Functional optical coherence tomography : spatially resolved measurements of optical properties
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CHAPTER 2

Theory

The advantage of OCT over other optical imaging techniques is that the spatial origin of the signal in the sample is known with high accuracy. This is achieved by combining coherence gating and confocal gating, which will be the subject of the present chapter, along with a mathematical treatment of the optical properties to be extracted from the OCT signal. This chapter introduces OCT in formulas and numbers. The equations found here serve as a starting point for the theory sections of the subsequent chapters.

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2.1 coherence gating

THE DETECTOR CURRENT FROM A MICHELSON INTERFEROMETER

Most principles of OCT are readily illustrated using a Michelson interferometer as depicted in the left panel of figure 2-1. The interferometer is illuminated by an optical field $E_0$ traveling in the source arm towards a 50/50 beam splitter. The sample arm and reference arm of the interferometer are terminated by the mirrors $S$ and $R$ respectively. The detector arm is terminated by a photo detector.

The lengths of the sample arm and reference arm are $l_s$ and $l_r$. The field at the detector $E_d$ is the superposition of the fields from the sample arm $E_s$ and reference arm $E_r$ and is recorded as a function of path length difference $\Delta l = 2(l_s - l_r)$. The factor 2 accounts for the fact that the light traverses the sample and reference arms twice. The photo detector current $i_d$ is proportional to the time averaged intensity on the detector:

$$i_d \propto \left\langle |E_d|^2 \right\rangle = \left\langle |E_s + E_r|^2 \right\rangle$$

(2-1)

The brackets denote integration over the detector response time. Expanding the quadrature term, $i_d$ can be separated into a term proportional to the total power in sample and reference fields, and an interferometric term of the product of $E_s$ and $E_r$,

$$i_d \propto |E_s|^2 + |E_r|^2 + \left\langle E_s E_r^* + E_r E_s^* \right\rangle$$

(2-2)

where $^*$ denotes the complex conjugate. From now on, only this latter part of $i_d$ will be considered. Because the optical frequencies ($\sim 10^{15}$ Hz) are much higher then the cut-off frequency of the detector (typically $\sim 10^8$ Hz, but up to $\sim 10^{11}$ Hz) the integration over the detector response time does not need to be carried out explicitly.

An expression for the interferometric signal is quickly derived because the reference field is simply a time shifted version ($\Delta t = \Delta l/c$, with $c$ the speed of light) of the sample field and both are proportional to the source field. Therefore this term is actually the autocorrelation function of the source field. According to the Wiener-Khinchine theorem [1], the autocorrelation $R_s(\Delta l)$ is the Fourier transform of the amplitude spectrum of the light source $S_s(k)$:

$$R_s(\Delta l) = \int S_s(k) \exp(jk\Delta l) dk.$$ Here $k$ is the wave number $k = 2\pi/\lambda$, and $\lambda$ is wavelength. Note the Fourier transform pair $k \leftrightarrow \Delta l$. The spectrum of a practical light source exists on a finite wavelength (-number) range, and is therefore written as $S_s(k-k_0)$ where $k_0$ is the (center) wave number. A well known property of Fourier transforms [1] says that a shift in the $k$-domain
leads to a modulation in the $\Delta l$-domain: $R_0(\Delta l)\exp(-jk_0\Delta l) = |S_0(k-k_0)\exp(jk\Delta l)|dk$. Consequently, the final expression for the detector current is given by

$$i_\phi(\Delta l) \propto R_0(\Delta l) \cos(k_0\Delta l) \quad (2-3)$$

Equation 2-3 shows that the detected interference pattern consist of an envelope $R_0(\Delta l)$ that is cosine modulated as a function of path length difference. In figure 2-1, right hand side, two examples of equation 2-3 are depicted, corresponding to a monochromatic (top) and a broadband (bottom) light source in the interferometer. The monochromatic light source has a spectrum that is confined in the $k$-domain and consequently the autocorrelation function in this case extends over a large part of the $\Delta l$-domain (top). Conversely, the broad band spectrum covers a large part of the $k$-domain, and so the autocorrelation is more confined in space, i.e. an interference pattern of sufficient amplitude will only exist on a small range of path length differences (bottom).

