PROCEEDINGS OF SPIE

Biophotonics: Photonic Solutions for Better Health Care IV

Jürgen Popp
Valery V. Tuchin
Dennis L. Matthews
Francesco S. Pavone
Editors

14–17 April 2014
Brussels, Belgium

Sponsored by
SPIE

Cosponsored by
B-PHOT—Brussels Photonics Team (Belgium)
FWO—Fonds Wetenschappelijk Onderzoek (Belgium)
Brussels-Capital Region (Belgium)
Ville de Bruxelles (Belgium)

Cooperating Organisations
CBO-BCO (Belgium)
European Laser Institute
Photonics 21 (Germany)
EOS—European Optical Society (Germany)

Published by
SPIE

Volume 9129

Proceedings of SPIE 0277-786X, V. 9129

Evaluation of the Doppler component contribution in the total backscattered flux for noninvasive medical spectroscopy

Denis Lapitan*, Dmitry Rogatkin
Moscow Regional Research and Clinical Institute "MONIKI" named after M. F. Vladimirskiy
Shepkina str. 61/2, Moscow, RF 129110

ABSTRACT

The widespread introduction of laser noninvasive diagnostic techniques in medicine gave rise interest to theoretical description of light propagation in turbid media. One of the purposes for that is a preliminary simulation of incoming radiation for diagnostic spectrophotometry equipment. For complex diagnostic devices combining the Laser Doppler Flowmetry (LDF) and the tissue reflectance oximetry (TRO) it is necessary to know a ratio of signals in each diagnostic channel for a proper choice of the radiation power of laser sources, sensitivity of photodetectors, etc. In LDF the light-beating backscattered signal mixed from moving red blood cells and static inhomogeneities inside the tissue is the useful signal, while in TRO both signals from static and moving scatterers are registered in the sum. The aim of our study was an estimation of the ratio between flux with the Doppler shifted signal and the total backscattered flux. For this purpose the simple analytical model describing the backscattered radiation for a two-layered tissue with different levels of blood volume in the second layer was under consideration. The physical model was based on the improved Kubelka-Munk approach. This approach involves an additional parameter of the density of scatterers, so it is useful for the Doppler signal intensity calculation as well. To assess the intensity of the Doppler component the single-scattering approximation inside the tissue's second layer was used. It was found that the fraction of the Doppler component in the total backscattered flux can vary in the range of 1-10% for the blood volume of 1-20%.

Keywords: Laser Doppler flowmetry, backscattering, blood volume, Kubelka-Munk approach, tissue, spectroscopy

1. INTRODUCTION

The widespread introduction of laser noninvasive diagnostic techniques in medicine gave rise interest to theoretical description of light propagation in turbid media, which, in particular, is a human skin. One of the purposes for that is the opportunity of a preliminary simulation of incoming radiation for diagnostic spectrophotometry equipment which allows for engineers to make a correct substantiation of technical requirements for the equipment[1]. For example, for complex diagnostic devices combining the Laser Doppler Flowmetry (LDF) and the tissue reflectance oximetry (TRO) it is necessary to know a ratio of signals in each diagnostic channel for a proper choice of the radiation power for laser sources, sensitivity of photodetectors, etc. In LDF the light-beating backscattered signal mixed from moving red blood cells (RBC) and static inhomogeneities inside the tissue is the useful signal[2,3], while in TRO both signals from static and moving scatterers are registered in the sum[1,4]. So, the ratio of them is very important.

Moreover, as it was shown by Bonner et al.[3], the light-beating phenomenon, when optical signals with the Doppler shifted wavelengths and without ones are mixed on photodetectors, leads to appearance of a low-frequency components in a spectral power density of the complex registered signal. The amplitude of the low-frequency components is the raw essential data to calculate the blood flow as an output of the diagnostics in LDF. But the basic theory was constructed by Bonner et al.[3] with a large number of assumptions, e.g. a small concentration of RBCs, isotropic illumination, etc. One of such assumptions is stationary amplitude of the reference beam scattered on motionless elements in tissues. Meanwhile, it is well-known that the total amplitude of the backscattered flux strongly and nonlinear depends on the blood volume in the tested tissue. It limits, particularly, the sensitivity of the tissues reflectance oximeters[1]. The same has to occur in LDF. If for LDF technique we formulate the initial illuminating optical field E_0 in the form

$$E_0 = A_0 e^{-i\omega_0 t} \tag{1}$$

*lapitandenis@mail.ru; phone/fax +7(495)6818984; www.medphyslab.com

Biophotonics: Photonic Solutions for Better Health Care IV, edited by Jürgen Popp, Valery V. Tuchin, Dennis L. Matthews, Francesco Saverio Pavone, Proc. of SPIE Vol. 9129, 91292X · © 2014 SPIE · CCC code: 0277-786X/14/$18 · doi: 10.1117/12.2051974

