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Contactless diagnostics of biophysical parameters of skin and blood on the basis of approximating functions for radiation fluxes scattered by skin

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Abstract. **Approximating expressions are derived to calculate spectral and spatial characteristics of diffuse reflection of light from a two-layer medium mimicking human skin. The effectiveness of the use of these expressions in the optical diagnosis of skin biophysical parameters (tissue scattering parameters, concentration of melanin in the epidermis, concentration of total haemoglobin and bilirubin in the tissues of the dermis) and content of haemoglobin derivatives in blood (oxy-, deoxy-, met-, carboxy- and sulfhaemoglobin) is analysed numerically. The methods are proposed to determine in real-time these parameters without contact of the measuring instrument with the patient's body.**

Keywords: *skin, diffuse reflection, biophysical parameters, haemoglobin derivatives, contactless methods.*

1. Introduction

The most widely used method of optical diagnostics of biological tissues is nowadays the method of diffuse reflectance spectroscopy, which allows the parameters affecting the process of radiation transfer in the tissue to be determined, i.e., the scattering coefficient, diameter of capillaries, concentration of optically active chromophores (oxyhaemoglobin, reduced haemoglobin, melanin, bilirubin, etc.). Many papers [1–11] are known, which are devoted to the determination of parameters of the tissue by spectral and spatial characteristics of radiation diffusely reflected by it. To this end, various models of radiative transfer in the tissue under study and mathematical algorithms for solving inverse problems are employed.

In cutting-edge analytical methods of the radiative transfer theory [5, 7–10, 12, 13], use is made of various approximations, in accordance with which the dominant process determining the attenuation of light in a medium and its separate layers is either absorption or scattering. These methods allow one to simply and quickly calculate the fluxes of radiation diffusely reflected in the medium by the specified structural and optical parameters of the medium. However, the accuracy of the calculations is reduced in this case and the assumptions of the techniques employed significantly limit the scope of their application. Numerical methods of the radiative transfer theory, such as the Monte Carlo method [14], the methods of discrete ordinates [15], 'adding-doubling' [15, 16], etc., being free from assumptions about the optical and structural properties of the medium, still require large computational costs and therefore are mainly used to solve research problems rather than find application in clinical practice.

It should be noted that even when the most accurate methods of the radiative transfer theory are used, an adequate determination of the parameters of skin by the spectral and spatial characteristics of its diffuse reflectance (DR) is challenging enough. This is due to the optical inhomogeneity of the object in question and to the necessity of its description by means of a large number of model parameters that must be simultaneously retrieved from the measurement data. Very often, the number of the model parameters needed exceeds the number of independent (i.e., complementary in the sense of the information content) measurements. In such cases, the retrieval procedure provides not one but a whole range of model solutions, acceptable in the sense of reproducibility of measurement results within experimental accuracy. In this regard, it is important to analyse what parameters of skin and with what accuracy can in principle be obtained with a minimal use of *a priori* information. In particular this applies to clinically relevant concentrations of haemoglobin derivatives (oxy-, deoxy-, carboxy-, met- and sulfhaemoglobin), noninvasive determination of which is complicated by the overlap of their absorption spectra and the uncertainty of the other parameters of skin, affecting the diffusely reflected radiation fluxes.

Contact of the device with the patient's skin (with some pressure) also has a significant impact on the accuracy of the skin parameters. At present, optical fibres deliver exciting radiation to the tissue and collect radiation scattered by this tissue. This requires a direct contact of the optical fibre sensor with the tissue, which, as shown in [17, 18], leads to a change in its optical parameters and distorts the measurement result. To exclude such a contact, a more complex measurement scheme is required which enables remote irradiation of the tissue site, fixation of radiation scattered by its internal layers and screening of radiation reflected by the surface layer.

The aim of this paper is to create the diffuse reflectance spectroscopy methods, which allow the parameters of the patient's skin and composition of haemoglobin with its basic forms (oxy- and deoxyhaemoglobin) and dishaemoglobin (carboxy-, met -, sulfhaemoglobin) taken into account to be determined quickly and contactlessly. This problem is solved by using analytical expressions that approximate the results of numerical calculations of spectral and spatial characteristics of diffuse reflectance of skin by varying its optical parameters in a wide range. The errors in determining the parameters of skin are analysed theoretically with the help of the data

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of the optical measurements with a minimal use of *a priori* information.

2. Optical measurements

One possible scheme of a contactless optical measuring device of skin parameters is shown in Fig. 1. The lens apparatus allows any diameter of the irradiation spot to be obtained, and a CCD camera allows a two-dimensional distribution of the radiation flux scattered by skin to be constructed. Thus, measurements can be performed remotely, i.e., without contact of the measuring instrument with the body of the patient. The angle of incidence of radiation on the skin should be selected such that radiation reflected from the surface (*7*) does not fall into the camera lens and only diffuse radiation reflected by the inner layers of the skin is recorded. The influence of radiation reflected from the surface on the detected optical signals can be also eliminated by mutually orthogonal polarisers (*5*) and (*8*) installed in the channels of delivery and detection of radiation. Since the radiation reflected by the surface retains its initial polarisation, the use of crossed polarisers makes it possible to block the signal components producing noise.

