedance plethysmography, and PPG. These methods have been employed selectively from time to time depending upon the application. For quick assessment of blood flow in the limbs, air displacement plethysmograph, commercially available as pulse volume recorder (PVR) has been in common use till late 1970s. Strain gauge plethysmography has been in common use for respiratory monitoring, nocturnal penile tumescence, and venous occlusion phlebogram. Volume displacement plethysmography and strain gauge plethysmography have a common limitation in accurate estimation of blood flow as they are unable to distinguish between change in the limb volume caused by flow of blood or that of any other fluid. Strain gauge plethysmography, however, is still a method of choice for monitoring of respiration and nocturnal penile tumescence.

Electrical impedance plethysmography is more direct than the above two methods, as it takes into cognizance the electrical resistivity of the blood. Since blood is a good conductor of electricity as compared with remaining constituents of the body, such as bone, muscle, fat, skin, etc., the amount of blood in any part of the body is inversely proportional to the electrical impedance offered by the body segment. Therefore, pulsatile blood volume changes in the limb segment caused by rhythmic contraction of the heart can be recorded as pulsatile impedance changes. Huge volume of work has been done on this technique by large number of researchers in India as well as abroad and it is still a method of choice for continuous monitoring of cardiac output noninvasively.[1-3] However, the method calls for placement of surface electrodes on the body surface of the subject, free environment from electrical noise, and stringent requirement on the specifications of the instrument from the consideration of patient safety. There is always a need for non-Ohmic method, which can estimate blood circulation quickly, easily and accurately.

Photoplethysmography,[4,5] based on the optical properties of the blood, is an ideal choice for the measurement of blood flow for two reasons: (1) There is no electrical contact between the patient and instrument, and (2) it is specific for

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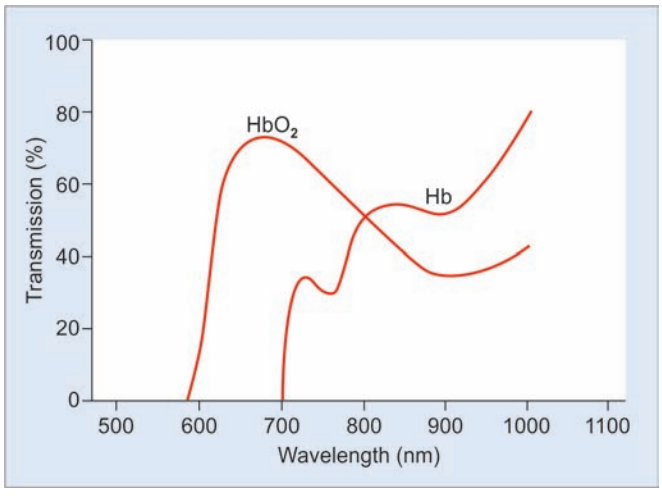
the blood unlike PVR and strain gauge plethysmography. Graph 1 shows the spectral transmission characteristics of oxy-hemoglobin (HbO_2) and reduced hemoglobin (Hb) in the visible and infrared regions of the electromagnetic waves.[6] As can be seen from the figure, transmission is highest for oxy-hemoglobin and reduced hemoglobin at wavelengths of 640 and 825 nm respectively, with common value at 805 nm. It increases for both beyond 900 nm. These characteristics are especially useful for monitoring oxygen saturation noninvasively in critically ill patients.

Graph 2 shows a typical PPG system in transmission mode. The light-emitting diode used as transmitter and photodiode used as receiver are mounted on the opposite side of the transducer cap or clip. It is energized with the help of square wave generator (100–500 Hz). Transmitted light received on the photodiode in the form of photocurrent is amplified and filtered with the help of 10 kHz low-pass filter. The output of filter is sampled and held with the logic input synchronized from square-wave generator. The output of sample and hold is amplified using differential amplifier. The direct current (DC) signal from the sample and hold is cancelled using a DC cancellation circuit as shown in the figure. The output of the differential amplifier (ΔP) can be recorded on a strip chart recorder or can be connected to an analog to digital converter (ADC) card for viewing it on personal computer (PC) monitor. For estimation of arterial blood flow, time derivative of ΔP signal is taken, known as dP/dt, and like ΔP it can be viewed on the monitor.



