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The theoretical model for fluorescent field calculation in non-homogeneous and scattering biological tissues

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ABSTRACT

The possibility of the fluorescence spectroscopy for diagnosing a pathology in human tissues is studied now very intensively. However, there are not much and good theoretical models to calculate the fluorescence intensity in scattering and absorbing non-homogeneous biological tissues. Moreover, such models are needed for up-to-date laser medical non-invasive diagnostic equipment and technique which run by principle of an inverse optical task solution. In order to obtain the acceptable model we used the Transport equation and multi-layered plane medium. The Method of Moments was used to solve the Transport equation with calculation of the moment of fluorescence flux at the last step of the solution.

1. INTRODUCTION

Last achievements in the field of the laser and optical diagnostic in medicine show 1-3 that a further development of this direction will impossible without attraction for the diagnostic results analysis and processing of good theoretical models of laser light interaction with biological tissues. And, first of all, it is referred to the laser clinical fluorescence diagnostic, based on a registration from a tissues surface the fluorescence flux intensity, induced by an external laser radiation, called also, the autofluorescence (AF) flux, using which it becomes possible to evaluate the physiological and functional state of human tissues and organs.

Not long ago a number of authors 4,5 had attempts to describe some theoretical approaches to the problem of AF radiation distribution inside and on surfaces of biological tissues. However, from our view point, the simplified approaches used by them don't allow to obtain acceptable qualitative models and were justifiable on the most initial stages only. For the correct interpretation of the diagnostic results it is advisable to have a possibility of more exact theoretical modelling of different situations for the reason, for example, to clarify an influence of optical characteristics of the biological medium on the energy and spatial parameters of its fluorescence radiation.

One of such approaches can be a method to solve the Transport equation (TE) using one or another approximation, if only the TE could be completed with fluorescence intensity. In our opinion, the most interesting approach is way to use the Method of moments (MM)[7], which does not require any limiting conditions on parameters of medium and can give a result with any level of accuracy by taking into account more senior members of equations system and using more detailed polynomial expansion.

Historically, MM was offered by Chandrosekhar 8 in 50-h s, but did not find a broad using, since in general case requires a lot of calculations. Today, with the high-speed personal computer appearance, time of calculation of an average difficulty problem does not exceed groups of ten seconds, that is acceptable for real-time systems even.

However, known on today decisions used MM[6-8], designed for the case of homogeneous medium without AF radiance. This work was made with the purpose of development of MM ideas to the general case of non-homogeneous biological tissues with AF phenomenon.

2. THEORY

If it is considered a plane incident wave and a seamy-infinite medium with plane boundary surface then the light intensity I is a function of one coordinate X and Transport equation has the form[6] :

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$$\cos\upsilon \frac{dI_\lambda(x,\upsilon)}{dx} = -(\chi_\lambda + \sigma_\lambda) I_\lambda(x,\upsilon) + \chi_\lambda \frac{B_\lambda(T)}{\pi} +$$

$$+ \frac{\sigma_\lambda}{4\pi} \int_{4\pi} \rho_\lambda(\upsilon,\upsilon',\varphi-\varphi') I_\lambda(x,\upsilon') d\omega'$$

(1)

where υ,υ' è φ,φ' - special angles for directions of propagating and scattering **l, l'**

β - scattering angle ; σ - scattering coefficient ; χ - absorption coefficient ;

ρ - scattering indicatrix ; ω - solid angle ; **B(T)** - head source function

The moment of light intensity is defined[7] as integral:

$$M_n(z) = 2\pi \int_{-1}^{1} I(z,\mu)\mu^n d\mu$$

where: n - is the order of the moment and:

$$dz_\lambda = (\chi_\lambda + \sigma_\lambda) dx, \quad \mu = \cos\upsilon$$

How it follows from the moment definition the M_o is 3-D density of energy of radiation and M_1 is a light flux. So, after a number of mathematical transformations steps the infinite equations system can be obtained[7] :

$$\frac{dM_{n+1}(z)}{dz} = -(1+\gamma) M_n(z) + \frac{1+(-1)^n}{2(n+1)} B^*(z) +$$