The width of the autocorrelation envelope is commonly characterized by the so-called coherence length of the light source. This leads to the following definition of coherence gating in OCT: interference will only be observed if the path length difference between sample arm and reference arm is less than the coherence length of the light source. We can now turn the argument around: if we see interference, and know the path length in the reference arm, we can calculate the path length in the sample arm, with an accuracy given by the coherence length. The width of the autocorrelation determines the axial resolution of the OCT system.

The detector signal in the cases of monochromatic and broadband light sources will be discussed in more detail below.

CASE A: MONOCHROMATIC LIGHT SOURCES
First, consider a purely monochromatic light source, i.e. emitting only at wave number $k_0$. Then the sample and reference field are proportional to

$$E_s \propto E_0 e^{ik_0z} \quad E_r \propto E_0 e^{ik_0z - 2\pi\nu z} \quad (2-4)$$

respectively, where $\nu_0$ is the center frequency of the light source. The interferometric signal is found by inserting eq. 2-4 in eq. 2-2 and retaining only the last term:

$$i_\phi(\Delta l) \propto |E_0|^2 \left(e^{ik_0\Delta l} + e^{-ik_0\Delta l}\right) \propto |E_0|^2 \cos(k_0\Delta l) \quad (2-5)$$

Equation 2.5 shows a cosine as a function of path length difference; see figure 2-1, top right. This is consistent with the Wiener-Khinchine theorem because the spectrum of a monochromatic source is given by $S_0(k) = \delta(k-k_0)$, where $\delta$ is a dirac-function. The Fourier transform of the dirac-function is a constant, the shift over $k_0$ again leads to modulation so that equation 2-5 follows.

CASE B: BROADBAND LIGHT SOURCES
Purely monochromatic light sources only exist in textbooks. Using the Wiener-Khinchine theorem, the detector current is written as the Fourier transform of the source spectrum,

$$i_\phi(\Delta l) \propto \text{Re} \int S_\phi(k-k_0) e^{ik\Delta l} dk = R_0(\Delta l) \cos(k_0\Delta l) \quad (2-6)$$
Equation 2-6 shows that broadband light sources can be treated as the superposition of many coherent, monochromatic light sources appropriately weighted by the power spectrum of the light source.

The light may travel in a dispersive medium. This is accounted for by introducing \( k \)-dependence of the path length \( l(k) \). Because of the broad bandwidth it is convenient to write phase terms \( \varphi(k) = kl(k) \) as series expansions around the center wave number \( k_0 \):

\[
\varphi(k) = \varphi(k_0) + (k - k_0) \frac{\partial \varphi(k_0)}{\partial k} \bigg|_{k=k_0} = k_0 l_\varphi + (k - k_0) l_g
\]

In the last term on the right hand side the definitions of phase delay \( l_\varphi = \varphi(k_0)/k_0 \) and of group delay \( l_g = \partial \varphi(k)/\partial k \) are used. Equation 2-6 can now be rearranged to

\[
i_d(\Delta l_r, \Delta l_c) \propto \text{Re}\left\{ e^{i k_0 k_0 S_{\varphi}(k)} e^{i(\Delta k) \Delta l_g} d(k - k_0) \right\} = R_0(\Delta l_g) \cos(k_0 \Delta l_g)
\]

As in equation 2-6, the detector signal is the Fourier transform of the source spectrum (autocorrelation function) and consists of an envelope as function of group delay difference, modulated as a function of phase delay difference.

Light sources commonly used in OCT have (approximately) Gaussian spectra \((\omega \text{ or } k\text{-domain})\); therefore the envelope of the autocorrelation \((t \text{ or } \Delta l\text{-domain})\) is also Gaussian. Both can be characterized by their 1/e radii \( w \), which are related through \( w_m = 2/w_k \). From an experimental point of view, it is more convenient to characterize the Gaussians by their full width at half maximum FWHM = 2\( w \sqrt{\ln 2} \). The FWHM of the \( R_0(\Delta l) \) will be \( 2l_c = 8\ln 2/\Delta k \) when the spectral FWHM bandwidth \( S_{\varphi}(k) \) is \( \Delta k \). Here we have implicitly defined the coherence length \( l_c \). Consequently, for Gaussian sources equation 2-8 can be written as

\[
i_d(\Delta l_r, \Delta l_c) \propto e^{-4\ln 2 \left( \frac{\Delta l_c}{2l_c} \right)^2} \cos(k_0 \Delta l_c)
\]

Equation 2-9 describes the situation illustrated in figure 2-1 right, bottom panel. In practice, only the envelope of the detector signal will be plotted, as a function of \( z = \frac{1}{2} \Delta l_g \) because this corresponds to a specific location of the mirror \( S \) (or depth inside a sample)

\[
i_d(z) \propto e^{-4\ln 2 \left( \frac{z}{l_c} \right)^2}
\]

where \( l_c \) is commonly expressed in terms of wavelength instead of wave number, i.e.