Graph 1: Transmission characteristics of oxy-hemoglobin and reduced hemoglobin in the visible and infra red regions of electromagnetic waves

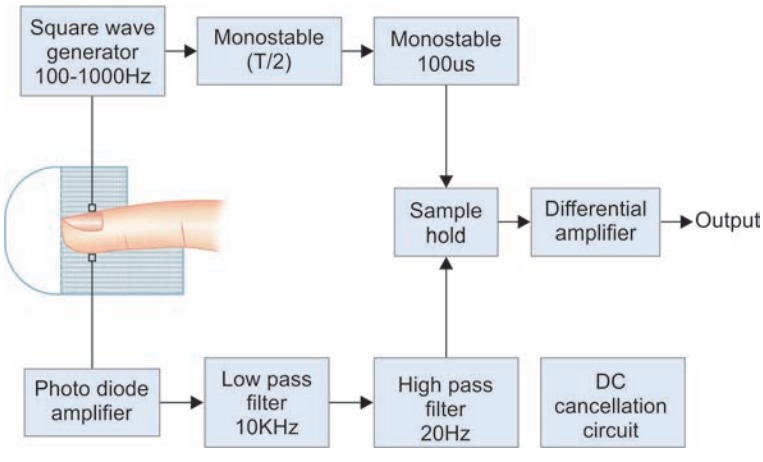
When the red light falls on finger/toe/earlobe, the light received on the other side through transmission depends on several factors, such as pulsatile blood volume in the arteries/arterioles (A), blood volume in the veins and tissues in the optical path (V), absorption in the skin and tissue pigments (T). "A" represents information on arterial blood, which is pulsatile and "V" and "T" represent the attenuation by venous blood and other tissue in the optical path, which are more or less constant.[7]

According to Beer–Lambert law, if the incident light intensity is I_0, a is the absorption coefficient for the dissolved solute in a solution with its concentration c, and L is the thickness of the solution measured along direction of light, intensity (I) of emergent light is given as:

$$I = I_0 e^{-aLc}$$

Assuming that the Beer–Lambert's law is valid for the whole blood, i.e., present in the finger/toe/earlobe, and that the attenuation of light by multiple scattering and reflection can be neglected, the intensity of transmitted light can be written as:

$$I = I_0 e^{-acL-\alpha' d-\alpha v}$$



Graph 2: Typical photo plethysmograph system. In transmission mode the light emitter and photo sensor are mounted on opposite side of the transducer cap or clip. The transmitted light produces proportional electric current in the sensor, which is amplified and processed to obtain change in blood volume as a function of time

where acL represents absorbance by nonblood compartment, d is quantity of blood present at the end of systole, α′ is the absorption coefficient of the blood at the end systole, v is the quantity of the arterial blood that flows into the finger/toe, and α is the absorption coefficient of the arterial blood.

This transmitted light, when falling on the photoelectrical element, produces electrical output with DC component corresponding to the venous blood and tissues in the optical path and an alternating current (AC) component corresponding to arterial flow. Thus

$$E_{DC+AC} = I_0 A e^{-\gamma acL - \gamma\alpha' d - \gamma\alpha v}$$

where A and γ are constants specific to the photoelectrical element. On similar lines, the DC component of the photoelectric output can be written as:

$$E_{DC} = I_0 A e^{-\gamma acL - \gamma\alpha' d}$$

Division of these equations leads to:

$$\frac{E_{DC+AC}}{E_{DC}} = e^{-\alpha\gamma v}$$

Taking natural logarithm on both sides leads to:

