Tutorial on Biomedical Optics

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Homework solutions available to instructors

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Chapters

1. Introduction to biomedical optics
2. Single scattering: Rayleigh theory and Mie theory
3. Monte Carlo modeling of photon transport
4. Convolution for broad-beam responses
5. Radiative transfer equation and diffusion theory
6. Hybrid model of Monte Carlo method and diffusion theory
7. Sensing of optical properties and spectroscopy
8. Ballistic imaging and microscopy
9. Optical coherence tomography
10. Mueller optical coherence tomography
11. Diffuse optical tomography
12. Photoacoustic tomography
13. Ultrasound-modulated optical tomography
Motivation for Biomedical Optics

1. Optical photons provide nonionizing and safe radiation for medical applications.

2. Optical spectra--based on absorption, fluorescence, or Raman scattering--provide biochemical information because they are related to molecular conformation.

3. Optical absorption, in particular, reveals angiogenesis and hypermetabolism, both of which are hallmarks of cancer; the former is related to the concentration of hemoglobin and the latter to the oxygen saturation of hemoglobin. Therefore, optical absorption provides contrast for functional imaging.

4. Optical scattering spectra provide information about the size distribution of optical scatterers, such as cell nuclei.

5. Optical polarization provides information about structurally anisotropic tissue components, such as collagen and muscle fiber.

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6. Optical frequency shifts due to the optical Doppler effect provide information about blood flow.

7. Optical properties of targeted contrast agents provide contrast for the molecular imaging of biomarkers.

8. Optical properties or bioluminescence of products from gene expression provide contrast for the molecular imaging of gene activities.


10. Optical transparency in the eye provides a unique opportunity for high-resolution imaging of the retina.
Optical Properties of Biological Tissue

- Basic properties
  - $n \, [-]:$ index of refraction; e.g., 1.37
  - $\mu_a \, [cm^{-1}]:$ absorption coefficient; e.g., 0.1
  - $\mu_s \, [cm^{-1}]:$ scattering coefficient; e.g., 100
  - $g \, [-]:$ scattering anisotropy, $<\cos\theta>$; e.g., 0.9

- Derived properties
  - $\mu_t \, [cm^{-1}]:$ total interaction (extinction) coefficient, $\mu_a + \mu_s$
  - $l_t \, [cm]:$ mean free path, $1/\mu_t$; e.g., 0.1 mm
  - $\mu_s' \, [cm^{-1}]:$ reduced scattering coefficient, $\mu_s(1 - g)$
  - $\mu_t' \, [cm^{-1}]:$ transport interaction coefficient, $\mu_a + \mu_s'$
  - $l_t' \, [cm]:$ transport mean free path, $1/\mu_t'$; e.g., 1 mm
  - $\mu_{eff} \, [cm^{-1}]:$ effective attenuation coefficient, $(3\mu_a \mu_t')^{1/2}$
  - $\delta \, [cm]:$ penetration depth, $1/(3\mu_a \mu_t')^{1/2}$; e.g., 5 mm

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Beer's Law

\[-\frac{dI}{I} = \mu_t \frac{dx}{dx}\]

\[I(x) = I(0)\exp(-\mu_t x) = I(0)\exp(-x/l_t)\]

- \(I\): ballistic intensity
- \(x\): pathlength
- \(\mu_t\): total interaction (extinction) coefficient
Spectra of Major Biological Absorbers

Near IR window: ~700 nm

• HbO₂
• Melanin
• Water

~1 µm penetration

2.95 µm

Absorption coefficient (cm⁻¹)

Wavelength (nm)
Near Infrared Window Near 700 nm

Absorption Coefficient (cm⁻¹)

Wavelength (nm)

- 7% Blood
- 75% Water
- Total

700 nm
Absorption Spectra of Pure Blood

- Soret band (420 nm) with approximately 3 µm penetration
- Q-band (540–580 nm) with approximately 30 µm penetration

100% deoxygenated
100% oxy
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Rayleigh Theory: Small Scatterer \((ka << 1)\)

Scattered intensity (unpolarized): 
\[ I(r, \theta) = \frac{(1 + \cos^2 \theta) k^4 |\alpha|^2}{2r^2} I_0 \]

\(r, \theta\): radial distance and polar angle of observation point

\(k = \frac{2\pi n_b}{\lambda}\): propagation constant

\(\alpha = \frac{n_{rel}^2 - 1}{n_{rel}^2 + 2} a^3\): polarizability

\(n_{rel} = n_s / n_b\): relative refractive index between sphere and background

\(a\): radius of scatterer

\(x = ka\)

Scattering efficiency: 
\[ Q_s = \frac{\sigma_s}{\pi a^2} = \frac{8x^4}{3} \left| \frac{n_{rel}^2 - 1}{n_{rel}^2 + 2} \right|^2 \]