$$+ \frac{\gamma}{2} \sum_{k=0}^{n} \frac{1+(-1)^k}{2} \frac{C_n^k C^{k/2}}{2^k} \Gamma_{n,k} \sum_{r=0}^{k/2} (-1)^r C_{k/2}^r M_{n-k+2r}(z),$$

$$n = 0,1,2,\ldots$$

(2)

where: B(z)=4B[T(z)], C- binomial coefficients, $\gamma = \sigma/\chi$ and

$$\Gamma_{n,k} = \int_0^\pi \rho(\beta) \sin^{k+1}\beta \cdot \cos^{n-k}\beta \cdot d\beta$$

- integral term of scattering.

In practice, to get a N-order approach the first N equations from (2) is keeping which contains **N+1** unknown moments $\grave{I}_0, \grave{I}_1, \ldots$ To obtain a rear equation it is necessary to enter a simplify assumption for the type of function **I(z, μ).** So, if we will assume that this function into the interval **μ ϵ [-1, 1]** can be described by the Legendre polynomials [8]:

$$I(z,\mu)=\sum_{k=0}^{N-1} b_k(z)P_k(\mu)$$

$$P_k(\mu)=\sum_{j=0}^{k} C_{j,N}\mu^{k-j}$$

(3)

where $\mathbf{P_k(\mu)}$ - Legendre polynomials of k-order,
then, by multiplying (2) on (3) and making the integrating:

$$\int_{-1}^{1}\{...\}\mu^n d\mu$$

the rear equation will written as follows:

$$\sum_{j=0}^{N} C_{j,N} M_{N-j}(z)=0$$

(4)

that is an equivalent of description of light intensity by using a series:

$$I(z,\mu)=\sum_{j=1}^{N} a_j(z)\mu^{N-j}$$

(5)

when:

$$M_n(z)=2\pi\sum_{j=1}^{N}\frac{1+(-1)^{N-j+n}}{N-j+n+1}a_j(z),\quad n=0,1,2,...$$

(6)

Under such assumptions the system (2) is reduced to following system:

$$\left.\begin{aligned}\frac{dM_1(z)}{dz}&=-M_0(z)+B^*(z)\\ \frac{dM_2(z)}{dz}&=-\mathrm{E}M_1(z)\\ M_2(z)&=\frac{1}{3}M_0(z)\end{aligned}\right\}\quad (7)$$

and to following equation:

$$\frac{d^2 M_1(z)}{dz^2} - 3\mathrm{E} M_1(z) = \frac{dB^*(z)}{dz}$$

which has a solution:

$$M_{0i}(z_i) = \alpha_i [A_i(z_i) - B_i(z_i) - E_{1i} e^{\alpha_i z_i} + E_{2i} e^{-\alpha_i z_i}]$$
$$M_{1i}(z_i) = A_i(z_i) + B_i(z_i) + E_{1i} e^{\alpha_i z_i} + E_{2i} e^{-\alpha_i z_i}$$

(8)

where:

$$A_i(z_i) = e^{-\alpha_i z_i} \int_0^{z_i} \frac{B^*(z')}{2} e^{\alpha_i z'} dz'$$
$$B_i(z_i) = e^{\alpha_i z_i} \int_0^{z_i} \frac{B^*(z')}{2} e^{\alpha_i z'} dz'$$
$$\alpha_i = \sqrt{3\mathrm{E}} = \sqrt{3(1+\gamma_i(1-0.5\Gamma_{1.0i}))}$$

(9)

and E_{ij} is integrating constants, determinate from boundary conditions.

When considering the non-homogenous biological tissues the latest one can be described as multi-layered plane medium (see fig.1) with different optical properties for each layer. And (8) is available for each "i" layer too.

For the determinations of E_{ij} it is necessary to formulate some corresponding external and between layers boundary conditions (see fig.2 and fig.3), where $\mathbf{r_i}$ and $\mathbf{q_i}$ is boundary surfaces indices of reflectance and transmittance. And it is necessary yet to transform them using (3)-(6) technique.

