Computer Methods and Programs in Biomedicine, 28 (1989) 257–269
Elsevier

CPB 00983

Section II. Systems and programs

Skin photoplethysmography – a review

A.A.R. Kamal [1,*], J.B. Harness [2], G. Irving [3] and A.J. Mearns [1,4]

[1] *Postgraduate school of Control Engineering,* [2] *Postgraduate School of Chemical Engineering,* [3] *Postgraduate School of Pharmacology, University of Bradford, Bradford, U.K., and* [4] *Bradford Royal Infirmary, Bradford, U.K.*

The photoplethysmograph has been used for over 50 years but there are still misconceptions in how and what is the information obtained. A photoplethysmograph signal from any site on the skin can be separated into an oscillating (a.c.) and a steady-state (d.c.) component, their amplitudes dependent upon the structure and flow in the vascular bed. Many simple applications are available: pulse counters, using the a.c. component, skin colour and haemoglobin saturation meters, using the d.c. component. The d.c. component of the photoplethysmograph signal is a function of the blood flux beneath the device. A good emitter for use in a photoplethysmograph of skin blood flow is one in the frequency range 600–700 nm and the best signal for a.c. analysis is obtained from the finger pulp. The frequency range of the electronic circuitry should be from 0.01 to 15 Hz, then all the information in the signal can be extracted about the autonomic nervous system control of the cardiovascular system, particularly between 0.01 and 2 Hz. Comparative studies may be drawn between similar skin sites on a subject or between subjects if the afferent inputs to the brain stem are controlled or driven at a known frequency. These afferents, inputs, will modulate the efferents, outputs, which generate variations in the a.c. component of the detected photoplethysmograph signal.

Photoplethysmography; Skin; Blood flow; Signal analysis

1. Measurement of skin blood flow

To date, a precise quantitative measurement of skin blood flow has proved to be impossible. The skin has a complex structure (see Fig. 1), and many factors affect the skin blood flow. Methods used to date for skin capillary blood flow measurement include skin thermometry [35], thermal clearance [36], laser Doppler plethysmography [34,58], radioactive isotope clearance [55,56], electrical impedance methods [18,53] and photoplethysmography [25,42], each having their own advantages and disadvantages. When choosing a method to measure skin blood flow it should be remembered that the ideal non-invasive technique should be safe, sensitive, reliable, reproducible, simple to use and inexpensive.

In skin thermometry the surface temperature is used as an indicator of changes in skin blood flow. It is predominantly sensitive to the component of

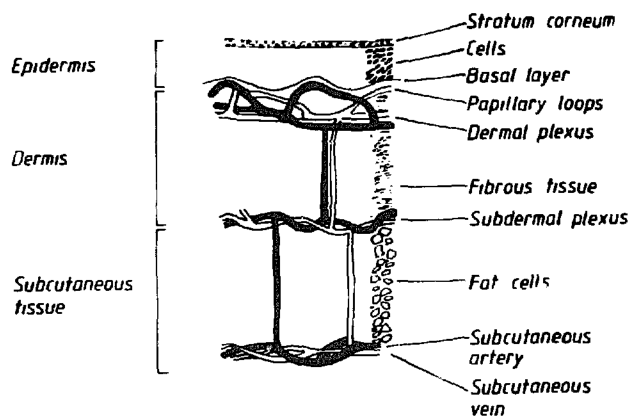

Fig. 1. Diagrammatic representation of skin and the cutaneous vascular system.

Correspondence: Dr. J.B. Harness, Department of Chemical Engineering, University of Bradford, Bradford BD7 1DP, U.K.
* Now at University of Bahrain, Gulf Polytechnique.

0169-2607/89/$03.50 © 1989 Elsevier Science Publishers B.V. (Biomedical Division)

DOCKET ALARM Find authenticated court documents without watermarks at docketalarm.com.

total skin blood flow that is employed for thermoregulation, with a reduced sensitivity to changes in nutritional capillary flow. It has the practical disadvantage of requiring an environment in which ambient temperature and humidity are kept constant. Thermal clearance or thermal conductance [9] methods assess the rate of removal of heat from a heated area at the centre of a probe by the skin's nutrient blood flow in the dermis. The thermal clearance transducer measures the temperature difference between a heated copper disc at the centre of the probe and an unheated, concentric copper annulus at its periphery. The main practical disadvantages are the relatively long lag period before a constant reading is obtained and the application of heat to the skin modifies local skin conditions.