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

Here \( \lambda_0 \) is the center wavelength of the light source spectrum and \( \Delta \lambda \) is its FWHM bandwidth. Equation 2-11 provides a practical definition of the coherence length of the light source and is commonly used to characterize the axial resolution that can be achieved by an OCT system.
In the derivation of equation 2-7 we have introduced dispersion by the \( k \)-dependence of the path length \( l(k) \). The refractive index is given by \( n(k) \) so that the phase terms \( \varphi(k) = kn(k)l \) can be written as \( \varphi(k) = kl(k) \) where \( l \) is (as before) the path length measured in air. From the definitions of phase delay and group delay we see that

\[
l_p = n(k_0)l; \quad l_g = n_g(k_0)l
\]

(2-12)

Here we used the definition of the group refractive index

\[
n_g = n + \frac{dn}{dk}
\]

(2-13)

Consequently, this means we have to alter the previous definition of coherence gating: we will only observe interference if the group path length difference between sample arm and reference arm is less than the coherence length of the light source and by knowing the group path length in the reference arm the group path length in the sample arm can be calculated with an accuracy given by the coherence length. Because the coherence length only depends on the light source, this actually means that the accuracy with which the geometrical path length in the sample is determined, is increased by \( n_g(k_0) \). Consequently, the axial resolution in such a medium will be improved by \( n_g(k_0) \).

1.350-
1.345-
1.340-
1.335-
1.330-
1.325-

\[600 \quad 700 \quad 800 \quad 900 \quad 1000\]

\textit{figure 2-2: group and phase refractive index of water. Data from [2]}

Note that the difference in group and phase refractive index can be quite large. Figure 2-2 shows the refractive indices of water in the wavelength range 600-1000 nm. The refractive index at 800 nm (the center wavelength of the Ti:Sapphire laser used in the experiments in this thesis) is 1.328; the group refractive index at this wavelength is 1.341. Using a bandwidth of 125 nm, this means the resolution of this OCT system (according to equation 2-13) is 2.3 \( \mu \text{m} \) in air and 1.7 \( \mu \text{m} \) in water.

FREQUENCY AND BANDWIDTH OF THE DETECTOR CURRENT

In `conventional` time-domain OCT, the detector current is recorded as function of path length difference, e.g. equation 2-9. To achieve this, the scanning mirror \( R \) is moved as a function of time. Consequently, the field in the reference arm is Doppler shifted, whereas the sample field is not. This causes a beat frequency in the interferometric part of the detector current. Because this Doppler shift is wavelength dependent, the detector current will have a certain center frequency and bandwidth. For completeness, we derive their expressions here.

The frequency at which a certain wave number appears in the detector current can be found (by definition) by differentiating the phase of equation 2-6 (using 2-7) with respect to time.

\[
2\pi f(k) = \frac{\partial \varphi}{\partial t} = k_0 \frac{\partial \Delta l}{\partial t} + (k - k_0) \frac{\partial \Delta l}{\partial t} = k_0 V_p + (k - k_0)V_g
\]

(2-14)
The last term on the right hand side defines the phase velocity $V_p$ and group velocity $V_g$ of the scanning delay line. The last two terms on the right hand side can be written in terms of wavelength,

$$f(\lambda) = \frac{V_p}{\lambda_0} + \left(\frac{1}{\lambda} - \frac{1}{\lambda_0}\right)V_g$$  \hspace{1cm} (2-15)

The center electrical frequency $f_0$ of the detector current is obtained from equation 2-15 using $\lambda = \lambda_0$; the electrical bandwidth $\Delta f$ is obtained from a Taylor expansion around the center wavelength,

$$f_0 = \frac{V_p}{\lambda_0}; \quad \Delta f = \frac{\Delta \lambda}{\lambda_0^2}V_g = \frac{V_g}{c} \left(\frac{\pi}{2\ln 2}\right)$$  \hspace{1cm} (2-16; 2-17)

The center frequency of the detector current depends on the phase scan velocity of the scanning delay line and center wavelength $\lambda_0$; the bandwidth depends on the group scan velocity of the scanning delay line and coherence length $\lambda_c$. The detection electronics have to support this (broad) bandwidth. Consequently, they are more susceptible to noise – i.e. there is a trade-off between resolution and signal to noise ratio.

