# TISSUE OPTICS

## Light Scattering Methods and Instruments for Medical Diagnostics

THIRD EDITION

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Valery Tuchin

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*To My Grandkids*
*Dasha, Zhenya, Stepa, Serafim, and Ksusha*

# Contents

# Nomenclature

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| $2l$ | separation between two point light sources formed in the nodal plane |
| $2R_a$ | diameter of circular aperture |
| $A = \log(1/R_d)$ | apparent absorbance |
| $\bar{a}$ | numerical coefficient, depending on the form of the diffusion equation |
| $a$ | radius of a scatterer (particle), nm or μm |
| $A$ | signal amplitude in the frequency-domain measuring technique |
| $A$ | acoustic amplitude |
| $A = \langle i \rangle^2$ | square of the mean value of the photocurrent (baseline of the autocorrelation function) |
| $A \cong \pi\,[\lambda_{exc}/(2\mathrm{NA})]^2$ | illuminated area |
| $a'$ | largest dimension of a nonspherical particle, nm or μm |
| $A_0$ | initial amplitude due to the instrumental response |
| $A_{ac}$ | ac component of the amplitude of the photon-density wave |
| $A_{dc}$ | dc component of the amplitude of the photon-density wave |
| $a_m$ | more probable scatterer radius, μm |
| $a_n$ and $b_n$ | Mie coefficients |
| $A(\mathbf{r})$ | describes the optical absorption properties of the tissue at $\mathbf{r}$ |
| $a_{sph}$ | radius of spherical particle |
| $a_T$ | thermal diffusivity of the medium, $m^2/s$ |
| $B_d$ | detection bandwidth |
| $b_s$ | accounts for additional irradiation of upper layers of a tissue due to backscattering (photon recycling effect) |
| $c$ | velocity of light in the medium, cm/s |
| $c_0$ | velocity of light in vacuum, cm/s |

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| $C_1$ and $C_2$ | concentrations of molecules in two spaces separated by a membrane |
| $C_{\mathrm{a}}(x, t)$ | concentration of the agent |
| $C_{\mathrm{a0}}$ | initial concentration of the agent |
| $c_{\mathrm{ab}}$ | concentration of absorber in μmol, mmol, or mol |
| $c_{\mathrm{b}}$ | blood specific heat, J/kgK |
| $C_{\mathrm{Hb}}$ | hemoglobin concentration |
| $C_{\mathrm{f}}(x, t)$ | fluid concentration |
| $c_P$ | specific heat capacity for a constant pressure, J/kgK |
| $c_{\mathrm{s}}$ | relative concentration of the scattering centers |
| $\bar{C}_{\mathrm{S}}$ | average concentration of dissolved matter in two interacting solutions |
| $c_{\mathrm{V}}$ | specific heat capacity for a constant volume, J/kgK |
| $C_{\mathrm{n}}^{\alpha}$ | Gegenbauer polynomials |
| $\langle C \rangle$ | average blood concentration |
| $\langle C \rangle V_{\mathrm{rms}}$ | blood flux or perfusion |
| $D = z\lambda/\pi L_{\varphi}^2$ | wave parameter |
| $D$ | photon diffusion coefficient, $\mathrm{cm}^2/\mathrm{s}$ |
| $D_{\mathrm{A}}$ | diattenuation (linear dichroism) |
| $D_{\mathrm{a}}$ | agent diffusion coefficient, $\mathrm{cm}^2/\mathrm{s}$ |
| $D_{\mathrm{B}}$ | coefficient of Brownian diffusion, $\mathrm{cm}^2/\mathrm{s}$ |
| $D_{\mathrm{f}}$ | fluid coefficient of diffusion, $\mathrm{cm}^2/\mathrm{s}$ |
| $D_{\mathrm{media}}\,(\lambda)$ | age-related optical density of transparent media of the eye |
| $d$ | sample (tissue layer or slab) thickness, cm |
| $\mathbf{D}^{-1}$ | inverse of the measurement matrix |
| $D_{\|\|}$ | dimension of incident light beam along the area where the total radiant energy fluence rate is maximal (determined from the $1/e^2$ level), cm |
| $D_{\perp}$ | dimension of incident light beam across the area where the total radiant energy fluence rate is maximal (determined from the $1/e^2$ level), cm |
| $d\Omega'$ | unit solid angle about a chosen direction, sr |
| $d_{\mathrm{av}}$ | average size of a speckle in the far-field zone |
| $D_{\mathrm{f}}$ | fractal (volumetric) dimension |
| $D_{\mathrm{I}}$, $D_{\mathrm{I}}(\Delta\xi)$ | structure function of the fluctuation intensity component |
| $d_{\mathrm{p}}$ | length of the space where the exciting and the probe laser beams are overlapped, cm |
| $d_{\mathrm{s}}$ | mean distance between the centers of gravity of the particles |
| $D_{\mathrm{T}}$ | coefficient of translation diffusion |
| $D_{\mathrm{Tf}}$ | coefficient of translation diffusion for fast process |

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|---|---|
| $D_{\mathrm{Ts}}$ | coefficient of translation diffusion for slow process |
| $D_{\mathrm{V}}$ | diameter of a microvessel |
| $d\bar{n}/\mathrm{d}\lambda$ | material dispersion, 1/nm |
| $dn/\mathrm{d}T$ | medium (tissue) refractive index temperature gradient, 1/°C |
| DPF | differential path length factor accounting for the increase in photon migration paths attributable to scattering |
| $dS$ | thermoelastic deformation, cm |
| $E$ | incident pulse energy, J |
| $E$ | electron charge |
| $E_0$ | incident laser pulse energy at the sample surface ($\mathrm{J/cm^2}$) |
| $E_{0\mathrm{j}}$ | scattering amplitude of an isolated particle, V/m |
| $E_{\mathrm{ref}}(\omega)$ | incident THz pulse amplitude |
| $E_{\mathrm{sample}}(\omega)$ | transmitted THz pulse amplitude |
| $\mathbf{E}_{\|\mathrm{i}}$ | electric field component of the incident light parallel to the scattering plane, V/m |
| $\mathbf{E}_{\perp\mathrm{i}}$ | electric field component of the incident light perpendicular to the scattering plane, V/m |
| $\mathbf{E}_{\|\mathrm{s}}$ | electric field component of the scattered light parallel to the scattering plane, V/m |
| $\mathbf{E}_{\perp\mathrm{s}}$ | electric field component of the scattered light perpendicular to the scattering plane, V/m |
| $\mathbf{E}_{\mathrm{s}}$ | scattered electric field vector, V/m |
| $E_{\mathrm{s}}$ | amplitude of a scattered wave, V/m |
| $E_{\mathrm{T}}$ | absorbed pulse energy, J |
| $E(0)$ | subsurface irradiance, $\mathrm{J/cm^2}$ |
| $F(\mathrm{Hct})$ | packing function of RBC |
| $F(\mathbf{r})$ | radiant flux density or irradiance, $\mathrm{W/cm^2}$ |
| $f(t, t')$ | describes the temporal deformation of a δ-shaped pulse following its single scattering |
| $f_{1,2}$ | volume fractions of tissue components |
| $f_{\mathrm{a}}$ | frequency of acoustic oscillations, Hz |
| $f_{\mathrm{c}}$ | volume fraction of the collagen in tissue |
| $f_{\mathrm{cp}}$ | volume fraction of the fluid in the tissue contained inside the cells |
| $f_{\mathrm{cyl}}$ | surface fraction of the cylinders' faces |
| $f_{\mathrm{D}}$ | Doppler frequency |
| $f_{\mathrm{Ds}}$ | Doppler frequency shift |
| $f_{\mathrm{f}}$ | volume fraction of the fibers in the tissue |
| $f_{\mathrm{ge}}$ | oscillator strength of transition between the ground and excited states |