The laser Doppler technique depends on the Doppler shift of coherent (laser) light 'back scattered', from moving red blood cells. This frequency shift is due to the velocity of blood cells (particles) within the tissue and, therefore, is related to tissue blood flow. To measure changes in nutritional blood supply the geometry of the capillary loops needs to be known which is an impossibility because of its random variations. Laser light, in the red region of the spectrum, penetrates further than incoherent light as the beam is narrower making the intensity per unit area greater rendering the laser Doppler method able to collect data from deeper lying blood vessels [48].

The radioactive isotope clearance technique involves the measurement of the clearance rate of intradermally injected radiopharmaceuticals, the most widely used tracer being ^{133}Xe. This method required access to a γ (gamma) camera or surface counting technique with exposure to a small amount of radiation and involves percutaneous injection. The trauma may be unacceptable to diseased skin and repeated measurement in the same patient is limited by the radiation dose.

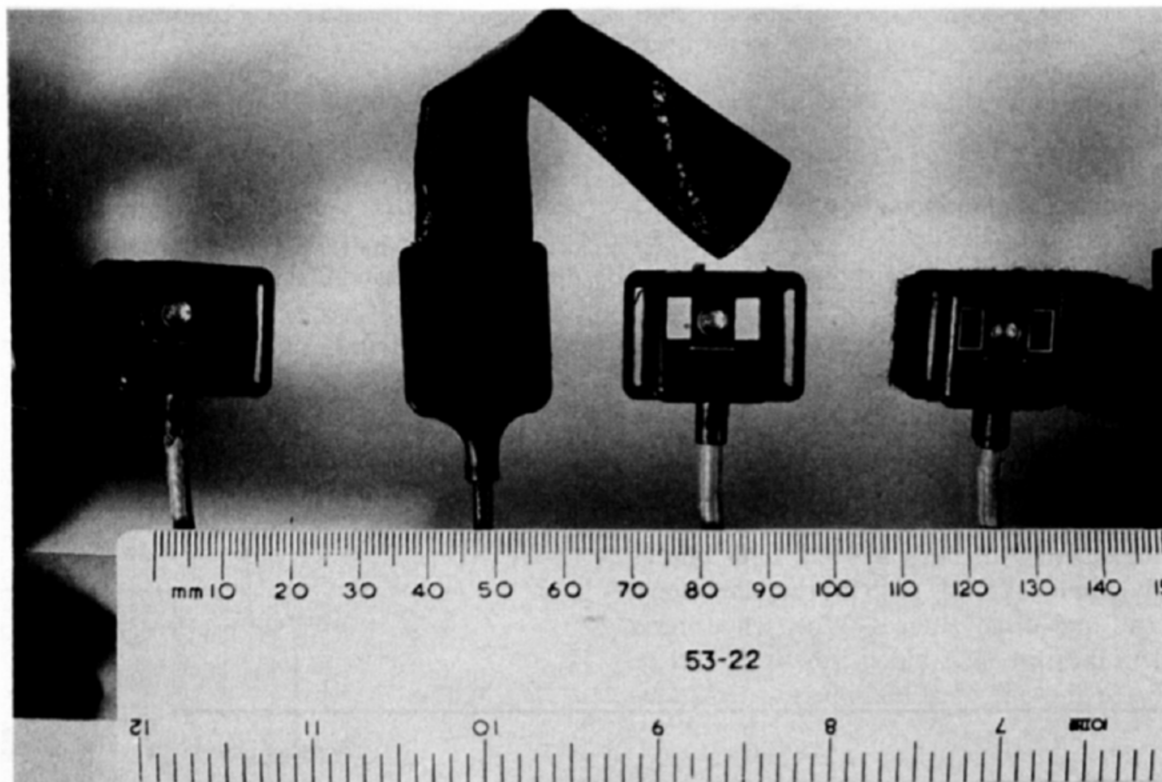

Fig. 2. Photograph of plethysmographs. From left to right: red LED photoplethysmograph, green LED photoplethysmograph, piezoelectric plethysmograph, and bulb photoplethysmograph.

