Biological and Medical Physics, Biomedical Engineering

Vladimir Blazek
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Steffen Leonhardt
Mandavilli Mukunda Rao *Editors*

Studies in Skin Perfusion Dynamics

Photoplethysmography and its Applications in Medical Diagnostics

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Preface

As technology advances, novel methods of measurements become feasible. These methods infuse further understanding of the underlying principles of operation and behavior of systems. Comprehension of the principles of operation and behavior of the system further accelerates discovery of novel methods of measurement and fuels further advancements. This is more evident in the field of medical electronics. This book deals with the development of new non-invasive methods of measurement and the underlying physiological aspects of blood perfusion in extremities such as skin, earlobe, and fingers. Editorial team and the authors of the book collaborated to unravel the novel methods of determination of blood perfusion dynamics and unravels the relation between the measured (quantified) results and the physiological phenomena. The results outlined in this book elucidate the decade-long synergetic research carried by the authors as well as research undertaken by them in their individual capacity. The authors strongly feel that the book will be engrossing to readers who wish to understand blood perfusion dynamics and its relation to the underlying physiological phenomena. Equally, this book provides deep insights to the readers who are involved in research leading to advance the noninvasive optical measurements of skin perfusion dynamics using photoplethysmography (PPG) and photoplethysmography imaging (PPGI) and its relation to not only the physiological but also psychological activities. Authors are indebted to their respective organizations and funding agencies for supporting the research activities whose outcomes culminated as this book. Special thanks are due to the (i) Federal Ministry of Education and Research (BMBF), Germany, (ii) Alexander von Humboldt Foundation (AvH), Germany, (iii) German Academic Exchange Service (DAAD), DFG (German Research Foundation) and (iv) Department of Biotechnology (DBT), India.

Happy reading!

Editorial team and authors

Acknowledgements

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Thanks are due to the *Centre for Continuing Education*, *IIT Madras* in Chennai for providing seed money in bringing out this book. The authors are also indebted to *Springer Nature* for their support in the publication of this book.

Last but not the least, the editors say thanks to all the individual authors of different chapters and scientific co-workers in their groups and laboratories, graduate and doctoral students for their engagement and collaboration.

Introduction

Aims and Results of Indo-European Research Activities "Studies of Neurological Induced Skin Perfusion Dynamics"

In recent years, the investigation and understanding of the interaction between tissue perfusion, brain activity and human hemodynamic are receiving much attention. Such investigations have been generally confined to few premier research institutions where expensive and sophisticated facilities like PET, MRI, etc., are available. However, recent advancements in optoelectronics and computer technology have accelerated the development of new measuring systems and methodologies for use in this medical field. Specifically, transcutaneous assessment of skin perfusion changes (blood volumetric measurement) through optical-sensor-based photoplethysmography (PPG) has rapidly gained an important role. This basically non-invasive measuring procedure is devoid of harmful radiation and ionizing phenomena, simple in construction and connection to the measuring set-up and is easy to use in all areas of human body. The relatively low cost of these sensors has resulted in their use in various medical fields and clinical applications. In the past, though, the application of PPG had been limited by technical difficulties involving calibration of the data.

The development of the quantitative PPG technique based on computer-aided data processing has removed this obstacle. In cooperation between the Indian Institute of Technology at Chennai and RWTH Aachen University, an Indo-German Project was initiated in 1996 for advanced studies in this research area. Measuring system designs, experimental details and some preliminary results obtained within the framework of this project are presented in this book. From the investigations carried out so far using the PPG sensors in conjunction with breathing sensors, it has been possible to monitor the 0.1–0.15 Hz rhythms in the arterial blood volumetric changes and to study the influence of breathing on them. These rhythms, which according to medical experts have relevance to psychosomatic conditions like stress or relaxation, can also be addressed to quantify the benefits or lack of ancient Indian practices like yoga and meditation. Using the PPG

techniques mentioned above, a first Indo-European project was initiated in 1996 for studying the effects of Indian relaxation techniques like pranayama, meditation, etc., in comparison with Western relaxation techniques like autogenic training. Many of the results obtained so far in this project have been presented at several international conferences and published in their proceedings. As a consequence, we now can constate that the Indian techniques of relaxation like yoga and meditation are very effective in generating low-frequency rhythms in the skin perfusion as monitored by the optical sensors. According to medical experts, these low-frequency rhythms have a very important influence on the human physiology and have potential therapeutic implications. We are now in the process of quantifying these rhythms under normal and controlled conditions with the help of data obtained from many subjects. We hope that these measurements will scientifically validate the efficacy of the ancient Indian relaxation techniques like yoga and meditation.