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| $F_{\text{int}}(\theta)$ | interference term taking into account the spatial correlation of particles |
| $f_n = g^n$ | $n$th order moment of the phase function |
| $f_{\text{nc}}$ | volume fraction of the nuclei in the tissue contained inside the cells |
| $f_{\text{or}}$ | volume fraction of the organelles in the tissue contained inside the cells |
| $f_{\text{p}}$ | pulse repetition rate |
| $f_{\text{r}}$ | fixed reference (lock-in) frequency |
| $f_{\text{RBCi}}$ | volume fraction of RBCs |
| $f_{\text{s}}$ | volume fraction of scatterers |
| $f_{\text{T}}$ | focal length of the thermal lens, cm |
| $F_{\text{v}}$ | total volume fraction of the particles |
| $f_x = (k_x/2\pi), f_y = (k_y/2\pi)$ | spatial frequencies |
| $f_\sigma$ | material fringe value |
| $F(\lambda)$ | packing factor of the particles |
| $\text{FP}(\omega)$ | reflection of pulses in a parallel plate: Fabry–Perot modes |
| $G$ | domain where radiative transport is examined |
| $G(f)$ | power spectrum with a Gaussian shape |
| $g$ | scattering anisotropy factor [mean cosine of the scattering angle $\theta$, $<\cos(\theta)>$] |
| $g_1(\tau)$ | first-order autocorrelation function (normalized autocorrelation function of the optical field) |
| $g_2(\Delta\xi)$ | normalized autocorrelation function of intensity fluctuations |
| $G_1(\tau)$ | autocorrelation function of the scalar electric field, $E(t)$, of the scattered light |
| $G_2(\tau)$ | autocorrelation function of intensity fluctuations |
| $\tilde{G}_2(\Delta\xi)$ | autocorrelation function of the fluctuation intensity component |
| $\tilde{g}_2$ | normalized autocorrelation function of the fluctuation intensity component |
| $g(r)$ | radial distribution function of scattering centers (local-to-average density ratio for scattering centers) |
| $G(r)$ | binary density–density correlation function |
| $g_{\text{d}}$ | scattering anisotropy factor of dermis |
| $g_{\text{e}}$ | scattering anisotropy factor of epidermis |
| $G_{\text{s}}$ | attenuation factor accounting for scattering and geometry of the tissue |
| $G_{\text{V}}$ | gradient of the flow rate |
| Hct | blood hematocrit |
| $H$ | tissue hydration |

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| $H(x, y, t) = (\lambda/2\pi\Delta n)\phi(x, y, t)$ | dynamic profile of the geometric thickness of the cell |
| $h$ | Planck's constant |
| $h$ | apparent energy transfer coefficient |
| $h(x, y, t) = \int [n(x, y, z, t) - n_0]\mathrm{d}z$ | two-dimensional distribution of optical path difference |
| $H(\mathbf{r}, \bar{t})$ | heating function, defined as the thermal energy per time and volume deposited by the light source in the close proportion to the optical absorption coefficient of interest |
| Hb | hemoglobin |
| $HbO_2$ | oxyhemoglobin |
| HbR | deoxyhemoglobin |
| $h\nu$ | photon energy |
| $h(x, y)$ | spatial variations in the thickness of the RPS |
| $I(\theta)/I(0) \equiv p(\theta)$ | normalized scattering indicatrix, 1/sr |
| $I(\theta)$ | scattering indicatrix (angular dependence of the scattered light intensity), W/cm$^2$sr |
| $i = (-1)^{1/2}$ | imaginary number |
| $I_{ac}$, $I_{dc}$ | ac and dc components of diffusely reflected intensity |
| $I_{AS}$, $I_S$ | intensity of the anti-Stokes and Stokes Raman lines for a given vibration state |
| $I_F$ | fluorescence intensity |
| $I_i$ | irradiance or intensity of the incident light beam, W/cm$^2$ |
| $\langle I \rangle$ | mean value of the intensity fluctuations |
| $<i^2(z)>$ | rms of photodetector heterodyning signal of the OCT system, obtained from probing depth $z$ |
| $I$ | refers to the irradiance or intensity of the light, W/cm$^2$ |
| $I(\mathbf{r}, \mathbf{s})$ | radiance (or the specific intensity) of average power flux density at point **r** in given direction **s**, W/cm$^2$ sr |
| $I(\mathbf{r}, \mathbf{s}, t)$ | time-dependent radiance (or specific intensity), W/cm$^2$ sr |
| $I(0)$ | intensity at the center of the beam |
| $I(d)$ | intensity of light transmitted by a sample of thickness $d$ measured by using a distant photodetector with a small aperture (online or collimated transmittance), W/cm$^2$ |
| $I$, $Q$, $U$, and $V$ | Stokes parameters |

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| $I_H$, $I_V$, $I_{+45^\circ}$, $I_{-45^\circ}$, $I_R$, and $I_L$ | light intensities measured with a horizontal linear polarizer, a vertical linear polarizer, a +45 deg linear polarizer, a –45 deg linear polarizer, a right circular analyzer, and a left circular analyzer in front of the detector, respectively |
| $I_{in}(\eta_c)$ | incident radiance angular distribution |
| $I_\Sigma(\theta)$ | angular distribution of the scattered intensity of a system of $N$ particles |
| $I_\Sigma(x, y)$ | intensity of light transmitted by an RPS |
| $I_{\|\|}$ and $I_\perp$ | intensities of the transmitted (scattered) light polarized in parallel or perpendicular to linear polarization of the incident light, respectively |
| $I(\theta)$ | angular distribution of the scattered light by a particle, W/cm$^2$sr |
| $I(2\omega)$ | SHG signal intensity |
| $I_0(\lambda)$ | spectrum of the incident light |
| $I_0$ | incident light intensity, W/cm$^2$ |
| $I_b$ | intensity of the uniform background light |
| $I_c(x,y)$ | intensity of light transmitted in the forward direction (the specular component) |
| $I_{F\|\|}$ and $I_{F\perp}$ | fluorescence intensities of light polarized in parallel or perpendicular to the exciting electric field vector |
| $\hat{I}_{2f}(t)$ | TPEF instant intensity collected by the optical system |
| $\left\langle \hat{I}_{2f} \right\rangle_{CW}$ | time-averaged over any period of time $T$, the TPEF intensity per a single molecule at CW laser excitation |
| $I_{HP}(x, y, z_0)$ | intensity distribution in the hologram plane (HP) |
| $I_{par}$ and $I_{per}$ | intensity images for light polarized in parallel or perpendicular to linear polarization of the incident light, respectively |
| $I_r(r)$ and $I_s(r)$ | intensity distributions of the reference and signal fields, respectively |
| $I_R$ and $I_S$ | intensity distributions of the reference and object fields, respectively |
| $I_{rest}$ and $I_{test}$ | light intensity detected when an object is at rest (brain tissue or skeletal muscle) or test (induced brain activity, cold or visual test, or training) |
| $I_s(x, y)$ | intensity of the scattered component |
| $I_{sp}$ | mean intensity of speckles |
| $<I_{x,y}>$ | mean value of CCD intensity counts at pixel ($x$, $y$) over $n$ frames |
| $J$ | flux of matter, mol/s/cm$^2$ |

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| $J_0$ | zero-order Bessel function |
| $J_1$ | first-order Bessel function |
| $J_S$ | dissolved matter flux |
| $J_W$ | water flux |
| $k = 2\pi/\lambda$ | wavenumber |
| $k_a$ | acoustic wave vector |
| $k_{ET}$ | rate constant of nonradiative energy transfer to adjacent molecules |
| $k_F$ | rate constant of the fluorescence transition to ground state $S_0$ (including its vibrational states) |
| $K$ | image contrast |
| $K, S$ | Kubelka–Munk parameters |
| $K_\varphi(\Delta x)$ | correlation coefficient of phase fluctuations of the boundary field |
| $k_B$ | Boltzmann constant |
| $k_{bvo}$ | modification factor for reducing the crosstalk between changes in blood volume and oxygenation |
| $k_G$ | gas heat conductivity, W/K |
| $k_i(\omega)$ | imaginary part of the photon-density wave vector, 1/cm |
| $k_{IC}$ | rate constant of internal conversion to ground state $S_0$ |
| $k_{ISC}$ | rate constant of intersystem crossing from singlet to triplet state $T_1$ |
| $k_r(\omega)$ | real part of the photon-density wave vector, 1/cm |
| $k_T$ | heat conductivity, W/K |
| $K_t(x, y)$ | temporal contrast of intensity fluctuations of laser scattered light at pixel $(x, y)$ |
| $l$ | thickness of a thin membrane |
| $L$ | total mean path length of a photon, cm |
| $L$ | tissue slab thickness, cm |
| $L = D\lambda/2l$ | period of interferential fringes ($D$ is the mean distance between eye nodal plane and retina) |
| $L_D$ | phenomenological coefficient characterizing the interchange flux induced by osmotic pressure |
| $L_\phi$ | correlation length of the phase fluctuations of the scattered field |
| $l_0$ | amplitude of longitudinal harmonic vibrations |
| $L_c$ | correlation length of the inhomogeneities (random relief) |
| $l_c$ | coherence length of a light source |
| $l_d = \mu_{eff}^{-1}$ | diffusion length, cm |
| $l_e$ | depth of light penetration into a tissue |