$$v = -1/\alpha\gamma \ln(E_{DC+AC}/E_{DC})$$
$$\text{or } v = -Y/\alpha\gamma$$

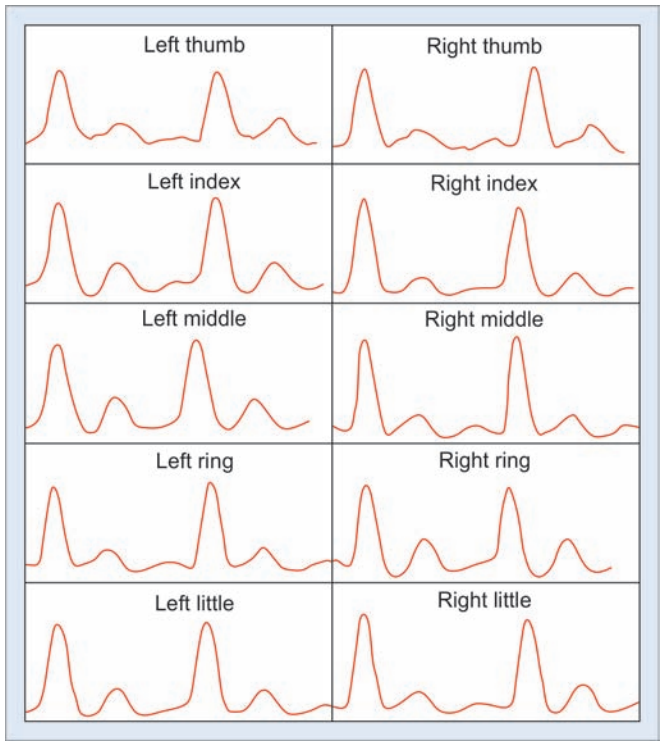
where Y is the logarithmic difference of E_{DC+AC} and E_{DC}.

This equation shows that the amount of blood entering the finger/toe during systole is directly proportional to the logarithmic difference of total photoelectric output and its DC component. This relation makes this technique far superior to air displacement and strain gauge plethysmography and can be used to assess the arterial blood flow in the extreme ends of the extremities.

CLINICAL APPLICATIONS

Estimation of Arterial Blood Flow in Toes/Fingers

As described above, it is possible to record the arterial blood flow in the fingers and toes of the subject and the PPG waveform can be analyzed to be normal or pathological depending upon the amplitude and morphology of the pulse. There are several conditions like Reynaud's phenomenon, radiation injury, etc., where assessment of arterial circulation in the digits is of prime importance. In such cases, PPG is performed in all the fingers in case of upper extremity disease and in all the toes in case of lower extremity disease. The data from fingers or toes can be compared to arrive at the diagnosis in the manner described by Iyer et al[8] for impedance plethysmography. The advantage of PPG over impedance plethysmography is the ease of application of the probe in case of former and cumbersomeness of application of electrodes in the latter. Graph 3 shows arterial blood flow waveforms (time derivative of PPG signal) recorded from upper extremities in a control subject.[9]