### 2.2 confocal gating

OCT can be regarded as an extension of confocal microscopy (CM). The optical arrangement of CM is shown in figure 2-3. An image of the source pinhole (sp) is created in the sample overlapping with an image of the detection pinhole (dp). Because of this arrangement, light scattered from outside that location is not imaged onto the detection pinhole, in other words detection of light scattered from outside the focal volume (symbolized by the ‘dot’ in figure 2-3) is suppressed.

![figure 2-3: confocal microscopy. The source pinhole (sp) is imaged in the tissue. Co-localized is an image of the detection pinhole (sp). The location of this focal volume is symbolized by the ‘dot’ in the sample.]

The resolution in CM thus depends on the size of the focal volume. As was discussed in chapter 1, figure 1-6, high numerical aperture (NA) optics provide a small depth of focus and small lateral spot size. The confocal system can be characterized by the detector signal when a small reflector is imaged. The response to this reflector as a function of its radial and axial position with respect to the focal volume is called the 2-dimensional point spread function (PSF).

OCT is also based on a confocal optical setup. In most clinical systems (and the setups used in the experiments in this thesis), single mode fibers (SMF) serve as the confocal pinholes. As
with CM, the lateral resolution is determined by the used optics whereas the axial resolution is
determined by the coherence length of the light source. The combination of coherence and
confocal gating provides for the high localization of the probe volume in OCT.

Using high NA optics in OCT, both high axial resolution and high lateral resolution can be
obtained. Because the (confocal) depth of focus in such a setup is limited, ideally the positions
of the coherence and confocal gates are matched throughout the depth scan. Unfortunately,
moving the focusing lens at high velocity is mechanically not possible and therefore clinical
OCT systems, (which rely on high imaging speed) usually deploy relatively low NA ‘fixed’
optics. This means that the strength of a reflection in the OCT image depends on its position
relative to the focus position. In other words, to quantitatively analyze such OCT data, the
PSF has to be known and taken into account.

In this section the PSF for SMF based OCT systems will be derived, using the coupling
efficiency \( \eta_c \) of Gaussian intensity profiles, launched from one SMF into another SMF using
an arbitrary optical system. A Gaussian beam is characterized by the waist \( w \) and its position
and the Rayleigh length \( Z_0 \) (half depth of focus). The Rayleigh length is given by:

\[
Z_0 = \frac{\pi w^2}{\lambda}
\]

(2-18)

with wavelength \( \lambda \) (in vacuum) and the index of refraction \( n \) of the medium. In calculating \( \eta_c \),
it has to be taken into account that only an effective beam, equivalent to the fundamental
mode of the receiving fiber can be coupled in. Specifically, the light from one SMF (mode
field diameter \( 2w_f \), Rayleigh length \( Z_f \) ) is imaged to a new waist \( w_i \) and Rayleigh length \( Z_i \).
The fundamental mode of the detection optical system and SMF is characterized by mode
field diameter \( 2w_r \), Rayleigh length \( Z_r \). The coupling efficiency can be calculated as the
overlap integral of the two Gaussian fields (and not their overlap area, as with multimode
fibers). Then, \( \eta_c \) depends on any losses due to offset \( \delta \) between the waist positions, lateral
misalignment \( x \), angular misalignments and mode field diameter mismatch between the two
beams (figure 2-4).

![Figure 2-4: Geometry of coupling light from a single mode fiber, via a lens system into another
lens/fiber system taking into account both axial (\( \delta \)) and lateral (\( x \)) misalignment, and mode field
diameter mismatch (\( 2w_f, 2w_r \)).](image)

In the following, angular misalignments will not be considered for simplicity. The radial
distribution of the Gaussian field can be written as

\[
E(r) = \sqrt{\frac{2}{\pi}} \frac{1}{w} e^{-\frac{r^2}{w^2}}
\]