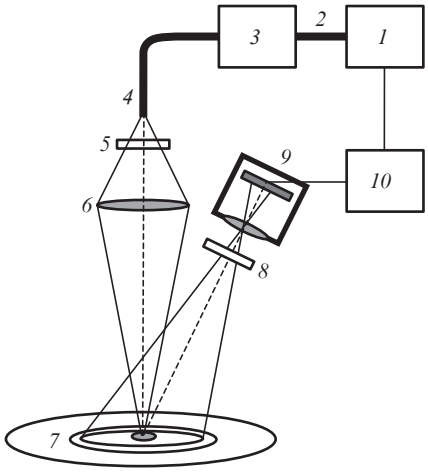

Figure 1. Scheme of the device for measuring spectral and spatial characteristics of diffuse reflectance of skin: (*1*) broadband light source; (*2*, *4*) transmitting optical fibres; (*3*) monochromator; (*5*, *8*) mutually orthogonal polarisers; (*6*) focusing lens; (*7*) surface; (*9*) monochrome CCD camera (black and white); (*10*) control unit of the radiation source and signal reception and processing.

Using the scheme under consideration, one can measure the total scattered radiation flux $F(\lambda)$ entering the camera lens and azimuthally averaged scattered radiation fluxes $F(\rho,\lambda)$ at different distances ρ from the centre of the irradiation spot. Measurements of $F(\lambda)$ allow one to determine the diffuse reflectance $R(\lambda)$ of skin by comparing the fluxes $F(\lambda)$, recorded for the object in question and for a reference diffuse reflector. The calibration in this case is not significantly complex and eliminates the influence of spectral characteristics of the optical system and the geometry of the experiment on the result of determining the unknown parameters of skin. Calibration measurements of $F(\rho,\lambda)$ are a rather complicated task because they assume production of calibration samples with optical parameters known in a wide spectral range, which are used in the Monte Carlo method [14] to calculate 'reference' signals recorded in the experiment. In this regard, in further consideration of such measurements we will use only difference signals of diffuse reflectance:

$$r(\rho,\lambda) = \ln\frac{P(\rho_0,\lambda)}{P(\rho,\lambda)},$$

where

$$P(\rho,\lambda) = 2\pi\int_{\rho-\Delta\rho/2}^{\rho+\Delta\rho/2} F(\rho,\lambda)\rho\mathrm{d}\rho$$

is the power of radiation that enters the camera lens from the skin area bounded by a ring of radius ρ and width $\Delta\rho$ and ρ_0 is the radius of the receiving ring which is the closest to the irradiation region.

3. Numerical calculation of diffuse reflectance characteristics of skin

The best method to calculate light scattering characteristics of a multilayer medium with no restrictions on its optical parameters and experimental geometry is today the Monte Carlo method. This method is based on a multiply repeated numerical experiment aimed at the calculation of a random trajectory of a photon in the medium under study, followed by a generalisation of the results. Each photon is characterised by its own 'weight', Cartesian coordinates, which specify its position in the medium, and direction cosines, which specify the direction of its movement. The initial 'weight' of each photon is equal to unity. When a photon 'wanders' in a semi-infinite medium (without horizontal boundaries and unlimited depth), its 'weight' is reduced due to the Fresnel reflection from the surface of the medium, as well as due to the processes of absorption and scattering in the medium. The photon trajectory can be traced to as long as its 'weight' becomes less than a predetermined value (in our calculations, 10^{-4}) or until the photon leaves the boundaries considered. Initial conditions for the input of the photons in the medium and conditions of their detection at given geometrical parameters of the experiment are determined on the basis of geometrical optics representations.

To calculate the diffuse reflectance characteristics of skin, $R(\lambda)$ and $r(\rho,\lambda)$, obtained from the measurements considered, of importance is the radial distribution of photons backscattered by the medium. The Monte Carlo method allows one to obtain it as an array $H[i]$, each element of which is equal to the total 'weight' of the photons emitted from the medium at a distance ρ_i from the centre of the irradiation spot within solid angle at which the camera lens is visible from the point of departure of the photon. The wavelength of light in the Monte Carlo method is implicitly specified through the optical parameters of the medium. To this end, use is made of the optical model of skin presented in [19]. The skin is modelled as a medium consisting of two layers (epidermis and dermis) with the same light scattering parameters and different absorption coefficients. The model parameters are as follows: n is the refractive index of skin; $\mu_t(\lambda_0)$ is the transport scattering coefficient of a connective tissue at $\lambda_0 = 600$ nm; ρ_{Mie} is the fraction of Mie scattering with respect to total scattering of the tissue at $\lambda = 400$ nm; x is the parameter of the spectral dependence of the Mie transport scattering coefficient; L_e is the epidermis thickness; f_m is the volume concentration of melanin in the epidermis; C_{bil} is the bilirubin concentration in the dermis; f_{bl} is the volume concentration of capillaries in the dermis; d_v is the average diameter of capillaries; C_{tHb} is the

concentration of total haemoglobin in blood; and S is the degree of blood oxygenation.

