Mathematical modelling of signals recorded in noninvasive medical laser fluorescence diagnosis

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Based on the Kubelka–Munk two-flux model modified by the authors, which makes it possible in one-dimensional problems to obtain exact analytical expressions for radiation fluxes at the boundary of a turbid medium, and Kokhanovsky's solution for the radiation flux of fluorescence, questions are considered of modelling the spectrum of stimulated endogenous fluorescence of biological tissues as applied to problems of noninvasive medical diagnosis. An analytical expression is presented for the spectral distortion function, which depends on the scattering and absorption properties of cellular biological tissues and blood. It is shown that the model spectra agree well with the experimental data. © *2013 Optical Society of America.*

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INTRODUCTION

Noninvasive *in vivo, in situ* laser fluorescence diagnosis (LFD) appeared as a new scientific diagnostic specialization in medicine around the mid-1980s.[1,2] Today many scientific groups worldwide are undertaking intense attempts to develop LFD now at the level of practical health maintenance, including the creation of systems to visualize the internal structures of biological tissues, using the radiation of stimulated endogenous fluorescence (autofluorescence) of biological tissues, and to visualize the structure of so-called diffusion fluorescence tomographs based on this.[3] However, a number of problems associated with the accuracy of such measurements, the quantitative determination of the concentration of active luminophores in the examination zone from the fluorescence intensity, the interpretation of the results of the total fluorescence spectra, etc., do not yet make it fully possible to implement these plans.[4] One serious problem in LFD is the problem of allowing for distortions of the fluorescence spectra when the *in vivo* spectrum recorded by the diagnostic device does not always correspond to the original fluorescence spectrum of the endogenous luminophores.[5] In the overwhelming majority of actual cases, such a situation arises because the tissue contains, besides the light-emitting luminophores, an even greater amount of substances that intensively absorb and scatter the light (for example, melanin in skin, hemoglobin in blood, etc.).

A number of authors have repeatedly attempted to construct theoretical models based on linear transport theory (TT) to calculate the spectra of endogenous fluorescence of biological tissues and to develop algorithms for correcting the spectra, taking into account plethora of the tissue and certain other factors (see, for example, Refs. 6–10). In particular, it has been shown that the fluorescence signal recorded *in vivo* from biological tissue depends in general not only on the fluorescence quantum yield and the concentration of fluorescent substance in the tissue but also has a complex and substantially nonlinear dependence on the overall optophysical properties of the tissue, formulated in terms of TT—the scattering transport coefficient μ_s, the absorption coefficient μ_a, etc.[7,8] However, until recently, all such work was based on some approximate methods or other of solving the transport problem—the method of moments,[7] the diffusion approximation,[3] simplified heuristic algorithms,[10] or on the basis of the well-known statistical method of random walk of a photon in a medium (the Monte Carlo method). Each of these approaches has definite drawbacks. Heuristic algorithms, as a rule, are applicable only for a chosen design of the diagnostic device. Approximate solutions possess low accuracy, while numerical methods like the Monte Carlo method require extensive calculations and do not provide a solution in the form of a closed analytical expression that could be easily analyzed on the subject of how one parameter or the other affects the final diagnostic result.

Recently A. Kokhanovsky proposed a rigorous analytical method of solving the fluorescence problem for the classical two-flux Kubelka–Munk (KM) approximation.[11] Also, the author showed in Ref. 12 the main source of errors of the KM model and proposed a version of their equation that makes it possible in one-dimensional (1D) problems to obtain today exact values for radiation fluxes at the boundary of a medium (for the fluxes recorded by a device). This opens up prospects for constructing simple analytical real-time algorithms that make it easy to analyze the distortions of the fluorescence spectra without resorting to complex multistep computations and numerical methods. The goal of this article is to use a combination of the modified two-flux KM model and

Kokhanovsky's solution as a basis to show the possibility of obtaining an exact analytical expression in terms of the 1D model for the distortion function of the fluorescence spectra, as well as to analyze this solution for agreement with typical experimental data.