So, our equations system will contain 2m unknown E_{ij} and 2m equations that allows to calculate E_{ij} from the algebraic line equations system:

$$\begin{cases} E_1^1 U_{11} + E_2^1 U_{12} + E_1^2 \cdot 0 + E_2^2 \cdot 0 + \ldots + E_1^m \cdot 0 + E_2^m \cdot 0 = W_1 \\ E_1^1 U_{12} + E_2^1 U_{22} + E_1^2 U_{23} + E_2^2 U_{24} + \ldots + E_1^m \cdot 0 + E_2^m \cdot 0 = W_2 \\ \cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots\cdots \\ E_1^m \cdot 0 + E_2^m \cdot 0 + \ldots\ldots\ldots\ldots\ldots + E_1^m U_{m,m-1} + E_2^m U_{m,m} = W_m \end{cases}$$

(10)

The next step of our approach is the determination of AF flux moments. In general cases, there is not any AF fluxes in the Transport theory. But there is the heat radiance (B[T]) in the Transport equation, which can be replaced, as we assume, by function of an AF flux. Let the **B(T)** is replaced by $\eta_i \chi_i \mathbf{Mo_i(z_i)}$, where η is the fluorescence efficiency,

because there is the evidence dependence of fluorescence energy on density of energy of the penetrated external radiation deep into the tissue. And, also, we assume that the wavelength of AF radiation is near to incident light wavelength towards using the same spectral optical properties of medium for external and AF radiation's. But them are not equal towards not taking into account any interference between them.

Thus, the solution of the problem is to consist of two steps. The first step is to calculate $M_o(z)$ and $M_1(z)$ for every layer from (8) under $A_i=B_i=0$ and using (10) for E_{ij} under boundary conditions of incident external flow. And the second step is to obtain $M_{1f}(z)$ and $M_{0f}(z)$ from (8) replacing B(T) as mentioned above and using (10) for new E_{ij} without external flow. And what's more , the integrals in (9) can be analytically taken for introduced AF source function . So, the AF flux distribution into a tissue can be obtained using this approach in form of $M_{1f}(z)$ moment.

3. RESULTS

Since for the non-invasive medical fluorescence diagnostic it is important a correct interpretation of diagnostic data obtained from flux intensity measured on the external border of tissues, then it is interesting to consider an influence of different optical tissue properties, especially σ and χ , on AF back-scattering (*backfluorescing*) intensity. Some results of computer modelling of that are presented in Fig.4-6.

Fig.4 presents the distribution of AF flux ($M_{1f}(x)$) in mono-layer tissue (h=1.5cm) under unit incident flux (Io=1) and η=0.1. Fig.5 presents the relation between boundary value of backfluorescing flux ($M_{1f}(0)$) and back-scattering flux of monolayer medium as a function of absorbency under the same conditions (h=1.5 cm, η=0.1, Io=1). And Fig.6 shows the changing of that relation when medium is two-layer tissue (the second layer is fluorescing and the first one is not) and the size of first layer is the changeable parameter.

As it can be seen from presented results, the functions are not line curves, so the real laser clinical diagnostic devices will give a small accuracy without using the principle of inverse optical task solution. Without one it turns to be highly problematic a determination of the main results of the fluorescence diagnostic - values of quantum efficiency of the fluorescence, values of volume concentration of active tissues fluorochromes and their location depth into a tissue.

4. CONCLUSION

As it follows from foregoing , the Method of moments would be successfully applied for theory modelling of light distribution into real scattering, non-homogeneous and fluorescing biotissues. Under a desire to raise accuracy of the MM it is possible to use some more high orders approach, for instance 4-h moment order, however that is not always justified. According to [7] , where the analysis of accuracy of MM was mentioned, even 2-h order approach gives a mistake not more then 10% in general case. The method itself, probably, is several difficult for a reproduction, but once mastered can give quite correct results. And could be applied as a part of base software of real laser clinical diagnostic equipment, which must run on the principle of inverse optical task analysis and which are now developing in various countries, including by authors of this report in Russia

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6. THE OFFER

Authors are looking for foreign collaborators for the ISTC research and development project No 1001 to internationally disseminate the results of the project.