DOCKET ALARM Find authenticated court documents without watermarks at docketalarm.com.

The basic technique applied in electrical impedance methods requires a high frequency, constant amplitude, current to pass through the segment of interest. The measured voltage appears as a result of the segment impedance. The electrode area and spacing, together with the choice of operating frequency determine the form of signal produced. The impedance techniques provide an indication of blood volume in deeper vessels. The main difficulty of this technique is to provide good contact between the skin and the electrodes.

Plastic piezoelectric microphones are now commercially available and they have many applications [23], they can be used as plethysmographs [45]; one is shown in Fig. 2. As piezoelectric plethysmographs they are used to measure the movement of the skin. A major disadvantage is that to obtain a reasonable signal their size has to be about 70 mm by 10 mm so the signal produced gives an indication of the skin movement over a relatively large area. The signal contains only an oscillating (a.c.) component because of the rapid decay of the acquired charge through its internal resistance and the impedance of the connected circuits. The lower frequencies are attenuated due to the rapid loss of the charge. No steady-state (d.c.) component is generated. The piezoelectric plethysmograph produces a signal which is the differential of the photoplethysmograph signal [45].

Plethysmography applies to the measurement or estimation of the fullness or volume of an object. Volume and strain gauge techniques remain true to this definition in the assessment of blood flow. Volumetric measurements of limbs were accurately taken well before the advent of electronic transducers and polygraphs [4,37,41]. Plethysmographs have been productively applied in peripheral circulatory studies [25,27,62] also to estimate arterial blood flow [22,33] and variations in vasomotor tone [28–30]. A recent review of volume plethysmography is given by Porter and Swain [50].

Photoelectric plethysmography, or photoplethysmography, was introduced almost simultaneously in 1938 by Hertzman [25] in the United States and Matthes and Hauss [42] in Germany but Hertzman [24] and Hertzman and Spielman [26] were the first to use the term 'Photoplethysmograph' and suggested that the resultant 'Plethysmogram' represented volumetric changes in the blood vessels of the skin. Hertzman [25] published his paper on the subject of photoplethysmography demonstrating the effect of cold and exercise on blood volume changes in the limb. He also established the validity of the method for estimating both skin blood flow and blood volume changes, where a steady blood flow appears as a constant volume.

2. Skin photoplethysmography

Photoplethysmography satisfies most of the conditions for a non-invasive technique to estimate skin blood flow and is ideally suited to situations which require measurement to be made over long periods. It is a technique that provides a signal proportional to changes in skin blood volume but does not produce a quantitative measure [15]. The d.c. component represents total red cell volume below the sensor plus some reflected components from within the skin (see below). The a.c. component is produced by the fluctuations in the blood volume below the sensor. The volume changes recorded sequentially reflect the variations in flow. Thus the a.c. component is a measure of changing flow. Its attraction is that it is the least invasive method and atraumatic, as well as being inexpensive. Fairs et al. [21] have recently demonstrated that photoplethysmography and Doppler flowmetry correlate well with venous occlusion plethysmography and stated that 'optical methods of skin blood flow measurement approach the ideal situation of non-invasion'.

Fig. 2 shows a photograph of photoplethysmographs constructed from two light sources and a detector. The signal produced by the photoplethysmograph depends upon the location and the properties of the subject's skin at that site, including the skin structure, the blood oxygen saturation, blood flow rate and the skin temperatures.

The importance of the spectral reflectance and transmittance of skin has long been recognised and many workers have used such measures to

DOCKET ALARM Find authenticated court documents without watermarks at docketalarm.com.

determine the state of the skin circulation. Dawson et al. [14], in an in vivo study of light absorption and scattering in skin, described a theoretical basis for the application of the logarithm of the inverse of reflectance (LIR). An instrument was constructed specifically for the measurement of LIR spectra in the assessment of skin colour. The spectrum of light reflected from the skin is related to the light absorbing and scattering structures within the skin. The clinical use of the instrument was also reported and the calculation of indices which may be used to quantify erythema and pigmentation of skin. From these observations Dawson et al. [14] concluded that the LIR spectra can be resolved into three principal components which correspond to two layers, one containing melanin and the other the subpapillary venous plexus, and a residual term comprising the contributions of fibrous protein, collagen and fat. Melanin absorbs strongly over the visible spectrum, its absorption increasing towards the ultraviolet while whole blood has a relatively small absorption at wavelengths greater than 620 nm, as illustrated in Fig. 3.

