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

$2l$	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

C_1 and C_2	concentrations of molecules in two spaces separated by a membrane
$C_a(x, t)$	concentration of the agent
C_{a0}	initial concentration of the agent
c_{ab}	concentration of absorber in μmol, mmol, or mol
c_b	blood specific heat, J/kgK
C_{Hb}	hemoglobin concentration
$C_f(x, t)$	fluid concentration
c_P	specific heat capacity for a constant pressure, J/kgK
c_s	relative concentration of the scattering centers
$\bar{C}_S$	average concentration of dissolved matter in two interacting solutions
c_V	specific heat capacity for a constant volume, J/kgK
C_n^{α}	Gegenbauer polynomials
$\langle C \rangle$	average blood concentration
$\langle C \rangle V_{rms}$	blood flux or perfusion
$D = z\lambda/\pi L_{\varphi}^2$	wave parameter
D	photon diffusion coefficient, cm^2/s
D_A	diattenuation (linear dichroism)
D_a	agent diffusion coefficient, cm^2/s
D_B	coefficient of Brownian diffusion, cm^2/s
D_f	fluid coefficient of diffusion, cm^2/s
$D_{media}\ (\lambda)$	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_{av}	average size of a speckle in the far-field zone
D_f	fractal (volumetric) dimension
D_I, $D_I(\Delta\xi)$	structure function of the fluctuation intensity component
d_p	length of the space where the exciting and the probe laser beams are overlapped, cm
d_s	mean distance between the centers of gravity of the particles
D_T	coefficient of translation diffusion
D_{Tf}	coefficient of translation diffusion for fast process

D_{Ts}	coefficient of translation diffusion for slow process
D_{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_{s}	amplitude of a scattered wave, V/m
E_{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_{a}	frequency of acoustic oscillations, Hz
f_{c}	volume fraction of the collagen in tissue
f_{cp}	volume fraction of the fluid in the tissue contained inside the cells
f_{cyl}	surface fraction of the cylinders' faces
f_{D}	Doppler frequency
f_{Ds}	Doppler frequency shift
f_{f}	volume fraction of the fibers in the tissue
f_{ge}	oscillator strength of transition between the ground and excited states

$F_{\text{int}}(\theta)$	interference term taking into account the spatial correlation of particles
$f_n = g^n$	nth order moment of the phase function
f_{nc}	volume fraction of the nuclei in the tissue contained inside the cells
f_{or}	volume fraction of the organelles in the tissue contained inside the cells
f_{p}	pulse repetition rate
f_{r}	fixed reference (lock-in) frequency
f_{RBCi}	volume fraction of RBCs
f_{s}	volume fraction of scatterers
f_{T}	focal length of the thermal lens, cm
F_{v}	total volume fraction of the particles
$f_x = (k_x/2\pi), f_y = (k_y/2\pi)$	spatial frequencies
f_σ	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 θ, $<\cos(\theta)>$]
$g_1(\tau)$	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_{d}	scattering anisotropy factor of dermis
g_{e}	scattering anisotropy factor of epidermis
G_{s}	attenuation factor accounting for scattering and geometry of the tissue
G_{V}	gradient of the flow rate
Hct	blood hematocrit
H	tissue hydration

$H(x, y, t) = (\lambda/2\pi\Delta n)\phi(x, y, t)$	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^2sr
$i = (-1)^{1/2}$	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 $\mathbf{r}$ in given direction $\mathbf{s}$, 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

I_H, I_V, I_{+45°, I_{-45°, 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

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_ϕ	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

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_∞	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

N	number of scatterers (particles)
$N = \theta/2\pi$	fringe order (θ 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 ∂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

$O(x, y, z = z_0)$	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)

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 ϕ
$\mathbf{r}$	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
$\bar{R}$	4×1 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

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 ∂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_Φ	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

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
α_{Hb}	spectrally dependent coefficient of the proportionality of hemoglobin imaginary refractive index on its concentration
α_i	incidence angle of the beam, angular degrees
β	coefficient of volumetric expansion, 1/K
β	modulation depth of photoelectric signal of the interferometer
β	factor that accounts for the conversion of optical power to the photodetector current
$\langle\beta\rangle$	orientation averaged first molecular hyperpolarizability
β_{sb}	parameter of self-beating efficiency
Γ	Grüneisen parameter (dimensionless, temperature-dependent factor proportional to the fraction of thermal energy converted into mechanical stress)
Γ_{eff}	effective shear rate
Γ_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
Δa	half-width of the radii distribution
$\Delta E_{vib} = h\nu_{vib}$	energy of the molecular vibration state

ΔF	width of the averaged spectrum
$\Delta\tilde{k}$	wavenumber shift
$\Delta L = \Delta(nh)$	optical length (relief) variations
Δn	difference in refractive indices
$\Delta n = (n_{\text{cell}} - n_0)$	difference between the average refractive index of the cell and the environment
Δn_{oe}	difference in refractive indices due to birefringence of form
Δp	change of pressure, Pa
Δp	hydrostatic pressure, Pa
$\Delta R^{\text{r}}(\lambda)$	differential residual polarization spectra
ΔV	change of illuminated volume caused by local temperature increase, m^3
Δw	change of radius of a cylinder illuminated by a laser beam caused by local temperature increase, cm
Δx	linear shift of the center of maximal diffuse reflection, cm
Δz	longitudinal displacement of the object
ΔT	local temperature increase, °C
ΔT	optical clearing (enhancement of transmittance)
Δx_{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 τ
ΔT_{S}	temperature change of a sample, °C
ΔT_{G}	temperature change of a surrounding gas, °C
Δt	time shift of the transmitted pulse peak
$\langle \Delta V^2 \rangle$	second moment of the particle velocity distribution (mean square velocity)