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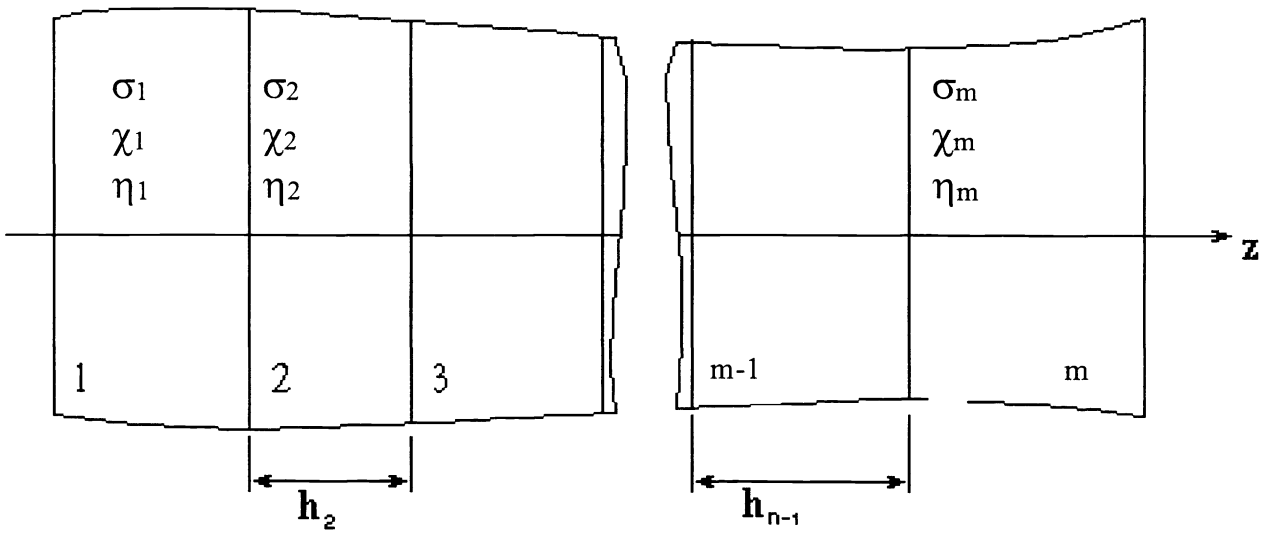
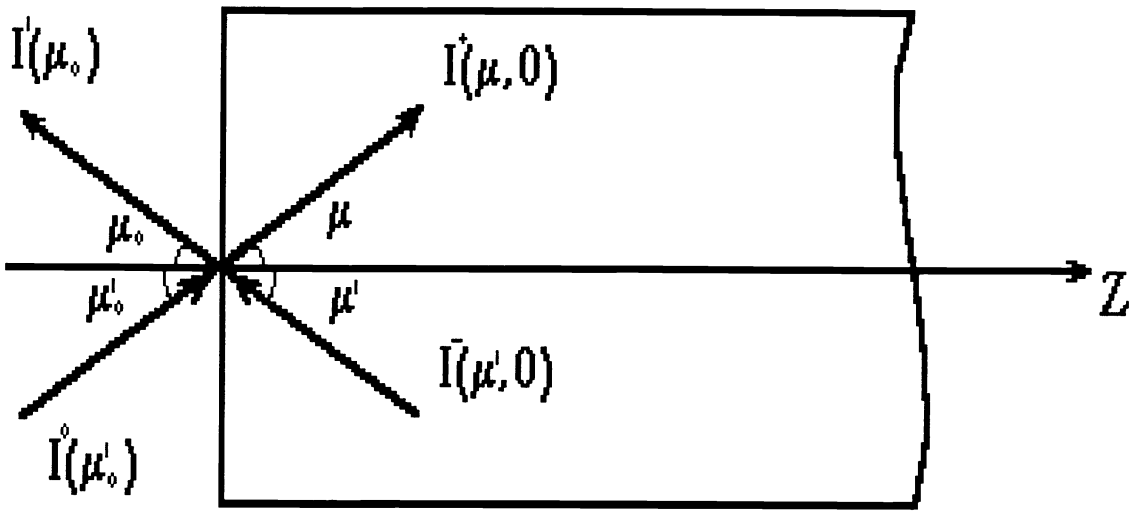
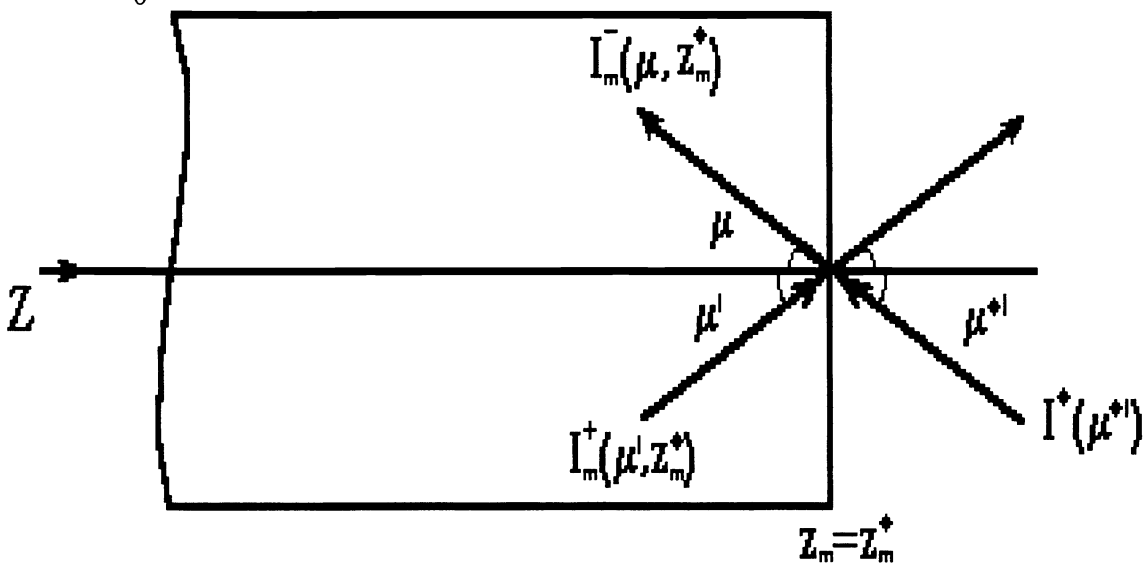