Scattering cross section: 
\[ \sigma_s = Q_s \pi a^2 \]

Scattering anisotropy: 
\[ g = 0 \]

Scattering coefficient: 
\[ \mu_s = N_s \sigma_s, N_s = \text{density of scatterers} \]
Scattering efficiency:

\[ Q_s = \frac{2}{x^2} \sum_{l=1}^{\infty} (2l + 1) \left( |a_l|^2 + |b_l|^2 \right) \]

Scattering anisotropy:

\[ g = \frac{4}{Q_s x^2} \sum_{l=1}^{\infty} \left[ \frac{l(l + 2)}{l + 1} \text{Re}(a_l a_{l+1}^* + b_l b_{l+1}^*) + \frac{2l + 1}{l(l + 1)} \text{Re}(a_l b_{l+1}^*) \right] \]

...
Mie Theory: Plot of Scattering Efficiency

Scattering efficiency $Q_s$

$\frac{x}{ka}$

Rayleigh approximation

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Mie Theory: Plot of Scattering Anisotropy

\[ x = ka \]

Anisotropy \( g \)

\( 10^{-1} \) \( 10^{0} \) \( 10^{1} \) \( 10^{2} \) \( 10^{3} \)

\( 0.1 \) \( 0.2 \) \( 0.3 \) \( 0.4 \) \( 0.5 \) \( 0.6 \) \( 0.7 \) \( 0.8 \) \( 0.9 \) \( 1.0 \)
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Sampling Random Variable: Inverse Distribution Method

\[ \int_a^\chi p(\chi)\,d\chi = \xi \]

\[ P(\chi) = \xi \]
Cumulative distribution function of step size:

\[ P(s) = 1 - \exp(-\mu_t s) \]

Inverse distribution method:

\[ 1 - \exp(-\mu_t s) = \xi \]

Sampled step size:

\[ s = -\frac{\ln(1 - \xi)}{\mu_t} \quad \text{or} \quad s = -\frac{\ln(\xi)}{\mu_t} \]
Sampling Scattering Angle

Henyey-Greenstein phase function:

\[ p(\cos \theta) = \frac{1 - g^2}{2(1 + g^2 - 2g \cos \theta)^{3/2}} \]

Sampled scattering angle:

\[
\cos \theta = \begin{cases} 
\frac{1}{2g} \left[ 1 + g^2 - \left( \frac{1 - g^2}{1 - g + 2g\xi} \right)^2 \right] & \text{if } g \neq 0 \\
2\xi - 1 & \text{if } g = 0 
\end{cases}
\]
Launch photon (dimensionless \( s_0 = 0 \))

Set new \( s_\) if \( s_0 = 0 \)

\( s_\) = \(- \ln(\xi)\)

Find distance to boundary \( d_b \)

Hit boundary: \( d_b \mu_i \leq s \) ?

\[ \begin{align*}
&\text{Y} \\
&\text{N} \\
&\text{Y} \\
&\text{N} \\
&\text{Y} \\
&\text{N} \\
&\text{Y} \\
&\text{N} \\
&\text{Y}
\end{align*} \]

Moves \( s_\) / \( \mu_i \)

Absorb

Scatter

Move \( d_b \)

\[ s_\) = s_\) - \( d_b \mu_i \]

Transmit/reflect

Photon dead?

Weight small?

Survive roulette?

Last photon?

End
Physical Meaning of Penetration Depth

![Graph showing the wide source with a penetration depth δ and the fluence depth where 1/e = 36.7%]

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Scattering Enhanced Internal Light Fluence

- Wide Source
- Source fluence
- Enhanced fluence

Depth [cm]

Internal Fluence [J/cm²]
Transition from Ballistic to Diffusive Regimes

Simulation software MCML available from http://oilab.seas.wustl.edu

Cloud center:

\[ z_c = l'_t \left[ 1 - \exp\left( -ct / l'_t \right) \right] \]

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Convolution is applicable to a system that is:
- Stationary (time-invariant)
- Linear
- Translation-invariant (shift-invariant).

\[
C(x, y, z) = \int_{-\infty}^{\infty} \int_{-\infty}^{\infty} G(x - x', y - y', z)S(x', y')dx'dy'
\]

- \(G\): impulse response to pencil beam
- \(S\): broad-beam source
- \(C\): broad-beam response

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Fluence Distribution: Pencil Beam vs Gaussian Beam

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Physical Quantities

Radiance \([Wm^{-2}sr^{-1}]\): 
\[
L(\vec{r}, \hat{s}, t) = \frac{dE}{(\hat{s} \cdot \hat{n})dAd\Omega dt}
\]

Fluence rate \([Wm^{-2}]\): 
\[
\Phi(\vec{r}, t) = \int L(\vec{r}, \hat{s}, t)d\Omega
\]