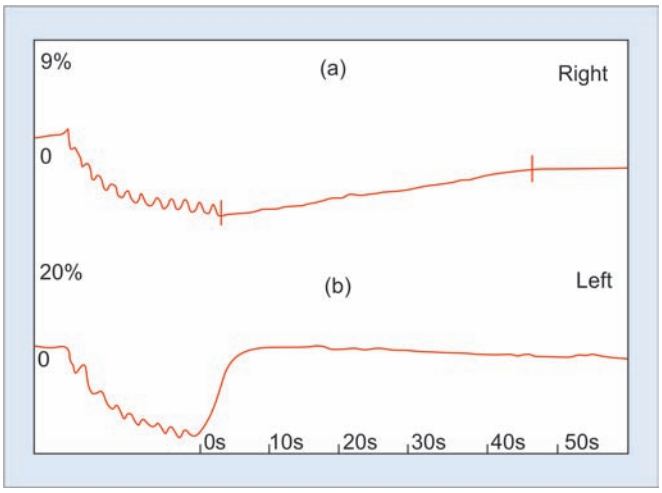


Graph 3: Photoplethysmography waveforms recorded from digits in a normal subject

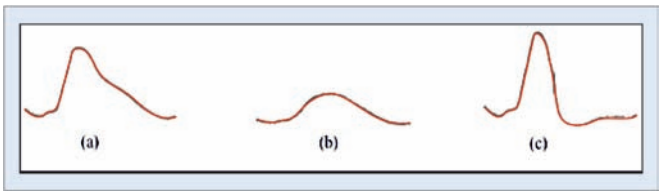
Venous Reflux Test

The venous reflux test, also called the muscle pump test, is an exercise test to diagnose insufficiencies of the venous valves in the lower extremities.[10] For this investigation, reflection mode PPG is used in place of the transmission type described hitherto. The patient is sitting on a height adjustable chair with knee extended to an angle of 110°. The reflectance PPG transducer is applied approximately 8 cm above the ankle between the inner and backside of the calf on a healthy skin. The patient then carries out dorsiflexion exercise to pump the blood out of the veins. For this, the patient must flex his foot upward above the heel and then relax. This exercise is repeated about 10 times. After finishing the exercise the patient must wait motionless for a period of 2 minutes to allow the refilling of the veins completely.

Graph 4 shows the venous reflux graph (a) in a normal leg and (b) in a diseased leg with incompetent venous valves. As can be seen from the figure, there are initial spikes in both the curves representing the motion artifact during exercise. The refilling takes about 50 seconds in a normal leg, whereas the same takes only 5 seconds in the leg with venous incompetence. This exercise test allows



Graph 4: Photoplethysmography waveforms recorded from lower extremities in a patient with venous incompetence in the left leg. As can be seen, the refilling time is greater than 40 secs in the normal leg(a) and less than 10secs in the leg (b) with venous incompetence (courtesy Ralf Schüler, Medis GmbH)



Graph 5A to C: Morphology of the PPG pulse (a) in a normal subject, (b) in a patient with arterial occlusion and (c) in a patient with generalized atherosclerosis. The normal pulse is characterized by fast rise, round crest and slow return to the base line with a discernible dicrotic notch as shown in (a). In case of an arterial occlusion, the rise is slow; the crest is round and broad with a slow return to the base line as shown in (b). In case of deficient arterial perfusion pressure, the rise of pulse is sharp, crest in rounded and small and a fast return to the base line as shown in (c).

a fast and noninvasive diagnosis and is the method of choice as a screening procedure.

Analysis of PPG Pulse Morphology

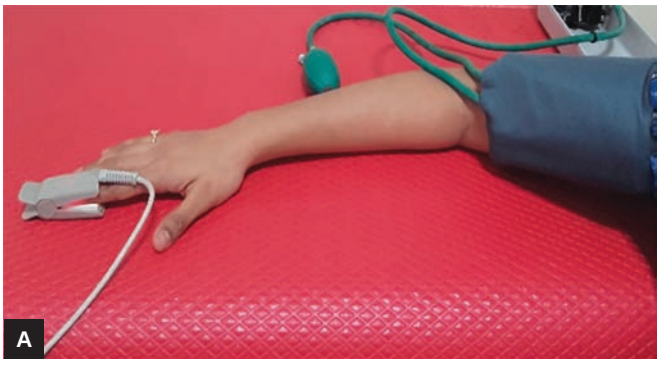
The shape of the PPG pulse depends on thickness of blood vessels, contractility of heart and vascular smooth muscle in the vessel wall. Therefore, condition of the blood vessel can be assessed from the morphology of the PPG pulse. For this examination, the patient lies on a couch usually in relaxed position. The probe is correctly applied on the tip of the finger or toe so as to cover the photometric sensor completely. The arterial pulse waves are recorded with the help of PPG equipment described above. Graph 5 shows three different types of arterial pulses recorded from the fingers or toes in various conditions. A physiologically normal pulse has fast slope, small crest, fast return to the baseline during systole, and slow return to the baseline during diastole as shown in Graph 5a. In case of an arterial occlusion, the crest is delayed and round, and the return to the baseline is also slow as shown in Graph 5b. In case of an insufficient arterial perfusion pressure, the pulse wave has a fast slope, small crest, and fast return to the baseline throughout as shown in Graph 5c.