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| $L_p$ | phenomenological coefficient indicating that volumetric flux can be induced by increasing hydrostatic pressure |
| $L_{pd}$ | phenomenological coefficient indicating, on one hand, the volumetric flux that can be induced for a membrane by osmotic pressure, and on the other, the efficiency of the separation of water molecules and dissolved matter |
| $l_{ph} = \mu_t^{-1}$ | photon mean free path, cm |
| $l_s = \mu_s^{-1}$ | scattering length, cm |
| $l_T$ | length of thermal diffusivity (thermal length), cm |
| $l_{tr} = (\mu_s' + \mu_a)^{-1}$ | photon transport mean free path (MFP), cm |
| $M$ | molecular weight |
| $M$ | optical magnification |
| $m \equiv n_s/n_0$ | relative refractive index of the scatterers |
| $M = I_1/I_0$ | intensity modulation depth, defined as the ratio between the intensity at the fundamental frequency, $I_1$, and the unmodulated intensity, $I_0$ |
| $\mathbf{M}$ | normalized 4 × 4 scattering matrix (intensity or Mueller's matrix) (LSM) |
| $M_0$ | zero moment of the power density spectrum, $S(\nu)$, of the intensity fluctuations |
| $M_1$ | first moment of the power density spectrum, $S(\nu)$, of the intensity fluctuations |
| $M_{ac}(x, f_x)$ | amplitude envelope of the reflected photon density standing wave at frequency $f_x$ |
| $M_{dc}(x)$ | spatially varying dc amplitude |
| $m_I$ | intensity modulation depth of the incident light |
| $M_{ij}$ | LSM elements, $i, j = 1–4$, 16 elements |
| $\overline{M}_{ij}$ | LSM element normalized to the first element |
| $M_{ij}{}^0$ | LSM elements of an isolated particle |
| $m_{RBC}$ | relative index of refraction of RBC |
| $M_q$ | mass of the charge of the molecule capable for oscillations at its own frequency at light excitation |
| $m_t$ | amount of dissolved matter at moment $t$ |
| $m_\infty$ | amount of dissolved matter at the equilibrium state |
| $m_U \equiv ac_{detector}/dc_{detector}$ | modulation depth of scattered light intensity |
| $n$ | relative mean refractive index of tissue and surrounding media |
| $n(\omega) = n'(\omega) - i{\cdot}n''(\omega)$ | complex refractive index |
| $n'(\omega)$ | real part of index of refraction |
| $n''(\omega) = \alpha(\omega){\cdot}c/\omega$ | imaginary part of index of refraction |
| $\bar{n}$ | mean refractive index of the scattering medium |

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| $N$ | number of scatterers (particles) |
| $N = \theta/2\pi$ | fringe order ($\theta$ is the optical phase) |
| $N_0$ | number of scatterers in a unit volume |
| $N_1(z) = z \cdot \mu_s^{ex}$ | average number of scattering events experienced by excitation light before it reaches the fluorophore ($z$ is the distance of fluorophore location) |
| $N_2(z) = z \cdot \mu_s^{em}$ | average number of scattering events experienced by the emitted light before it exits the medium ($z$ is the distance of fluorophore location) |
| $\bar{N}$ | outside vector normal to $\partial G$ |
| $n_{2f}$ | rate of two-photon excitation |
| $n_0$ | refractive index of ground matter |
| $\bar{n}_0$ | average background index of refraction |
| $n_c$ | refractive index of collagen fibers |
| $n_{cp}$ | refractive index of cytoplasm |
| $n_e$ | extraordinary refractive index |
| $n_f$ | refractive index of tissue fibers (collagen and elastin) |
| $n_{g0}$ | refractive index of the ground material of a tissue |
| $\bar{n}_{g1}$ | effective (mean) group refractive index of a tissue |
| $n_{g2}$ | group refractive index of the homogeneous reference medium (air) |
| $n_g$ | group refractive index |
| $n_{gs}$ | group refractive index of scatterers |
| $n_{H_2O}$ | refractive index of water |
| $N_i = f_{RBCi}/V_{RBCi}$ | number of RBCs in a unit volume of blood |
| $N_{int} = [\arcsin(\lambda/2l)]^{-1}$ | density of interferential fringes per degree of the view angle (angular resolving power of the eye or retinal visual acuity) |
| $n_{is}$ | refractive index of the ISF |
| $n_{nc}$ | refractive index of cell nucleus |
| $n_o$ | ordinary refractive index |
| $n_{or}$ | refractive index of cell organelles |
| $N_p$ | number of particle diameters |
| $n_s$ | refractive index of scattering centers (particles) |
| $\bar{n}_s$ | refractive index of a scattering particle, determined by averaging refractive indices of tissue components |
| $\bar{n}_{sc}$ | average refractive index of eye sclera |
| $N_{sp}$ | number of speckles within the receiving aperture |
| NA | numerical aperture of the objective or fiber |
| $n(x, y)$ | spatial variations in the refractive index of the random phase screen |
| $\bar{n}_t$ | average refractive index of the tissue |

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| $O(x, y, z = z_0)$ | object wave |
| OD | optical density |
| osm | osmolarity |
| $p$ | packing dimension |
| $p$ | porosity coefficient |
| $P$ | laser beam power, W |
| $P$ | induced polarization |
| $P(t)$ | instantaneous power of the radiation within illuminated area $A$ |
| $P_a$ | coefficient of permeability |
| $P_{ave} = (\tau_p \cdot f_p)P_{peak}$ | average power |
| $P_0$ | average incident power, W |
| $P_C = V/I = [Q^2 + U^2]^{1/2}/I$ | degree of circular polarization |
| $P_{FL} = (I_{F\|\|} - I_{F\perp})/(I_{F\|\|} + I_{F\perp})$ | degree of linear polarization of fluorescence |
| $P_L = (I_{\|\|} - I_\perp)/(I_{\|\|} + I_\perp)$ | degree of linear polarization |
| $P_L^r(\lambda)$ | residual polarization degree spectra |
| $P_{min}$ | minimal detectable signal power |
| $p(I)$ | intensity probability density distribution function |
| $p(s)$ | distribution function of photon migration paths in the medium |
| $p(\mathbf{s}, \mathbf{s}') = p(\theta)$ | scattering phase function (probability density function for scattering in the direction, $\mathbf{s}'$, of a photon travelling in direction $\mathbf{s}$), 1/sr |
| $p_{GK}(\theta)$ | Gegenbauer kernel phase function (GKPF) |
| $p_{HG}(\theta)$ | Henyey–Greenstein phase function (HGPF) |
| $P_{peak}$ | peak power |
| $P_R$ and $P_S$ | powers of the reference and object beams of OCT interferometer |
| PI | polarization degree image |
| $P_n^1(\cos\theta)$ | Legendre polynomials |
| $p(\Delta L)$ | probability density distribution function of relief variations |
| $p(\mathbf{r}, \bar{t})$ | acoustic wave |
| $\mathbf{P}^{(3)}$ | third-order polarization |
| $pix$ | pixel size |
| $q$ | charge of molecule capable of oscillations at its own frequency at light excitation |
| $q$ | spatial modulation frequency of fringes |
| $\mathbf{q}$ | scattering vector |
| $\|\mathbf{q}\|$ | value of scattering vector |
| $q(\mathbf{r})$ | source function (i.e., number of photons injected into the unit volume) |

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| $Q$, $U$, and $V$ | the extents of horizontal linear, 45 deg linear, and circular polarization, respectively |
| $Q_a$ | asymmetry parameter of intensity fluctuations |
| $q_b$ | blood perfusion rate (1/s), defined as the volume of blood flowing through unit volume of tissue in one second |
| $Q_s$, $Q_s(a_{sph}, n_s, n_I)$ | factor of scattering efficiency |
| $R(x, y, z = z_0)$ | reference wave |
| $r$ | transverse spatial coordinate |
| $r = \frac{I_{\|\|} - I_\perp}{I_{\|\|} + 2I_\perp}$ | polarization anisotropy |
| $r_F = (I_{F\|\|} - I_{F\perp})/(I_{F\|\|} + 2\, I_{F\perp})$ | fluorescence polarization anisotropy |
| $\mathbf{R}(\phi)$ | Stokes rotation matrix for angle $\phi$ |
| $\mathbf{r}$ | radius vector of a scatterer or a given point at which the radiance is evaluated, cm |
| $R$ | radius of membrane (of a cell or tumor necrotic core) |
| $R(z)$ | backscattering or reflectance in OCT |
| $r_{\perp\|\|}(\tau)$ | cross-correlation function (correlation coefficient) for two polarization states |
| $R_{\|\|}(\lambda)$ and $R_\perp(\lambda)$ | reflectance spectra at parallel and perpendicular orientations of polarization filters |
| $\hat{R}$ | reflection operator |
| $\bar{R}$ | $4 \times 1$ response vector corresponding to the four retarder/analyzer settings |
| $R_a$ | reflectance from the backward surface of the sample impregnated by an agent |
| $R_\theta(\lambda)$ | spectrum of light scattered under the angle $(\theta + d\theta)$ |
| $r_0$ | radius of the incident light beam, cm |
| $R_{bd}$ | distance between the axis of exciting laser beam and the acoustic detector, cm |
| $R_d$ | diffuse reflectance |
| $R_d(k)$ | diffuse reflectance of spatially modulated photon density waves |
| $R_F = [(n-1)/(n+1)]^2$ | coefficient of Fresnel reflection |
| $R_G$ | gas cell radius, cm |
| $r_h$ | hydrodynamic radius of a particle |
| $R_o$ | dimension (radius for a cylinder form) of a bio-object, cm |
| $r_p$ | radius of the pinhole |
| $r_{RBC}$ | radius of RBC |
| $r_s$ | radius of the scattered beam in the observation plane |