THEORETICAL FORMULATION AND SOLUTION OF THE PROBLEM

This section discusses the well-known general formulation of the photometric 1D KM problem in a medium with fluorescence,[11] when the left boundary of the medium ($x = 0$) is illuminated by an external flux of radiation Φ_0 with wavelength λ_1, and two oppositely directed fluxes $i(x)$ and $j(x)$ with initial wavelength λ_1 propagate inside the medium along the x axis. Because light is absorbed and scattered in the medium, these fluxes are partially absorbed, are converted into each other, and also cause stimulated emission of fluorescence of the luminophores found in the medium. This causes additional similar fluorescence fluxes $I(x)$ and $J(x)$ with wavelength $\lambda_2 > \lambda_1$ to be formed in the medium (Fig. 1). Some wave properties of the radiation are neglected in this model because of its very simple photometric (energy) formulation and the one-dimensional calculational scheme.[12]

When diagnostic measurements are made from the front (illuminated) surface of the biological tissue, a device records the output of fluxes $j(0)$ and $J(0)$ from the medium. This will interest us in the process of obtaining exact analytical solutions for them. In such a formulation of the problem, the fluxes $i(x)$, $j(x)$, $I(x)$, and $J(x)$ can be derived from two connected systems of first-order linear differential equations:

$$\begin{cases} di_{\lambda 1}(x)/dx = -\beta_1(\lambda_1) i_{\lambda 1}(x) + \beta_2(\lambda_1) j_{\lambda 1}(x) \\ dj_{\lambda 1}(x)/dx = \beta_1(\lambda_1) j_{\lambda 1}(x) - \beta_2(\lambda_1) i_{\lambda 1}(x) \end{cases} \quad (1)$$

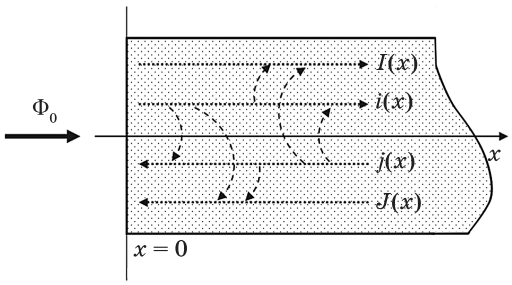

FIG. 1. Formulation of the problem of radiation propagation in a medium with fluorescence. See text for explanation.

and

$$\begin{cases} dI_{\lambda 2}(x)/dx = -\beta_1(\lambda_2) I_{\lambda 2}(x) + \beta_2(\lambda_2) J_{\lambda 2}(x) + F_{12}(x) \\ dJ_{\lambda 2}(x)/dx = \beta_1(\lambda_2) J_{\lambda 2}(x) - \beta_2(\lambda_2) I_{\lambda 2}(x) - F_{12}(x) \end{cases} \quad (2)$$

where $\beta_1(\lambda)$ and $\beta_2(\lambda)$ are called, respectively, the attenuation (extinction) coefficient and the radiation-backscattering coefficient. They determine the optical properties of the radiation-propagation medium (the biological tissue). According to Ref. 12, in the modified version, unlike the standard KM model, coefficients $\beta_1(\lambda)$ and $\beta_2(\lambda)$ are fairly complex functions of the absorption coefficients $\mu_a(\lambda)$, the density μ_ρ of inhomogeneities in the medium, and the Fresnel reflectance $R(\lambda)$ at the boundaries of the inhomogeneities inside the medium:

$$\beta_1 = \omega \frac{\mu_a(\lambda) - \mu_\rho \ln(1 - R(\lambda)) + \mu_\rho \ln(1 - \omega(\lambda)) + \sqrt{\omega(\lambda)^2 - R(\lambda)^2 e^{-2\mu_a(\lambda)/\mu_\rho}}}{\sqrt{\omega(\lambda)^2 - R(\lambda)^2 e^{-2\mu_a(\lambda)/\mu_\rho}}},$$

$$\beta_2(\lambda) = R(\lambda) e^{-\mu_a(\lambda)/\mu_\rho} \frac{\mu_a(\lambda) - \mu_\rho \ln(1 - R(\lambda)) + \mu_\rho \ln(1 - \omega(\lambda)) + \sqrt{\omega(\lambda)^2 - R(\lambda)^2 e^{-2\mu_a(\lambda)/\mu_\rho}}}{\sqrt{\omega(\lambda)^2 - R(\lambda)^2 e^{-2\mu_a(\lambda)/\mu_\rho}}}, \quad (3)$$

where we introduce the notation $\omega(\lambda) = (1 - (1 - R(\lambda)) e^{-2\mu_a(\lambda)/\mu_\rho})/2$.