Haemoglobin absorbs strongly in the yellow band of the visible spectrum. Oxygenated and de-oxygenated blood have similar absorption coefficients at wavelengths greater than 805 nm [11], but below 805 nm their absorption coefficients greatly diverge with those of oxygenated greater than the de-oxygenated blood [61]. The differential haemoglobin saturation level is significant when considering total blood volume. Recently, devices based on the photoplethysmograph have been available for use in anaesthesia which produce a pulse rate and percentage oxygen saturation of haemoglobin (pulse oximetry).

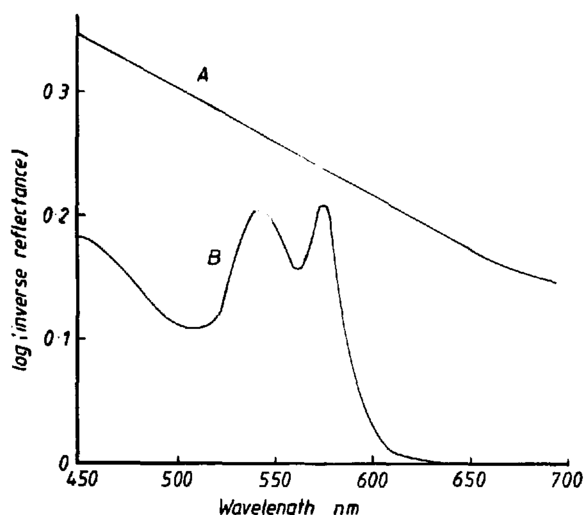

Fig. 3. Absorption curves for melanin and blood in vitro. (*A*) Melanin; (*B*) whole blood.

3. Photoplethysmograph operation

The construction of a photoplethysmograph requires a light source and a detector. Their relative positions may vary in individual designs. On certain areas of the body, such as the ear lobe and fingers, it is possible to have the light source and the detector opposite each other on the skin surface, an arrangement known as transmission mode, but this limits the application possibilities. A more acceptable arrangement, known as reflection mode [46], is such that the light source and the photodetector are placed side by side, and this arrangement can be applied to any part of the body. The principle of operation of the photoplethysmograph is based on the assumption that light is attenuated when it is shone on to the skin and the attenuation shows variation depending on the volume of blood entering the tissue under observation. This attenuation is due to reflection, scattering and absorption of light. Such absorption of light depends not only upon the skin pigments, melanin and other substances which absorb specific spectral bands, see Fig. 3, but also upon a scattering action due to the structural inhomogeneities in the skin. Absorption of light may depend on haematocrit and on the orientation of red cells within the vessels, an explanation suggested by Hocherman and Polti [32].

The wavelength of the source used is of significant importance. Light sources that operate in the near red (600–700 nm) region of the spectrum are most effective because haemoglobin is the major protein present which changes with time and scatters the light in this region. In this area of the spectrum the absorption of skin pigments, oxyhaemoglobin, haemoglobin and bilirubin with the exception of melanin fall to their minima.

DOCKET ALARM
Find authenticated court documents without watermarks at docketalarm.com.

Another factor which makes this part of the spectrum, 600–700 nm, favourable is that the skin not only has minimum absorption but also the difference in the optical density of the skin due to erythema is negligible [3]. With pulsating flow, there is a variation in the light received at the detector on the skin surface [20], but the pulsatile component is largely independent of wavelength in the range 660–805 nm. Challoner [12] confirmed this by comparing the outputs of photoplethysmographs operating at 650 nm and 805 nm, and found that their pulsatile outputs were substantially the same. Although the pulsatile component at heart rate does not require a critical narrow spectral range, the values of the lower frequency components are better detected using a light emitter in the range 600–700 nm. Much of the skin has a poor pulsatile component but the precapillary activity is present throughout.