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| $R_s$ | reflectance from the backward surface of the control sample |
| $r_{sd}$ | distance between light source and detector at the tissue surface (source–detector separation), cm |
| $R(\eta'_c, \eta_c)$ | reflection redistribution function |
| $\tilde{R}_p(\omega)$ | complex reflection coefficient ($p$-polarization) |
| $RL(\omega)$ | reflection losses at the boundaries of the sample |
| $RT\Delta C_S$ | osmotic pressure |
| $s$ | total photon path length (or mean path length of a photon) |
| $S$ | hemoglobin oxygen saturation |
| $S$ | heat source term, W/m$^3$ |
| $S$ | sample area |
| $S_D$ | surface of detection |
| $\mathbf{S}$ | Stokes vector |
| $\mathbf{S}_s$ | Stokes vector of the scattered light |
| $\mathbf{S}_i$ | Stokes vector of the incident light |
| $\mathbf{s}$ and $\mathbf{s}'$ | directions of photon travel or unit vectors for incident and scattered waves |
| $\|s\| = 2k\sin(\theta/2)$ | magnitude of the scattering wave vector, $k = 2\pi\bar{n}/\lambda_0$ |
| $\mathbf{S}_0$ | unit vector of the direction of the incident wave |
| $\mathbf{S}_1$ | unit vector of the direction of the scattered wave |
| $S(\mathbf{r}, \mathbf{s})$ | incident light distribution at $\partial G$ |
| $S(f)$ | power spectrum of intensity fluctuations of the speckle field |
| $S(q)$ | structure factor |
| $S_3(\theta)$ | 3D structure factor |
| $S_2(\theta)$ | 2D structure factor |
| $S(\omega)$ | spectrum of intensity fluctuations |
| $S_{1-4}$ | elements of the amplitude scattering matrix (S-matrix) or Jones matrix |
| $S_r(t)$ | surface radiometric signal |
| $S(\bar{t})$ | describes the shape of the irradiating pulse |
| $sO_2$ or $SO_2$ | hemoglobin saturation with oxygen |
| $T$ | absolute temperature |
| $T$ | exposure time, s |
| $T(\mathbf{r})$ | change in tissue temperature at point $\mathbf{r}$ |
| $T(\eta'_c, \eta_c)$ | transmission redistribution function |
| $T(\omega)$ | transmission spectrum on terahertz |
| $T_0(\omega)$ | medium transmission spectrum through which the THz pulse is travelling |
| $t$ | time, s |
| $t_0$ | spatially independent amplitude transmission of the RPS |

| | |
|---|---|
| $t_1$ | first moment of the distribution function, $f(t, t')$; time interval of an individual scattering act, s |
| $t_2 = l/(\mu_t c)$ | average interval between interactions, s |
| $T_a$ | acoustic wave period |
| $T_a$ | arterial blood temperature, K |
| $t_b$ | blood temperature |
| $T_c(\lambda)$ | collimated transmission spectrum |
| $T_c$ | collimated transmittance |
| $T_d$ | diffuse transmittance |
| $T_s$ and $T_e$ | temperature of the tissue surface and environment, respectively |
| $t_s(x, y)$ | amplitude transmission coefficient of an RPS |
| $T_t = T_c + T_d$ | total transmittance |
| $T_t(\lambda)$ | total transmission spectrum |
| $T_\theta(\lambda)$ | transmission spectrum when a measuring system with a finite angle of view is used (collimated light beam with the addition of a forward-scattered light in the angle range 0 to θ is detected) |
| $U(\mathbf{r})$ | total radiant energy fluence rate, W/cm$^2$ |
| $\langle U \rangle$ | averaged amplitude of the output signal of the homodyne interferometer |
| $U_m$ | maximum of the total radiant energy fluence rate, W/cm$^2$ |
| $V$ | illuminated volume |
| $V$ | volume of the tissue sample |
| $V(t) = \int H(x, y, t)dxdy$ | momentary volume of the cell |
| $v$ | velocity of motion of the object with respect to the light beam |
| $V_C$ | volume of collagen fibers |
| $V_e$ | volume of an erythrocyte |
| $V_F$ | flow velocity |
| $V_M$ | molecular volume |
| $v_{sh}$ | shear rate |
| $\bar{V}(z)$ | contrast of average intensity fringes |
| $V_\Phi$ | phase velocity of a photon-density wave, cm/s |
| $V_0$ | contrast of the interference pattern in the initial laser beam |
| $v_a$ | velocity of acoustic waves in a medium, m/s |
| $V_I$ | contrast of the intensity fluctuations |
| $v_p$ | radius (in optical units) of conjugate pinholes of a confocal microscopic system |
| $V_P$ | contrast of the polarization image |
| $V_{RBC}$ | RBC volume, μm$^3$ |
| $V_{rms}$ | root-mean-square speed of moving particles |

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|---|---|
| $V_s$ | velocity of a moving particle |
| $\bar{V}_S$ | partial mole volumes of dissolved matter |
| $v_{sh}$ | shear rate |
| $V_V$ | parameter directly proportional to the flow velocity |
| $\bar{V}_W$ | partial mole volumes of water |
| $w$ | laser (Gaussian) beam radius (or radius of a cylinder illuminated by a laser beam), cm |
| $w_H$ | radius of the beam at $1/e$, at a probing depth of OCT in the absence of scattering, cm |
| $w_p$ | probing laser beam radius, cm |
| $w_0$ | radius of the Gaussian beam waist, cm |
| $x^0$ | fixed point at the plane where speckles are observed |
| $x = 2\pi a/\lambda$ | size (diffraction) parameter $z$ linear coordinate (depth inside the medium), cm |
| $\overline{\mathbf{Z}}$ | normalized phase matrix |
| $z_0 = (\mu_s')^{-1}$ | transport scattering length, cm |

**Greek**

| | |
|---|---|
| $\alpha(z)$ | reflectivity of the sample at depth of $z$ |
| $\alpha(\omega)$ | absorption coefficient on terahertz |
| $\alpha_{Hb}$ | spectrally dependent coefficient of the proportionality of hemoglobin imaginary refractive index on its concentration |
| $\alpha_i$ | incidence angle of the beam, angular degrees |
| $\beta$ | coefficient of volumetric expansion, 1/K |
| $\beta$ | modulation depth of photoelectric signal of the interferometer |
| $\beta$ | factor that accounts for the conversion of optical power to the photodetector current |
| $\langle\beta\rangle$ | orientation averaged first molecular hyperpolarizability |
| $\beta_{sb}$ | parameter of self-beating efficiency |
| $\Gamma$ | Grüneisen parameter (dimensionless, temperature-dependent factor proportional to the fraction of thermal energy converted into mechanical stress) |
| $\Gamma_{eff}$ | effective shear rate |
| $\Gamma_T$ | relaxation parameter |
| $\gamma = c_P/c_V$ | ratio of specific heat capacities |
| $\gamma_{11}(\Delta t)$ | degree of temporal coherence of light |
| $\Delta\psi$ | phase shift in a measuring interferometer, degrees |
| $\Delta a$ | half-width of the radii distribution |
| $\Delta E_{vib} = h\nu_{vib}$ | energy of the molecular vibration state |

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|---|---|
| $\Delta F$ | width of the averaged spectrum |
| $\Delta\tilde{k}$ | wavenumber shift |
| $\Delta L = \Delta(nh)$ | optical length (relief) variations |
| $\Delta n$ | difference in refractive indices |
| $\Delta n = (n_{\text{cell}} - n_0)$ | difference between the average refractive index of the cell and the environment |
| $\Delta n_{\text{oe}}$ | difference in refractive indices due to birefringence of form |
| $\Delta p$ | change of pressure, Pa |
| $\Delta p$ | hydrostatic pressure, Pa |
| $\Delta R^{\text{r}}(\lambda)$ | differential residual polarization spectra |
| $\Delta V$ | change of illuminated volume caused by local temperature increase, $m^3$ |
| $\Delta w$ | change of radius of a cylinder illuminated by a laser beam caused by local temperature increase, cm |
| $\Delta x$ | linear shift of the center of maximal diffuse reflection, cm |
| $\Delta z$ | longitudinal displacement of the object |
| $\Delta T$ | local temperature increase, °C |
| $\Delta T$ | optical clearing (enhancement of transmittance) |
| $\Delta x_{\text{T}}$ | amplitude of mechanical oscillations, cm |
| $<\Delta n>$ | mean refractive index variation |
| $\Delta\Phi$ | phase shift relative to the incident light modulation phase (phase lag), degrees |
| $\Delta\Phi_0$ | initial phase due to the instrumental response |
| $\Delta\phi_{HP}(x, y, z_0) =$ $\phi_R(x, y, z_0) - \phi_O(x, y, z_0)$ | phase difference between waves $O$ and $R$ in plane $z = z_0$ |
| $\Delta\theta$ | angular width of the coherent peak in backscatter, angular degrees |
| $\Delta\lambda$ | bandwidth of a light source |
| $\Delta\xi$ | change in variable |
| $\Delta\Psi_{\text{I}}(r)$ | deterministic phase difference of the interfering waves |
| $\Delta\Phi_{\text{I}}(r)$ | random phase difference |
| $\Delta\Phi_{\text{I}}(r)$ | time-dependent phase difference related to the motion of an object |
| $\Delta\varphi_s(x, y, z_0)$ | phase change attributable to the object |
| $<\Delta r^2(\tau)>$ | mean-square displacement of a particle within time interval $\tau$ |
| $\Delta T_{\text{S}}$ | temperature change of a sample, °C |
| $\Delta T_{\text{G}}$ | temperature change of a surrounding gas, °C |
| $\Delta t$ | time shift of the transmitted pulse peak |
| $\langle \Delta V^2 \rangle$ | second moment of the particle velocity distribution (mean square velocity) |