The mean density μ_ρ of inhomogeneities in the medium is determined[12] from the mean number N of inhomogeneities at which light is scattered divided by the thickness H of the section of biological tissue under consideration (Fig. 1):

$$\mu_\rho = N/H.$$

The systems of Eqs. (1) and (2) are connected via the function $F_{12}(x)$ that describes the formation of the fluorescence radiation inside the medium,

$$F_{12}(x) = \frac{1}{2}[i\lambda_1(x) + j\lambda_1(x)]\mu_{af}(\lambda_1)\varphi_{12}\Phi_0, \quad (4)$$

where $\mu_{af}(\lambda_1)$ is the absorption coefficient of the initial radiation by the active luminophor inside the biological tissue at wavelength λ_1, and φ_{12} is the quantum yield of fluorescence at wavelength λ_2 when the fluorescence is excited by radiation at wavelength λ_1 (the conversion coefficient of radiation $\lambda_1 \to \lambda_2$).

The system of Eqs. (1)–(4) with the corresponding very simple boundary conditions [left boundary ($x = 0$) $i_{\lambda 1}(0) = \Phi_0$ and $I_{\lambda 2}(0) = 0$; right boundary ($x = H$) $j_{\lambda 1}(H) = J_{\lambda 2}(H) = 0$] makes it possible to solve analytically the formulated problem for the fluxes $j_{\lambda 1}(0)$ and $J_{\lambda 2}(0)$.

In the case of the approximation of a semi-infinite medium ($H \to \infty$), the solution of the system of Eqs. (1) for the sum of fluxes $i_{\lambda 1}(x)$ and $j_{\lambda 1}(x)$ can be written in the form[11]

$$i_{\lambda 1}(x) + j_{\lambda 1}(x) = \Phi_0(1 + r_{\infty \lambda 1}) e^{-\alpha_{\lambda 1} x}, \quad (5)$$

while the solution for $j_{\lambda 1}(0)$ can be written as

$$j_{\lambda 1}(0) = \Phi_0 r_{\infty \lambda 1}, \tag{6}$$

where in the solutions we use the notation $r_{\infty\lambda 1} = (\beta_2(\lambda_1))/(\beta_2(\lambda_1) + \alpha_{\lambda 1})$ and $\alpha_{\lambda 1} = \sqrt{\beta_1^2(\lambda_1) - \beta_2^2(\lambda_2)}$.

Making the substitutions (5) → (4) → (2) and solving the system of Eqs. (2) for $J_{\lambda 2}(x)$ by the standard method of differentiation, we get for $J_{\lambda 2}(x)$ the following second-order differential equation:

$$\frac{d^2 J_{\lambda 2}(x)}{dx^2} - \alpha_{\lambda 2} \frac{dJ_{\lambda 2}(x)}{dx} = -(\beta_1(\lambda_2) + \beta_2(\lambda_2))F(x) - \frac{dF(x)}{dx}. \tag{7}$$

As shown by Kokhanovsky,[11] Eq. (7) is easy to solve analytically for $J_{\lambda 2}(x)$. However, other boundary conditions were used in its solution, since in his problem the medium was simultaneously illuminated at both wavelengths λ_1 and λ_2, and therefore we cannot directly use that solution here. However, in our formulation of the problem and in the case of flux $J_{\lambda 2}(0)$, which comes out of the biological tissue from its front surface, the solution by Kokhanovsky's method with the boundary conditions indicated above in the approximation of a semi-infinite medium ($H \to \infty$) takes the form

$$J_{\lambda 2}(0) = \Phi_0 \mu_{af}(\lambda_1)\varphi_{12} \frac{(1 + r_{\infty\lambda 1})(1 + r_{\infty\lambda 2})}{2(\alpha_{\lambda 1} + \alpha_{\lambda 2})}. \tag{8}$$

The product $\Phi_0 \mu_{af}(\lambda_1)\varphi_{12}$ determines the initial undistorted fluorescence spectrum. Thus, the distortion of the spectrum is determined by coefficient γ, equal to

$$\gamma = \frac{(1 + r_{\infty\lambda 1})(1 + r_{\infty\lambda 2})}{2(\alpha_{\lambda 1} + \alpha_{\lambda 2})}, \tag{9}$$

where $r_{\infty\lambda 2} = (\beta_2(\lambda_2))/(\beta_1(\lambda_2) + \alpha_{\lambda 2})$ and $\alpha_{\lambda 2} = \sqrt{\beta_1^2(\lambda_2) - \beta_2^2(\lambda_2)}$.