Fig. 1. The multi-layered plane medium as a middle of non-homogenous biological tissue



$$I_1^+(\mu,0) = \int_0^1 I_1^-(-\mu',0)\, r_1^0(\mu,\mu')\, d\mu' +$$

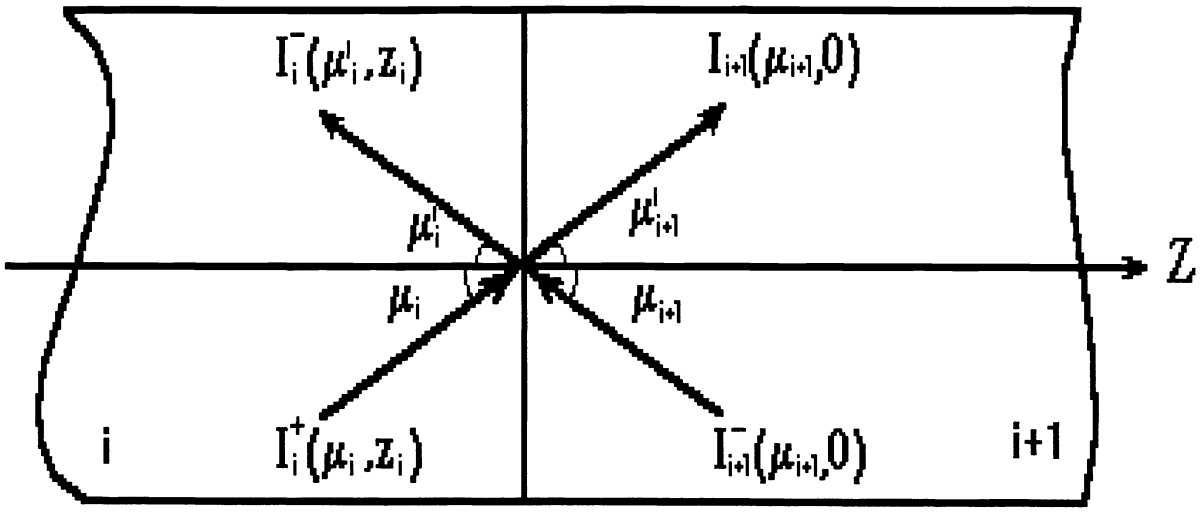
$$+ \int_0^1 q_1^0(\mu,\mu'_0)\, I^0(\mu'_0)\, d\mu'_0$$