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|---|---|
| $\delta = 2\pi d\Delta n/\lambda_0$ | phase delay (retardance) of optical field |
| $\delta$ | penetration depth of the field into tissue or fluid |
| $\delta_{CCD} = pix/M$ | resolution of CCD camera |
| $\delta_F = V_F\tau_L$ | motion distortion due to cell displacement during the exposure or the time between the two probe pulses |
| $\delta_n$ and $\delta_d$ | parameters related to the average contributions per photon free path and scattering event, respectively, to the ultrasonic modulation of light intensity |
| $\delta_{oe} = 2\pi\ d\Delta n_{oe}/\lambda_0$ | phase delay of optical field due to birefringence |
| $\delta_{OPT} = 0.61\lambda/NA$ | optical resolution of the microscope objective |
| $\delta_{PT}$ | image resolution |
| $\delta_T \equiv l_T = (4a_T\tau_L)^{1/2}$ | thermal resolution |
| $\delta p(\omega)$ | amplitude of harmonically modulated pressure, Pa |
| $\delta p(t)$ | time-dependent change of pressure, Pa |
| $\partial G$ | boundary surface of domain $G$ |
| $\partial n/\partial p$ | adiabatic piezo-optical coefficient of the tissue |
| $\Delta z_{opt}$ | optical path length |
| $\epsilon(\omega)$ | dielectric function (permittivity) |
| $\epsilon_0$ | low-frequency permittivity |
| $\epsilon_{ab}$ | absorption coefficient, measured in $mol^{-1}\ cm^{-1}$ |
| $\varepsilon_\lambda^d$ | extinction coefficient of deoxyhemoglobin, measured in $mol^{-1}\ cm^{-1}$ |
| $\varepsilon_\lambda^o$ | extinction coefficient of oxyhemoglobin, measured in $mol^{-1}\ cm^{-1}$ |
| $\varepsilon_\lambda$ | extinction coefficient at wavelength $\lambda$, in $mol^{-1}\ cm^{-1}$ |
| $\varepsilon_{HbO_2}(\lambda_i)$ and $\varepsilon_{HbR}(\lambda_i)$ | molar extinction coefficients of oxyhemoglobin and deoxyhemoglobin, respectively |
| $\phi(x)$ | spatially modulated phase due to the object |
| $\phi_{O_0}(x, y, z_0)$ | phase of the object wave itself |
| $\eta$ | absolute viscosity of the medium |
| $\eta(a)$ or $\eta(2a)$ | radii ($a$) or diameter ($2a$) distribution function of scatterers |
| $\eta_c$ | cosine of the polar angle |
| $\eta_F$, $\eta = \eta(\lambda_{em})$ | fluorescence quantum yield |
| $\eta_q$ | quantum efficiency of the detector |
| $\eta'(2a)$ | correlation-corrected distribution $\eta(2a)$ |
| $\theta$ | scattering angle, angular degrees |
| $\theta_I$ | angle between the wave vectors of the interfering fields |
| $\theta_{rnd}^{GK}$ | GKPF random scattering angle |
| $\theta_{rnd}^{HG}$ | HGPF random scattering angle |

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|---|---|
| $\kappa$ | coefficient taking into account the collection efficiency of the fluorescent photons |
| $\Lambda = \frac{\sigma_{sca}}{\sigma_{ext}} = \frac{\mu_s}{\mu_t}$ | albedo for single scattering (characterizes the relation of scattering and absorption properties of a tissue) |
| $\Lambda' = \frac{\mu_s'}{\mu_a + \mu_s'}$ | transport albedo |
| $\Lambda_\Phi$ | photon-density wavelength, cm |
| $\Lambda_I$ | spacing of interference fringes |
| $\lambda = \lambda_0/\bar{n}$ | wavelength in the scattering medium, nm |
| $\lambda_0$ | wavelength of the light in vacuum, nm |
| $\lambda_{1f}$ | wavelength necessary to excite the fluorescence at single-photon absorption |
| $\lambda_2 \cong 2\lambda_{1f}$ | wavelength necessary to excite the fluorescence at two-photon absorption |
| $\lambda_{exc}$ and $\lambda_{em}$ | wavelengths of excitation and emission, respectively |
| $\lambda_p$ | wavelength of the probe beam, nm |
| $\mu_a'$ | absorption coefficient at the thermal radiation emission wavelength, 1/cm |
| $\mu_a$ | absorption coefficient, 1/cm |
| $\mu_b$ | volume-averaged backscattering coefficient, 1/cm sr |
| $\mu_{eff} = [3\mu_a(\mu_s' + \mu_a)]^{1/2}$ | effective attenuation coefficient or inverse diffusion length, 1/cm |
| $\mu_{eff}' = \sqrt{\mu_{eff}^2 + k_x^2 + k_y^2}$ | scalar attenuation coefficient of spatially modulated photon density waves |
| $\mu_{ge}$ | change in dipole moment between ground and excited states |
| $\mu_n$ | $n$-order statistical moment ($n$ = 1,2,3,. . .,) |
| $\mu_s' = (1-g)\mu_s$ | reduced (transport) scattering coefficient, 1/cm |
| $\mu_s$ | scattering coefficient, 1/cm |
| $\mu_s^{ex}$ | scattering coefficient of the excitation light, 1/cm |
| $\mu_s^{em}$ | scattering coefficient of the emitting light, 1/cm |
| $\mu_t = \mu_a + \mu_s$ | extinction coefficient (interaction or total attenuation coefficient), 1/cm |
| $\mu_{tr} = \mu_a + \mu_s'$ | transport coefficient |
| $\lvert\mu(z)\rvert$ | modulus of the transverse correlation coefficient of the complex amplitude of the scattered field |
| $\nu_I$ | exponential factor of the spatial intensity fluctuations |
| $\xi = x$ or $t$ | spatial or temporal variable |
| $\xi_I$ | characteristic depolarization length for linearly ($i = L$) and circularly ($i = C$) polarized light |
| $\rho$ | medium density, kg/m$^3$ |

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|---|---|
| $\rho$ | polarization azimuth |
| $\rho$ | distance from collimated sources |
| $\rho_a$ | volume density of absorbers, 1/cm$^3$ |
| $\rho_b$ | blood density (kg/m$^3$) |
| $\rho_G$ | gas density, kg/m$^3$ |
| $\rho_s$ | volume density of the scatterers, 1/cm$^3$ |
| $\rho(s)$ | probability density function of the optical paths |
| $\sigma$ | half-width of particle size distribution |
| $\sigma = -(L_{pd}/L_p)$ | molecular reflection coefficient |
| $(\sigma_1 - \sigma_2)$ | difference in the in-plane principle stress |
| $\sigma_2$ | two-photon absorption cross section, GM |
| $\sigma_{abs}$ | absorption cross section of a particle, cm$^2$ |
| $\bar{\sigma}_{abs}$ | specific absorption coefficient, cm$^{-1}$ |
| $\sigma_b$ | effective backscattering cross section |
| $\sigma_{ext}$ | extinction cross section of a particle, cm$^2$ |
| $\sigma_f$ | photon absorption cross section |
| $\sigma_h$ | standard deviation of the altitudes (depths) of inhomogeneities |
| $\sigma_I$ | standard deviation of the intensity fluctuations |
| $\sigma_L$ | standard deviation of relief variations (in optical lengths) |
| $\sigma_m$ | width of the skewed logarithmic distribution function for the volume fraction of particles of diameter $2a$ |
| $\sigma_s(2a_i)$ | optical cross section of an individual particle with diameter $2a_i$ and volume $v_i$, cm$^2$ |
| $\sigma_{sca}$ | scattering cross section of a particle, cm$^2$ |
| $\bar{\sigma}_{sca}$ | specific scattering coefficient, cm$^{-1}$ |
| $\Sigma_{sca}$ | scattering cross section for the system of particles, cm |
| $\sigma_\phi$ | standard deviation of the phase fluctuations of the scattered field |
| $\sigma_I^2$ | variance of the intensity fluctuations |
| $\sigma_s^2$ | spatial variance of the intensity in the speckle pattern |
| $\sigma_U^2$ | variance of the output signal of the homodyne interferometer |
| $\sigma_{x,y}$ | standard deviation of the CCD intensity counts at pixel $(x, y)$ over the $n$ frames |
| $\tau$ | delay time, s |
| $\tau$ | lifetime of the excited state, s |
| $\tau = \int_0^s \mu_t ds$ | optical thickness |
| $\tau_a = 1/\mu_a c$ | average travel time of a photon before being absorbed, s |