The succeeding chapters, in full or part, describe the results of the research works carried out by the respective authors. Most of these results have been published by the authors themselves in different scientific forums. The aim of bringing all these results together under one unifying umbrella of this book is to provide an overall glimpse of the commonality in the techniques used for different and very much differing medical applications. Moreover, the value of some chapters should be seen in the historical context to understand the broad experimental and appreciate the innate clinical relevance of photoplethysmography. However, it should also be noted here that some chapters provide new results or extend the previously proven PPG applications to new, mesmerizing measurements. The authors hope that the next generation of scientists/engineers will carry this work forward in the years to come so that the general public, both in the east and in the west, will benefit from these practices in their lives.

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Dr. Mandavilli Mukunda Rao was a Post-doctoral Fellow at the University of Illinois, USA. He is a retired professor of of Electrical Engineering at the Indian Institute of Technology Madras where he was teaching in the area of Laser and Optical Communication. He has published a book on optical communication and several research papers in reputed journals. His research interests include Optical Non-invasive Diagnostics. He spent several years at the RWTH Aachen University in Germany, first as DAAD Fellow (1970-1972) and then as Alexander von Humboldt Fellow (1978-1979). He is currently an Honorary Research Professor at Sri Ramachandra University, Chennai.

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Chapter 1
Skin Perfusion Studies: Historical Notes and Modern Measuring Strategies Using Non-invasive Photoplethysmographic Sensor Concepts

Vladimir Blazek

Abstract For adequate skin perfusion rhythmicity assessment, sensor technology must be used, which fulfills basic demands such as unobtrusiveness and continuous monitoring with spatial resolution photoplethysmography (PPG) and its modern camera-based imaging variant (PPGI) ideally meet these requirements, and they are generally accepted in the field of noninvasive medical diagnostics. PPG can work in reflective or transmissive mode and detects blood volume changes in the vascular plexus within the region of transilluminated tissue. The PPG and PPGI signals comprise a complex of pulsatile wave formations (AC) associated with cardiac, respiratory, and different nervous system activities, which are superimposed to a non-pulsatile baseline (DC) due to optical damping of bloodless tissue. Although most of the PPG applications in medical diagnostics are today devoted to recording cardiac rhythmicity, the strength and future of PPG lie in detecting the distributed and, in some cases, highly autonomous skin perfusion dynamics below the frequencies of the "central oscillators", namely the heartbeat and breathing. This chapter presents selected activities and results of the bilateral and interdisciplinary long-term cooperation between IIT Madras in Chennai and RWTH Aachen University in Aachen in this exciting research field of the dermal perfusion dynamics.

1.1 Introduction

The Englishman William Harvey (1578–1657) was the first physician to correctly describe the dynamics of blood circulation after many false interpretations and working hypotheses presented by others. Nevertheless, he considerably underestimated the pumping function of the heart. He assumed that half an ounce (18 g) of blood is normally pumped per minute by the left ventricle; he then multiplied this amount by 1000 heartbeats per half an hour and concluded that 1000 oz of blood has