$$I_m^-(\mu,z_m^*) = \int_0^1 I^+(\mu',z_m^*)\, r_m^*(\mu,\mu')\, d\mu'$$

$$I^*(\mu^{*'}) = 0$$

Fig. 2. External boundary conditions



$$I_i^-(-\mu_i', z_i^*) = \int_0^1 I_i^+(\mu_i, z_i^*)\, r_i^*(\mu_i', \mu_i)\, d\mu_i +$$

$$+ \int_0^1 q_{i+1,i}^0(\mu_i', -\mu_{i+1})\, I_{i+1}^-(-\mu_{i+1}, 0)\, d\mu_{i+1}$$

$$I_{i+1}^+(\mu_{i+1}', 0) = \int_0^1 I_{i+1}^-(-\mu_{i+1}, 0)\, r_{i+1}^0(\mu_{i+1}', -\mu_{i+1})\, d\mu_{i+1} +$$

$$+ \int_0^1 q_{i,i+1}^*(\mu_{i+1}', \mu_i)\, I_i^+(\mu_i, z_i^*)\, d\mu_i$$

Fig. 3. Boundary conditions between layers

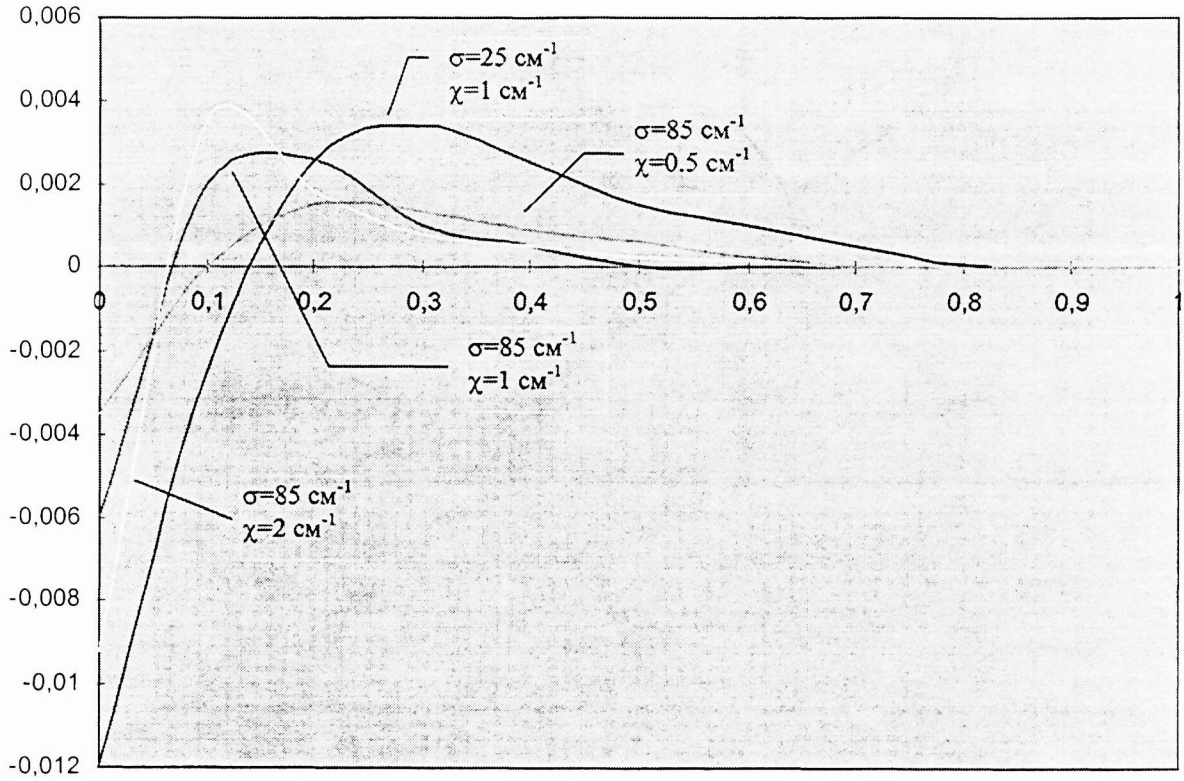


Fig. 4. Distribution of autofluorescence flux into mono-layered tissue.