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|---|---|
| $\tau_c$ | correlation time of intensity fluctuations in the scattered field, s |
| $\tau_d, \tau_{oa}$ | time delay between optical and acoustical pulses, s |
| $\tau_L$ | duration of a laser pulse, s |
| $\tau_{NR}$ | nonradiative relaxation time, s |
| $\tau_p$ | pulse duration, s |
| $\tau_{PH}$ | time to response of the photodetector, s |
| $\tau_r$ | time constant of rotational diffusion, s |
| $\tau_{RT}$ | characteristic rise time, s |
| $\tau_{TA}$ | temperature-averaging time within the biological cell |
| $\tau_{th}$ | time delay for the thermal lens technique, s |
| $\tau_T$ | thermal relaxation time, s |
| $\tau_B^{-1} \equiv \Gamma_T$ | characterizes the random (Brownian) flow |
| $\tau_S^{-1} \cong 0.18 G_V \lvert\bar{q}\rvert l_{tr}$ | characterizes the directed flow |
| $\Phi(x, y)$ | random phase shift introduced by the RPS at the $(x, y)$ point |
| $\Phi_p(\omega)$ | phase lag of harmonically modulated pressure, deg |
| $\phi(t)$ | phase shift defined by a scatterer position |
| $\varphi$ | angle of observation and azimuthal angle, angular deg |
| $\varphi$ | volume fraction of particles |
| $\varphi_d$ | deflection angle of a probe laser beam, angular degrees |
| $\chi^{(n)}$ | $n$th order nonlinear susceptibility |
| $\left[\chi^{(3)}_{nonres} + \chi^{(3)}_{res}\right]$ | third-order optical susceptibility, presented as a sum of the nonresonant and resonant contributions |
| $\Psi(z)$ | heterodyne efficiency factor |
| $\Omega$ | solid angle, sr |
| $\Omega_v$ | frequency of harmonic vibrations |
| $\omega = 2\pi f$ | modulation frequency, 1/s |
| $\omega_a$ | fundamental acoustic frequency |
| $\omega_{ge}$ | energy difference between the ground and excited states |
| $\omega_p$ | packing factor of a medium filled with a volume fraction $f_s$ of scatterers |
| $(\omega t - \theta)$ | phase of the photon-density wave |

# Acronyms

| | |
|---|---|
| ac | alternating current |
| ADC | amplitude- (or analog-) digital convertor |
| AF | autocorrelation function |
| AF | autofluorescence |
| AHA | α-hydroxy acid |
| ALA | aminolevulinic acid |
| AO | acousto-optical |
| AOD | acousto-optical deflector |
| AOM | acousto-optic modulator |
| AOT | acousto-optic tomography |
| APD | avalanche photodetector |
| ALA | δ-aminolevulinic acid |
| ATR | attenuated total reflection |
| ATR-FTIR | attenuated total reflectance Fourier transform infrared |
| AW | acoustic waves |
| BEM | boundary-element method |
| BSA | bovine serum albumin |
| BW | birefringent wedges |
| CARS | coherent anti-Stokes Raman scattering |
| CBF | cerebral blood flow |
| CCD | charge-coupled device |
| CDI | coherent detection imaging |
| CEA | carotid endarterectomy |
| CFD | constant-fraction discriminator |
| CIE | Commission Internationale de l'Eclairage (the French title of the International Commission on Illumination) |
| CIN | cervical intraepithelial neoplasia |
| CIS | carcinoma *in situ* |
| CM | confocal microscopy |
| cmOCT | correlation map OCT |
| CMOS | complementary metal-oxide semiconductor |
| CNT | carbon nanotube |

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|---|---|
| CP-OCT | cross-polarization OCT |
| CPU | central processing unit |
| CRI | contrast of refractive index |
| CSF | cerebrospinal fluid |
| CT | computed tomography |
| CUDA | Compute Unified Device Architecture |
| CW | continuous wave |
| Cyt-*c* | cytochrome *c* |
| DBM | double-balanced mixer |
| dc | direct current |
| DCF | double-clad fiber |
| dcOCT | double correlation OCT |
| DCS | diffusion-correlation spectroscopy |
| DeoxyHb | deoxyhemoglobin |
| DG | delay generator |
| DHM | digital holographic microscope |
| DIS | double integrating sphere |
| DLP | digital light processing |
| DMD | digital micromirror device |
| DMSO | dimethyl sulfoxide |
| DNA | deoxyribonucleic acid |
| DOCP | degree of circular polarization |
| DOCT | Doppler OCT |
| DOLP | degree of linear polarization |
| DOP | degree of polarization |
| DOPA | 3,4-dihydroxyphenylalanine |
| DOPE | dioleoylphosphatidylethanolamine |
| DPF | differential path length factor |
| DPS OCT | differential phase-sensitive OCT |
| DPSS | diode pumped solid state |
| DT | diffusion theory |
| DTC | disseminated tumor cell |
| DWS | diffusion wave spectroscopy |
| EB | Evans Blue |
| EDL | extensor digitorum longus |
| EDTA | ethylenediaminetetraacetic acid |
| EEM | excitation–emission map |
| ENT | ear, nose, and throat |
| ESCC | esophageal squamous cell carcinoma |
| ESR | erythrocyte sedimentation rate |
| FAD | flavin dinucleotide |
| FD | frequency domain |
| FDA | Food and Drug Administration |
| FD-LUM | frequency-domain luminescence |

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|---|---|
| FD-OTR | frequency-domain OTR |
| FD-PTR-LUM | frequency-domain photothermal radiometry luminescence |
| FDPM | frequency-domain photon migration |
| FDTD | finite-difference time domain |
| FF-OCT | full-field OCT |
| FFT | fast Fourier transform |
| FG | function generator |
| FLIM | fluorescence lifetime imaging microscopy |
| FLMA | fractional laser microablation |
| FMN | flavin mononucleotide |
| FOV | field-of-view |
| FRAP | fluorescence recovery after photobleaching |
| FWHM | full-width half-maximum |
| GFP | green fluorescent protein |
| GHb | glycated hemoglobin |
| GK | Gegenbauer kernel |
| GKPF | Gegenbauer kernel phase function |
| GM | Goeppert Mayor |
| GNP | gold nanoparticle |
| GNR | gold nanorod |
| GNT | golden carbon nanotube |
| GPM | goniophotometric measurements |
| GPU | graphics processing unit |
| GRIN | gradient index |
| HCM | human cervical mucus |
| Hct | hematocrit |
| HDL | high-density lipoprotein |
| H&E | hematoxylin and eosin |
| HEM | human epidermal membrane |
| HG | Henyey−Greenstein |
| HGPF | Henyey–Greenstein phase function |
| HP | hologram plane |
| HPD | hematoporphyrin derivative |
| HPM | Hilbert phase microscopy |
| HRS | hyper-Rayleigh scattering |
| HWHM | half-width half-maximum |
| IAD | inverse adding-doubling |
| IC25 | Infracyanine 25 |
| ICG | indocyanine green |
| IF | intermediate frequency |
| IFS | interfibrillar spacing |
| IMC | inverse Monte Carlo |
| IMS | intermolecular spacing |
| IOC | immersion optical clearing |

| | |
|---|---|
| IQ | in-phase quadrature |
| IR | infrared |
| IS | integrating sphere |
| KDP | kalium dihydrophosphate |
| KMM | Kubelka–Munk model |
| LASCA | laser speckle contrast analysis |
| LAT | lung adenocarcinoma tumor |
| LBG | lung benign granulomatosis |
| LD | laser diode |
| LDA | laser Doppler anemometer |
| LDI | laser Doppler imaging |
| LDL | low-density lipoprotein |
| LDM | laser Doppler microscope |
| LED | light-emitting diode |
| LID | lattice of islet damage |
| LIPT | laser-induced pressure transient |
| LITT | laser-induced interstitial thermal therapy |
| LO | local oscillator |
| LPF | low-pass filter |
| LSCC | lung squamous cell carcinoma |
| LSI | laser speckle imaging |
| LSLO | line-scanning laser ophthalmoscope |
| LSM | light-scattering matrix |
| LSMM | laser scattering matrix meter |
| LSS | light scattering spectroscopy |
| LVDS | low-voltage differential signaling |
| MAR | modified amino resin |
| MB | methylene blue |
| MBG | mean blood glucose |
| MC | Monte Carlo |
| MCA | multi-channel analyzer |
| M-CARS | multiplex coherent anti-Stokes Raman scattering |
| MCML | Monte Carlo modeling of photon transport in multilayered tissues |
| MCP-PMT | multichannel plate-photomultiplier tube |
| MED | minimal erythema dose |
| MFP | mean free path length |
| MIM | multispectral imaging micropolarimeter |
| MIR | middle infrared |
| MNP | magnetic nanoparticle |
| MO | micro-objective |
| MONSTIR | multichannel optoelectronic near-infrared system for time-resolved image reconstruction |
| MPM | multiphoton microscopy |