Fluence \([Jm^{-2}]\): 
\[
F(\vec{r}) = \int_{-\infty}^{+\infty} \Phi(\vec{r}, t)dt
\]

Current density \([Wm^{-2}]\): 
\[
\vec{J}(\vec{r}, t) = \int \hat{s}L(\vec{r}, \hat{s}, t)d\Omega
\]

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Radiative Transfer Equation (Boltzmann Equation)

\[
\frac{\partial L(\vec{r},\hat{s},t)}{\partial t} = -\hat{s} \cdot \nabla L(\vec{r},\hat{s},t) - \mu_t L(\vec{r},\hat{s},t) + \mu_s \int_{4\pi} L(\vec{r},\hat{s}',t)P(\hat{s}' \cdot \hat{s})d\Omega' + S(\vec{r},\hat{s},t)
\]

Change rate of energy density

\{Dimension of \( L/c = J \, m^{-3} \, sr^{-1} \}\}

Divergence

Extinction

Scattering contribution

Source
**Diffusion Theory**

Diffusion expansion of radiance:

\[ L(\vec{r}, \hat{s}, t) = \frac{1}{4\pi} \Phi(\vec{r}, t) + \frac{3}{4\pi} \vec{J}(\vec{r}, t) \cdot \hat{s} \]

Fick's law: \[ \vec{J}(\vec{r}, t) = -D \nabla \Phi(\vec{r}, t) \]

Diffusion coefficient: \[ D = \frac{1}{3(\mu_a + \mu_s')} \]

Diffusion equation:

\[ \frac{\partial \Phi(\vec{r}, t)}{\partial t} = \nabla \cdot \left[ -D \nabla \Phi(\vec{r}, t) \right] \]

\[ -\nabla \cdot [D \nabla \Phi(\vec{r}, t)] \]

Change rate of energy density

\[ \left\{ \text{Dimension of } \Phi/c = \text{J m}^{-3} \right\} \]

\[ -\mu_a \Phi(\vec{r}, t) \]

Absorption

\[ + S(\vec{r}, t) \]

Source

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Impulse Responses

\[ \Phi(\vec{r}, t) = \frac{c}{(4\pi Dct)^{3/2}} \exp \left( - \frac{r^2}{4Dct} - \mu_a ct \right) \]

\[ \int \Phi(\vec{r}, t) d\vec{r} = c \exp(-\mu_a ct) \]

\[ \Phi(\vec{r}) = \frac{1}{4\pi Dr} \exp(-\mu_{eff} r) \]

Effective attenuation coefficient: \( \mu_{eff} = \sqrt{\frac{\mu_a}{D}} \)

\[ \Phi_{1D}(z) = \frac{\mu_{eff}}{2\mu_a} \exp(-\mu_{eff} |z|) \]

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Boundary Condition

\[
\int_{\hat{s} \cdot \hat{n} > 0} L(\vec{r}, \hat{s}, t) \hat{s} \cdot \hat{n} d\Omega = 0
\]

In diffusion approximation:
\[
\Phi(\vec{r}, t) - 2D \frac{\partial \Phi(\vec{r}, t)}{\partial z} = 0
\]

Extrapolated boundary:
\[
\Phi(z = -2D, t) = \Phi(z = 0, t) - 2D \frac{\partial \Phi(\vec{r}, t)}{\partial z} \bigg|_{z=0} = 0
\]

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Diffuse Reflectance

(a) Pencil beam

(b) Similarity relation

(c) Isotropic source

(d) Extrapolated boundary & Method of image

\[ \mu_a = \mu_{a1} \]
\[ \mu_s = \mu_{s1} (1 - g_1) \]
\[ g_2 = 0 \]

\[ I_t' \]

\[ I_t' + 2z_b \]
Photon Propagation Regimes

- Mean free path: $l_t = 0.1 \, \text{mm} (0.2 \, \text{ps})$
- Transport mean free path: $l_t' = 1 \, \text{mm} (2 \, \text{ps})$

- Ballistic regime:
  - Pathlength $ct < l_t = 0.1 \, \text{mm}$
  - Probability of no scattering $> \exp(-1) = 37\%$

- Quasi-ballistic regime:
  - Pathlength $ct = l_t - l_t' = 0.1 - 1 \, \text{mm}$
  - Probability of no scattering $= \exp(-1) - \exp(-10) = 0.37 - 0.45 \times 10^{-4}$

- Quasi-diffusive regime:
  - Pathlength $ct = l_t' - 10l_t' = 1 - 10 \, \text{mm}$
  - Photon-cloud center distance to final position $= [\exp(-1) - \exp(-10)] \, l_t'$

- Diffusive regime:
  - Pathlength $ct > 10l_t' = 10 \, \text{mm}$
  - Photon-cloud center distance to final position $< \exp(-10) \, l_t'$

$P(ct) = \exp(-ct / l_t)$

$l_t' - z_c = l_t' \exp(-ct / l_t')$
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Hybrid Model for a Slab