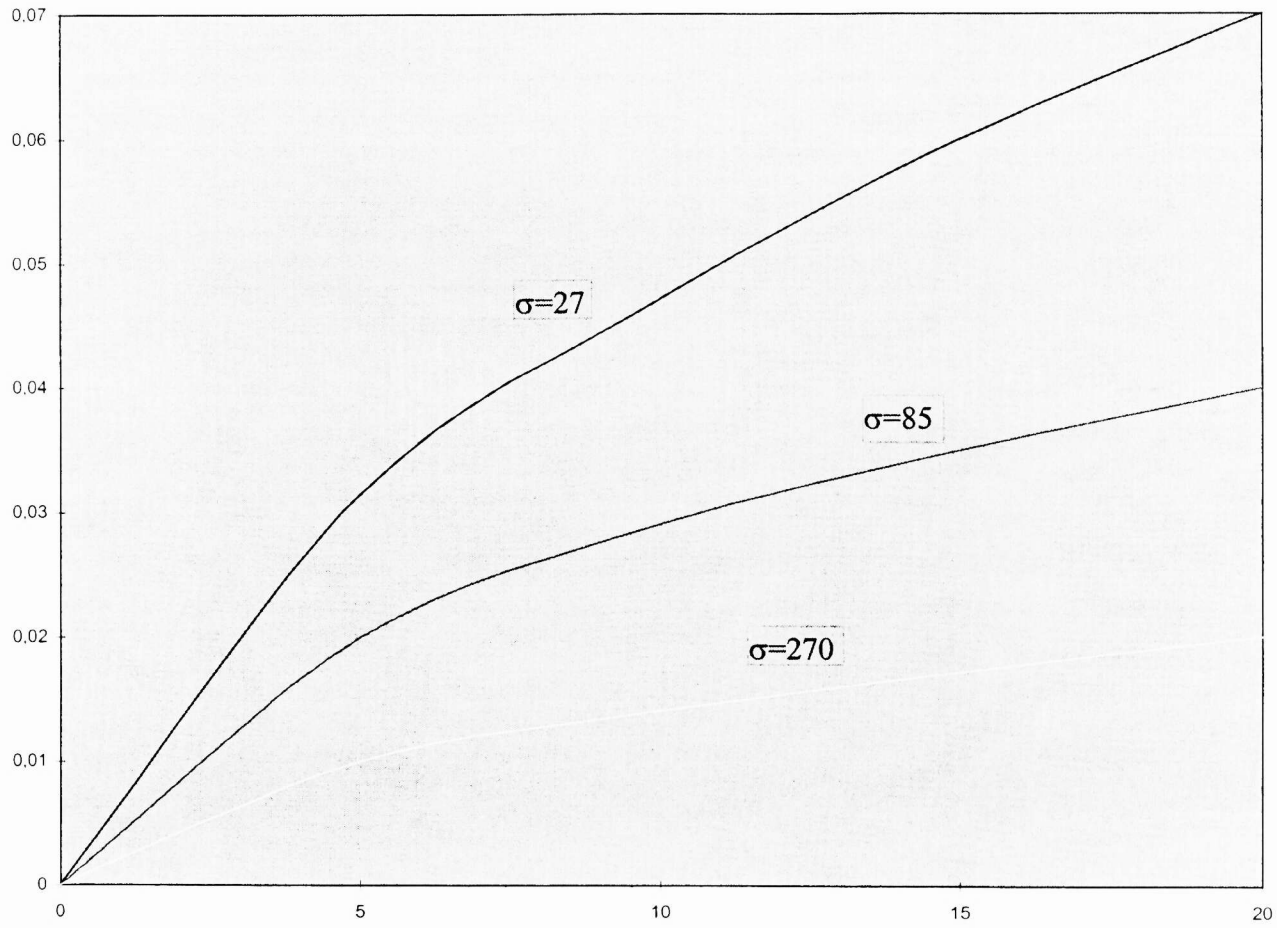


Fig. 5. Relation between autofluorescence flux and backscattered incidental flux on external surface of mono-layered tissue as function of σ and χ. I_0=1, η=0.1, h=1.5 cm.