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|---|---|
| MPS | maximum permissible exposure |
| MPT | multiphoton tomography |
| MR | magnetic resonance |
| MRI | MR imaging |
| MSOAT | multispectral optoacoustic tomography |
| MTF | modulation transfer function |
| MTT | meal tolerance test |
| NA | numerical aperture |
| NAD | nicotinamide adenine dinucleotide |
| $NAD^+$ | oxidized form of NAD |
| NADH, NAD·H | reduced form of NAD |
| NADP·H | reduced form of NAD phosphate |
| NIR | near infrared |
| NIRS | near infrared spectroscopy |
| NL | normal lung |
| NP | nanoparticle |
| OA | optoacoustic |
| OAT | OA tomography |
| OCA | optical clearing agent |
| OCE | optical coherence elastography |
| OCI | optical coherence interferometry |
| OCM | optical coherence microscopy |
| OCP | optical clearing potential |
| OCT | optical coherence tomography |
| OCTSS | OCT signal slope |
| OD | optical density |
| OFDI | optical frequency-domain imaging |
| OGTT | oral glucose tolerance test |
| OMA | optical multichannel analyzer |
| OMAG | optical microangiography |
| OPD | optical path difference |
| OPO | optical parametric oscillator |
| OR-PAM | optical resolution PAM |
| OT | optothermal |
| OTR | optothermal radiometry |
| OxyHb | oxyhemoglobin |
| PA | photoacoustic |
| PAM | photoacoustic microscopy |
| PBS | phosphate buffered solution |
| PC | personal computer |
| PD | photodetector |
| PDF | probability distribution function |
| PDMD | phase-delay measurement device |
| PDT | photodynamic therapy |

| | |
|---|---|
| PDWFCS | photon-density wave fluctuation correlation spectroscopy |
| PEG | polyethylene glycol |
| PG | propylene glycol |
| PHA | pulse-height analysis |
| PhS-OCT | phase-sensitive OCT |
| PhS-SSOCT | phase-stabilized swept-source OCT |
| PM | polarization-maintaining |
| PMT | photomultiplier tube |
| POS | polyorganosiloxane |
| PPG | polypropylene glycol |
| PpIX | Protoporphyrin IX |
| PRS | polarized reflectance spectroscopy |
| PSF | point-spread function |
| PS-OCT | polarization-sensitive OCT |
| PS-OLCR | phase-sensitive optical low-coherence reflectometer |
| PT | photothermal |
| PTFC | PT flow cytometry |
| PTI | PT imaging |
| PTM | PT microscopy |
| PT-OCT | photothermal OCT |
| PTR | PT radiometry |
| PVA-C | polyvinyl alcohol cryogel |
| PVDF | polyvinyldenefluoride |
| PY | Percus–Yevick |
| QD | quantum dot |
| QELS | quasi-elastic light scattering |
| RA-SHG | random access second-harmonic generation |
| RBC | red blood cell |
| RC | relative contrast |
| RCM | reflection confocal microscopy |
| RC-PACT | ring-shaped confocal photoacoustic computed tomography |
| RF | radio frequency |
| RGA | Rayleigh–Gans approximation |
| RI | refractive index |
| rms | root mean square |
| RNA | ribonucleic acid |
| RNFL | retinal nerve fiber layer |
| ROI | region of interest |
| RPS | random phase screen |
| RSODL | rapid scanning optical delay line |
| RTE | radiative transfer equation |
| RTT | radiation transfer theory |
| RTV | room-temperature vulcanizing |
| RVA | retinal visual acuity |

| | |
|---|---|
| SAW | surface acoustic wave |
| SC | stratum corneum |
| SD-OCM | spectral-domain OCM |
| SD-OCT | spectral-domain OCT |
| SEM | standard error of the mean |
| SERS | surface-enhanced Raman scattering |
| SF | spatial filter |
| SFD | spatial-frequency domain |
| SFDI | spatial frequency-domain imaging |
| SHG | second harmonic generation |
| SIV | statistical intensity variation |
| SL | sonoluminescence |
| SLD | superluminescent diode |
| SLM | spatial light modulator |
| SLN | sentinel lymph nodes |
| SLT | SL tomography |
| SMF | skeletal muscle fibers |
| SMI | spatially modulated imaging |
| SMLB | spatially modulated laser beam |
| *s*-MTF | spatial modulation transfer function |
| SNR | signal-to-noise ratio |
| SOCS | skull optical clearing solution |
| SOI | scattering orientation index |
| SPD | sonophoretic delivery |
| SPEF | single-photon excitation fluorescence |
| SPR | spatially resolved reflectance |
| SPS | spatial phase shift |
| *s*-PSF | spatial point-spread function |
| SRR | spatially resolved reflectance |
| SSB | single sideband |
| SSOCT | swept-source OCT |
| SSS | superior sagittal sinus |
| ST | *Staphylococcus* toxin |
| STFT | short time Fourier transform |
| svOCT | Speckle variance OCT |
| SWI-OCT | shear wave imaging OCT |
| TA | thermoacoustic |
| TAC | time-to-amplitude convertor |
| TD | time-domain |
| TDM | time division multiplex |
| TDM | transillumination digital microscopy |
| TEWL | transepidermal water loss |
| TGS | thermal gradient spectroscopy |
| THb | total hemoglobin |

| | |
|---|---|
| TMP | trimethylolpropanol |
| TMR | transverse microradiography |
| *t*-MTF | temporal modulation transfer function |
| TOAST | time-resolved optical absorption and scattering tomography |
| TPEF | two-photon-excited fluorescence |
| *t*-PSF | temporal point-spread function |
| TRS | time-resolved spectroscopy |
| UHP | ultra-high performance |
| US | ultrasound |
| UV | ultraviolet |
| VLDL | very low density lipoprotein |
| VOA | variable optical attenuator |
| WBC | white blood cell |
| WP | Wollaston prism |
| VRTE | vector radiative transfer equation |
| VTW | virtual transparent window |
| WDM | wavelength division multiplex |
| WHO | World Health Organization |
| WMC | “white” Monte Carlo |

# Preface to the First Edition

Many up-to-date medical technologies are based on recent progress in physics, including optics.[1–102] An interesting example relevant to the topic of this tutorial is provided by computer tomography.[1,4] X-ray, magnetic resonance, and positron-emission imaging techniques are extensively used in high-resolution studies of both anatomical structures and local metabolic processes. Another safe and technically simple tool currently in use is diffuse optical tomography.[1,3,4,6,15,28,71]

From the viewpoint of optics, biological tissues and fluids (blood, lymph, saliva, mucus, gastric juice, urine, aqueous humor, and semen) can be separated into two large classes.[1–40,40–69,92–97,101] The first class includes strongly scattering (opaque) tissues and fluids, such as skin, brain, vessel walls, eye sclera, blood, and lymph. The optical properties of these tissues and fluids can be described within the framework of a model of multiple scattering of scalar or vector waves in a randomly nonuniform absorbing medium. The second class consists of weakly scattering (transparent) tissues and fluids, such as cornea, crystalline lens, vitreous humor, and aqueous humor of the front chamber of the eye. The optical properties of these tissues and fluids can be described within the framework of a model of single scattering (or low-step scattering) in an ordered isotropic or anisotropic medium with closely packed scatterers with absorbing centers.

The vector nature of light waves is especially important for transparent tissues, although much attention has recently focused on the investigation of polarization properties of light propagating in strongly scattering media.[3,5,6,8–10,23,28,43,59–64,69,70] In scattering media, the vector nature of light waves is manifested as the polarization of an initially nonpolarized light beam or as the depolarization (generally, change in the character of polarization) of an initially polarized beam propagating in a medium. Similar to coherence properties of a light beam reflected from or transmitted through a biological object, polarization parameters of light can be employed as a selector of photons originating from different depths in an object.

The problems of optical diagnosis and spectroscopy of tissues are concerned with two radiation regimes: continuous wave and time resolved.[1,3,4,6,12,14,15,28,31,71,92] The latter is realized by means of the exposure of a scattering object to short laser pulses ($\sim 10^{-10}$ to $10^{-12}$ s) and the

subsequent recording of scattered broadened pulses (time-domain method), or by irradiation with modulated light, usually in the frequency range 50 to 1000 MHz, and recording the depth of modulation of scattered light intensity and the corresponding phase shift at modulation frequencies (frequency-domain or phase method). The time-resolved regime is based on the excitation of the photon-density wave spectrum in a strongly scattering medium, which can be described in the framework of the nonstationary radiation transfer theory (RTT). The continuous radiation regime is described by the stationary RTT.