4. Analytical calculation of diffuse reflectance characteristics of skin

Despite all its merits the Monte Carlo method is not convenient for practical use, since it does not allow experimental data to be processed in real time. In this regard, we have developed simple and fast methods for calculating diffuse reflectance characteristics of skin, measured by the above-described device. The methods are based on analytical expressions that approximate the results of calculation of $R(\lambda)$ and $r(\rho,\lambda)$ by the Monte Carlo method in the approximation of the model from paper [19]. For these expressions to be derived, random values of the model parameters were generated from the ranges of their variation for light and moderately pigmented human skin (according to the classification [20]): $n = 1.4–1.5$, $\mu_t(\lambda_0) = 30–110$ cm^{-1}, $\rho_{Mie} = 0.1–0.6$, $x = 0.5–1.0$, $L_e = 50–150$ μm, $f_m L_e = 0.5–10$ μm, $f_{bl} = 0.2\%–7\%$, $C_{tHb} = 120–200$ g L^{-1}, $d_v = 5–60$ μm, $C_{bil} = 0.1–50$ mg L^{-1}, $S = 40\%–98\%$. With each realisation of the model parameters we calculated the absorption coefficients of the epidermis $\mu_{ae}(\lambda)$ and the dermis $\mu_{ad}(\lambda)$ as well as the transport scattering coefficient $\mu_t(\lambda)$ and the scattering anisotropy factor $g(\lambda)$ of the tissue at 30 wavelengths in the spectral range from 450 to 800 nm. As a scattering phase function of the tissue, use was made of the Henyey–Greenstein function with the parameter $g(\lambda)$.

In accordance with the generated values of n and L_e, as well as with the calculated values of $\mu_{ae}(\lambda)$, $\mu_{ad}(\lambda)$, $\mu_t(\lambda)$ and $g(\lambda)$, we used the Monte Carlo method to simulate the spectral coefficients $R(\lambda)$ and the signals $r(\rho,\lambda)$ corresponding to the particular geometry of the experiment. Thus, an ensemble of 10^3 random realisations of $R(\lambda)$ and $r(\rho,\lambda)$ was formed. The spectral values for all optical parameters and diffuse reflectance characteristics of skin are combined into a single data set: $n = 1.35–1.50$, $L_e = 50–150$ μm, $\mu_{ae} = 0.9–180$ cm^{-1}, $\mu_{ad} = 0.2–30$ cm^{-1}, $\mu_t = 5–80$ cm^{-1}, $\mu_t/\mu_{ae} = 0.15–35$, $\mu_t/\mu_{ad} = 0.7–150$, and $R = 0.01–0.57$ [the range $r(\rho)$ depends on the geometry of the measurement]. Such an approach to obtaining analytical expressions that approximate the results of numerical calculations of diffuse reflectance characteristics of the tissue allows one to take into account the physical conditionality of the optical parameters of the tissue and the relations between them, which are typical for the considered spectral range, as well as to exclude the combination of optical parameters that do not occur in reality.

The calculations of diffuse reflectance of skin show that at different angles of incidence θ of radiation onto skin the variations of θ in the range 0–30° almost have no effect on the value of the diffuse reflectance. Thus, at not very large angles of incidence of probing radiation the diffuse reflectance of skin is determined only by its optical and structural parameters. In accordance with the principle of optical 'adding' of the layers [9, 15, 16], a general expression for the diffuse reflectance of a two-layer medium has the form:

$$R = \frac{(1-f)(1-f^*)R_{12}}{1-f^*R_{12}^*}, \qquad (1)$$

where $f = (1-n)^2/(1+n)^2$ is the reflectance of normally incident light from the medium surface; f^* is the reflectance of the medium surface illuminated by a diffuse flow from inside, whose dependence on the refractive index n, as shown in [12], is described with a high accuracy by a polynomial

$$f^* = -1.4399n^{-2} + 0.7099n^{-1} + 0.6681 + 0.0636n; \qquad (2)$$

and R_{12} and R_{12}^* are the reflectances of a two-layer medium without account for an external border with directed and diffused light, respectively. Expression (1) takes into account the fact that the luminous fluxes, multiply reflected from the inner boundary of the medium, form an infinitely decreasing geometric progression with the ratio $f^*R_{12}^*$. The coefficients R_{12} and R_{12}^* are presented by us in the form of products of the optical transmission of the epidermis and dermis:

$$R_{12} = \exp\{-\mu_{ae}L_1\}\exp\{-\mu_{ad}L_2\}, \qquad (3)$$

$$R_{12}^* = \exp\{-\mu_{ae}L_1^*\}\exp\{-\mu_{ad}L_2^*\}, \qquad (4)$$

where L_1 and L_2 are the 'effective' paths travelled by light in the epidermis and dermis, given its multiple scattering and re-reflection between these layers of skin under directional illumination of skin; and L_1^* and L_2^* are the same paths but under diffuse illumination of skin. The L_1 and L_2 were calculated by formulas

$$L_1 = \alpha L_e + L_e\sum_{m=1}^{3}\left[A_m\left(\frac{\mu_{ae}}{\mu_t}\right)^m + B_m\left(\frac{L_e}{\delta_d}\right)^m\right], \qquad (5)$$

$$L_2 = \gamma\delta_d + \delta_d\sum_{m=1}^{3}\left[C_m\left(\frac{\mu_{ad}}{\mu_t}\right)^m + D_m\left(\frac{L_e}{\delta_d}\right)^m\right], \qquad (6)$$

where $\delta_d = [3\mu_{ad}(\mu_{ad}+\mu_t)]^{-1/2}$ is the depth of light penetration into the dermis (in the diffusion approximation); and α, γ, A_m, B_m, C_m and D_m are the coefficients obtained by approximating the results of numerical calculations of R (Table 1). Similar expressions, but with other coefficients (α^*, γ^*, A_m^*, B_m^*, C_m^* and D_m^*), and used for the L_1^*, L_2^* (see Table 2).