(2-19)
The overlap integral can be calculated at any position in the optical system. For simplicity, we choose the waist position of the receiving optical system. The Gaussian field of equation 2-19 will diverge from waist \( w_1 \) position over the distance \( \delta \) to:

\[
E_r(r) = \frac{1}{\sqrt{\pi w_1^2}} \exp \left( -\frac{r^2}{w_1^2} \right) \exp \left( -\frac{ikr^2}{2R_1} \right) \exp \left( -i[k\delta - \theta'] \right)
\]  \hspace{1cm} (2-20)

with \( w'_1 = w'_1(\delta) = w_1 \sqrt{1 + \delta^2/Z_r^2} \quad R'_1 = R_1(\delta) = \delta(1 + Z_r^2/\delta^2) \quad \theta' = \arctan(\delta^2/Z_r^2) \)  \hspace{1cm} (2-21)

The field of the fundamental mode \( E_r(r) \) of the receiving fiber is simply given by equation 2-19. For these fields, the coupling coefficient (overlap integral) is calculated as:

\[
\eta_c = \int E_r E'_r \, dr
\]  \hspace{1cm} (2-22)

The power transmission \( T \) is then given by \( \eta_c \eta_c^* \) (see [3] for details):

\[
T = \frac{4 \left( \frac{w_r}{w_1} \right)^2}{\left( \frac{\delta}{Z_r} \right)^2 + \left( \frac{w_r}{w_1} \right)^2 + 1} \exp \left( -2 \left( \frac{w_r^2}{w_1^2} + \left( \frac{x}{w_r} \right)^2 \right) \left( \frac{\delta}{Z_r} \right)^2 + \left( \frac{w_r^2}{w_1^2} + 1 \right) \right)
\]  \hspace{1cm} (2-23)

The Rayleigh length \( Z_r \) is defined similar to equation 2-18. This expression is a function of the parameters of the Gaussian beams only (and their misalignment). From this general expression, three forms of the PSF will be derived.

CASE A: RESPONSE TO POINT REFLECTOR
Consider a small point reflector, somewhere in the sample arm beam. We can think of the light reflected back by this point into the OCT system as a beam with a small waist (corresponding to the size of the point reflector), with waist position at the position of the point reflector. The response to this point reflector (PSF) can then be calculated from equation 2-23. Now \( d, x \) are the coordinates of the point reflector with respect to the center of the focal volume of the beam, \( w_r \) describes the fundamental mode of the probe beam, and \( w_1 \ll w_r \). This yields for the (normalized) point spread function:

\[
PSF(d, x) \approx \frac{1}{\left( \frac{d}{Z_r} \right)^2 + 1} \exp \left( -\frac{-2(x/w_r)^2}{\left( \frac{d}{Z_r} \right)^2 + 1} \right)
\]  \hspace{1cm} (2-24)

(after first re-arranging the term before the exponential, by multiplying the nominator and denominator with \( [w_1^2/w_r^2] \), the Rayleigh length \( Z_r \) is defined similar to equation 2-18.). The normalization factor (of course) depends on \( w_1 \) and is given by \( (2w_1^2/w_r^2)^2 \). Figure 2-5 shows a surface rendering (left) and contour plot of this point spread function, using \( w_r = 4 \mu m \); \( \lambda = 800 \)
nm; \( Z_r = 65 \, \mu m \). These numbers closely match our laboratory setup, see chapters 3 and 4. Reflector size is \( w_r = 100 \, nm \).

CASE B: RESPONSE TO SPECULAR REFLECTION

Specular reflection occurs at smooth interfaces such as mirrors, air-glass or air-water boundaries and is governed by Fresnel’s laws of reflection. The PSF in this case can be measured as the detector signal when moving a mirror through the focus of the beam. Taking into account that in our OCT systems the same fibers and lenses are used for delivery and collection of the light, i.e. \( w_i = w_p \), the geometry can be depicted as in figure 2-6 (where the mirror is not drawn, rather the beam paths are “folded” around the location of the mirror). Lateral and angular offsets are not present.

When the mirror is positioned at axial distance \( d \) from the focus, the actual distance between the waist of incident and receiving beams is given by \( 2d \). Inserting this in equation 2-23 yields the PSF for specular reflection:

\[
T_s(d) = \frac{1}{\left( \frac{d}{Z_r} \right)^2 + 1}
\]  

(2-25)

with \( d \) the distance of the reflecting object to the waist position of the beam. The axial PSF of equation 2-25 equals that of equation 2-24 for zero lateral offset.

