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Biophysics

Photoplethysmography as Time-Dependent Optical Spectroscopy of Skin

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Photoplethysmography (PPG) is a photometric technique that is widely used in the detection of time-dependent blood volume changes in the peripheral tissues of the body. Despite the long history of research, the detailed mechanism of this phenomenon is still a matter of debate. Based on the above, our goal is to determine the mechanism of the PPG-signal formation. In this paper, we analyze a series of observations obtained using reflection-mode PPG. In our experiments, photoplethysmograms were recorded in the wavelength range of 400 – 1000 nm. Recordings were made for 10 s and the time step was 16.5 ms. Measurements were carried out *in vivo* on the projection of the radial artery of the wrist. The observed photoplethysmograms are described by modification of the physiological model of the interaction of light with living tissue proposed several years ago. According to this model, it is the pulsating transmural pressure of the radial artery that increases/decreases the density of capillaries in the dermis, thereby modulating the volume of blood in the capillary bed. The photoplethysmogram observed in the green/blue range of the optical spectrum was due to the modulation of the blood volume in the capillary bed. In the yellow-red and near-infrared ranges, the PPG signal was a modulated blood volume in the capillary bed and artery. For these ranges, differences in the PPG signal shapes are not observed. Differences are observed only in intensities, which are proportional to the amount of blood in the area of interaction. The PPG signal is also modulated by the respiratory rate. *© 2022 Bull. Georg. Natl. Acad. Sci.*

multi-wavelength PPG, modified physiological model of PPG, simultaneous recording of blood pulsations, respiratory modulations

In this paper, we discuss PPG signals recorded *in vivo* on our spectroscopic setup from the wrists of volunteers on the projection of the radial artery, and in our analysis, we are based on a recently proposed model [1], which takes into account the elastic deformation of the dermis by large blood vessels, and in our opinion, more correctly describes the origin of light modulation.

A modified physiological model of PPG. In general, the optical wavelength and the spatial orientation of the sensor relative to the irradiated

area are the two main factors affecting the optical parameters of the skin, as well as the actual appearance of the PPG signal recorded by the experimental setup [2]. Based on this, if we consider the origin of PPG from the point of view of the wavelengths that form the signal, then we will come to the well-known contradictions between the experimental data and the predictions of the theoretical model [3].

To overcome these contradictions, a group of scientists proposed a new physiological model [1, 3]. It is based on the well-known physiological postulate that significant fluctuations in pulse pressure occur only in the arteries [4]. According to the authors of [3]: these fluctuations lead to modulation at the heart rate of both the blood volume in the arteries and the transmural pressure. Green light and light with a shorter wavelength are not modulated by arterial blood volume pulsations due to their low tissue penetration (≤0.6 mm) [5]. However, in the systole phase, the increasing transmural pressure compresses the connective tissue of the dermis in certain places, depending on the peculiarities of the anatomy of the examined subject. The dermis contains both blood and lymphatic capillaries, which are incompressible and do not pulsate with the heart rate. However, due to the contraction of the dermis, the distance between adjacent capillaries decreases, resulting in the modulation of capillary density in synchrony with transmural pressure at the local measurement site [1]. This change in capillary density leads to temporal modulation of the light parameters since it affects absorption and scattering coefficients. In other words, the PPG waveform arises from the modulation of blood volume in the capillary bed, which is induced by the pulsating transmural pressure of the arteries.

A simplified concept of the proposed model is shown in Fig. 1.

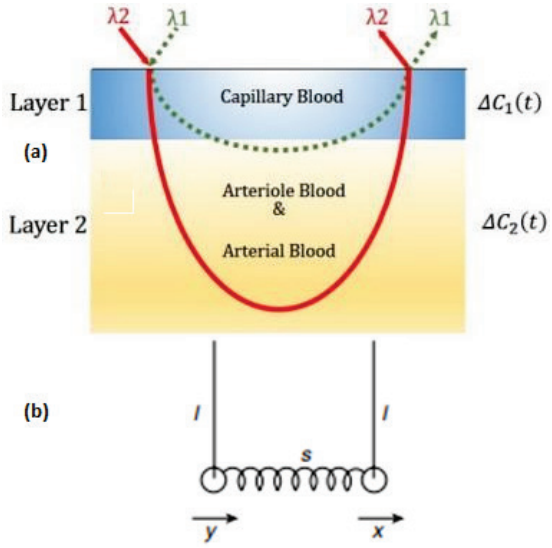

Fig. 1. (a) Two-layer and two-wavelength-range light-tissue interaction model. (b) Artery and microcapillary bed as two coupled identical oscillators.