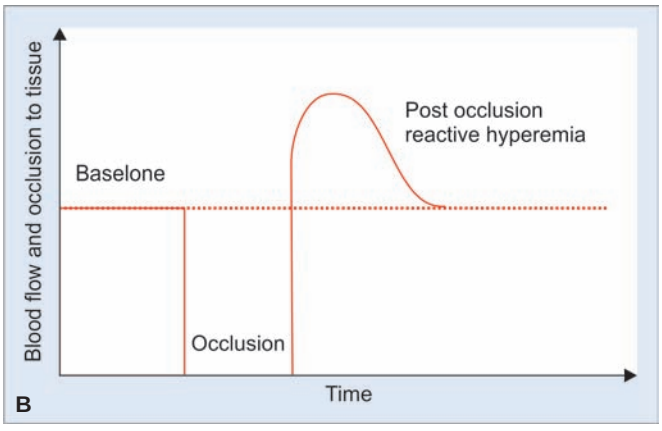
Sherebrin and Sherebrin[11] have performed harmonic analysis of peripheral pulse in three age groups of 10 to 29, 30 to 59, and 60 to 89 years. They have selected these age groups since they have noted in their other experiments that there was a marked decrease in extensibility in human aortas above the age of 30 years and a further change beyond about 60 years. The power spectrum of 2nd to 6th harmonics has shown considerable decrease in the power of 2nd and 6th harmonics at $p < 0.05$. The 2nd harmonic power was significantly different between the youngest and both the older age groups. The 6th harmonic was significantly different between the youngest and oldest group. Their most important observation has been marked decrease in the relative power of the 2nd harmonic with age.

Endothelium Function

Endothelium is single layer of cell lining forming the interior layer of blood vessels and serves as interface between the blood circulating in lumen and outer wall of the vessel. These cells line entire circulatory system from heart to smallest capillary. Endothelial cells are involved in many vascular aspects like vasoconstriction, vasodilation, blood clotting, atherosclerosis, angiogenesis, inflammation, and swelling. Endothelium synthesizes and releases several vasoactive factors like nitric oxide which play important role in maintaining normal function. Disorders like peripheral vascular disease may lead to endothelial dysfunction. These diseases can be diagnosed from pulse wave amplitude (PWA) using finger plethysmograph. Endothelium dysfunction can also detect cardiovascular disease in early stages and can be considered a precursor to coronary artery disease. Analysis of PWA during reactive hyperemia maybe used to study peripheral vascular endothelial dysfunction.

Reactive hyperemia is temporary increase of blood flow to an area as a result of ischemia, or an arterial blockage. Reactive hyperemia is measured by inducing temporary occlusion with the help of a tourniquet for a period of about 5 minutes that gives better results.[12,13] Graph 6a shows the placement of tourniquet above elbow and PPG probe in the index finger. A trace of baseline PPG wave for 30 seconds is obtained with patient in sitting. Ischemic phase is induced by inflating tourniquet to 30 mm Hg higher than the systolic pressure. The cuff is deflated suddenly at the end of 3/5 minutes and postischemic PPG tracing is recorded for about 120 seconds. Amplitude of the systolic peak of the base-



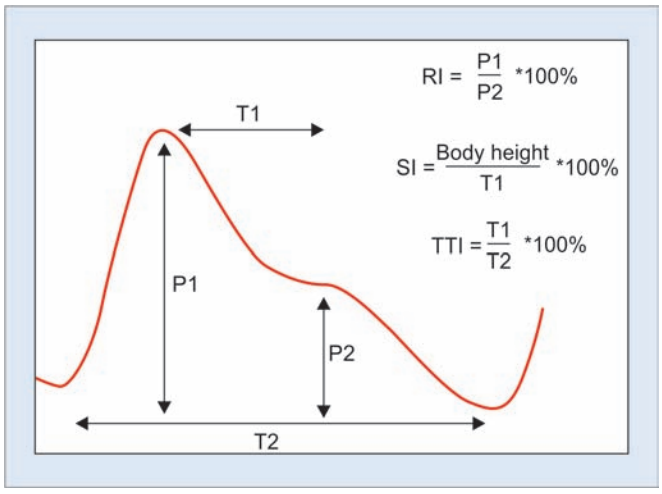


Graph 6A and B: Experiment setup for placement of tourniquet and PPG probe with the patient in supine (a). Plot of amplitude of systolic wave during baseline recording, during occlusion and post ischemia is shown in (b). The crest value divided by baseline around 1.3 is considered normal

line PPG as well as that postischemia is plotted as shown in Graph 6b. Endothelial dysfunction is considered to be present if the postischemic systolic amplitude did not increase by more than 30% in comparison to the baseline value.