Incident beam

Isotropic source

Scattering slab

$z_c$

$d$

$z_b$

Extrapolated boundary

$i = -1$

$i = 0$

$i = 1$

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Accuracy and Speed of Hybrid Model

<table>
<thead>
<tr>
<th>( d ) (cm)</th>
<th>( \mu_a ) (cm(^{-1}))</th>
<th>( T_{MC} ) (s)</th>
<th>( T_H ) (s)</th>
<th>( T_{MC}/T_H )</th>
</tr>
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<td>10</td>
<td>0.01</td>
<td>6684</td>
<td>23</td>
<td>291</td>
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<tr>
<td>10</td>
<td>0.1</td>
<td>2589</td>
<td>23</td>
<td>113</td>
</tr>
<tr>
<td>10</td>
<td>1</td>
<td>679</td>
<td>23</td>
<td>30</td>
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<tr>
<td>3</td>
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<td>2095</td>
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<td>91</td>
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<tr>
<td>3</td>
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<td>1961</td>
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<td>1</td>
<td>1</td>
<td>583</td>
<td>23</td>
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</table>

\( n_{rel} = 1.37 \)

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Beer's law for ballistic transmission: \( I_s = I_0 \exp(-\mu_t d) \)

Absorbance (optical density, OD = 10 dB): \( A = -\log_{10} \frac{I_s}{I_0} \)

Extinction coefficient: \( \mu_t = -\frac{1}{d} \ln \frac{I_s}{I_0} = (\ln 10) \frac{A}{d} = 2.303 \frac{A}{d} \)
Molar Extinction Spectra of Hemoglobin

Isosbestic point

<table>
<thead>
<tr>
<th>nm</th>
<th>259.93</th>
<th>339.54</th>
<th>390.01</th>
<th>422.05</th>
<th>452.36</th>
<th>500.11</th>
<th>529.24</th>
<th>545.26</th>
<th>570.18</th>
<th>584.09</th>
<th>796.80</th>
</tr>
</thead>
</table>

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Oximetry

Measured absorption coefficients:

\[ \mu_a (\lambda_1) = \ln 10 [ \varepsilon_{ox} (\lambda_1) C_{ox} + \varepsilon_{de} (\lambda_1) C_{de} ] \]

\[ \mu_a (\lambda_2) = \ln 10 [ \varepsilon_{ox} (\lambda_2) C_{ox} + \varepsilon_{de} (\lambda_2) C_{de} ] \]

Concentrations of oxygenated and deoxygenated hemoglobin:

\[ C_{ox} = \frac{1}{\ln 10} \frac{\varepsilon_{de} (\lambda_2) \mu_a (\lambda_1) - \varepsilon_{de} (\lambda_1) \mu_a (\lambda_2)}{\varepsilon_{de} (\lambda_2) \varepsilon_{ox} (\lambda_1) - \varepsilon_{de} (\lambda_1) \varepsilon_{ox} (\lambda_2)} \]

\[ C_{de} = \frac{1}{\ln 10} \frac{\varepsilon_{ox} (\lambda_1) \mu_a (\lambda_2) - \varepsilon_{ox} (\lambda_2) \mu_a (\lambda_1)}{\varepsilon_{de} (\lambda_2) \varepsilon_{ox} (\lambda_1) - \varepsilon_{de} (\lambda_1) \varepsilon_{ox} (\lambda_2)} \]

Oxygenation saturation and total concentration of hemoglobin:

\[ SO_2 = \frac{C_{ox}}{C_{ox} + C_{de}}, \quad C_{Hb} = C_{ox} + C_{de} \]
Measurement of Tissue Optical Properties

Reflectance (1/cm²) vs Horizontal Axis, x (cm)

- Monte Carlo
- Diffusion

Determined by $\delta$
Normal Versus Oblique Incidence Reflectometry

(a)

(b)

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Diffuse Reflectance: Normal vs Oblique Incidence

Reflectance [cm$^{-2}$]

Horizontal Axis x [cm]

$0^\circ$  
$45^\circ$ Shifted  
$45^\circ$

1 mfp'

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Spectroscopic Oblique Incidence Reflectometry

White-light source → Probe → Imaging spectrograph → CCD → Computer

9 collection fibers

1 source fiber

Air → Scattering medium

Q-band

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1. $100 \text{ fs} \times (3 \times 10^8 \text{ m/s}) = 30 \mu\text{m}$
2. $\exp(-\mu_t d) = \exp(-100 \times 0.3) = \exp(-30) = 120 \text{ dB}$
Spatial-frequency Filtered Imaging

(a)

Laser \rightarrow \text{Scattering medium} \rightarrow \text{Lens} \rightarrow \text{Pinhole} \rightarrow \text{Detector}

(b)

Laser \rightarrow \text{Beam expander} \rightarrow \text{Scattering medium} \rightarrow \text{Lens} \rightarrow \text{Pinhole} \rightarrow \text{Lens} \rightarrow \text{CCD}
Polarization-difference Imaging

\[ I_{//}(x, y) = I_b(x, y) + \frac{1}{2} I_{nb}(x, y) \]

\[ I_{\perp}(x, y) = \frac{1}{2} I_{nb}(x, y) \]

\( I_b \): Ballistic intensity.
Assumed polarized.