Our measurements were carried out on the surface of the skin, in the wavelength range of 400-1000 nm. However, blue and green light only reaches the superficial capillary bed, and yellow light can reach arterioles in the dermis, while longer wavelengths such as red and NIR can penetrate the skin and reach arteries in the subcutaneous tissue. The investigated spectral range reduces these three layers to two: violet-green light affects the sub-epidermal layer with capillaries and red and NIR the dermal layer with arterioles and subcutaneous tissue with arteries. In addition, it should be taken into account that yellow, red, and NIR radiation on the way to the detector passes through the capillary bed twice and acquires additional modulation. Thus, according to the modified physiological model [1,3], the vascular network can be represented as a two-layer medium, the physical model of which is two coupled identical oscillators [6] (Fig.1).

According to the modified physiological model, any change in internal conditions, such as those caused by changes in venous pressure, mussel constriction, or changes in lymph volume, also affects the PPG waveform.

It should be noted that the validity of the physiological model was tested on the wrist but at a distance from the projection of the radial artery [1, 3]. In our case, the measurements were carried out directly on the projection of the artery, that is, in those places where PPG signals are caused not only by transmural pressure but also by changes in blood volume, as well as their superposition. It is clear that, according to this model near the artery, green and shorter wavelengths describe skin pulsations caused by transmural pressure, while yellow, red, and near-infrared radiation generally describe both processes, both transmural pressure and changes in blood volume. When approaching the artery, the modulations caused by changes in blood volume will intensify, and the modulations in capillary bed caused by transmural pressure will significantly decrease down to negligible smallness.

Such studies are very important for those medical applications that use pulse oximeters operating in reflection mode to avoid erroneous interpretation of the measurement. And, in fact, in places far from the artery, the PPG waveform occurs due to the modulation of blood volume in the dermis, the oximeter measures oxygen saturation in the capillaries, not in the arteries. Although reflection mode oximeters work with yellow, red and near-infrared light, which penetrates much deeper than green light, the effect of dermal compression should be significant, since any light, as already noted, interacts twice with the upper layer of the dermis before reaching the photodetector [1, 3]. In this case, the pulse oximeter measures oxygen saturation, not in the arterial but in the capillary blood.

A typical PPG waveform is shown in Fig. 3 for several successive pulses. As you can see, it consists of two different components: alternating (AC), changing in time with a frequency of about one Hz, and slowly changing base (DC-level). Within our model of PPG signals, the AC component is due to absorption due to the pulse-added arterial blood volume of transmural pressure, while the background (DC) component with various lower-frequency components is associated with respiration, sympathetic nervous system activity, and thermoregulation [7, 8].

As a result of modifying models presented in works [9-11], to describe our experiments, we get the following expression for the time dependent reflection intensity:

$$I(t) = k_1 \cdot \Delta C_1(t) \cdot e^{-i\varphi_1} + k_2 \cdot \Delta C_2(t) \cdot e^{-i\varphi_2}, \quad (1)$$

where k_1 and k_2 are experimentally determined proportionality coefficients.

It follows from Equation 1 that some points should be observed on the skin, where the fluctuations caused by transmural and arterial pressure are in opposite phases. In these cases, PPG signals should not be observed, and if the phases coincide, this signal will be maximum. Probably the difficulty of observing the PPG signal is related to this.

From our model it also follows that:

- For violet-green ($\lambda 1$) regions of the visible spectrum, $k_1 \cdot \Delta C_1(t) \cdot e^{-i\varphi_1}$ and accordingly at different points of the skin surface the measured PPG signal will be out of phase. And the modulation of different colors of the fixed region $\lambda 1$ will be in-phase. Indeed, all this is experimentally confirmed (see [1] and the referenced literature).
- For yellow-near IR (up to 1μm) ($\lambda 2$) regions $I(t)$ of the visible spectrum, the signal is proportional to the amplitudes of conditionally arterial and transmural oscillations. If either term dominates, then the modulation of the different colors of light in the $\lambda 2$ region will still be in-phase, respectively, on φ_1 or φ_2, and if both terms are commensurate, then the modulation phase will be determined by the $\varphi_1 - \varphi_2$ difference.

The obtained theoretical results will use to interpret our measurements.

Experimental setup. Our experiments were carried out on the wrist, the signal-detector distance was 3mm. Fig. 2 shows a diagram of the experimental setup. An AOC-100 endoscope with a halogen lamp (former USSR) was used as the light source.

Reflection spectra were recorded on a CCD spectrometer (Ocean FX, Ocean Optics, United States). Transmission of exciting radiation to the skin and transmission of the fluorescence signal from the sample to the spectrometer was performed using a special optical fiber 5 mm in diameter (former USSR). The reflected light was collected at a distance of 3 mm from the edge of the illuminated point using a fiber optic probe, which is a bundled-together fiber with a diameter of 400 microns.