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to be pumped in one hour. It appeared logical to him that such a large amount of blood could not be regenerated in any way within our body—an idea based on the erroneous theories of blood circulation proposed by Galen of Pergamon (physician/philosopher c. AD 129 to c. 201) that were popular at that time. Nevertheless, he forged ahead and gained valuable insight into the closed human circulatory system based on simple quantitative examination. Today, we know that the driving force of our blood circulation is based on the difference in pressure between the arteries and veins. The pulsed high pressure in the arteries funnels the blood until the blood pressure in the veins reaches a steady-state low pressure. The human vascular system (with an integral length of hundreds of kilometers or more) circulates about 6 L of blood through our body in just one minute, powered by our heart (weighing only 350 g) acting as a pump and impulse generator. The transportation capacity of such an extensive vascular network (without losses) is about 10,000 L per day. The phenomenon of rhythmic fluctuation due to arterial blood pressure was experimentally discovered in the eighteenth century. In 1726, the Reverend Stephen Hales (1677–1761), an English clergyman who pioneered quantitative experimentation in plant and animal physiology was the first to observe the magnitude of arterial blood pressure and its pulsation in an invasive manner. Figure 1.1 illustrates the experiment he conducted to determine the arterial blood pressure of a horse.

After the first continuous recording of blood pressure, an extensive series of investigations have taken place, all dealing with the problem of how to explain the rhythmic fluctuation of blood flow. However, even until now, a complete understanding of the underlying mechanisms that control the formation of such rhythms is still lacking.

A practical, non-invasive way to acquire information on peripheral venous and/or arterial hemodynamics is by use of optoelectronics paired with quantitative photoplethysmography (PPG). An optoelectronic biosensor concept is introduced that is capable of identifying rhythms from several sensors in combination with acquisition of data on, for example, respiration, ECG and body movement. Depending on the area measured and the purpose of measurement, the optoelectronic sensor can be used in either reflection or transmission mode. The data can then be analyzed using high-time resolution and displayed in time and frequency domains [3].

This chapter presents various possibilities related to the PPG measuring concept by means of examples and perfusion protocols. Current research focuses not only on the so-called central rhythms and their correlation with heartbeat and respiratory rate, but also on the perfusion frequency range around 0.1 Hz. However, assessment and interpretation of these perfusion rhythms are often hindered by the fact that these patterns have a very strong spatial variability and are highly transient [4].

Nowadays, new information about the rhythmic phenomena in skin perfusion is available based on the relationship between blood volume rhythms and respiratory dynamics, evaluation of the hemodynamic-related effect of autogenous training, analysis of the pulse waveform parameters, and/or pulse wave transient time. Using new camera-based sensor and signal processing strategies, a recently developed photoplethysmographic setup allows contactless measurements of cutaneous perfusion with spatial resolution.

Fig. 1.1 A spectacular observation by Hales, measuring arterial blood pressure by means of a glass tube placed in the carotid artery of a horse lying down [1, 2]

1.2 Rhythmic Phenomena in Dermal Perfusion: A Brief Introduction

Before discussing our experimental results and PPG findings, we present a brief overview of rhythmical skin perfusion phenomena based on physiologically-related publications. To this chapter makes no claim to completeness, but seeks only to classify these phenomena and thus facilitate the understanding of the perfusion time series and graphs portrayed in the following chapters.

When human skin is irradiated with infrared light, a large proportion of the photons injected into the tissue is scattered or reflected, and the remaining part is absorbed. If the photons interact with haemoglobin (red blood cells), then the absorption increases. Since the blood volume in the skin is not constant, the amount of reflected light varies inversely with the abundance of blood in the irradiated part of the skin. Thus, variations, e.g., vascular cross-section, cause the rhythmic abundance of blood, making these rhythms particularly easy to find and important for diagnostic

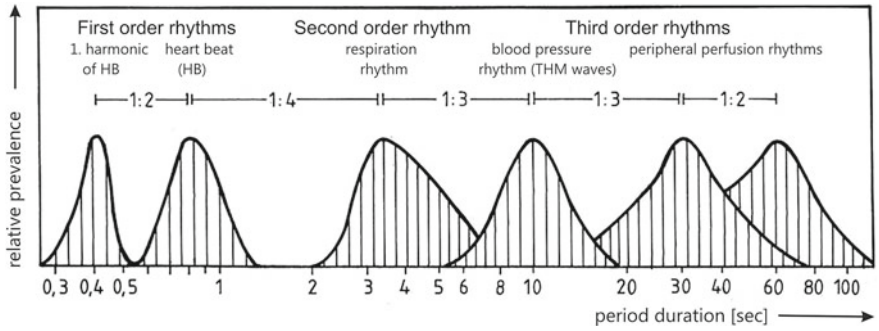

Fig. 1.2 Schematic presentation of some typical rhythmical patterns in the skin perfusion (modified after [5] and H. Schmid-Schönbein, Aachen, personal communication)

purposes. These are the following well-known rhythmical fluctuations [5–18], (see also Fig. 1.2).