This coefficient is a function of the wavelength of the radiation and depends in a complex way on the optical properties $\beta_1(\lambda)$ and $\beta_2(\lambda)$ of the propagation medium of the radiation, so that there is no simple normalization of $J_{\lambda 2}(0)$ to $j_{\lambda 1}(0)$ or Φ_0 in Eq. (8) that makes it possible to eliminate it. Only in the ideal case of "grey" biological tissue, if all of its optical properties are independent of wavelength ($r_{\infty\lambda i} = \text{const}_i$ and $\alpha_{\lambda j} = \text{const}_j$), for the two wavelengths λ_2 and λ_3 and two luminophores f_1 and f_2 will the ratio of the recorded fluorescence signals equal the ratio of the signals for the undistorted spectra:

$$\frac{J_{\lambda 2}(0)}{J_{\lambda 3}(0)} = \frac{\mu_{af1}(\lambda_1)\varphi_{12}}{\mu_{af2}(\lambda_1)\varphi_{13}}. \tag{10}$$

However, in the general case of actual clinical situations, to obtain the original (undistorted) spectrum, the value of γ needs to be accurately known in the entire working range of wavelengths, since the dependence of γ on the optical properties of the medium in principle is not linear and not monotonic.

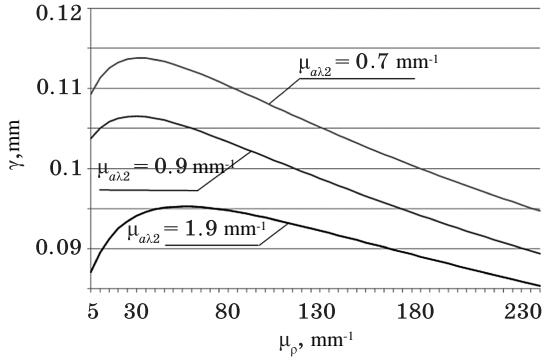

FIG. 2. Parameter γ versus the density of scatterers. $R(\lambda_1) = 0.03$, $R(\lambda_2) = 0.02$, $\mu_{a\lambda 1} = 4$ mm^{-1}.

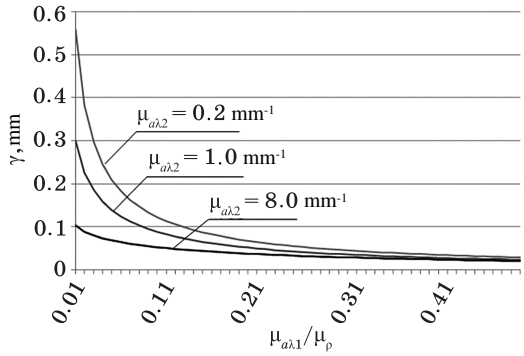

FIG. 3. Parameter γ versus the ratio $\mu_a(\lambda_1)/\mu_\rho$. $R(\lambda_1) = 0.03$, $R(\lambda_2) = 0.02$, $\mu_\rho = 50$ mm^{-1}.

As an illustration of this last statement, Fig. 2 shows how coefficient γ according to Eq. (9) depends on the density μ_ρ of the inhomogeneities (scatterers) inside the medium, while Fig. 3 shows how γ depends on the ratio $\mu_a(\lambda_1)/\mu_\rho$, also calculated from Eq. (9), using Eq. (3). Both dependences, as we shall see, have a nonlinear character and are far from obvious *a priori*.