where: A_0 is the amplitude of the initial optical field, ω_0 – circular frequency of illuminating radiation, t – time,

as well as if we formulate the backscattered field E_d with the Doppler shifted frequency in the form

$$E_d = A_d \cdot e^{-i(\omega_0+\omega_d)t} \tag{2}$$

where A_d is the amplitude of the E_d, ω_d is frequency shift due to the Doppler effect, then the total backscattered field E_Σ reaching the photodetector can be expressed as follows:

$$E_\Sigma = A_S e^{-i\omega_0 t} + A_d \cdot e^{-i(\omega_0+\omega_d)t} \tag{3}$$

where A_s is the amplitude of the backscattered field E_s scattered from the motionless components inside the tissues.

The light-beating signal of these two components produces a low-frequency output voltage from the photodetector. It is well-known equation[2,3]. But if we take into account an amplitude modulation of the E_s as follows

$$E_S = A_S(1 + k\cos\Omega t) \cdot e^{-i\omega_0 t} \tag{4}$$

where k<<1 is the depth of modulation, Ω is the frequency of that, then one can obtain easily that:

$$E_\Sigma = A_S e^{-i\omega_0 t} + \frac{kA_S}{2}(e^{-i(\omega_0-\Omega)t} + e^{-i(\omega_0+\Omega)t}) + A_d \cdot e^{-i(\omega_0+\omega_d)t} \tag{5}$$

In the equation (5) the second and the third components of the sum don't differ among themselves, especially when Ω is of the same order as ω_0, and it can lead to mistakes in calculations of blood flow. Therefore, the ratio between kA_s and A_d become the key parameter for the correct interpretation of the LDF data.

So, the aim of our study was an evaluation of the possible ratio between flux with the Doppler shifted signal and the total backscattered flux in typical diagnostic tasks. For this purpose the simple analytical model describing the backscattered radiation for a two-layered tissue with different levels of blood volume in the second layer was under consideration. Several experimental measurements to verify the model were executed as well.

2. THE SIMPLE ANALYTICAL MODEL

The investigated biological tissue (human skin, for example) was split on two main layers differing in their optical properties: a first layer without blood vessels (like epidermis of the skin) and the second layer - all remaining tissue – is filled with blood (like derma). The first layer has a finite width H_1 while the second layer is a semi-infinite ($H_2 \to \infty$), since, in most cases, the light doesn't pass through the second layer (Fig. 1). To find the power of the backscattered flux $F_{BS} \sim |E_\Sigma|^2$ the improved Kubelka-Munk (KM) two-flux approach[5] was used. This approach differs from the classic KM model[6] by introducing of the complex coefficients of equations β_1 and β_2 describing more precisely attenuation and backscattering processes on the elementary path-length dx in the general case. It allows anyone to obtain exact analytical solutions for the boundary fluxes – backscattered and transmitted by the tissue fluxes[5]. Moreover, this approach involves an additional parameter of density of scatterers (μ_ρ), so it is useful for the Doppler signal intensity calculation as well.

Like the classic KM model this approach takes into consideration two radiative fluxes passing through the light-scattering medium in two opposite directions – forward and backward. On the Figure 1 the fluxes passing in our two-layered model tissue are denoted by solid arrows. Backscattering processes are denoted by dotted arrows. F_0 – the incident flux illuminating the tissue, F_{BS} – the total backscattered flux, β_{11}, β_{12} – the attenuation and backscattering coefficients defining the optical properties of the first layer[5], β_{21}, β_{22} – the same ones defining the optical properties of the second layer, V_b (in relative units; V_b=0….1) – the relative fraction of blood (total haemoglobin volume) in the second layer which is an integral parameter characterizing both the total volume of circulating blood in the inspected tissue and the degree of filling of superficial structures of the layer by blood. So, the total optical properties of the two-layered tissue are different at various levels of blood fraction in the second layer.