1.2.1 Heart Rate (Pulse-Synchronous Rhythms)

During a heartbeat, changes of blood pressure and blood circulation occur below the skin. The observed/imaged waveform changes with the distance from the heart. The arteries in the heart's vicinity are distensible; they accumulate blood during the contraction of the heart and dispense it again over the entire period. This is called the "Windkessel effect". The resting frequency of 1–1.2 Hz is significantly higher than the other investigated fluctuations.

Moreover, in the air-chamber integer multiples of the heartbeat—the harmonics—are generated by reflections. Above these frequencies, the measurement only picks up disturbances which must be filtered out.

1.2.2 Breathing Frequency (Respiratory-Synchronous Rhythms)

Many large vessels, arteries and veins lie in the vicinity of the lungs. The lungs rhythmically press on this system with a pressure of a few mmHg. This affects the arterial system with a central pressure of 100 mmHg only minimally. But on the veins, with a mean pressure of 1 mmHg to 4 mmHg this breathing influence is experienced. After each inhalation and during diastole, the venous system pumps more blood back into the right ventricle than in the exhaled state in order to increase the pumping and the arterial blood pressure. Strength and shape of the blood pressure will be

influenced by the form of respiration. One distinguishes between thoracic breathing, diaphragmatic breathing, and mixed forms of both.

Another important factor is that through the respiration-induced effect known as respiratory sinus arrhythmia (RSA), occasional phase jumps in the heart rate are noticed, which always have a certain phase relationship with the respiration rate. The exact sequence is unclear, but there seems to be a synchronization mechanism between respiration and heart activity. Finally, there exist vasomotor effects (vascular muscle movements) synchronous to breathing, which are driven by synchronized neuronal activity. It would therefore be conceivable that the vasomotor centre in the brain is connected through the respiration centre. However, it is not yet clear if both these alleged centres could be driven by nerve impulses from the same region of the brain stem. The respiratory rate at rest is usually at 0.2 Hz to 0.4 Hz (in the frequency range of the middle PPG spectrum (see) in the logarithmic scale).

1.2.3 Vasomotor Rhythms

The investigation of the vasomotor system really began with the work of French physiologist Claude Bernard (1813–1878), who demonstrated that a section of the sympathetic nervous system in a rabbit caused dilatation of the vessels of ear and that simulation of the peripheral cut end of the nerve caused constriction [6, 7]. His famous quotation may be worth noting in this context:

> I consider the hospital the antechamber of medicine; it is the first place where the physician makes his observations. But the laboratory is the temple of the science of medicine

Each human organ is perfused with oxygenated blood through a capillary vascular network. This takes care of the nutrient intake, the residual material dissipation and temperature regulation. The structure is as follows: branching off from the arteries are the arterioles (diameter see). From this point on, one speaks of "microcirculation". The venules collect the blood at the opposite ends of the microcirculation system and pass it back into the veins. Between arterioles and venules are two types of connections: the arteriovenous anastomosis, a short circuit which is closed when required, and the metarteriole, the main blood-flow path through the capillary network. At the junctions are ring muscles (sphincter precapillaris), which regulate blood flow through the capillaries. The walls of the capillaries consist of a single cell-layer separating the blood vessel (intravascular layer) from the cell gap (interstitium). The pressure decreases about 50% in the arterioles.

The vessel diameter is therefore well-regulated. According to Hagen-Poiseuille's law, the resistance R of a tube like an artery is defined as [17]:

$$R = \frac{8 \cdot v \cdot l}{\pi \cdot r^4}, \text{ with: } v = \text{viscosity}, l = \text{length and } r = \text{radius of the artery.} \quad (1.1)$$

This mechanism regulates the blood volume flow in the vascular plexus. Arterioles and precapillary sphincter are considered to be resistance vessels. Several different control mechanisms exist, which are all interrelated and together affect the blood distribution:

- neural (nervous) influence (from the brain, almost exclusively based on sympathetic activity),
- systemic humoral influence (control by hormones),
- local metabolic influence,
- hormonal influence (due to inflammation or allergies),
- self-regulation (mainly in the brain and in the kidneys),
- influence through local chemo-receptors (in skeletal muscles, with the nerves, then signaling the blood distribution).