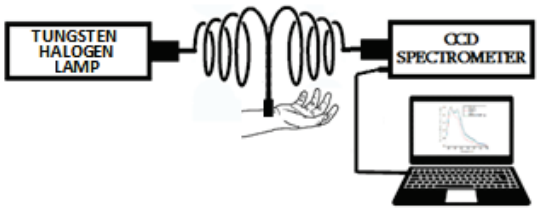

Fig. 2. Measurement site and experimental setup.

Experiments were carried out on the wrist of volunteers. In particular, on the volar side of the left hand of physiologically healthy volunteers. We have measured characteristic, time-dependent spectral curves in the spectral range 400-1000 nm. The experiments were performed with the permission of the Medical Ethics Commission of the Georgian National Center for Disease Control& Public Health (Protocol #2019-43) and with the informed consent of all volunteers.

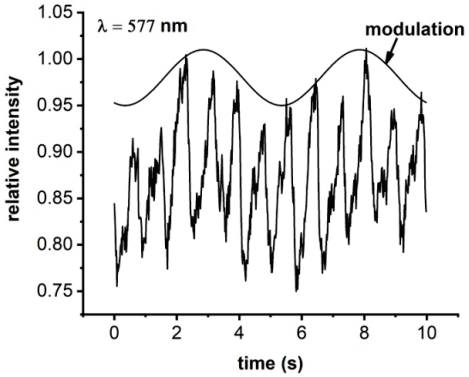

Fig. 3. PPG signal measured at 577 nm.

Significant result #1. It follows from Equation (1) that the reflected signal should be a superposition of periodic functions of two different frequencies (corresponding to the heart rate + the corresponding transmural pressure and respiration). Indeed, this is confirmed by our results (Fig. 3).

Significant result #2. As we know, light with a wavelength of 577 nm reaches the arterioles and arteries. Therefore, photons with a longer wavelength of 577 nm will also reach them, and based on our model (Equation 1), their period, shape, and peak values should match. As can be seen from the graph (Fig. 4) and the model, this theoretical prediction is carried out with high accuracy (Table).

Table. The standard deviation of the error at different wavelengths for 10 s and $\Delta t = 16$ ms.

wavelength, nm	root-mean-square deviation(RMSD)
515	9.5×10^{-2}
577 - 900	$\approx 1\times10^{-2}$
950	2.2×10^{-2}

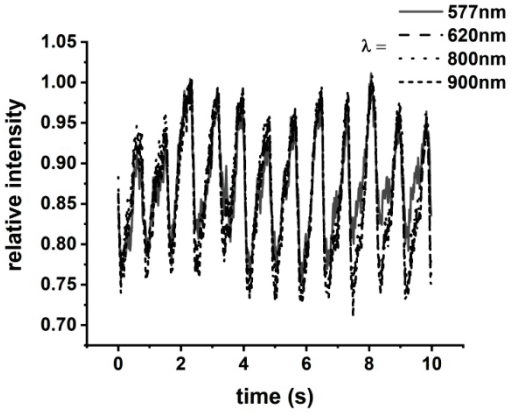

Fig. 4. PPG signal over the radial artery measured at 577, 620, 800 and 900 nm.

We will arrive at the same result if we look at this question in the following way. Using the nominal tissue sound velocity of 1540 m/s and the wave ratio $\nu = f\lambda$, we can calculate the tissue wavelength $\lambda = 1540(\text{m/s})/1-1(\text{Hz}) = 1540-775(\text{m})$ for a sound wave with a frequency of 1-2 Hz. For such wavelengths and at a constant distance between the two oscillators of 3 mm (artery and microcirculatory layer), the phase difference does not change and at this distance, the peaks should coincide with each other. That is we get the same result.

Significant result #3. For light with a wavelength of $\lambda < 577$ nm, the oscillations must be capillary, and from Equation 1 we obtain $k_1 \cdot \Delta C_1(t) \cdot e^{-i\varphi_1}$. Since these reflected light oscillations are caused by transmural pressure oscillations in capillary density and respiration, thereforethe position and periods of peak values of these fluctuations should coincide with the same data for wavelengths $\lambda \geq$ 577 nm. And this is true (Fig.5).

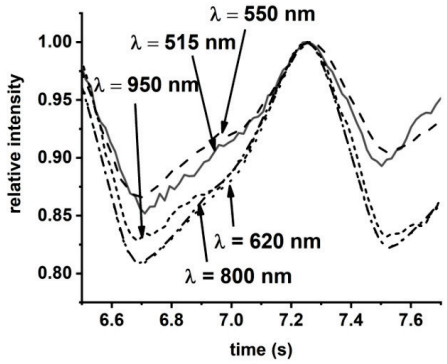

Fig. 5. Synchronized single oscillations of PPG at different wavelengths. Here everywhere smoothing is done at 15 points.