\( I_{nb} \): Non-ballistic intensity.
Assumed unpolarized.

\[ I_b(x, y) = I_{//}(x, y) - I_{\perp}(x, y) \]
Confocal Microscopy

Diagram:

- Detector
- Confocal aperture
- In-focus rays
- Out-of-focus rays
- Point source
- Illuminating aperture
- Objective lens
- Dichroic mirror
- In-focus plane
- Sample
Two-photon Microscopy: Schematic

- Source
- Dichroic mirror
- Lens
- Detector
- Sample
Two-photon Microscopy in Comparison to Confocal Microscopy

- A more localized excitation volume leads to reduced photo-bleaching.
- A longer excitation wavelength leads to increased penetration because both the absorption and the reduced scattering coefficients are decreased in the typical spectral region.
- No pinhole is needed.
- An ultrashort pulsed laser is used.
- Scattering contrast is not directly measured.
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Principle of Time-domain Optical Coherence Tomography

SLD: Superluminescent diode
NBS: Non-polarizing beam splitter

Reference arm

Sample arm

Sample

Lens

Photodiode

SLD

Mirror

NBS
Michelson Interferometer with a Monochromatic Source

\[ E_R = E_{R0} \exp[-i(2k_R l_R - \omega t)] \]
\[ E_S = E_{S0} \exp[-i(2k_S l_S - \omega t)] \]
\[ I = |E_R + E_S|^2 \]
\[ I = E_{R0}^2 + E_{S0}^2 + 2E_{R0}E_{S0} \cos[2(k_S l_S - k_R l_R)] \]

In free space

Phase difference: \( \Delta \phi = 2k(l_S - l_R) = 2\pi \frac{\Delta l}{\lambda / 2} \)

Arm-length difference: \( \Delta l \)

Sustained oscillation with \( \Delta l \).
Coherence Length

- Defined as the spatial full width at half maximum (FWHM) of the autocorrelation function of the electric field.

Autocorrelation function:

\[ C\{E(t)\} = \int_{-\infty}^{+\infty} E(t)E(t + \tau)dt \]

Coherence length for a Gaussian spectrum:

\[ l_c = \frac{4 \ln 2}{\pi} \frac{\lambda_0^2}{\Delta\lambda} \]

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Michelson Interferometer with a Low-coherence Source: Basic OCT

\[ I_{AC} \propto \exp \left[ -16 \ln 2 \left( \frac{\Delta l}{l_c} \right)^2 \right] \cos(2k_0\Delta l) \]

Coherence length: \( l_c = \frac{4 \ln 2}{\pi} \frac{\lambda_0^2}{\Delta \lambda} \)

Axial resolution: \( \Delta z_R = \frac{l_c}{2} \)

Lateral resolution: \( \Delta x_R = \frac{4 \lambda_0}{\pi} \frac{f}{D} \)

For example:
\( \lambda_0 = 830nm, \Delta \lambda = 20nm, l_c = 30 \mu m \)
Demodulation of OCT Signals: Simulation

MATLAB program:

% Use SI units throughout
% center wavelength
lambda0 = 830E-9;
% bandwidth (delta lambda)
dlambda = 60E-9;
% speed of light
c = 3E8;

% coherence length
lc = 4*log(2)/pi*lambda0^2/dlambda
% number of sampling points
N = 2^12;
% array for Delta_l
dl = lc*linspace(-2,2, N);
% propagation constant
k0 = 2*pi/lambda0;
...

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MATLAB Program: Original Interferogram

- subplot(4, 1, 1)  % interferogram
- Iac = exp(-16*log(2)*(dl/lc).^2) .* cos(2*k0 * dl);
- plot(dl/lc, Iac, 'k')
- title('(a) Interferogram')
- xlabel('$\Delta l/l_c$')
- ylabel('Signal')
- axis([-0.6, 0.6, -1, 1])
- ...

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MATLAB Program: Rectified Interferogram

- subplot(4, 1, 2) % rectified interferogram
- lrec = abs(lac);
- plot(dl/lc, lrec, 'k')
- title('(b) Rectified interferogram')
- xlabel('\Deltal/l_c')
- ylabel('Signal')
- axis([-0.6, 0.6, -1, 1])
- ...