Skin perfusion is also supported by influences from the temperature control-loop. The local mechanisms are mostly more dominant than global mechanisms. The interrelation of the above-mentioned mechanisms is currently not clear: they all together, maybe in different ways and intensities contribute to the generation of the vasomotor rhythms. Especially waves with a duration of 5–7/min (fast wave types of third order, also called Traube-Hering-Mayer (THM) waves) are prevalent in blood pressure recordings, while waves with a periodic length of about 1/min are dominant in peripheral perfusion (skin, muscle). These dominant rhythms are called 10 s- and 1min-rhythms according to their preferred frequency.

The 10 s- and the breathing-rhythm show coupling in form of relative coordination according to Golenhofen and Hildebrand [5]. The mechanism of this coupling is still debated after many years of research. Since the 1 min-rhythm of dermal perfusion is characterized by compensation of blood-content variations in connected vessel districts nearby, the central pressure fluctuations probably don't play a part in these rhythms. The frequencies of all these fluctuation patterns are usually at see and are at the bottom of a PPG signal spectrum.

1.2.4 Perfusion Rhythms and the Vegetative Nervous System

All major vascular and organ functions are regulated and controlled by the autonomic nervous system. This consists of two parts, the sympathetic and the parasympathetic. They branch out from the spinal canal at the top of the chest and are regulated by the medullary control centres in the brain. The sympathetic nervous system drives the body and accelerates body activities. Parasympathetic activity inhibits body activity. During physical exercise, the parasympathetic nervous system adjusts itself more quickly to the new situation compared to the sympathetic and the organism experiences oxygen- and nutrient-deficiency; this is moderated by reserves in the blood.

The above-mentioned rhythms are mainly triggered by sympathetic nerves. During anaesthesia, the decaying sympathetic becomes active first. The previously

made measurements on subjects who are under anaesthesia or just awakening as well as from anaesthetized animals are therefore not meaningful. Since the frequency spectrum and probably also the operating and control parameters of all these loops overlap, causal investigations hardly make sense. They should include the entire contiguous vegetative scheme. Many vegetative rhythms fluctuate in frequency, if they are assessed over long periods of time. Mostly, they are synchronized with each other at integer harmonics.

1.2.5 Rhythmic Perfusion Patterns in Peripheral Venous Network Related to Active Body Exercise

The main application of photoplethysmography to map venous blood flow has been en vogue for more than 30 years and provides functional evaluation of total blood displacement in the venous system of the upper extremities. To obtain a PPG for venous blood flow analysis, the PPG sensor is fixed about 10 cm above the inner ankle using a double adhesive ring. The seated patient performs the classical, worldwide standardized muscle pump test (MPT): 8 dorsal extensions in 16 s [19–24]. In an adult with healthy leg veins, the venous blood pool that has been pumped by the dorsal flexions uphill, back to the heart will not flow back due to of the venous valves. As a result the venous blood volume in the foot/leg part reduces which causes the PPG signal to rise. From the venodynamic behavior during such active MPT exercise, several functional parameters like venous refilling time and venous drainage can be calculated (see Chap. 5).