MODELLING THE EXPERIMENTAL SPECTRA

The advantages of Eqs. (6) and (8) consist of their obvious analytical form, which makes it easy to calculate the complete fluorescence spectrum and spectrum of radiation backscattered by biological tissue, recorded by the device in the process of diagnosis in the entire range of wavelengths of the recording and excitation of fluorescence. Figure 4 demonstrates such typical experimentally recorded spectra. Spectra that are similar in shape but with weaker resolution in wavelength are shown in Ref. 13. In this sense, they are fairly representative, and therefore we specially chose them as an example, since their interpretation, as we shall see below, can be erroneous. The spectra of Fig. 4 are recorded *in vivo* on the LAKK-M diagnostic complex when fluorescence is excited by the narrow-band UV radiation of an LED with maximum at the line $\lambda_1 = 365$ nm.[14] Fluorescence region I

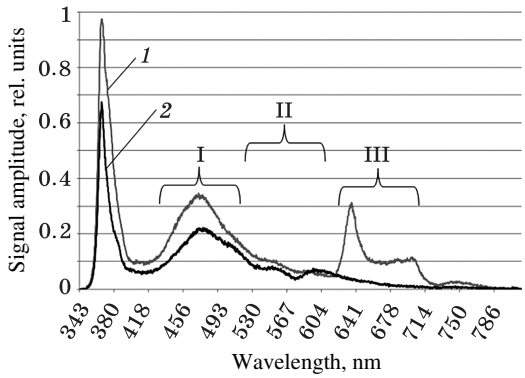

FIG. 4. Experimental spectra of endogenous fluorescence, recorded *in vivo* on the LAKK-M diagnostic complex with fluorescence excited by the narrow-band emission of a UV LED with a maximum at the line $\lambda = 365$ nm. 1—Rat-tail skin, 2—mucous membrane of the human soft palate. I—the region where collagen, elastin, NADH, keratin, etc., fluoresce; II–the region where flavoproteins and lipofuscin fluoresce; III—the region where porphyrins fluoresce.

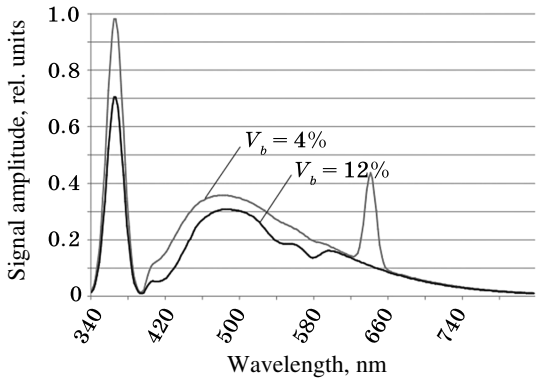

FIG. 5. The results of modelling the experimental spectra shown in Fig. 4. Only one principal maximum of protoporphyrin IX was modelled for porphyrin in the region $\lambda = 640$ nm, $S_tO_2 = 95\%$. The total density of scatterers in the tissue was $\mu_\rho = 100$ mm^{-1}.

corresponds to the fluorescence of such endogenous luminophores in biological tissue as elastin, collagen, keratin, NADH (nicotinamide), etc. NADH, flavines, and lipofuscin most actively fluoresce in region II. Region III most clearly reflects the presence of protoporphyrin IX, chlorophyll, and a number of other substances in biological tissue by fluorescence.

To equalize the amplitudes of backscattered radiation (the left peak in the graphs) and fluorescence radiation (in the longer-wavelength region), attenuating optical filters made from colored optical glass[15] of type OS-13, KS-15, etc., are used in the optical layout of the LAKK-M diagnostic system to attenuate the recorded backscattered radiation by about a factor of 10^3.[14] Therefore, the graphs of Fig. 4 show reduced amplitudes of the signals of backscattered radiation by comparison with their actual values, and the spectra was theoretically modelled in our paper using Eq. (8) and taking into account the spectral response of the filter that is used. The optical properties of the biological tissue were specified in the modelling by typical values of $\mu_a(\lambda)$, μ_ρ, and $R(\lambda)$, taking into account the known spectral data on the optical properties of oxygenated and reduced hemoglobin of the blood. Different possible values of the volume plethora V_b of the tissue and tissue saturation of the oxyhemoglobin S_tO_2 in the blood were also allowed for.[16] The biological tissue itself was represented as a macrohomogeneous semi-infinite continuous light-scattering and light-absorbing medium–matrix, in which the blood and various luminophores are distributed uniformly over the entire volume in different concentrations.