Table 1. Coefficients of approximation formulas for L_1 и L_2.

m	A_m	B_m	C_m	D_m
1	–0.2113	–0.2852	2.1706	–2.9394
2	0.0454	–2.3016	–0.4702	3.4548
3	–0.0038	1.6987	–0.1525	–2.3147

Note: $\alpha = 2.6774$, $\gamma = 5.0046$.

Table 2. Coefficients of approximation formulas for L_1^* и L_2^*.

m	A_m^*	B_m^*	C_m^*	D_m^*
1	0.3576	9.0946	4.1821	–11.5106
2	–0.2002	–24.2959	–8.7959	11.0631
3	0.0281	15.5773	5.4954	–3.8394

Note: $\alpha^* = 3.7608$, $\gamma^* = 4.3750$.

Formulas (1)–(6) approximate the results of numerical calculation of diffuse reflectance of skin with an error not exceeding 5% in the whole range of R. The correlation coefficient between the diffuse reflectances of skin, calculated by the Monte Carlo method and formulas (1)–(6), is 0.9997. Thus, knowing structural and optical parameters of skin the proposed approximation formulas allow its diffuse reflec-

tance to be calculated explicitly with an accuracy of the Monte Carlo method.

The relationship of the signal $r(\rho)$ with the optical and structural parameters of skin can be described by the formula:

$$r(\rho) = a_{0,0}(\boldsymbol{s},\rho) + \sum_{m=1}^{3} a_{1,m}(\boldsymbol{s},\rho)(n-1)^m + \sum_{m=1}^{3} a_{2,m}(\boldsymbol{s},\rho)\mu_t^m + \sum_{m=1}^{3} a_{3,m}(\boldsymbol{s},\rho)\mu_{ad}^m + \mu_t \sum_{m=1}^{3} a_{4,m}(\boldsymbol{s},\rho)\left(\frac{\mu_t}{\mu_{ad}}\right)^m + \sum_{m=1}^{3} a_{5,m}(\boldsymbol{s},\rho)\left(\frac{\mu_t}{1+g}\right)^m + \sum_{m=1}^{3} a_{6,m}(\boldsymbol{s},\rho)(\mu_{ae}L_e)^m + \sum_{m=1}^{3} a_{7,m}(\boldsymbol{s},\rho)(\mu_{ad}\delta_d)^m + L_e \sum_{m=1}^{3} a_{8,m}(\boldsymbol{s},\rho)\left(\frac{\mu_{ae}}{\mu_t}\right)^m + \delta_d(\lambda) \sum_{m=1}^{3} a_{9,m}(\boldsymbol{s},\rho)\left(\frac{\mu_{ad}}{\mu_t}\right)^m + k_e L_e \sum_{m=1}^{3} \left[a_{10,m}(\boldsymbol{s},\rho)\left(\frac{L_e}{\delta_d}\right)^m + a_{11,m}(\boldsymbol{s},\rho)\left(\frac{\mu_{ae}}{\mu_t}\right)^m\right] + \mu_{ad}\delta_d \sum_{m=1}^{3} a_{12,m}(\boldsymbol{s},\rho)\left(\frac{L_e}{\delta_d}\right)^m, \quad (7)$$

where $a_{i,m}$ are the approximation coefficients and $\boldsymbol{s}$ is the vector of the geometric parameters of the experiment. As an example, consider the approximation of the signals $r(\rho)$ by formula (7), which are calculated by the Monte Carlo method for a particular experimental geometry. We assume that skin is illuminated by a light beam 0.2 mm in diameter along the normal, and diffuse radiation is recorded from four concentric rings with widths of 0.4 mm at distances ρ = 0.4, 0.8, 1.2 and 1.6 mm from the centre of the irradiation spot. Since the dimensions of the irradiation spot and the area of registration of the radiation scattered by skin is many times smaller than the diameter of the CCD camera lens, then roughly the same fraction of the diffuse flux is fixed by the camera from each ring. In this connection, the difference signals $r(\rho) = \ln[P(\rho_0 = 0.4\text{ mm})/P(\rho)]$ are virtually independent of the position of the lens relative to the skin surface under study. This fact allows one, in the calculation of the signals $r(\rho)$, to take into account all the photons emitted from receiving rings on the surface of the skin surface (in all directions), and thereby to reduce the number photon trajectories simulated by the Monte Carlo method. The coefficients in formula (7) corresponding to the geometry of the experiment under consideration, are obtained by least squares method based on the simulated data. Equation (7) (with the found coefficients) approximates the results of numerical calculations of $r(\rho)$ with a root-mean-square error of 1.0%, 1.6% and 2.5% for ρ = 0.8, 1.2 and 1.6 mm, respectively. An increase in the approximation error of $r(\rho)$ with an increase in ρ is associated with the statistical 'noise' inherent in Monte Carlo method.