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MATLAB Program: Spectrum of Rectified Interferogram

- subplot(4, 1, 3) % spectrum of the rectified interferogram
  - Frec1 = fft(Irec)/sqrt(N); % order of frequencies:
    - % 0,1...(N/2-1),-N/2,-(N/2-1)...-1
  - Frec2 = fftshift(Frec1); % shifted order of frequencies:
    - % -N/2,-(N/2-1)...-1, 0,1...(N/2-1)
  - dfreq = 1/(4*lc); % bin size = 1/sampling range
  - freq = dfreq*(-N/2:N/2-1); % frequency array
  - plot(freq*lambda0, abs(Frec2), 'k')
  - title('(c) Spectrum of the rectified interferogram')
  - xlabel('Frequency (1/\lambda_0)')
  - ylabel('Amplitude')
  - axis([-10, 10, 0, 5])
- ...
MATLAB Program: Envelopes

- subplot(4, 1, 4) % envelope
- % cut-off frequency for filtering
- freq_cut = 1/lambda0/2;
- % convert freq_cut to an array index
- i_cut = round(freq_cut/dfreq);
- Ffilt = Frec1; % initialize array
- Ffilt(i_cut:N-i_cut+1) = 0; % filter
- % inverse FFT then take the amplitude
- Ifilt = abs(ifft(Ffilt))*sqrt(N);
- plot(dl/lc, Ifilt/max(Ifilt), 'k')

lac_en = exp(-16*log(2)*(dl/lc).^2); % envelope
hold on;
plot(dl(1:N/32:N)/lc, lac_en(1:N/32:N), 'ko')
hold off;
title('(d) Envelopes')
xlabel('\Delta l/\ell_c')
ylabel('Signals')
axis([-0.6, 0.6, -1, 1])
legend('Demodulated','Original')

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Fourier-domain OCT: System

Reference mirror

Lens

Low-coherence light source

Beam splitter

Lens

Grating-based spectrometer

Virtual reference plane in sample arm

Object

Lens

Lens

Photodiode array

z

z₀
Fourier-domain OCT: Theory

\[ E_R(\omega) = E_0(\omega) r_R \exp[-i(2k_R(\omega)l_R - \omega t)] \]

\[ E_S(\omega) = E_0(\omega) \int_{-\infty}^{+\infty} r'_S(l_S) \exp[-i(2k_S(\omega)l_S - \omega t)] \, dl_S \]

If dispersion free, \( k_R / n_R = k_S / n_S = k = \omega / c \)

\[ I(k) = |E_R(kc) + E_S(kc)|^2 \]

\[ I(k) = S(k) \left\{ r^2_R + 2r_R \int_{-\infty}^{+\infty} r'_S(l_S) \cos[2k(n_Sl_S - l_R)] \, dl_S + \right. \]

\[ \left. \left[ \int_{-\infty}^{+\infty} r'_S(l_S) \exp[-i2k(n_Sl_S)] \, dl_S \right]^2 \right\} \]
Simulated Fourier-domain OCT: Two Back-scatterers

- % Use SI units throughout
- \( \lambda_0 = 830E-9 \);
- \( d\lambda = 20E-9 \); % FWHM
- \( n_s = 1.38 \); % refractive index of sample
- \( l_s1 = 100E-6 \); % location of scatterer 1
- \( l_s2 = 150E-6 \); % location of scatterer 2
- \( r_s1 = 0.50 \); % reflectivity of scatterer 1
- \( r_s2 = 0.25 \); % reflectivity of scatterer 2
- \( k_0 = 2\pi/\lambda_0 \);
- % FWHM bandwidth of \( k \)
- \( \Delta k = 2\pi d\lambda / \lambda_0^2 \);
- % standard deviation of \( k \)
- \( \sigma_k = \Delta k / \sqrt{2\log(2)} \);
- \( N = 2^{10} \); % # of sampling points
- % # of SD to plot on each side of \( k_0 \)
- \( n_s = 5 \);
- ...

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Simulated Fourier-domain OCT: Original Interferogram

- ...
- subplot(4,1,1); % Generate the interferogram
- k = k0 + sigma_k*linspace(-nsigma,nsigma, N); % array for k
- S_k = exp(-(1/2)*(k-k0).^2/sigma_k^2); % Gaussian source PSD
- E_s1 = rs1*exp(i*2*k*ns*ls1); % sample electric field from scatter 1
- E_s2 = rs2*exp(i*2*k*ns*ls2); % sample electric field from scatter 2
- I_k1 = S_k .* abs(1 + E_s1 + E_s2).^2; % interferogram (r_R = 1)
- plot(k/k0,I_k1/max(I_k1), 'k');
- title('Interferogram');
- xlabel('Propagation constant k/k_0');
- ylabel('Normalized intensity');
- axis([0.9 1.1 0 1]);
- ...