1.3 Photoplethysmography—Historical Notes

For many years, classical photoplethysmography has been one of the most popular non-invasive methods for functional monitoring of peripheral vascular (venous and/or arterial) status. After ground-breaking works by Cartwright [25], Haxthausen, Mathes [26], and Molitor et al. [27], in 1937 Alrick B. Hertzman (1898–1991), a physiologist at St. Louis University School of Medicine, discovered the relationship between the intensity of backscattered polychromatic light and blood volume in the skin [28]. The instruments consisted of three essential components which are still essential in modern systems: a light source, a light detector and a registration unit. He called the device Photoelectric Plethysmograph and summarized his findings as follows ([29], p. 336) (Fig. 1.3):

> The volume pulse of the skin as an indicator of the state of the skin circulation at rest
>
> Amplitude of volume pulse as a measure of the blood supply of the skin

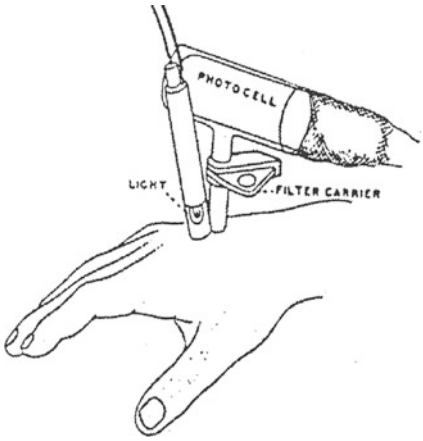

Fig. 1.3 Hertzman´s photoplethysmographic sensor with polychromatic light source, optical filter and photocell detector positioned over the skin of the hand [29]

Following these discoveries, many enhancements of the basic measuring principle have been developed: however, these could only make their way into daily usage in clinics and cardiovascular labs because of the continuous rapid developments in photonic components and microprocessor technology.

1.4 Photoplethysmography—Biophysical Fundamentals

In the skin, induced infrared light is most strongly absorbed by blood, particularly by its hemoglobin content, and not by surrounding skin tissues (Fig. 1.4). Therefore, the amount of reflected infrared light increases in the measurement window when the surface area of blood vessels decreases. A reduction of blood vessel surface area is caused by decreased blood volume [3, 20]. It follows that the PPG signal, which detects the amount of reflected infrared light, displays these changes in blood volume in the cutaneous and partially the subcutaneous vessel plexus. In addition to the very small, periodically changing arterial signal, the sensor signal consists of a high constant part (light scattering in tissue) and a quasi-static vein signal (Fig. 1.5).

It can clearly be seen from Fig. 1.5 that the PPG signal is firstly composed of a very large static component that is due to a large part of measuring light passing only through skin, tissue, or bone (without interaction with blood vessels). The second biggest part of the detected light is attenuated/modulated by venous blood volume changes in the transilluminated tissue volume. This component varies slowly due to respiration, vasomotor and vasoconstriction activity, and also thermoregulation [30–34]. The smallest PPG signal component is proportional to the number of photons passing arterial and terminal micro-vessels; this component will mainly possess peripheral blood volume pulse dictated by the heart beat (central oscillator in

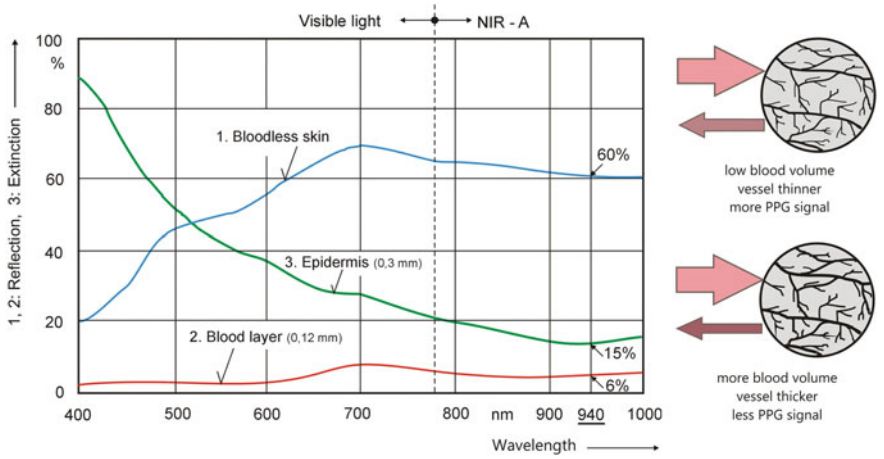

Fig. 1.4 Typical optical properties of human skin and blood in the visible and near-infrared area of the spectrum (**left**). The diagram shows the reflection spectra of anaemic skin in vivo, a 0.3 mm epidermal layer and of a 0.12 mm thick blood layer on glass. The difference in reflectivity between tissue and blood leads to a high optical contrast between skin and dermal vessel plexus. The optical attenuation of epidermis is lowest at wavelengths of about 930 nm and increases with decreasing wavelengths. Illustration of a transilluminated skin vessel plexus in the measurement area explaining the correlation between blood volume and PPG signal (**right**), modified after [20]