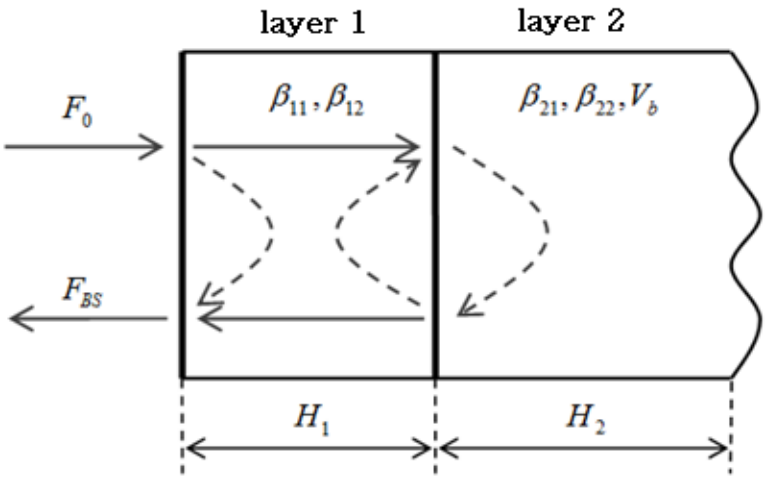

Figure 1. Two light fluxes passing through our two-layered tissue model in forward and backward directions.

The Gurevich's analytical expressions presented in Ref.[5] allow us to calculate F_{BS} for our two-layered turbid medium in the case of multiple scattering inside each layers as follows:

$$F_{BS} = F_0\left[\frac{P_1\left(1-e^{-2L_1H_1}\right)}{1-P_1^2e^{-2L_1H_1}} + \frac{P_2\left(1-P_1^2\right)^2 e^{-2L_1H_1}}{\left(1-P_1^2e^{-2L_1H_1}\right)\left(1-P_1P_2-P_1(P_1-P_2)e^{-2L_1H_1}\right)}\right] \tag{6}$$

where:

$L_i = \sqrt{\beta_{i1}^2 - \beta_{i2}^2}$, $P_i = \left(\beta_{i1} - L_i\right)/\beta_{i2}$,

$$\beta_{i1} = \omega_i \cdot \frac{\mu_{ai} - \mu_{\rho i}\ln(1-R_i) + \mu_{\rho i}\ln(1-\omega_i + \sqrt{\omega_i^2 - R_i^2\exp(-2\mu_{ai}/\mu_{\rho i})})}{\sqrt{\omega_i^2 - R_i^2\exp(-2\mu_{ai}/\mu_{\rho i})}},$$

$$\beta_{i2} = R_i \cdot \exp(-\mu_{ai}/\mu_{\rho i}) \cdot \frac{\mu_{ai} - \mu_{\rho i}\ln(1-R_i) + \mu_{\rho i}\ln(1-\omega_i + \sqrt{\omega_i^2 - R_i^2\exp(-2\mu_{ai}/\mu_{\rho i})})}{\sqrt{\omega_i^2 - R_i^2\exp(-2\mu_{ai}/\mu_{\rho i})}}, \tag{7}$$

and $\omega_i = \dfrac{1-(1-2R)\cdot\exp(-2\mu_{ai}/\mu_{\rho i})}{2}$.

In all these equations μ_{ai} [cm^{-1}] is the classic absorption coefficient, which corresponds to the same one of the general transport equation[6]. $\mu_{\rho i}$ [cm^{-1}] is the average density of heterogeneities inside the medium along the pass-length dx; and R_i is the Fresnel coefficient of reflection on the boundaries of the heterogeneities. All these parameters are the function of wavelength λ in the general case. The index "i" characterizes the layer's number (i=1, 2).

At numerical calculations and computing with the use of (6) and (7) the absorption coefficient for the first layer was defined as[7]

$$\mu_{a1}(\lambda) = 27\cdot\exp(-0{,}006\lambda) \quad . \tag{8}$$

The absorption coefficient for the second layer was calculated as a well-known mixture[4]

$$\mu_{a2}(\lambda) = \mu_{a1}(\lambda)\cdot(1-V_b) + (\mu_{aHBO2}(\lambda)\cdot S_tO_2 + \mu_{aHB}(\lambda)\cdot(1-S_tO_2))\cdot V_b \ , \tag{9}$$

where: μ_{aHBO2} is the absorption coefficient of the oxyhemoglobin in blood, μ_{aHB} is the absorption coefficient of the deoxyhemoglobin in blood; $S_tO_2 = 0{,}7$ (70%) is the mean tissue oxyhemoglobin saturation in relative units. Approximate values of the average density of heterogeneities were taken from Ref.[6]: for the first layer $\mu_{\rho 1}$=100 cm^{-1} and for the second layer it was calculated as the mixture

$$\mu_{\rho 2} = \mu_{\rho 1} \cdot (1 - V_b) + \mu_{\rho b} \cdot V_b , \tag{10}$$

where $\mu_{\rho b}$=100 cm^{-1} is the average density of red blood cells (RBC) in blood.