The results of modelling the experimental spectra shown in Fig. 4 are presented in Fig. 5. Only the one principal maximum of protoporphyrin IX in the $\lambda_2 = 640$ nm region was modelled for porphyrin. The tissue saturation of oxyhemoglobin is chosen to equal $S_tO_2 = 95\%$ for both cases. The total density of scatterers in the tissue is $\mu_\rho = 100$ mm^{-1}. $R(\lambda)$ was calculated for each wavelength as the Fresnel reflection coefficient at the water/air boundary. Both figures demonstrate extremely good qualitative and quantitative coincidence of the spectra for the chosen values of V_b. It is important to point out that the small visible increase of the amplitude in spectrum 2 in Fig. 4 in the $\lambda_2 = 604$ nm region can be treated as an increased concentration of fluorescent flavines or lipofuscin in the tissue. Such a treatment is sometimes encountered in certain papers. However, this "increase" is only a consequence of the absorption of the fluorescence emission by the blood. Figure 6 shows model fluorescence spectra of biological tissue for various values of V_b and S_tO_2 of the blood when there is no change in the luminophore concentration. As the plethora and the tissue saturation of oxyhemoglobin in the blood increase, a distortion of the true spectrum just appears in the form of an overall nonlinear decrease of the amplitude of the recorded signals and the appearance of characteristic hemoglobin dips in the $\lambda_2 = 530$–580 nm region.

Sometimes, when there are definite combinations of the emission spectrum of the source, the spectral attenuation function of the optical filter in a device, and the optical properties of a test object, it is possible to observe the appearance of cutouts (notches, gaps) in the backscattering spectrum of the radiation. An example of an experimentally recorded cutout in a spectrum is shown in Fig. 7 for the radiation of a He–Ne laser when an optical cutoff filter made from KS-17 colored optical glass is used in the device. Figure 8 shows a version of a theoretical model problem in which such a cutout also appears

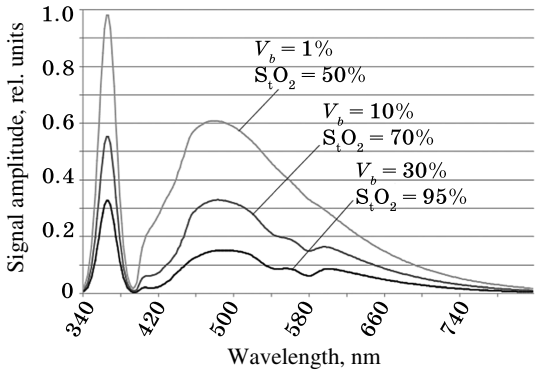

FIG. 6. Dependence of the fluorescence spectra on the volume plethora of the tissue in the examination zone and the degree of tissue saturation of oxyhemoglobin.

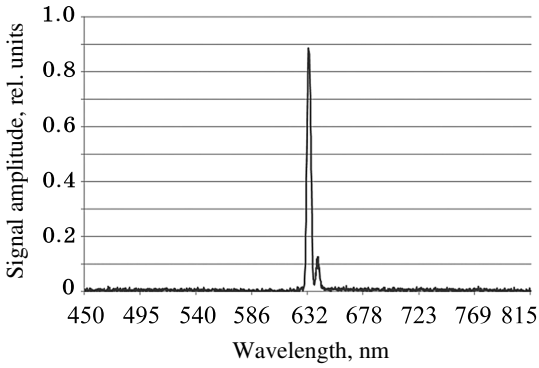

FIG. 7. Experimentally recorded appearance of a cutout in the backscattering spectrum of the radiation of a He–Ne laser.

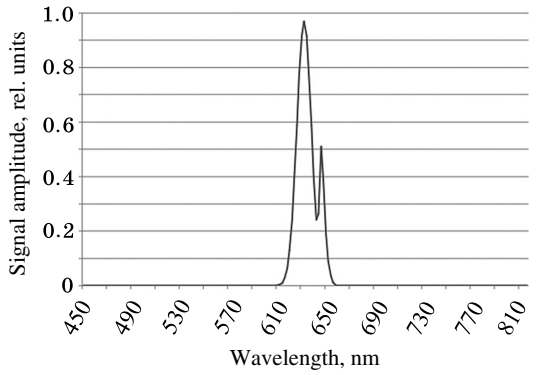

FIG. 8. Modelling of a cutout. The filter parameters correspond to KS-17 colored optical glass according to GOST 9411-75.[15]

according to the results of the computations. Thus, a comparison of the experimental and theoretically computed fluorescence spectra and the spectra of backscattered radiation of the fluorescence-excitation source shows that the proposed model and the algorithm for calculating the spectra can describe the actual situations fairly adequately.