Cardiovascular Indices

The hardening or stiffening of arteries is age related and can be accelerated by some medical conditions, like renal disease, diabetes mellitus, etc. Arterial stiffness is also associated with hypertension which is a risk factor for stroke and coronary artery disease. In stiffer arteries, pulse travel faster from the heart to the periphery, thus increasing the arterial pulse wave velocity.[14] The forward pressure pulse augmented by a fast returning reflected wave indicates arterial stiffness. Stiffness index (SI), transit time index (TTI), and reflection index (RI) give information about arterial stiffness and vascular tone. The SI is calculated from the body height (in meters) divided by the time delay (in seconds) between the pulse systolic peak and the point of inflection on the reflection wave (units m/s), TTI is the normalized transit time with respect to the cardiac cycle time and the RI is obtained as the percentage ratio of the height of the dicrotic notch to the systolic pulse height as shown in Graph 7.



Graph 7: Computation of reflection index, stiffness index and transit time index from the PPG signal. T2 represents one cardiac cycle. T1 is the time elapsed between the peak of the systolic wave (amplitude P1) and the point of inflection on the reflection wave (amplitude P2) and represents transit time of the pulse wave

Continuous Monitoring of Oxygen Saturation in the Blood

This is the most popular and most commonly used application of PPG. As far as intensive care monitoring is concerned, it is next to electrocardiography. Noninvasive blood gas monitoring is essential for the patient with cardiorespiratory complications. Transmittance plethysmography provides a very safe and simple solution to this problem.[7] As described in preceding section, the oxy-hemoglobin has maximum transmission at 650 nm and has transmission equal to that of reduced hemoglobin at 805 nm. Therefore, transmitted light at 650 nm gives an estimate of oxy-hemoglobin and that at 805 nm gives an estimate of total hemoglobin. Thus oxygen saturation of the blood, abbreviated as spO_2, is given as:

$$spO_2 = A - B\frac{\alpha^{650}}{\alpha^{805}}$$

where A and B are constants related to the absorption coefficient of hemoglobin and oxy-hemoglobin respectively.

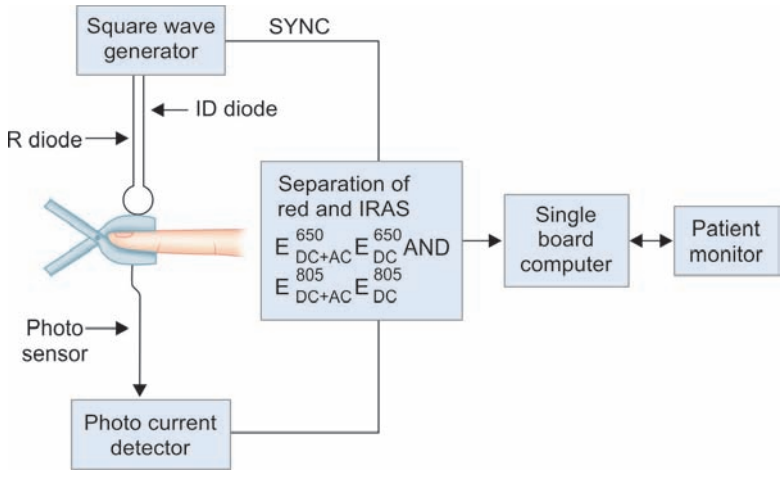
In terms of Y (defined as the logarithmic difference of E_{DC+AC} and E_{DC}), absorption coefficient is expressed as:

$$Y^{650} = -\alpha^{650}\gamma; \text{ and } Y^{805} = -\alpha^{805}\gamma$$

Therefore, spO_2 can be given as:

$$spO_2 = A - B\frac{Y^{650}}{Y^{805}}$$

Thus, it is possible to continuously monitor oxygen saturation of the blood noninvasively by photoplethysmographic method.