The Fresnel reflection coefficients were calculated with the use of the well-known data on the refractive index $n_{water}(\lambda)$ for water and the refractive index $n_{air}(\lambda)$ for air:

$$R(\lambda) = \left(1 - \frac{n_{water}(\lambda)}{n_{air}(\lambda)}\right)^2 \Big/ \left(1 + \frac{n_{water}(\lambda)}{n_{air}(\lambda)}\right)^2 \tag{11}$$

To assess the intensity of the Doppler component in the total detected flux F_{BS} the single-scattering approximation inside the second layer of the tissue was used. In this approximation the secondary scattering process of the reverse flux in tissue is neglected[8]. Using expressions for transmitted and backscattered fluxes for a single layer of a turbid medium[8], the analytical solution for the power of the backscattered radiation for our two-layered tissue can be written as:

$$F_{BS,\sin gle} = F_0 R \left[\frac{e^{-\mu_{a1}/\mu_{\rho 1}} (1 - Y_1^{\mu_{\rho 1} H_1})}{1 - Y_1} + \frac{e^{-\mu_{a2}/\mu_{\rho 2}} (1 - Y_1) Y_1^{\mu_{\rho 1} H_1} (1 - R)^{\mu_{\rho 1} H_1}}{(1 - Y_1)(1 - Y_2) - R^2 e^{-\mu_{a1}/\mu_{\rho 1}} e^{-\mu_{a2}/\mu_{\rho 2}} (1 - Y_1^{\mu_{\rho 1} H_1})} \right] \tag{12}$$

where $Y_i = (1 - R_i) e^{-2\mu_{ai}/\mu_{\rho i}}$. To extract the power of the Doppler component $F_d \sim |E_d|^2$ from the total backscattered flux (12) the difference in values of $F_{BS,\ single}$ for cases of the second layer filled with blood and not filled was used:

$$F_d = F_{BS,\sin gle}(V_b \neq 0) - F_{BS,\sin gle}(V_b = 0) . \tag{13}$$

3. RESULTS OF THEORETICAL SIMULATIONS

At the first step with the use of (6)-(11) the full spectra of the backscattered flux F_{BS} for different theoretical levels of blood volume (V_b=0…1) at H_1=20 μm and F_0=1 were calculated in the waveband 440-950 nm (Fig. 2).

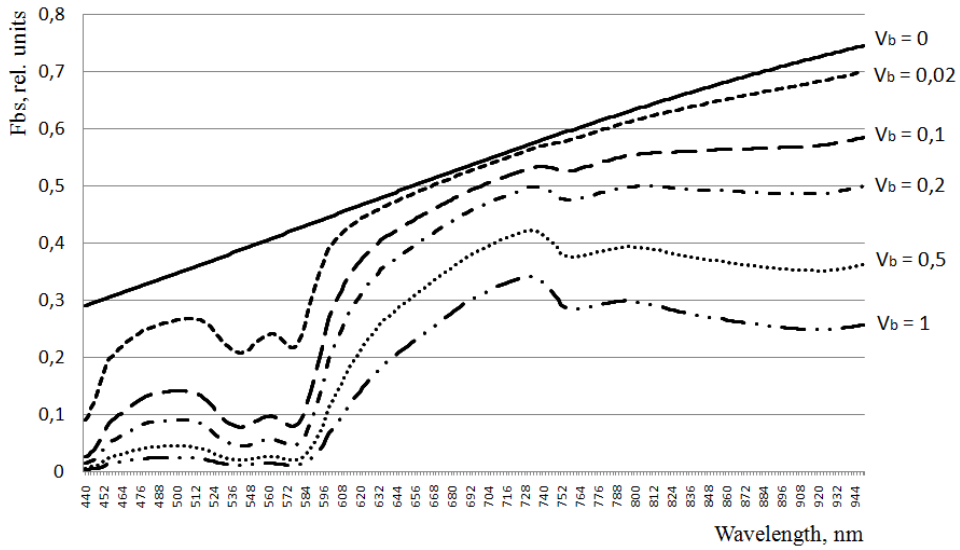

Figure 2. Spectra of backscattered light for different theoretical levels of blood volume in the second layer.

Figure 2 shows that the power of F_{BS} decreases with increasing of V_b. This dependence corresponds well to real situations because blood is a good absorber of optical radiation. "Cavities" at wavelengths of λ~540 nm and λ~576 nm correspond to the absorption peaks of oxyhemoglobin and at λ~757 nm of deoxyhemoglobin in the absorption spectra of hemolyzed blood. For human tissues the level of blood volume in superficial tissue layers in a normal state is in the range of 0,01÷0,2 rel. uns. As can be seen from Fig. 2 the power of registered flux for these values varies considerably and can be changed by almost 2 times for some parts of the spectrum. So, the key parameter among all other actual optical and physics properties of two-layered tissues is the level of blood volume in the second layer.