CASE C: RESPONSE TO DIFFUSE REFLECTION

In the case of diffuse reflection, in analogy of the paper of de Grauw et al. [4], illumination of an object at distance \( d \) from the waist position of the incoming beam will form a secondary source. This source will be treated as a new beam with waist \( \omega' \) and Rayleigh length \( Z'_r \) which will then overlap with the incoming beam (figure 2-7).
The propagation of the incident beam to the scattering location is calculated in the same way as for equation 2-20. From:

\[ w_i(d) = w_i \sqrt{1 + \frac{d^2}{Z_i^2}} \]

\[ Z_i(d) = Z_i \left(1 + \frac{d^2}{Z_i^2}\right) \]  

(2-26)

By using the result in equation 2-23, the axial PSF for diffuse reflection can be described as:

\[ T_d(d) = \frac{1}{\left(\frac{d}{2Z_i}\right)^2 + 1} \]  

(2-27)

i.e. for diffuse reflection, the depth of focus is doubled compared to the case of specular reflection. In the derivation of equation 2-27 we assume the beam is not distorted prior to, or after backscattering. The validity of this assumption will be experimentally tested in chapter 4.

2.3 light-tissue interaction in OCT

In the derivations in section 2.1, we have only considered a single reflector in the sample arm. If we probe, for example, a piece of tissue, the recorded OCT signal will depend on the optical properties of the tissue. As argued before, measurement of the optical properties can help to differentiate between different tissues. We start by deriving a general expression for the OCT signal from a ‘reflecting’ sample; and then briefly introduce the optical properties of interest. We proceed by giving expressions for the detector current in two cases: assuming single backscattering and when assuming multiple, forward scattering.

THE OCT SIGNAL FROM A SCATTERING SAMPLE

We start by deriving a general expression for the detector current, when the mirror S in figure 2-1 is replaced by an arbitrary sample. The total field returning from this sample at the detector is a superposition of time-shifted input fields, each weighted with the appropriate reflection coefficient corresponding to the individual reflections. Therefore, the sample field \( E_s \) can be expressed as the convolution of source field \( E_0 \) with the depth dependent electric field scattering coefficient \( h(z) \).

\[ E_s(z) = E_0(z) \otimes h(z) \]  

(2-28)

Here, \( z \) is the depth into the sample. Based on the discussion of section 2-1, the interferometric part of the detector current is the convolution of the sample field as given by equation 2-28,
with the reference field as before. Both the sample field and reference field are proportional to input field $E_0$ hence the detector current as function of $z$ can be written as:

$$i_s(z) \propto h(z) \otimes R_s(z)$$  \hspace{1cm} (2-29)

Consequently, the interaction of the electric field with the sample and subsequent mixing with the reference field "mathematically reduces" to the interaction of the autocorrelation-interferogram with the sample. Writing the Fourier transform of both sides of equation 2-29 yields

$$I_s(k) \propto H(k)S_s(k)$$  \hspace{1cm} (2-30)

which shows that the Fourier transform of the detector current is simply the source spectrum, multiplied by the spectral properties of the sample $H(k)$. The depth dependent reflection coefficient $h(z)$ (and its Fourier transform $H(k)$) are characterized by the local variation of the refractive index and the round-trip attenuation of the light in the sample. For quantitative assessment of optical properties from the OCT signal, $h(z)$ and $H(k)$ and thus the detector signal have to be expressed in terms of these properties.

THE OPTICAL PROPERTIES OF (BULK) TISSUE

The relevant optical properties of (bulk) tissue are the refractive index, absorption coefficient, scattering coefficient and scattering anisotropy. The refractive index and its influence on the OCT signal have already been discussed in section 2-1. Absorption by a single particle (or molecule) is governed by its absorption cross section $\sigma_a$. A medium containing many absorbers is then characterized by the absorption coefficient $\mu_a = N\sigma_a$, where $N$ is the number of particles per unit volume. The absorption coefficient equals the probability of absorption per unit path length. Likewise, scattering by a single particle is characterized by the scattering cross section $\sigma_s$; for a medium the scattering coefficient $\mu_s$ (mm$^{-1}$) is the probability of scattering per unit path length. Their sum is the (total) attenuation coefficient $\mu_t$, its reciprocal is the mean free path, i.e. the expected value of the path length of photon travels without interaction. If a photon is scattered, its direction may be changed. The probability function of the scattering angle is called the phase function. Whenever possible, the Heney-Greenstein phase function is used, which is described as a function of one parameter only, the scattering anisotropy $g$ (between $-1$ and 1) which by definition is the expected value of the cosine of the scattering angle. A $g$-value of 1 means purely forward directed scattering (i.e. no change of direction); a value of $-1$ means purely backward directed scattering. If $g = 0$, there is equal probability of scattering into all angles.