The signal detected by the photoplethysmograph consists of a steady component (d.c.), which is related to the relative vascularisation of the tissue, and a pulsatile component (a.c.), which is related to changing blood pulse volume [24]. The resultant signal is a measure of expansion of skin vessels (predominantly arterial) which is a summation effect of the arterial pulse and the opposing elastic properties of the vessel wall. The amplitude of the volume pulsation with each heart beat is closely correlated with the flow. Both amplitude of pulsation and blood flow serve as an index of the state of contraction of the walls of the blood vessels and hence of the activity of the sympathetic nervous system [10].

Roberts [52] in a study of fundamental aspects of the optical properties of blood in motion, outlined a review of mathematical analyses of light scattering and diffusion processes taking place in blood and proposed that light diffusion through blood, from a source outside a blood vessel, can diffuse preferentially in the direction of motion of blood which is added to the static diffusion process. Roberts [52] demonstrated that a reflectance photoplethysmograph, of reasonable size (not incorporating fibre optics or miniature transducers), constructed as a detector placed between two uncollimated light sources would be relatively insensitive to small positional changes in measuring blood flow either over a diffuse vascular bed or over a single artery.

4. LED photoplethysmograph and amplifier

The problem with using tungsten filament bulbs is the excessive heat produced. The frequency content of the light emitted from tungsten fillament bulbs is in the infrared area of the spectrum. The ratio of heat to light output is large, therefore the heating of the skin can be a limiting factor. We have found that usually the bulb fails when the filament partially shorts out producing extra light and heat. This will disturb the calibration of the photoplethysmograph and may cause burning of the skin. Normally a reflection type photoplethysmograph is used which incorporates a detector mounted in between two light sources or a light source alongside the detector. We have re-

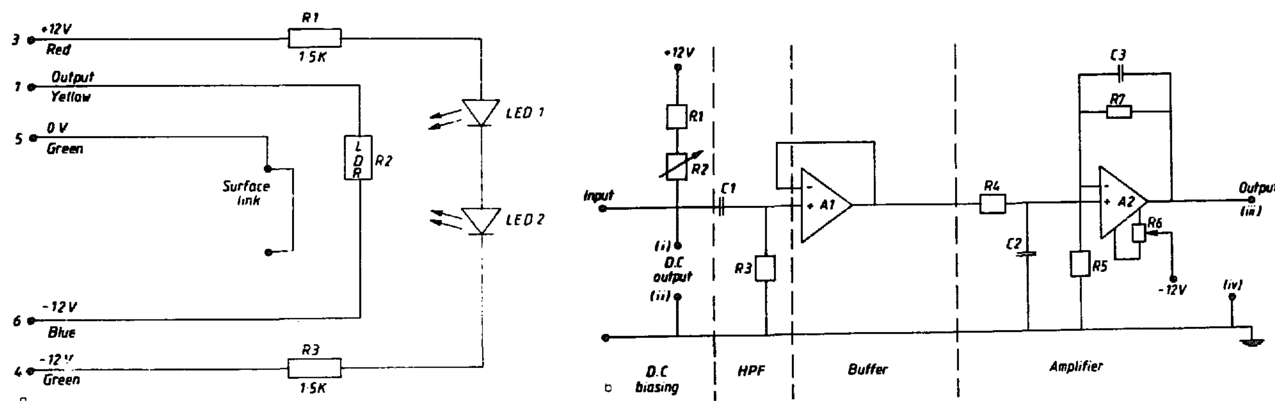

Fig. 4. (*a*) Diagrammatic representation of the photoplethysmograph electrical circuit. (*b*) Circuit diagram of the photoplethysmograph amplifier. Typical values are R1,6 100 k; R2 500 k; R3,7 1 M; R4,5 15 k; C1 10 μF; C2 0.022 μF; C3 100 pF; A1,2 324E1.

DOCKET ALARM Find authenticated court documents without watermarks at docketalarm.com.

DOCKET ALARM

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts

Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research

With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips

Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS

Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS

Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS

Sync your system to PACER to automate legal marketing.

WHAT WILL YOU BUILD? | sales@docketalarm.com | 1-866-77-FASTCASE

fastcase®
Smarter legal research.