Graph 8: Schematic block diagram of a fingertip oxymeter. The red and infrared light emitting diodes are alternatively switched on with the help of square wave and corresponding photo current are sensed and amplified by the photo current detector. The output of the photo current detector is separated into DC and AC components of infrared and red lights and fed to single board computer

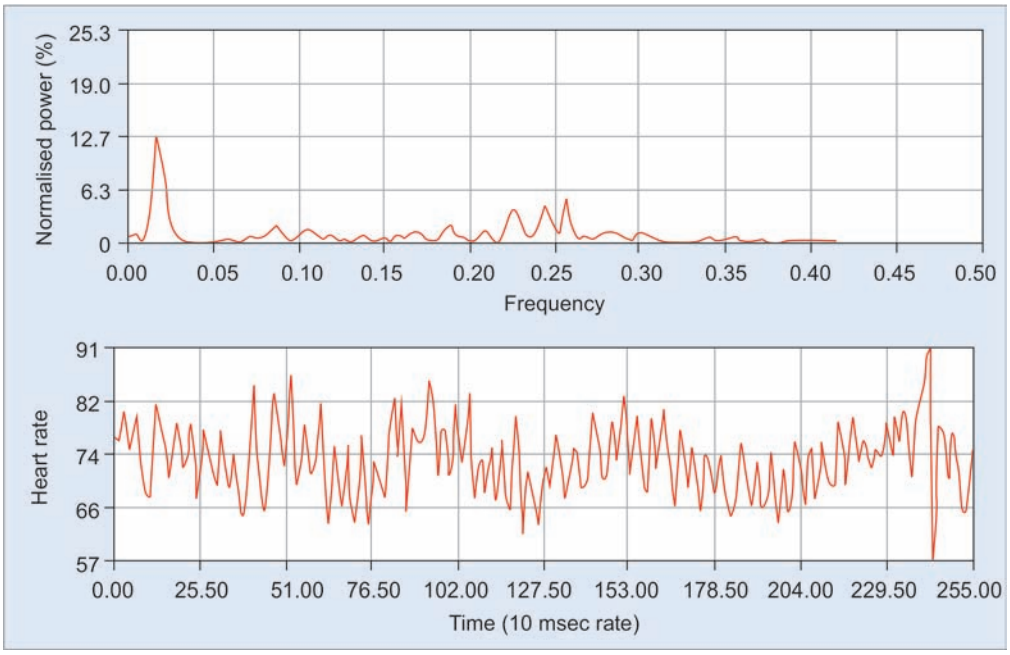
Graph 8 shows a typical spO_2 monitoring system. It comprises a clip type transducer on which red light emitter, infrared light emitter, and photosensor are mounted along with the cushions on the opposite sides in the inner surface as shown in the figure. The light emitters are sourced from a square-wave generator, which alternately puts-on the red and infrared light. Corresponding transmitted light is sensed by the photosensor and converted into electrical signal by photodetector. With the help of synchronization signal from square-wave generator, the red and infrared signals are separated to obtain, E^{650}_{DC+AC}, E^{650}_{DC}, E^{805}_{DC+AC}, E^{805}_{DC}. These signals are then given to the ADC inputs of a single board computer, which computes spO_2 as per above equation and displays the same along with any of the four voltage signals. Single board computer is linked to patient monitor through a serial link. The correlation between the oxygen saturation values measured by PPG method and conventional radiometric method has been observed to be 0.983, and it is observed to be within ±5% of that obtained by blood gas analysis. Thus, it is an ideal method for continuous monitoring for oxygen saturation noninvasively.