Thus, expression (1)–(7) allow one to calculate quickly and accurately the experimentally measured quantities in the approximation of a two-layer medium mimicking the skin tissue. As an example of such calculations Fig. 2 presents the dependences of $R(\lambda)$ and $r(\rho,\lambda)$ calculated numerically and analytically for the following values of the model parameters: n = 1.45, $\mu_t(\lambda_0)$ = 63 cm^{-1}, ρ_{Mie} = 0.4, x = 0.6, L_e = 100 μm, f_m = 3%, C_{bil} = 4 mg L^{-1}, f_{bl} = 1%, d_v = 15 μm, C_{tHb} = 150 g L^{-1}, S = 75%. One can see that the difference between them is within the error of the Monte Carlo method.

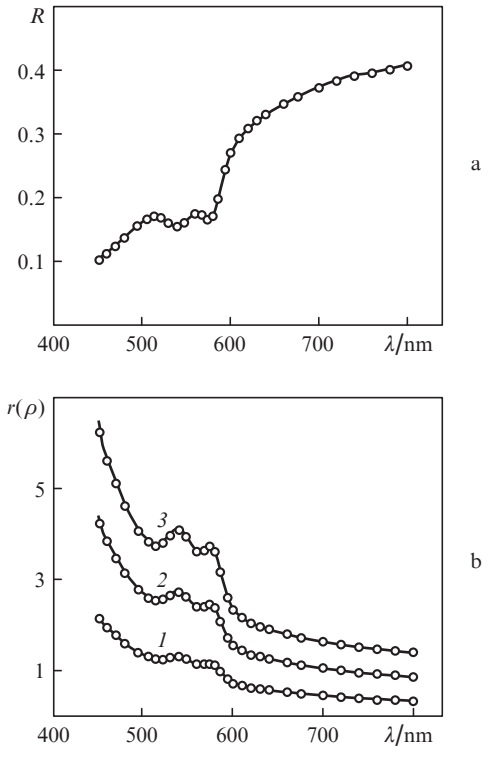

Figure 2. (a) Diffuse reflectance spectra of skin and (b) difference signals of light diffusely reflected by skin at ρ_0 = 0.4 mm and ρ = (*1*) 0.8, (*2*) 1.2, (*3*) 1.6 mm, modelled by the Monte Carlo method (points) and calculated analytically (curves) for the same model parameters.

5. Analysis of the inverse problem solution

We will analyse theoretically the errors in determining the parameters of skin and blood by using the data of the considered optical measurements. The inverse problem is solved by minimising the discrepancy between the experimental and theoretically predicted spectrum of $R(\lambda)$ or the spectral and spatial profile of $r(\rho,\lambda)$:

$$G^2 = \frac{1}{N_\lambda} \sum_{k=1}^{N_\lambda} \omega_k^2 [\ln R(\lambda_k) - \ln \tilde{R}(\boldsymbol{x},\lambda_k)]^2, \quad (8)$$

$$U^2 = \frac{1}{N_\rho N_\lambda} \sum_{i=1}^{N_\rho} \sum_{k=1}^{N_\lambda} v_{ik}^2 [r(\rho_i,\lambda_k) - \tilde{r}(\boldsymbol{x},\rho_i,\lambda_k)]^2, \quad (9)$$

where $R(\lambda_k)$ and $r(\rho_i,\lambda_k)$ are the experimental diffuse reflectance characteristics of skin; $\tilde{R}(\boldsymbol{x},\lambda_k)$ and $\tilde{r}(\boldsymbol{x},\rho_i,\lambda_k)$ are similar model characteristics; $\boldsymbol{x} = (x_m)$ is the vector of the model parameters to be determined; N_λ is the number of wavelengths of the optical probing; N_ρ is the number of spatial rings of registration of scattered radiation; and ω_k and v_{ik} are the weighting coefficients that are inversely proportional to the root-mean-square measurement errors. In the case of joint measurements of $R(\lambda)$ and $r(\rho,\lambda)$, as a solution to the inverse problem we select the set of $\boldsymbol{x}$ parameters, which provides a minimum of the functional $G^2 + U^2$.