CONCLUSION

An analytically rigorous solution of the problem of theoretically modelling the excited endogenous fluorescence of biological tissues as applied to problems of noninvasive medical diagnosis has been proposed in this paper in terms of the two-flux Kubelka–Munk model and Kokhanovsky's solution for fluorescence radiation. An adequate description of the experimentally recorded *in vivo* fluorescence spectra of actual biological tissues has been demonstrated. The resulting solution of Eq. (9) for the distortion function of the spectra shows that this function (coefficient γ) in principle nonlinearly and nonmonotonically depends on the optical properties of the radiation-recording medium. Therefore, in the general case of actual clinical diagnostic examinations for obtaining the initial (undistorted) spectrum, an accurate value of γ is necessary in the entire working range of wavelengths for each patient and each of its regions of examination. Accordingly, all studies oriented to the solution of the problem of quantitatively processing fluorescence spectra in practical medicine must today be directed to methods of determining γ and the errors of these methods.

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[1]V. B. Loschenov, V. I. Konov, and A. M. Prokhorov, "Photodynamic therapy and fluorescence diagnostics," Laser Phys. **10**, 1188 (2000).

[2]M. A. Mycek and B. W. Pogue, *Handbook of Biomedical Fluorescence* (Marcel Dekker Inc., New York, 2003).

[3]F. Leblond, S. Davis, P. Valdes, and B. Pogue, "Pre-clinical whole-body fluorescence imaging: review of instruments, methods and applications," J. Photochem. Photobiol., B **98**, 77 (2010).

[4]P. Bonfert-Taylor, F. Leblond, R. Holt, K. Tichauer, B. Pogue, and E. Taylor, "Information loss and reconstruction in diffuse fluorescence tomography," J. Opt. Soc. Am. A **29**, 321 (2012).

[5]D. A. Rogatkin, "Instrumental and methodological errors of measurements in noninvasive medical spectrophotometry," in *Materials of the Third Eurasian Congress with Respect to Medical Physics and Engineering, Medical Physics-2010* (MGU, Moscow, 2010), pp. 38–41.

[6]W. J. M. Putten and M. J. C. Gemert, "A modeling approach to the detection of subcutaneous tumours by haematoporphyrin-derivative fluorescence," Phys. Med. Biol. **28**, 639 (1983).

[7]D. Rogatkin, V. Svirin, and G. Hachaturyan, "The theoretical model for fluorescent field calculation in nonhomogeneous and scattering biological tissues," Proc. SPIE **3563**, 125 (1998).

[8]D. A. Rogatkin and V. V. Tchernyi, "Mathematical simulation as a key point of the laser fluorescence diagnostic technique in oncology," Proc. SPIE **4059**, 73 (2000).

[9]E. Baraghis, A. Devor, Q. Fang, V. Srinivasan, W. Wu, D. Boas, S. Sakadzic, F. Lesage, C. Ayata, and K. Kasischke, "Two-photon microscopy of cortical NADH fluorescence intensity changes: correcting contamination from the hemodynamic response," J. Biomed. Opt. **16**, 106003 (2011).

[10]S. Kanick, D. Robinson, C. Sterenborg, and A. Amelink, "Extraction of intrinsic from single-fiber fluorescence measurements on a turbid medium," Opt. Lett. **37**, 948 (2012).

[11]A. A. Kokhanovsky, "Radiative properties of optically thick fluorescent turbid media," J. Opt. Soc. Am. A **26**, 1896 (2009).

[12]D. A. Rogatkin, "On a feature in determining the optical properties of turbid biological tissues and media in calculational problems of medical noninvasive spectrophotometry," Medits. Tekhn. No. 2, 10 (2007).

[13]A. R. Subbotin, T. A. Savel'eva, and S. A. Goryaĭnov, "Algorithm for processing the fluorescence spectra of protoporphyrin IX and the endogenous fluorophores in glial tumors of the brain," in *Collection of the Materials of the Fifth Troitsk Conference on Medical Physics and Innovation in Medicine*, Troitsk, 2012, vol. **1**, pp. 268–269.

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

[15]GOST 9411–75, "Optical colored glass," Izd. Standartov, Moscow, 1976.

[16]D. A. Rogatkin, "Physical principles of optical oximetry," Medits. Fiz. No. 2, 97 (2012).