Objective Assessment of ANS

The ANS or the involuntary part of the nervous system tracks the requirement of different organ or systems of the body and keeps on modifying the physiological activity through parameters, such as heart rate; respiration rate; stroke output; peripheral blood flow; systolic, diastolic and mean blood pressures; body temperature; peristalsis; secretion of endocrinal and salivary glands; glucose-glycogen conversion; motility of large and small intestines; secretion of urine; and so on. Autonomic activity is initiated at the levels below, cerebrum, implying that it does not get stimulated voluntarily. However, the body may perceive the effect of stimulation, such as increase in the heart rate; the rate and force of heart beat; the secretion of the glands and alimentary track; the contraction of involuntary muscles and the size of pupil of the eye. Since the ANS performs the task of increasing or decreasing the activity of any particular system, it is further divided into two parts: Sympathetic and parasympathetic nervous system. These two have opposite effects on a particular system, meaning, that if sympathetic system increases the activity of a particular organ, the parasympathetic decreases activity of the same and *vice versa*.

Sympathetic stimulation (SS) prepares the body to deal with excitement and with stressful situations, e.g., strengthening its defenses in danger and in extremes of environmental conditions. It is often said that SS mobilizes the body for fight or flight. On the contrary, parasympathetic stimulation (PS) has a tendency to slow down body processes except the digestion, urinary excretion, and sex organs. Its effect is similar to that of peacemaking, allowing restoration processes to occur quietly and peacefully. Due to the nature of functions described earlier, the rhythm of PS lies in the higher frequency band (0.1–0.4 Hz) than that of the SS (0.01–0.1 Hz). These rhythms are objectively estimated from heart rate variability (HRV) obtained from processing of electrocardiographic (ECG) signal or blood flow signal.[15-18]

Graph 9 shows HRV in time and frequency domain obtained from PPG, which is similar to that obtained from electrocardiography. Similarity between HRV obtained from PPG and ECG renders PPG as a simple, reliable, and quick method for the objective assessment of ANS.



Graph 9: Heart rate variability in time (lower) and frequency (upper) domain recorded from a control subject with the help of photoplethysmography. The variability spectrum appears more or less similar to that obtained from electrocardiography

Table 1: Photodetector output of transmitted radiation through finger/earlobe

Sl. no.	*Blood glucose*	*Output of photodetector at different wavelengths of incident radiation*				
		565 nm	*650 nm*	*940 nm*	*1310 nm*	*1550 nm*
1	91	0.12	0.70	2.00	0.80	1.20
2	164	0.10	1.10	2.50	0.60	0.52
3	122	0.20	0.70	2.00	0.90	0.76
4	108	0.16	0.70	2.00	0.80	1.40

Prospective Method for Blood Glucose Monitoring

Visible light and infrared spectroscopy is being explored for the past few decades for the noninvasive personal monitoring of blood glucose keeping in view of the fact that more than 600 million people in the world and 60 million people in India suffer from type II diabetes. 10% of these patients require strict vigilance and hence, multiple needle pricks every day. It has been observed that some wavelengths are more sensitive to blood glucose concentration. Table 1 gives the PPG output in volts for different incident radiations at different blood glucose levels in a human subject. Appreciable fall in photodetector output at wavelengths 1310 and 1550 nm, with increase in blood glucose, can be noted from the table. In contrast, output at 650 and 940 nm shows increase, and 565 nm give unpredictable output. Though the observations appear impressive, they have to be reproducible in large number and wide variety of subjects. The studies carried out to date suggest that PPG cannot be implemented as a noninvasive analytic method; however, it can be used in a limited way for personal monitoring. Even to this extent it may give relief to some percentage of patients from multiple needle pricks.[19]

CONCLUSION

Photoplethysmography is used worldwide for the noninvasive monitoring of oxygen saturation of blood and is an essential instrument for every critical care unit and intensive care unit. As described earlier, this technique is very useful in monitoring digital blood flow in Reynaud's and similar diseases, where established methods like color Doppler are of little help. Morphology analysis of the PPG pulse has several parameters like power of higher harmonics, endothelial index, SI, TTI, and RI, which all have potential to reveal cardiovascular risk at early stages. These have not been sufficiently explored for their benefits and need more emphasis.[20] Its application in personal monitoring of blood glucose is worth further investigation. Simplicity of usage and extremely low cost of this modality makes it a method of choice for developing countries like India for host of applications described above.

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