At the second step with the use of (12)-(13) the backscattered from the RBC Doppler component F_d was computed as an increment in the total backscattered flux with growth of the density of RBC ($\mu_{\rho b}$) in the second layer of the tissue. At calculations $\mu_{\rho b}$ was varied from 100 to 1000 cm^{-1} (100, 500, 1000 cm^{-1}) and the intensity of the Doppler component was computed at wavelength λ = 800 nm for different levels of blood volume (V_b = 0; 0,1; 0,2; 0,3; 0,4; 0,5). The dependencies of F_d on the V_b were constructed. They are presented in the Figure 3. As it can be seen from the Figure 3, the dependence of F_d on the V_b of the second layer is quite linear for small values of $\mu_{\rho 1}$ (Fig. 3a) and becomes more nonlinear (close to the quadratic dependence) with increasing of $\mu_{\rho 1}$ (Fig. 3b and 3c). Thus, nonlinearity of the registered signal is caused by the amount of scatterers in the tissue.

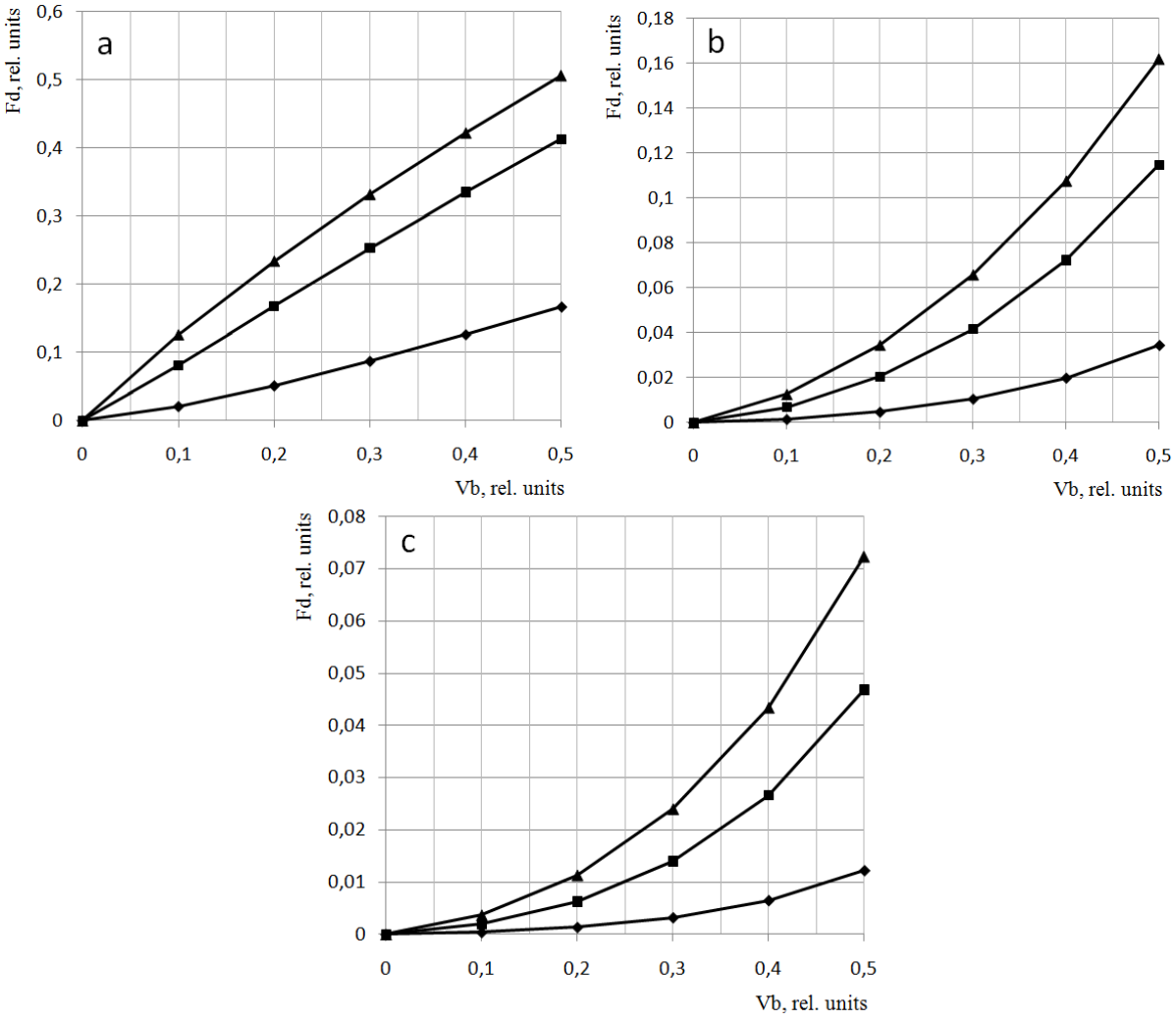

Figure 3. Dependences of the Doppler component F_d on the blood volume of the second layer for different values of $\mu_{\rho b}$ and $\mu_{\rho 1}$: a) $\mu_{\rho 1}$ = 100 cm^{-1}, b) $\mu_{\rho 1}$ = 500 cm^{-1}, c) $\mu_{\rho 1}$ = 1000 cm^{-1}. - $\mu_{\rho b}$ = 100 cm^{-1}, - $\mu_{\rho b}$ = 500 cm^{-1}, - $\mu_{\rho b}$ = 1000 cm^{-1}.

The ratio of the F_d to the total backscattered flux ($F_d/F_{BS,single}(V_b \neq 0)$) was calculated for different values of $\mu_{\rho b}$ and $\mu_{\rho 1}$ (Fig. 4). As it follows from the Figure 4, the fraction of the Doppler component in the total backscattered flux can vary in the range of 0,1÷10% for the normal blood volume of 0,01÷0,2 rel. un. These results are qualitatively corresponds to results obtained by Starukhin[9], when the similar calculations were carried out on the basis of the Monte Carlo simulation.