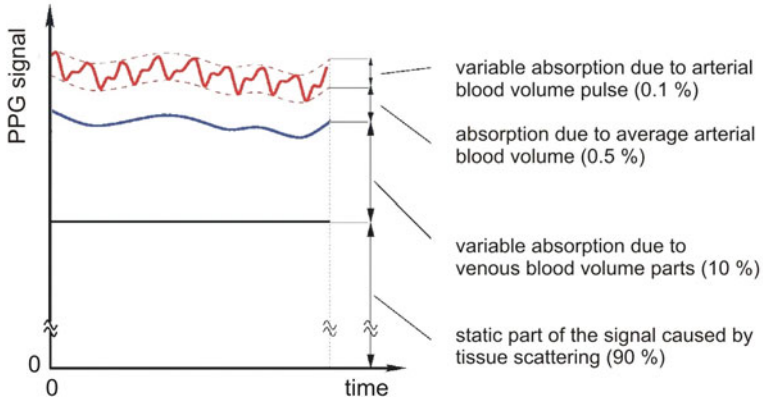

Fig. 1.5 Synthesis of the rPPG signal. The intensity of the backscattered light (subsurface reflection) encodes the PPG signal and depends partially on the blood volume in arterial and venous vessels in the measuring zone. A separation of the venous and arterial perfusion components are possible by selective post-processing of the signal, modified after [21]

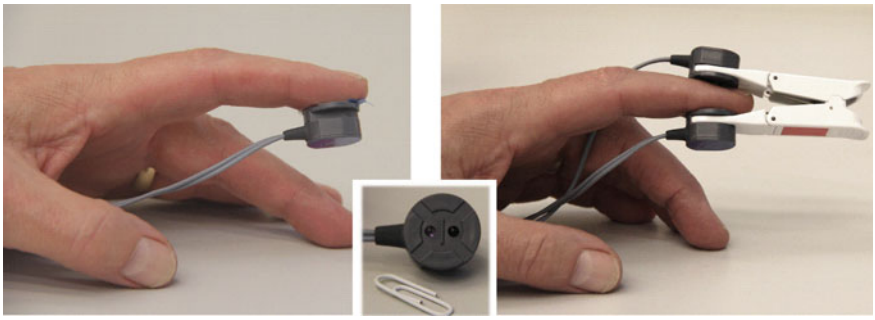

Fig. 1.6 Typical PPG sensors in reflection (**left**) and transmission (**right**) mode. Each sensor consists in its minimal configuration of one light source (LED) and one light detector (Si photodiode). Pulse oximetric sensors, a sub group of PPG sensors, consists of mostly two selective light sources and one detector, which is sensitive for both working wavelengths

our cardiovascular system). Last two PPG signal components depend on (possible) illumination artefacts (e.g., ambient light coupling into the sensor) and quantization noise in the sensor close A/D signal conversion:

$$S_{\mathrm{PPG}}(x, y, t) = S_T(x, y) + S_V(x, y, t) + S_A(x, y, t) + S_{\mathrm{err}}(x, y, t) + S_{\mathrm{qn}}(x, y, t) \tag{1.2}$$

Examples of early PPG sensors working in reflective (rPPG) or transmitive (tPPG) mode is shown in Fig. 1.6.

1.5 Detecting Light Attenuation Changes in Biotissue as a Function of Blood Volume

Biological tissue is a highly scattering and non-homogenous material concerning electromagnetic radiation at frequencies of about 300 THz (near-infrared). Mainly the spreading of photons with this energy content inside the tissue is of high interest in therapeutic and diagnostic applications of medical optoelectronics [35].