At the stage of deriving approximating expressions (3)–(7) we modelled an ensemble of 10^3 random realisations of $R(\lambda)$ and $r(\rho,\lambda)$. The calculation was carried out for 30 values of λ from the range 450–800 nm. Geometric parameters of the measuring scheme at which the signals $r(\rho,\lambda)$ were calculated are mentioned above. Ranges of variations in the

model parameters, corresponding to the simulated ensemble of realisations of $R(\lambda)$ and $r(\rho,\lambda)$, fully cover all possible values of the parameters for light and moderately pigmented skin. In this regard, this ensemble can be used to assess the accuracy of the solution of the inverse problem. To this end, we performed iterations over all the realisations of $R(\lambda)$ and $r(\rho,\lambda)$ and for each of them we minimised residuals (8) and (9) by the Levenberg–Marquardt algorithm [21]. The coefficients ω_k were taken equal to 1.0, which corresponds to the same range of measurement error in $R(\lambda_k)$. The coefficients v_{ik} are taken equal to 0.5 at $\lambda_k < 600$ nm and to 1.0 at $\lambda_k \geqslant 600$ nm, which is due to the rapid attenuation of the optical signal with increasing distance from the illumination site and to significant difference in the measurement errors of $r(\rho_i,\lambda_k)$ in spectral regions of strong ($\lambda < 600$ nm) and weak ($\lambda = 600-900$ nm) light absorption in skin. The retrieved values of the model parameters $\boldsymbol{x}^*$ were compared with their exact values $\boldsymbol{x}$. After that we calculated the average error δx_m of the parameter retrieval, the correlation coefficient γ_m between x_m and x_m^*, as well as informativeness I_m of solving the inverse problem with respect to the parameter x_m (as a ratio of the *a priori* and *a posteriori* uncertainties in x_m). We considered the most important parameters of skin: the concentration of bilirubin in the dermis tissues, C_{bil} (mg L^{-1}); the concentration of total haemoglobin, $F_{\text{tHb}} = f_{\text{bl}}C_{\text{tHb}}$ (g L^{-1}); the haemoglobin oxygen saturation, S (%); the average diameter of capillaries, d_{v} (μm); the thickness of the epidermis, L_{e} (μm); the integral content of melanin in the epidermis, $\Phi_{\text{m}} = f_{\text{m}}L_{\text{e}}$ (μm); and the parameters C_{t} (cm^{-1}) and v of the spectral dependence of the transport scattering coefficient of skin, $\mu_{\text{t}}(\lambda) = C_{\text{t}}(632/\lambda)^v$, in the range 600–700 nm. The estimates of the accuracy of the parameter retrieval by the data of the optical measurements in question are shown in Table 3.

The presented results provide a glimpse of what parameters of skin and with what accuracy can be obtained by the spectral and spatial characteristics of its diffuse reflectance in the case of minimal use of *a priori* information. One can see that the measurements of $R(\lambda)$ allow sufficiently accurate determination of the parameters F_{tHb}, S, Φ_{m} and C_{bil}. At the same time, the informativeness of these measurements with respect to the skin scattering parameters C_{t} and v is low. These parameters are determined much more accurately on the basis of measurements of $r(\rho,\lambda)$, and the accuracy of their determination depends strongly on the configuration of the rings of radiation registration. With the above configuration of the light receiving rings, the measurements of $r(\rho,\lambda)$ allow almost a twofold increase in the accuracy of determining the parameters C_{t} and v as compared to measurements of $R(\lambda)$.

However, the highest accuracy of determining these parameters is achieved in the case of joint measurements of $R(\lambda)$ and $r(\rho,\lambda)$. In this case, the correlation coefficients between the exact and retrieved skin values of skin scattering parameters are almost equal to unity. Joint processing of $R(\lambda)$ and $r(\rho,\lambda)$ can also improve the accuracy of determining the parameters F_{tHb}, S, Φ_{m} and C_{bil}, but the higher accuracy in this case is not as significant as for C_{t} and v. The accuracy of d_{v} estimation by the measurement data of $R(\lambda)$ and $r(\rho,\lambda)$ (both separately and jointly) obviously does not meet the requirements of modern medical diagnostics. For d_{v} to be determined more accurately, it is necessary to extend the spectral range to shorter wavelengths, where the effect of localised light absorption by blood vessels is more pronounced [22]. We should also pay attention to the low informativeness of the retrieved parameters of the epidermis, L_{e} and Φ_{m}, from the difference signals $r(\rho,\lambda)$, which is explained by approximately the same magnitude of the optical path travelled by light in the epidermis for closely located rings of registration of light scattered by skin.

6. Determination of haemoglobin derivatives in blood

The analysis of the content of various types of haemoglobin in blood is an essential clinical procedure for a reliable assessment of the current condition of the patient and the forecast of critical states in toxicology, anesthesiology, resuscitation and intensive therapy. The method currently used involves taking a blood sample, its processing in the transforming solution to destroy erythrocytes and the resulting direct photometric test. Due to the spectral overlap of haemoglobin derivatives, with substantially complete similarity of spectra of oxyhaemoglobin (HbO_2) and carboxyhaemoglobin (COHb) and the proximity of characteristic absorption bands of methaemoglobin (MetHb) and sulfhaemoglobin (SHb), the photometry of blood is performed at 128 wavelengths with a 1.5-nm step [23]. This method is not enough effective and fraught with a painful and uncomfortable procedure of using venous or finger-prick blood samples. Therefore, of great interest are noninvasive methods of monitoring the content of haemoglobin in the blood derivatives.