Conclusion

The PPG method is less than 100 years old, but a special interest in its application in new areas has arisen in recent years. As studies by various scientific groups show, the PPG method has greatly expanded the scope of its application since its inception. Using the PPG method, in addition to traditional areas of application such as determining the hemodynamic parameters of the body, registering the volumetric velocity of venous blood flow, assessing fluctuations in tissue volume, determining the tone and capacity of veins, monitoring the work of the heart with the ability to record various types of arrhythmias, and even determining some biochemical parameters of blood gives new unlimited possibilities for the development of the method in different areas of research.

The model proposed in [3] and taken by us as the primary and modified model of the interaction of light with biological tissue, which is based on the representation of changes in the optical density of capillaries and dermis as a response to pulsations of arterial transmural pressure, explains the mechanism of modulation of PPG signals, in which one of the low-frequency components of the signal is associated with breathing. Moreover, selective PPG using different wavelengths provides an interesting opportunity to study tissue layer by layer. All these examples testify to ever new, promising and limitless areas of application of the PPG method.

It should be especially emphasized that the defining significance and attractiveness of the PPG method are given by its absolute non-invasiveness and the comparative cheapness of the optoelectronic hardware.

Our research group is going to continue to work on a deeper and more thorough study of the nature and mechanisms of light modulation that determines the formation of PPG signals.

ბიოფიზიკა

ფოტოპლეთიზმოგრაფია როგორც კანის დროზე დამოკიდებული ოპტიკური სპექტროსკოპია

ზ. მელიქიშვილი*, თ. მედოიძე*, ზ. ჯალიაშვილი*, ა. გამყრელიძე**, ნ. იმნაიშვილი*

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**ივანე ჯავახიშვილის სახ. თბილისის სახელმწიფო უნივერსიტეტი, ზუსტ და საბუნებისმეტყველო მეცნიერებათა ფაკულტეტი, თბილისი საქართველო

(წარმოდგენილია აკადემიის წევრის რ. გამყრელიძის მიერ)

ფოტოპლეთისმოგრაფია (PPG) – ფოტომეტრული მეთოდია, რომელიც ფართოდ გამოიყენება ორგანიზმის პერიფერიულ ქსოვილებში სისხლის მოცულობის დროზე დამოკიდებული ცვლილებების გამოსავლენად. მიუხედავად კვლევების ხანგრძლივი ისტორიისა, ამ მოვლენის დეტალური მექანიზმი დღემდე დისკუსიის საგანს წარმოადგენს. ყოველივე ზემოაღწერილიდან გამომდინარე, ჩვენი მიზანია PPG სიგნალის ფორმირების მექანიზმის განსაზღვრა მაჯის არეში. ნაშრომში გაანალიზებულია არეკვლის რეჟიმში მიღებული PPG სიგნალების სერია. ექსპერიმენტებში ვარეგისტრირებდით ფოტოპლეთიზმოგრამებს ტალღების 400-1000 ნმ დიაპაზონში. ჩაწერები მიმდინარეობდა 10 წმ ხანგრძლივობით, დროითი 16,5 მწბიჯით. *in vivo* ექსპერიმენტები ტარდებოდა მაჯის არეში. დამზერილი ფოტოპლეთიზმოგრამები აღიწერება რამდენიმე წლის წინ შემოთავაზებული სინათლისა და ცოცხალი ქსოვილის ურთიერთქმედების მოდიფიცირებული ფიზიოლოგიური მოდელის საშუალებით, რომელიც მიღებული შედეგების ახსნის საშუალებას იძლევა. აღნიშნული მოდელის თანახმად დერმაში კაპილარული ქსელის სიმკვრივის გაზრდა/შემცირებას იწვევს სწორედ სხივური არტერიის ტრანსმურალური წნევის პულსაციები, რაც, თავის მხრივ, ამოდულირებს სისხლის მოცულობას კაპილარულ ქსელში. ფოტოპლეთიზმოგრამა, რომელიც დაიმზირება ოპტიკური სპექტრის მწვანე-ლურჯ უბანში, განპირობებული იყო კაპილარულ ქსელში სისხლის მოცულობის მოდულაციით, ხოლო ყვითელ-წითელ და ახლოინფრაწითელ უბანში PPG სიგნალი წარმოადგენს კაპილარული ქსელისა და არტერიული სისხლის ერთობლივ მოდულაციას. ამ დიაპაზონებისთვის PPG სიგნალების ფორმებს შორის განსხვავება არ დაიმზირება. განსხვავება შეინიშნება მხოლოდ ინტენსივობებში, რომლებიც დაკვირვების არეში სისხლის რაოდენობის პროპორციულია. PPG სიგნალი ასევე მოდულირდება სუნთქვის სიხშირით.

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