A typical skin cross-section is shown in Fig. 1.7a. When optical radiation is sent into the tissue, some photons are reflected directly at the skin surface (Fig. 1.7b), another fraction will be distributed in the tissue through absorption or scattering, while the remaining photons will travel into deeper layers, either straight through (ballistic photons) or after a number of scattering collisions [20, 35].

Typical values for the absorption and scattering coefficients range from 0.05 mm^{-1} to 0.15 mm^{-1} (μ_a) and 3 mm^{-1} to 10 mm^{-1} (μ_s) in the near-infrared wavelength range (800 nm to 1000 nm) in skin tissue. Monte Carlo simulations show that the free photon path between two collisions is around 0.24 mm and the mean scattering-to-absorption probability ratio approximately 50 [36, 37].

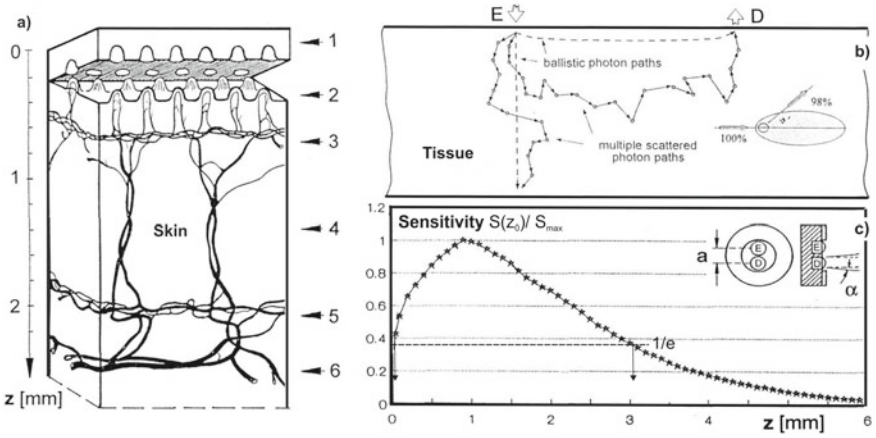

Fig. 1.7 Light propagation in dermal tissue. **a** Schematic structure of skin perfusion. 1: epidermis, 2: capillaries, 3: plexus superficialis, 4: vasa communicantia, 5: plexus profundus, 6: subcutis. **b** Possible photon paths in tissue. **c** Calculated relative sensitivity of a reflective optical sensor as a function of skin depth (modified after [20] and [35])

Therefore, the optical attenuation in skin can be calculated to about 7000 dB/m. Because of this, detector and light source of optical sensors are often placed in a single encasement next to each other on the skin surface. These sensors work in reflection mode. Transmission mode sensors is only used at fingertips or earlobes, where the distance between source and detector is not too large [35].

The effective measurement depth of the reflective PPG sensors as well as its sensitivity can be adjusted—besides by changing the wavelength—by varying its geometry. Distance (a) and axis alignment of both components as well as the beam angles of the opening (numerical aperture NA) affect these characteristics. For example a typical rPPG sensor (900 nm wavelength) with $a = 6$ mm, right-angled positioning and NA = 0.09 ($\alpha = \pm 5°$), has its main detection area between 0.1 mm and 3.1 mm skin depth [20, 35]. (decrease of maximum sensitivity to 1/e, Fig. 1.7c). The resulting measurement volume is about 100 mm^3. In this case, only around 120 photons per million reach the detector and can be used for further signal processing.

A sensor sensitivity profile can be also calculated when the light intensity at different depths locations are regarded.

$$S(z_0) = \frac{I(z_0)}{I_{ges}} = \frac{\int_{-y_{\max}}^{y_{\max}} \int_{-x_{\max}}^{x_{\max}} I_q(x, y, z_0) \cdot I_d(x, y, z_0) \cdot \mathrm{d}x \cdot \mathrm{d}y \cdot \mathrm{d}z}{I_{ges}}. \quad (1.3)$$

Last but not least, the knowledge of the basic optical skin parameters (absorption coefficient $\mu_a(\lambda)$, scattering coefficient $\mu_s(\lambda)$ and anisotropy factor $g(\lambda)$) makes the determination of the light penetration depth in tissue possible (see Chap. 9).