Many modern medical technologies employ laser radiation and fiber optic devices.[1–7] Because the application of lasers in medicine has both fundamental and technical purposes, the problem of coherence is critical for the analysis of the interaction of light with tissues and cell ensembles. On one hand, this problem can be considered in terms of the loss of coherence due to the scattering of light in a randomly nonuniform medium with multiple scattering, or to the change in the statistics of speckle structures of the scattered field. On the other hand, this problem can be interpreted in terms of the appearance of an amplified, coherent, sharply directed component in backscattered radiation under conditions when a tissue is probed with an ultrashort laser pulse.[1,3,73,74] The coherence of light is of fundamental importance for the selection of photons that have experienced few or zero scattering events, as well as for the generation of speckle-modulated fields from scattering phase objects with single and multiple scattering.[1,3,75–77] Such approaches are important for coherent tomography, diffractometry, holography, photon-correlation spectroscopy, laser Doppler anemometry, and speckle interferometry of tissues and fluxes of biological fluids.[1,3,5,15,22,28,76–83] The use of optical sources with short coherence length creates new opportunities in coherent interferometry and tomography of tissues, organs, and blood flows.[1,3,8,17,18,77,84]

The transparency of tissues reaches its maximum in the near infrared (NIR), which is associated with the fact that living tissues do not contain strong intrinsic chromophores that absorb radiation within this spectral range. Light penetrates into a tissue for several centimeters, which is important for the transillumination of thick human organs (such as brain or breast). However, tissues are characterized by strong scattering of NIR radiation, which prevents one from obtaining clear images of localized inhomogeneities arising in tissues owing to various pathologies; e.g., tumor formation, local increase in blood volume caused by a hemorrhage, or growth of microvessels. Strong scattering of NIR radiation also imposes certain requirements on the power of laser radiation, which should be sufficient to ensure the detection of attenuated fluxes. Special attention in optical tomography and spectroscopy is focused on the development of methods for the selection of image-carrying photons or the detection of photons providing the information concerning the optical parameters of the scattering medium. These methods employ the results of fundamental studies devoted to the propagation of laser beams in scattering media.[1,3,4,6,15,28,31,71,92]

Another important area in which deep tissue probing is practiced is reflecting spectroscopy, e.g., optical oxymetry for the evaluation of the degree of hemoglobin

oxygenation in working muscular tissue, the diseased neonatal brain, or the active brain of adults.[1,3,4]

This tutorial is primarily concerned with recently developed light-scattering techniques for quantitative studies of tissues and cell ensembles. It discusses the results of theoretical and experimental investigations into photon transport in tissues and describes methods for solving direct and inverse scattering problems for random media with multiple scattering and quasi-ordered media with single scattering, to model different types of tissue behavior. The theoretical consideration is based on stationary and nonstationary radiation transfer theories for strongly scattering tissues, Mie theory for transparent tissues, and the numerical Monte Carlo method, which is employed for the solution of direct and inverse problems of photon transport in multilayered tissues with complicated boundary conditions.

These are general approaches extensible to the examination of a large number of abiological scattering media. Many known methods of scattering media optics (e.g., the integrating sphere technique) were perfected when used in biomedical research. Concurrently, new measuring systems and algorithms for the solution of inverse problems have been developed that are useful for scattering media optics in general. Moreover, the improvement of certain methods was undertaken only because they were needed for tissue studies; this is especially true of the diffuse photon-density wave method, which is promising for the examination of many physical systems: aqueous media, gels, foams, air, and aerosols.

Based on such fundamental optical phenomena as elastic and quasi-elastic (static and dynamic) scattering, diffraction, and interference of optical fields and photon-density waves (intensity waves), we will discuss optical methods and instruments that offering promise for biomedical applications. Among these are spectrophotometry and polarimetry; time-domain and frequency-domain spectroscopy and imaging systems; photon-correlation spectroscopy; speckle interferometry; coherent topography and tomography; phase, confocal, and heterodyne microscopy; and partial coherence interferometry and tomography.

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**Valery Tuchin**
**April 2000**

# Preface to the Second Edition

This is the second edition of the tutorial on *Tissue Optics: Light Scattering Methods and Instruments for Medical Diagnosis*, first published in 2000. The last seven years since the printing of the first edition of the book have seen intensive growth of research and development into tissue optics, particularly in the field of tissue diagnostics and imaging.[103–144] Further developments in light-scattering techniques have been made for the quantitative evaluation of optical properties of normal and pathological tissues and cell ensembles. New results on theoretical and experimental investigations into light transport in tissues have been found, as have methods for solving direct and inverse scattering problems for quasi-ordered media and random media with multiple scattering. A few specific fields, such as optical coherence tomography (OCT),[108–111,115,116,126,127,129,130,136,142] and polarization-sensitive technologies,[129,130,135,136,138,139] which are very promising for optical medical diagnostics and imaging, have developed rapidly over the last few years. The optical clearing method, based on reversible reduction of tissue scattering through refractive index matching of scatterers and ground matter, has also been of great interest for research and application since the last edition.[129,132,136,139,140] Further developments in Raman and vibrational spectroscopies[104,105,123,130,132,136,143] and multiphoton microscopy[114,119,122,130,132,136,137] applied to morphology and the functioning of living cells and tissues have been provided by many research groups.

This new edition of this book is conceptually the same as the first. It is also divided into two parts: Part I describes the fundamentals and basic research of tissue optics, and Part II presents optical and laser instrumentation and medical applications. The author has corrected misprints, updated the references, and added some new results, primarily on measurements of tissue optical properties (Chapter 2) and polarized light interaction with turbid tissues (Section 1.4). Recent results on polarization imaging and spectroscopy techniques (Chapter 7), and on OCT developments and applications (Chapter 9) are also overviewed. Materials on controlling tissue optical properties (Chapter 5) and optothermal and optoacoustic interactions of light with tissues (Section 1.5) are updated. Brief descriptions of fluorescent, nonlinear, and inelastic light scattering spectroscopies are provided in Chapter 1.

I am grateful to Sharon Streams for her suggestion to prepare the second edition of the tutorial and for her assistance in editing of the book. I also would like to thank Merry Schnell for her assistance on the final stage of book editing and production.

I am very thankful to attendees of my short courses "Coherence, Light Scattering, and Polarization Methods and Instruments for Medical Diagnosis," "Tissue Optics and Spectroscopy," "Tissue Optics and Controlling of Tissue Optical Properties," and "Optical Clearing of Tissues and Blood," which I have given during SPIE Photonics West Symposia, SPIE/OSA European Conferences on Biomedical Optics, and OSA CLEO/QELS Conferences over the last seven years, for their stimulating questions, fruitful discussions, and critical evaluations of presented materials. Their responses were very valuable for preparation of this edition. My joint chairing with Joseph A. Izatt and James G. Fujimoto of the SPIE Conference on Coherence Domain Optical Methods and Optical Coherence Tomography in Biomedicine also was very helpful.

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**Valery Tuchin**
**June 2007**

# Preface to the Third Edition

The idea to publish the third edition of this book was stimulated by several factors and strongly supported by SPIE Press staff. A couple of years ago, SPIE Press received requests to republish this book in Russian by Fizmatlit Publishers (Moscow) and in Japanese by Optronics (Tokyo). Since the second edition of the English language book was issued seven years ago, and accounting for rapid developments in the field of tissue optics and corresponding optical medical instrumentation, the author offered to provide the further updates of this book to SPIE Press before its translation. In addition, the book structure was changed to provide more convenient and readable presented materials. The third edition contains 14 chapters instead of 9, as in the second edition. In addition, chapters related to optical coherence tomography, digital holography and interferometry, controlling of optical properties of tissues, nonlinear spectroscopy, and imaging were substantially updated.

Since the second edition of *Tissue Optics*, many other monographs, special issues of journals, and conference proceedings have been published related to tissue optics and biophotonics. This highlights the urgency of this research field and education, as well as the growing market for biomedical optics, medical lasers and fibers, optical biosensors, high-speed digital cameras, other devices for medical diagnostics and treatment, and skill training.[6,116,118,137,145–210] These books and journals address similar issues to those discussed in this monograph; in many ways, they are essentially complementary to *Tissue Optics* and can be recommended for more in-depth study of selected topics.

The previous editions of *Tissue Optics* contained two glossaries on (1) physics, statistics, and engineering; and (2) medicine, biology, and chemistry. These glossaries have been considerably updated and were recently published as a separate book, V.V. Tuchin, *Dictionary of Biomedical Optics and Photonics*, SPIE Press (2012) (see Ref. 210). Therefore, the third edition does not contain Glossaries because the reader can use this published dictionary instead.

The book is intended for researchers, teachers, and graduate and undergraduate students specializing in the physics of living systems, biomedical optics and biophotonics, laser biophysics, and applications of lasers in biomedicine. This

monograph can be useful as a textbook for students of physical, engineering, biological, and medical specialties.

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