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Simulated Fourier-domain OCT: IFT of Original Interferogram

- ...
- subplot(4,1,2); % Inverse Fourier transform (IFT) of the interferogram
- spec1=abs(fftshift(ifft(I_k1))/sqrt(N));
- dls_prime = 1/(2*nsigma*sigma_k/(2*pi)); % freq bin size = 1/sampling range
- ls_prime = dls_prime*(-N/2:N/2-1); % frequency array
- plot(ls_prime/(2*ns),spec1/max(spec1), 'k'); % scale the frequency
- title('Inverse Fourier transform of the interferogram');
- xlabel('Depth ls (m)');
- ylabel('Relative reflectivity');
- axis([-2*ls2 2*ls2 0 1]);
- ...

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Simulated Fourier-domain OCT: IFT of Deconvolved Interferogram

- subplot(4,1,3); % IFT of the deconvolved interferogram
- spec1_norm = abs(fftshift(ifft(I_k1./S_k)))/sqrt(N);
- dls_prime = 1/(2*nsigma*sigma_k/(2*pi)); % freq bin size = 1/sampling range
- ls_prime = dls_prime*(-N/2:N/2-1); % frequency array
- plot(ls_prime/(2*ns),spec1_norm/max(spec1_norm), 'k'); % scale the frequency
- title('Inverse Fourier transform of the deconvolved interferogram');
- xlabel('Depth ls (m)');
- ylabel('Relative reflectivity');
- axis([-2*ls2 2*ls2 0 1]);
- ...

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Simulated Fourier-domain OCT: IFT of Deconvolved Differential Interferogram

- ...
- subplot(4,1,4); % IFT of the deconvolved differential interferogram
- \[ I_k2 = S_k \cdot \text{abs}(-1 + E_s1 + E_s2)^2; \]
  % interferogram
- \[ \text{delta}_I_k = I_k1 - I_k2; \]
- \[ \text{spec2} = \text{abs}(\text{fftshift}(\text{ifft}(\text{delta}_I_k./S_k)))/\sqrt{N}; \]
- \[ \text{plot}(\text{ls_prime}/(2*ns), \text{spec2}/\text{max}(\text{spec2}), 'k'); \]
- \[ \text{title('Inverse Fourier transform of the deconvolved differential interferogram')}; \]
- \[ \text{xlabel('Depth } l_s \text{ (m)')}; \]
- \[ \text{ylabel('Relative reflectivity')}; \]
- \[ \text{axis([-2*ls2 2*ls2 0 1])}; \]
Simulated Fourier-domain OCT: A Single Back-scatterer

Interferogram

Normalized intensity

Propagation constant $k/k_0$

IFT of the interferogram

Relative reflectivity

Depth $l_s$ (m)

$10^{-4}$

IFT of the deconvolved interferogram

Relative reflectivity

Depth $l_s$ (m)

$10^{-4}$

IFT of the deconvolved differential interferogram

Relative reflectivity

Depth $l_s$ (m)

$10^{-4}$

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\[ \Delta l(t) = \Delta l_0 - v_R t \]

\[ \Delta \phi = 2k_0 \left( \Delta l_0 - v_R t \right) = \frac{4\pi}{\lambda_0} \left( \Delta l_0 - v_R t \right) \]

\[ f_R(\lambda_0) = \frac{1}{2\pi} \left| \frac{d\Delta \phi(t)}{dt} \right| = \frac{2v_R}{\lambda_0} \]

\[ f_{AC} = \frac{1}{2\pi} \left| \frac{d\Delta \phi(t)}{dt} \right| = \frac{2}{\lambda_0} \left( \nu_S \cos \theta - v_R \right) \]
Composition of OCT Signals

- Source coherence length = 15 microns
- Absorption coefficient = 1.5 /cm
- Scattering coefficient = 60 /cm
- Anisotropy factor = 0.9
Decay rate of class I signal: $\sim \mu_t$
Number of Scatters versus Depth

- **Class I**
- **Class II**

![Graph showing the number of scatters versus depth for Class I and Class II.](http://oilab.seas.wustl.edu)
Chapter 10

1. Introduction to biomedical optics
2. Single scattering: Rayleigh theory and Mie theory
3. Monte Carlo modeling of photon transport
4. Convolution for broad-beam responses
5. Radiative transfer equation and diffusion theory
6. Hybrid model of Monte Carlo method and diffusion theory
7. Sensing of optical properties and spectroscopy
8. Ballistic imaging and microscopy
9. Optical coherence tomography
10. **Mueller optical coherence tomography**
11. Diffuse optical tomography
12. Photoacoustic tomography
13. Ultrasound-modulated optical tomography
Polarization States

Elliptical

Linear

Circular
Stokes Vector Measured by OCT

\[ S = \begin{bmatrix} S_1 \\ S_2 \\ S_3 \\ S_4 \end{bmatrix} = \begin{bmatrix} I_H + I_V \\ I_H - I_V \\ I_P - I_M \\ I_R - I_L \end{bmatrix}, \quad I_{Total} = I_H + I_V \\
= I_P + I_M \\
= I_R + I_L \]