In this thesis, independent scattering will be assumed (and was already assumed deriving equations 2-28 to 2-30). Strictly speaking, this means that the scattered field by one particle is not influenced by the field scattered by other particles of the studied medium. In other words, there is no strict relation between the phases of the different scattered fields. In terms of low-coherence illumination this means that we assume that the scatterers are separated by more than one coherence length. Even if this requirement is not fulfilled, it can in general be overcome by sufficient volumetric averaging. However, in closely packed media, effects such as shielding may occur, effectively lowering the scattering cross section of the particle. In many practical cases, e.g. scattering from dense media such as blood, the assumption of independent scattering may not hold and as a direct consequence, the scaling of the microscopic cross sections to macroscopic coefficients with concentration can be questionable.
CASE A: SINGLE BACKSCATTERING

Consider a homogeneous sample in the sample arm. The locations of coherence and confocal gates are matched. We first calculate backscattering coefficient \( h(z) \) in a one-dimensional approximation, and consider independent, single backscattering only.

Then the probability of backscattering is independent of \( z \) and the input field is attenuated according to Beer’s law. Consequently, \( h(z) \) is proportional to

\[
h(z) \propto e^{-2\alpha z} e^{-k^2 z}
\]

(2-31)

where the factor 2 accounts for round-trip attenuation, and \( \alpha \) is the field attenuation coefficient. The light intensity returning from the sample \( I_s \), will be proportional to

\[
I_s \propto |E_z| = |h(z)h(z)^*|
\]

(2-28) were equation 2-28 is used. The coefficient \( \alpha \) is then related to the attenuation coefficient \( \mu \), through:

\[
I_s ... e^{-\mu z}
\]

(2-32)

Using the \( h(z) \) of equation 2-31 and 2-32 in equation 2-29 yields for the detector current:

\[
i(z) \propto \int_i R_s(z-z')e^{-\mu z'}dz' = e^{-\mu z}
\]

(2-33)

The last approximation holds when the width of \( R_s \) is much less then the mean free path; i.e. when \( l_s \ll 1/\mu \), the autocorrelation function can be approximated by a delta function \( \delta(z-z') \). This is the widely used single backscattering model. Note that if the tissue is layered, with the given assumptions this equation holds inside each layer. The attenuation coefficient is a function of wave number (see figure 1-1 for example). From equation 2-30, \( H(k) \) can be written as the Fourier transform of 2-31:

\[
H(k) = \int e^{-\mu(k)z} e^{-k^2 z} dz = \frac{1}{\mu(k)}
\]

(2-34)

Here the Fourier transform pair is \( k \leftrightarrow \Delta l = 2\pi \) as before. The second integral on the right hand side of equation 2-34 shows that \( H(k) \) is a the sum of attenuations \( e^{-\mu k z} \) due to single backscattering at all depths \( z \) in the sample. The local spectral properties of a sample are of more interest. The local spectrum of the detector current \( I_s(k) = S_s(k) \) \( H_s(k) \) is calculated from:

\[
H_s(k) = \int e^{-\mu(k)z} dz = \frac{1}{\mu(k)} e^{-\mu(k)z} \cdot \{1 - e^{-\mu(k)\Xi}\} = \Xi e^{-\mu(k)\Xi}
\]

(2-35)

The approximation in the last term on the right hand side holds if the observation window \( \Xi \) is small compared to the mean free path length \( 1/\mu \).