$\delta = 2\pi d\Delta n/\lambda_0$	phase delay (retardance) of optical field
δ	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
δ_n and δ_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
δ_{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
∂G	boundary surface of domain G
$\partial n/\partial p$	adiabatic piezo-optical coefficient of the tissue
Δz_{opt}	optical path length
$\epsilon(\omega)$	dielectric function (permittivity)
ϵ_0	low-frequency permittivity
ϵ_{ab}	absorption coefficient, measured in $mol^{-1}\ cm^{-1}$
ε_λ^d	extinction coefficient of deoxyhemoglobin, measured in $mol^{-1}\ cm^{-1}$
ε_λ^o	extinction coefficient of oxyhemoglobin, measured in $mol^{-1}\ cm^{-1}$
ε_λ	extinction coefficient at wavelength λ, 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
η	absolute viscosity of the medium
$\eta(a)$ or $\eta(2a)$	radii (a) or diameter ($2a$) distribution function of scatterers
η_c	cosine of the polar angle
η_F, $\eta = \eta(\lambda_{em})$	fluorescence quantum yield
η_q	quantum efficiency of the detector
$\eta'(2a)$	correlation-corrected distribution $\eta(2a)$
θ	scattering angle, angular degrees
θ_I	angle between the wave vectors of the interfering fields
θ_{rnd}^{GK}	GKPF random scattering angle
θ_{rnd}^{HG}	HGPF random scattering angle

κ	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
Λ_Φ	photon-density wavelength, cm
Λ_I	spacing of interference fringes
$\lambda = \lambda_0/\bar{n}$	wavelength in the scattering medium, nm
λ_0	wavelength of the light in vacuum, nm
λ_{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
λ_{exc} and λ_{em}	wavelengths of excitation and emission, respectively
λ_p	wavelength of the probe beam, nm
μ_a'	absorption coefficient at the thermal radiation emission wavelength, 1/cm
μ_a	absorption coefficient, 1/cm
μ_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
μ_{ge}	change in dipole moment between ground and excited states
μ_n	n-order statistical moment (n = 1,2,3,. . .,)
$\mu_s' = (1-g)\mu_s$	reduced (transport) scattering coefficient, 1/cm
μ_s	scattering coefficient, 1/cm
μ_s^{ex}	scattering coefficient of the excitation light, 1/cm
μ_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
ν_I	exponential factor of the spatial intensity fluctuations
$\xi = x$ or t	spatial or temporal variable
ξ_I	characteristic depolarization length for linearly ($i = L$) and circularly ($i = C$) polarized light
ρ	medium density, kg/m^3

ρ	polarization azimuth
ρ	distance from collimated sources
ρ_a	volume density of absorbers, $1/cm^3$
ρ_b	blood density (kg/m^3)
ρ_G	gas density, kg/m^3
ρ_s	volume density of the scatterers, $1/cm^3$
$\rho(s)$	probability density function of the optical paths
σ	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
σ_2	two-photon absorption cross section, GM
σ_{abs}	absorption cross section of a particle, cm^2
$\bar{\sigma}_{abs}$	specific absorption coefficient, cm^{-1}
σ_b	effective backscattering cross section
σ_{ext}	extinction cross section of a particle, cm^2
σ_f	photon absorption cross section
σ_h	standard deviation of the altitudes (depths) of inhomogeneities
σ_I	standard deviation of the intensity fluctuations
σ_L	standard deviation of relief variations (in optical lengths)
σ_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
σ_{sca}	scattering cross section of a particle, cm^2
$\bar{\sigma}_{sca}$	specific scattering coefficient, cm^{-1}
Σ_{sca}	scattering cross section for the system of particles, cm
σ_ϕ	standard deviation of the phase fluctuations of the scattered field
σ_I^2	variance of the intensity fluctuations
σ_s^2	spatial variance of the intensity in the speckle pattern
σ_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
τ	delay time, s
τ	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

τ_c	correlation time of intensity fluctuations in the scattered field, s
τ_d, τ_{oa}	time delay between optical and acoustical pulses, s
τ_L	duration of a laser pulse, s
τ_{NR}	nonradiative relaxation time, s
τ_p	pulse duration, s
τ_{PH}	time to response of the photodetector, s
τ_r	time constant of rotational diffusion, s
τ_{RT}	characteristic rise time, s
τ_{TA}	temperature-averaging time within the biological cell
τ_{th}	time delay for the thermal lens technique, s
τ_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
φ	angle of observation and azimuthal angle, angular deg
φ	volume fraction of particles
φ_d	deflection angle of a probe laser beam, angular degrees
$\chi^{(n)}$	nth 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
Ω	solid angle, sr
Ω_v	frequency of harmonic vibrations
$\omega = 2\pi f$	modulation frequency, 1/s
ω_a	fundamental acoustic frequency
ω_{ge}	energy difference between the ground and excited states
ω_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

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

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

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
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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
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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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