4 independent measurements needed.

\[ I_x \propto A_{OCTx}^2 \]

\[ x: \text{polarization states of the reference beam.} \]

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\[ S_{out} = MS_{in} \]

\[
M = \begin{bmatrix} M_0, M_1, M_2, M_3 \end{bmatrix}
\]

\[ S_H = MS_{Hi} = M_0 + M_1 \]
\[ S_V = MS_{Vi} = M_0 - M_1 \]
\[ S_P = MS_{Pi} = M_0 + M_2 \]
\[ S_R = MS_{Ri} = M_0 + M_3 \]

\[
M = \frac{1}{2} \left[ S_H + S_V, S_H - S_V, 2S_P - S_H - S_V, 2S_R - S_H - S_V \right]
\]
Serial Mueller OCT
Raw Polarized Images and Mueller Images (750x500 microns)

Source

H

V

P

R

HH
HV
HP
HR

M_{11}
M_{12}/M_{11}
M_{13}/M_{11}
M_{14}/M_{11}

M_{21}/M_{11}
M_{22}/M_{11}
M_{23}/M_{11}
M_{24}/M_{11}

M_{31}/M_{11}
M_{32}/M_{11}
M_{33}/M_{11}
M_{34}/M_{11}

M_{41}/M_{11}
M_{42}/M_{11}
M_{43}/M_{11}
M_{44}/M_{11}

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7 real independent parameters in a Jones matrix.

\[
\mathbf{E} = \begin{bmatrix} \mathbf{E}_H \\ \mathbf{E}_V \end{bmatrix}
\]

\[
\mathbf{J} = \begin{bmatrix} J_{11} & J_{12} \\ J_{21} & J_{22} \end{bmatrix}
\]

\[
\mathbf{E}_{OUT} = \mathbf{J}\mathbf{E}_{IN}
\]
Jones Reversibility Theorem

\[
J = J_{SB} J_{M} J_{SI} = J_{SI}^T J_{SI} = J^T
\]

- Reduces to 5 real independent parameters in a Jones matrix.

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Parallel Mueller OCT

[Diagram of a Mueller OCT setup including components such as mirrors, lenses, beam splitters, polarizing elements, and photodiodes.]

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**Mueller Images of Porcine Tendon**  
*(0.5 mm × 1 mm)*

- 10 micron resolution
- ~1 mm imaging depth
- Birefringence: \((4.2 \pm 0.3) \times 10^{-3}\) (e.g., density of collagen)
- Orientation: accurate to <\(5^\circ\) (e.g., direction of collagen)
- Diattenuation: 0.26/mm (e.g., property of collagen)

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Chapter 11

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10. Mueller optical coherence tomography
11. Diffuse optical tomography
12. Photoacoustic tomography
13. Ultrasound-modulated optical tomography
## Modes of Diffuse Optical Tomography

<table>
<thead>
<tr>
<th>Mode</th>
<th>Source light $\Phi_s(\vec{r}', t')$</th>
<th>Re-emitted light $\Phi_m(\vec{r}, t; \vec{r}', t')$</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Time domain</strong></td>
<td>Impulse: $\delta(\vec{r}')\delta(t')$</td>
<td>Time-resolved: $\Phi_m(\vec{r}, t; \vec{r}', t')$</td>
</tr>
<tr>
<td><strong>Frequency domain</strong></td>
<td>Amplitude-modulated: $\delta(\vec{r}')[D_s + A_s \cos(\omega t + \phi_s)]$</td>
<td>Amplitude-modulated: $D_m(\vec{r}; \vec{r}') + A_m(\vec{r}; \vec{r}') \cos(\omega t + \phi_m(\vec{r}; \vec{r}'))$</td>
</tr>
<tr>
<td><strong>Direct current</strong></td>
<td>DC: $D_s \delta(\vec{r}')$</td>
<td>DC: $D_m(\vec{r}; \vec{r}')$</td>
</tr>
</tbody>
</table>
Time-domain System

Reference

Photodiode
Fast fan-out module
Amplifier & timing discriminator
Delay

Variable optical attenuator

Long-pass filter
Pre-amplifier
Picosecond time analyzer

Fiber switch

Polymer fiber

Constant fraction discriminator

Micro-channel plate PMT

32 detection fiber bundles

Object

Computer

Pulsed laser

Nuetral density filter
Shutter
Fiber coupler
32 source fibers
Direct-current System
Frequency-domain System

- Power supply
- Signal generator 100.000 MHz
- Signal generator 100.001 MHz
- Time base
- Fiber-optical bundles
- Laser diode
- Linear translation stage
- Object
- Filter wheel
- Band-pass filter
- Linear translation stage
- PMT
- A/D board
- Computer

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