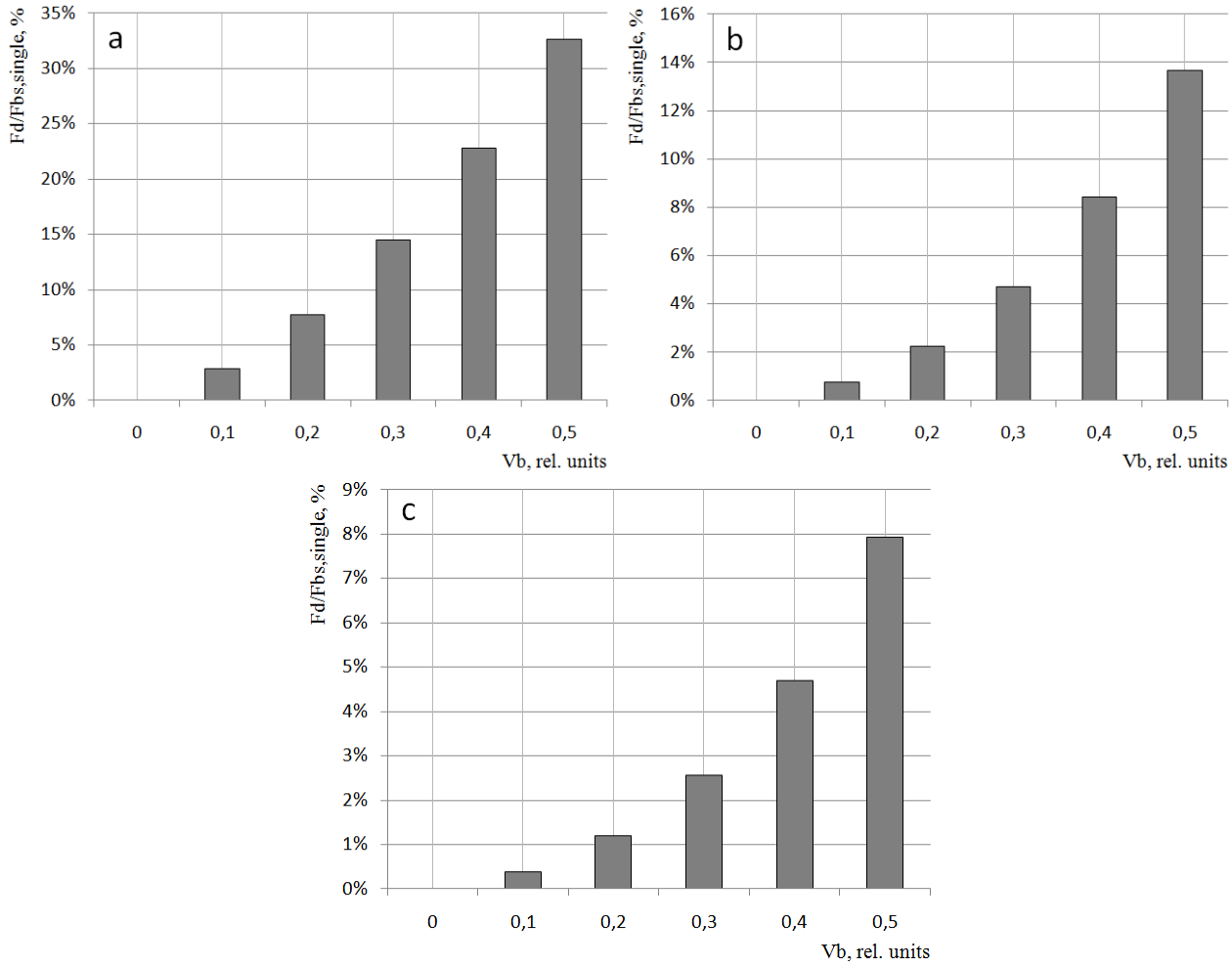

Figure 4. Contribution of the Doppler component F_d in the total backscattered flux F_{BS} as a function of the blood volume in the second layer for different values of $\mu_{\rho b}$ and $\mu_{\rho 1}$: a) $\mu_{\rho 1} = \mu_{\rho b} = 100$ cm^{-1}, b) $\mu_{\rho 1} = \mu_{\rho b} = 500$ cm^{-1}, c) $\mu_{\rho 1} = \mu_{\rho b} = 1000$ cm^{-1}.

4. EXPERIMENTAL RESULTS AND COMPARISON

To compare theoretical results with some experimental data we have carried out several experimental measurements with the use of the commercial tissue reflectance oximeter "Spectrotest" and a multifunctional laser noninvasive diagnostic system "LAKK-M" (Lazma Ltd., RF)[10]. By using the "LAKK-M" system the white light reflectance spectra from skin and mucosa of a healthy man were measured (Fig. 5). The shape and amplitude of these curves are very similar to the theoretically calculated spectra presented in the Figure 2. In our opinion, it proves in some ways the objectivity and