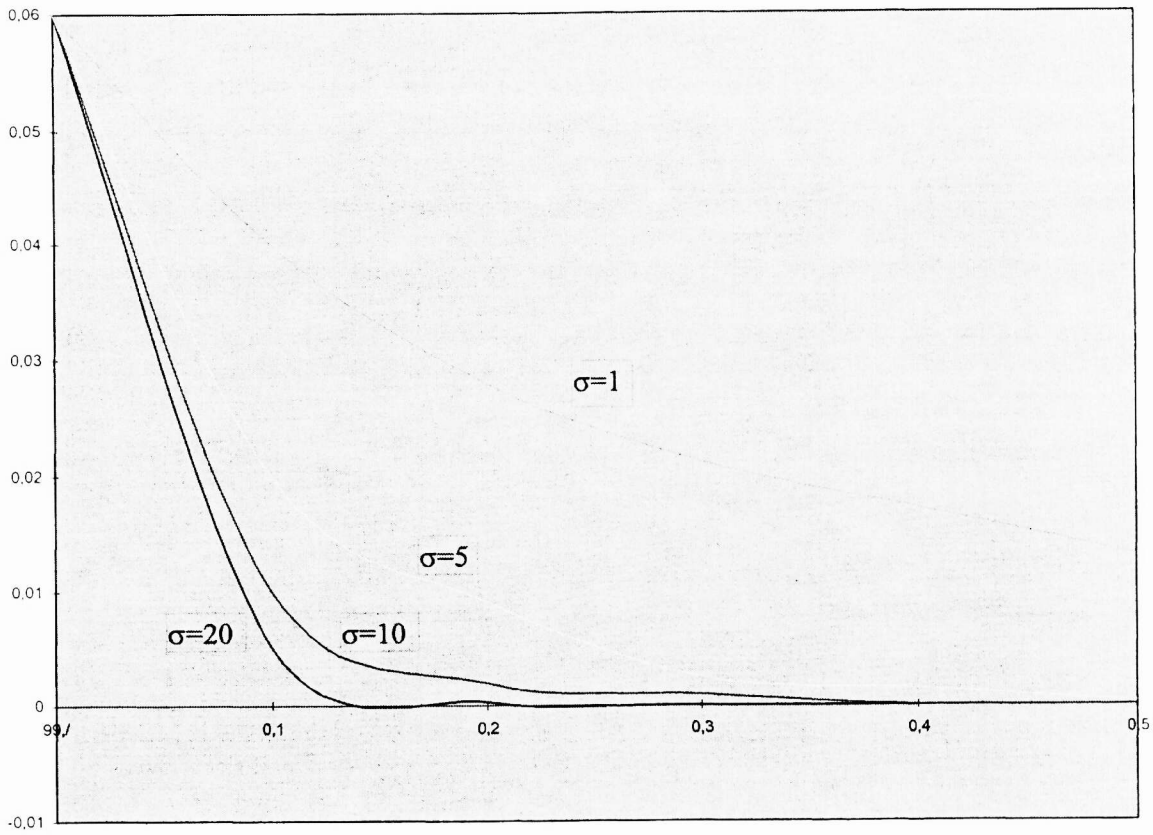


Fig. 6. Relation between autofluorescence flux and backscattered incidental flux on external surface of two-layered tissue estimated for different size of non-fluorescent first layer