Consider the possibility of a rapid analysis of haemoglobin concentration in blood on the basis of measurements of the spectral and spatial characteristics of diffuse reflectance of skin and on the basis of the developed analytical methods for calculating the measured characteristics. We will conduct the study by using the optical model of skin [19], in which, in addition to oxy- and deoxyhaemoglobin (Hb), we addition-

Table 3. Evaluation of the accuracy of retrieval of the model parameters under the conditions of their total variability.

x_m	Measured quantities								
	$R(\lambda)$			$r(\rho,\lambda)$			$R(\lambda)$ and $r(\rho,\lambda)$		
	δx_m (%)	γ_m	I_m	δx_m (%)	γ_m	I_m	δx_m (%)	γ_m	I_m
F_{tHb}	5.6	0.996	12.2	6.2	0.995	10.6	4.7	0.997	13.5
S	2.8	0.992	8.0	3.4	0.984	6.3	3.1	0.986	6.5
C_{bil}	8.0	0.983	6.1	6.4	0.985	6.8	4.8	0.992	8.8
d_{v}	19.5	0.898	1.7	26.4	0.813	1.4	23.8	0.838	1.6
Φ_{m}	9.2	0.995	6.6	62.6	0.719	0.97	5.6	0.996	9.4
L_{e}	14.4	0.831	1.7	36.6	0.344	0.8	11.1	0.914	2.4
C_{t}	9.1	0.942	2.8	4.7	0.981	5.4	1.3	0.999	16.5
v	9.7	0.908	2.2	5.1	0.970	4.0	1.9	0.994	10.8

ally take into account the presence of COHb, MetHb and SHb in blood. With these haemoglobin derivatives taken into account the spectral dependence of the absorption coefficient of blood is described by the expression:

$$k_{\rm bl}(\lambda) = \ln 10 \frac{C_{\rm tHb}}{\mu_{\rm tHb}} \{ S\varepsilon_{\rm HbO_2}(\lambda) + C_{\rm MetHb}\varepsilon_{\rm MetHb}(\lambda) + C_{\rm COHb}\varepsilon_{\rm COHb}(\lambda) + C_{\rm SHb}\varepsilon_{\rm SHb}(\lambda) + (1 - S - C_{\rm MetHb} - C_{\rm COHb} - C_{\rm SHb})\varepsilon_{\rm Hb}(\lambda) \}, \quad (10)$$

where $\mu_{\rm tHb} = 64500$ g mol^{-1} is the molar mass of haemoglobin; S, $C_{\rm MetHb}$, $C_{\rm COHb}$ and $C_{\rm SHb}$ are the relative concentrations of HbO_2, MetHb, COHb and SHb as part of the total haemoglobin; and $\varepsilon_{\rm HbO_2}$, $\varepsilon_{\rm Hb}$, $\varepsilon_{\rm MetHb}$, $\varepsilon_{\rm COHb}$ and $\varepsilon_{\rm SHb}$ are the molar absorption coefficients of haemoglobin derivatives in cm^{-1} mol^{-1} L^{-1} [24]. In other respects, the model [19] remains unchanged. Based on this model, we used the Monte Carlo method to calculate 350 realisations of fluxes of radiation diffusely reflected by skin in the spectral range 450–800 nm in steps of 5 nm. The calculation of $r(\rho,\lambda)$ was carried out for the geometric parameters of the experiment, corresponding to $\rho_0 = 0.4$ mm and $\rho = 0.8$, 1.2, 1.6 mm. The ranges of variations in the model parameters corresponding to the resulting ensemble of realisations of $R(\lambda)$ and $r(\rho,\lambda)$ are given in [19] with the only difference that in our case the concentration of bilirubin in the tissues of the dermis, $C_{\rm bil}$, varies from 0 to 5 mg L^{-1} (normal level of bilirubin), and the concentration of blood vessels $f_{\rm bl}$ varies in the range from 1% to 3%, which is typical of normal (nonmalignant) skin. Based on the literature data [25–30], for concentrations $C_{\rm MetHb}$, $C_{\rm COHb}$ and $C_{\rm SHb}$ we used the ranges of 1%–20%, 1%–20% and 0.2%–10%, respectively.

For each realisation of $R(\lambda)$ and $r(\rho,\lambda)$, using the developed methods for calculating the diffuse reflectance characteristics of skin and the Levenberg–Marquardt algorithm [21] we carried out the minimisation of functionals (8), (9) and retrieved the model parameters. Figure 3 compares the known concentrations of HbO_2, MetHb, COHb and SHb and those retrieved from the signals $r(\rho,\lambda)$ at a considered variation in the parameters of skin. The correlation coefficients between the known and retrieved values of the concentrations, obtained by solving the inverse problem for diffuse reflectance of skin and signals $r(\rho,\lambda)$, are shown in Table 4. It is evident that the considered measurements have a high sensitivity to the presence of all haemoglobin derivatives in blood. It is noteworthy that the joint interpretation of measurements of $R(\lambda)$ and $r(\rho,\lambda)$ does not increase the accuracy of determi-