reliability of both our theoretical model and computational results. By using oximeter "Spectrotest" several output voltages U_i from the photodiode amplifier were registered in different waveband during the changes of blood volume in skin of healthy volunteer at an occlusive test. This device measures the tissue oxyhemoglobin saturation S_tO_2 and the blood volume V_b when skin is irradiated by 5 LEDs operating in the infrared, red, yellow, green and blue wavebands. In experiments the voltages were registered at moments when the blood volume had reached magnitudes of 0,1 and 0,2 rel.

un. in the phase of the post-occlusive reactive hyperemia. Then the ratio of voltages $U_{Vb=0,1}/U_{Vb=0,2}$ was calculated. Also the similar theoretical ratio for backscattered fluxes $F_{BS,Vb=0,1}/F_{BS,Vb=0,2}$ was calculated for the same wavebands. The results are summarized in Table 1.

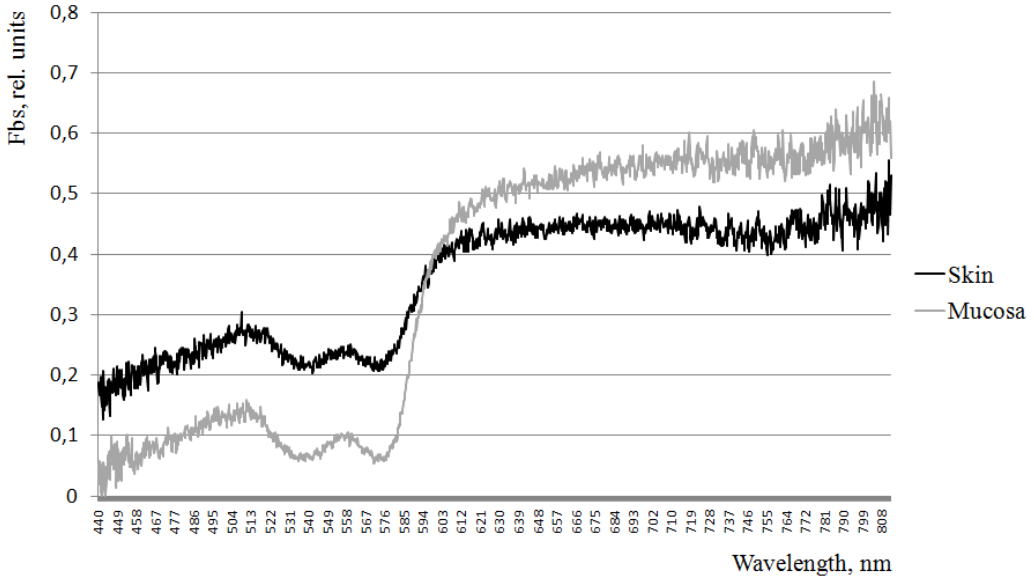

Figure 4. The experimentally measured reflectance spectra from skin and mucosa of healthy man.

Table 1. Ratios of output voltages from the "Spectrotest" photodiode amplifier for 5 different spectral bands and theoretical ratios of backscattered fluxes at V_b = 0,1 and 0,2 rel. un.

	Waveband, nm				
	Infrared, 900-950 nm	Red, 650-690 nm	Yellow, 565-590 nm	Green, 520-550 nm	Blue, 460-490 nm
$U_{Vb=0,1}/U_{Vb=0,2}$	1,18±0,08	1,04±0,07	1,80±0,15	2,01±0,32	2,30±0,46
$F_{BS,Vb=0,1}/F_{BS,Vb=0,2}$	1,17	1,10	1,66	1,71	1,64

As one can see from the Table 1, the intensity of simulated backscattered fluxes and the experimentally measured output voltages from the real diagnostic device are changed almost equally when changing levels of blood volume in the inspected tissue.

5. CONCLUSION

The theoretical simulation of light propagation in two-layered biological tissue with variable blood volume in the second layer was carried out. The used general approach was the improved Kubelka-Munk two-flux 1D approach[5] which was extended to the case of two layers of turbid medium. The model allowed us to calculate the power of the backscattered radiation depending on the level of blood fraction in the second layer. To evaluate the contribution of the Doppler component in the total detected backscattered flux the single-scattering approximation inside the second tissue's layer was used as well. The backscattered radiation from the red blood cells (RBC) having the Doppler-shifted wavelengths was computed as the increment in the total backscattered flux with growth of the density of RBC in the second layer of the tissue. The dependence of the Doppler component's magnitude on the blood volume in the second layer was estimated. It was found that the fraction of the Doppler backscattered component in the total backscattered radiation can vary in the range of 1-10% for the normal blood volume content in tissue of 1-20%. Basing on these results we can predict that the input optical radiation for real laser Doppler flowmeters contains a lot of amplitude-modulated nose in accordance with our equation (5). It can lead to mistakes in calculation of blood flow in LDF, especially in calculation of different blood flow fluctuations (rhythms) which frequently are used as an additional diagnostic factor when testing the microvasculature in clinics. So, the problem of the amplitude-modulated nose in LDF needs to be investigated in detail in the nearest future.

REFERENCES

[1] Dunaev, A. V., Zherebtsov, E. A., Rogatkin, D. A., Stewart, N. A. and Sokolovski, E. U., "Substantiation of medical and technical requirements for noninvasive spectrophotometric diagnostic devices," J. of Biomed. Optics 18(10), 107009 (2013).

[2] Rajan, V., Varghese, B., Leeuwen, T. G. and Steenbergen, W., "Review of methodological developments in laser Doppler flowmetry", Lasers Med Sci. 29, 269-283 (2009).

[3] Bonner, R. F. and Nossal, R.,"Model for laser Doppler measurements of blood flow in tissue", Appl. Opt. 20, 2097–2107 (1981).

[4] Tuchin, V. V. (Ed.), [Handbook of Optical Biomedical Diagnostics], SPIE Press, Bellingham (2002).

[5] Rogatkin, D. A., "A specific feature of the procedure for determination of optical properties of turbid biological tissues and media in calculation for noninvasive medical spectrophotometry," Biomedical engineering 41(2), 59-65 (2007).

[6] Ishimaru, A., [Wave Propagation and Scattering in Random Media, Volume I: Single scattering and transport theory], Academic Press, New York, 572p. (1978).

[7] Iyad, S., Saidi, [Transcutaneous optical measurement of hyperbilirubinemia in neonates], Doctor of Philosophy dissertation, Rice University, Houston, 234p. (1992).

[8] Dmitriev, M. A., Feducova, M. V., Rogatkin, D. A., "On one simple backscattering task of the general light scattering theory," Proc. SPIE 5475, 115-122 (2004).

[9] Starukhin, P.Yu., [Mathematical simulation of radiation transfer processes in multilayered medium with moving scatterers], Doctor of Philosophy dissertation (*in Russian*), Publishing house of Saratov State Technical University, Saratov, 20p. (2011).

[10] Rogatkin, D. A, Lapaeva, L. G, Petritskaya, E. N., Sidorov, V. V. and Shumskiy, V. I., "Multifunctional laser noninvasive spectroscopic system for medical diagnostics and metrological provisions for that," Proc. SPIE 7368, 73681Y, (2009).