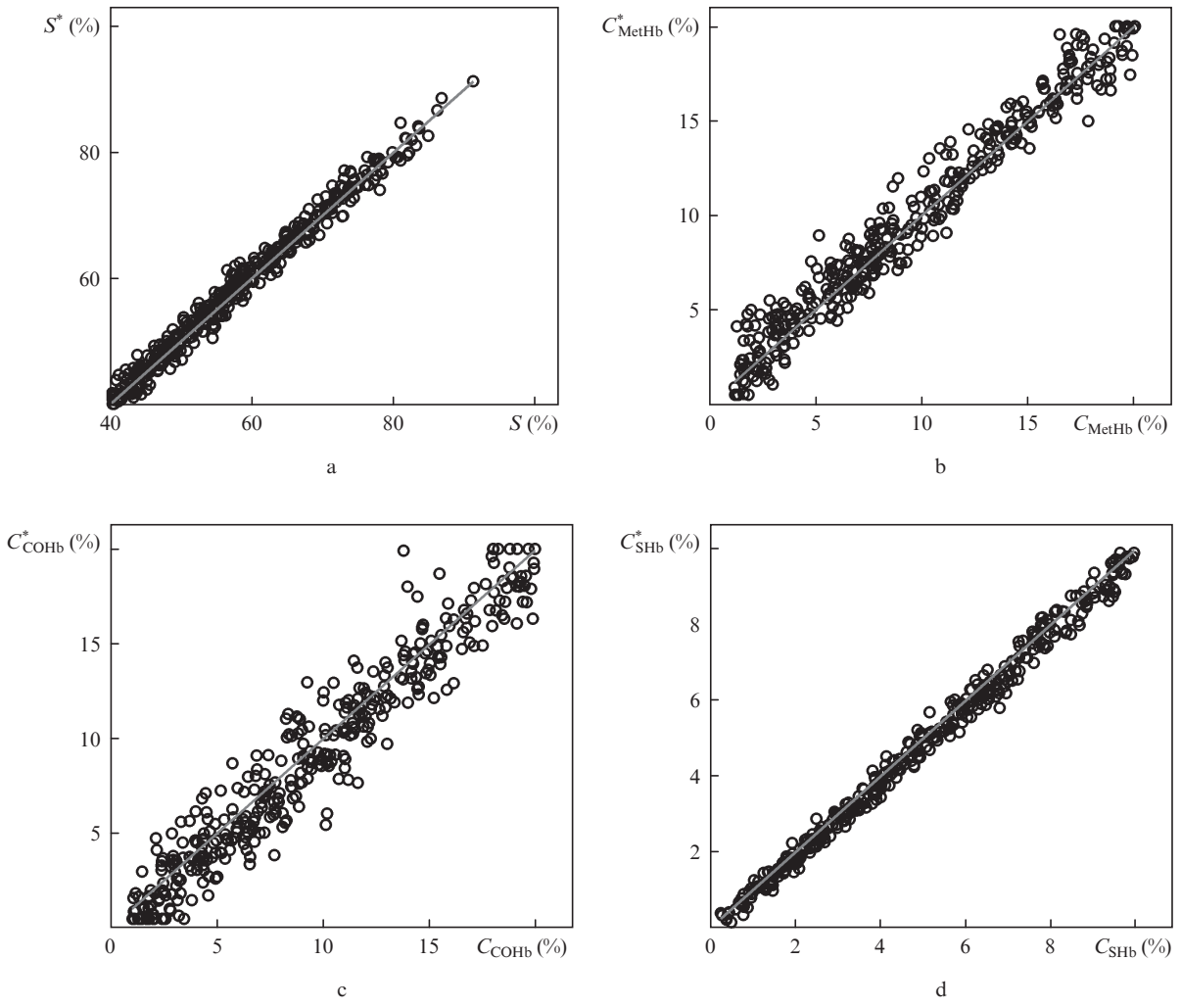

Figure 3. Comparison of the known (x axis) and retrieved [from the signals $r(\rho, \lambda)$] concentrations (y axis) of haemoglobin derivatives in blood. Straight lines in the figures correspond to the exact equality of known and retrieved parameters.

Table 4. Correlation coefficients between exact and retrieved values of concentrations of haemoglobin derivatives in blood.

Parameter	Measure quantities		
	$R(\lambda)$	$r(\rho,\lambda)$	$R(\lambda)$ and $r(\rho,\lambda)$
S	0.993	0.991	0.991
C_{MetHb}	0.994	0.980	0.982
C_{COHb}	0.935	0.965	0.962
C_{SHb}	0.997	0.996	0.992

nation of the searched-for parameters. Possibly, this result, to some extent, can be explained by the coefficients ω_i and v_{ij} [formulas (8) and (9)] used to solve the inverse problem.

It should be noted that the use of difference signals $r(\rho,\lambda)$ for determining the haemoglobin composition is more preferable because the corresponding measuring device does not require calibration, which enhances its serviceability and excludes additional costs on periodic calibration. The methods developed for calculating $r(\rho,\lambda)$ allow the interpretation of experimental data in real time. In this case, the sensitivity of the signals $r(\rho,\lambda)$ to small variations in the haemoglobin composition can be easily enhanced by increasing the gauge length, i.e., the distance between the region of irradiation of the tissue and the region of registration of scattered light.

The considered approaches to the optical diagnostics of the parameters of skin and blood are the basis of precise and easy-to-use optical measuring instruments, which have such practically important advantages as noninvasiveness, contactlessness, gaugelessness and measurement efficiency. These measuring devices can be widely used in medical diagnosis and therapy.

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