Localized spectroscopic information at \( z \) is obtained from time-frequency analysis like a windowed short time Fourier transform (STFT), on a segment of \( i_s(z) \). Note that for a non-homogeneous medium, still assuming single, independent backscattering, the amplitude of \( H(k) \propto \exp(-\mu(k,z')dz') \)
CASE B: MULTIPLE FORWARD SCATTERING

A model taking into account multiple scattering (neglecting absorption) was derived by Thrane et al [5]. Rather then calculating the detector current, statistical averages are computed. The OCT signal is expressed as the mean square signal current and is computed from the integral of sample and reference fields over the detector area. To this end, first the mean backscattered irradiance distribution \( \langle I_\theta(r) \rangle \) at the 'reflection site', i.e. the location of the coherence gate is calculated:

\[
\langle I_\theta(r) \rangle \propto \exp(-\mu_s z) \exp\left(-r^2/W_h^2\right) + \left[1 - \exp(-\mu_s z)\right] \exp\left(-r^2/W_s^2\right)
\]  

Here \( r \) is the radial coordinate as before. The first term on the right-hand side is the remaining un-scattered distribution i.e. attenuated according to Beer’s law thus proportional to \( \exp(-\mu_s z) \), the second term represents a broader ‘halo’ due to multiple forward scattering, i.e. proportional to \( [1-\exp(-\mu_s z)] \). The quantities \( W_h \) and \( W_s \) are the 1/e intensity radii of the probe beam without and with scattering, respectively. They are given by:

\[
W_h^2 = W_0^2 \left( \frac{z_{cf} - z}{n} \right)^2 + \left( \frac{f}{kW_0} \right) \left( \frac{z_{cf} - z}{nW_h} \right)^2
\]

\[
W_s^2 = W_h^2 + \left( \frac{2}{k\rho(z_{cf}, z)} \left[ f - \frac{z_{cf} - z}{n} \right] \right)^2
\]

Here, \( W_0 \) is 1/e intensity radius of the probe beam at the position of the focusing lens, \( z_{cf} \) and \( z \) are the locations of the confocal and coherence gate in the tissue; \( f \) is the focal length of the lens; \( n \) is the index of refraction and \( \rho(z_{cf}, z) \) is the lateral coherence length given by:

\[
\rho(z_{cf}, z) = \sqrt{\frac{3}{\mu_s z}} \frac{\lambda}{\pi \theta} \left( \frac{nf}{z} - \frac{z_{cf} - z}{z} \right)
\]

where \( \theta \) is the root mean square scattering angle, related to the scattering anisotropy of the sample through \( \theta = \sqrt{2(1-g)} \). The OCT signal can then found to be proportional to [5,6]:

\[
i_\theta(z) \propto \frac{1}{W_h} \left[ \exp(-2\mu_s z) + 2 \exp(-\mu_s z) [1 - \exp(-\mu_s z)] + [1 - \exp(-\mu_s z)] \frac{W_h^2}{W_s^2} \right]^{1/2}
\]
2.4 optical properties

In the previous section the optical properties of bulk tissue were briefly introduced. In this section some underlying physical principles are discussed. The interaction of light with a medium is due to fluctuations in the refractive index $m$ (where the fluctuations can be discrete particles or more continuous variations). The refractive index is a complex quantity, and a function of frequency $n(\omega)=n(\omega)+i\kappa(\omega)$. By the principle of causality, $n(\omega)$ and $\kappa(\omega)$ are related through Kramers-Kronig relations,

$$n(\omega)-1 = \frac{2}{\pi} \mathcal{P} \int_{0}^{\infty} \frac{\omega' \kappa(\omega')}{\omega^2 - \omega'^2} \, d\omega'$$ (2-41)

and the inverse transform given by,

$$\kappa(\omega) = \frac{2\omega}{\pi} \mathcal{P} \int_{0}^{\infty} \frac{n(\omega')-1}{\omega^2 - \omega'^2} \, d\omega'$$ (2-42)

Where $\mathcal{P}$ denotes the Cauchy principal value of the integral. In principle, all problems in optics are solved by solving Maxwell’s equations. Following the notation of Van der Hulst [7], these are given by:

$$\nabla \times \vec{H} = jkm^2 \vec{E}$$
$$\nabla \times \vec{E} = -jk\vec{H}$$ (2-43)

A solution of 2-43 for a homogeneous medium corresponds to a plane wave. A plane wave traveling in the $z$-direction is given by $E = \exp(jkmz - j\omega t)$, so:

$$E = \exp(-kz)\exp(jkmz - j\omega t)$$ (2-44)

which means the wave is damped when the imaginary part of the refractive index is non-zero. The absorption coefficient $\mu_a$ of the medium is then given by $2\kappa$ or, rearranging, the imaginary part of the refractive index is given by

$$\kappa(\omega) = \frac{\mu_a(\omega)}{2\omega}$$ (2-45)

where $c$ is the speed of light in vacuum. Understandably, $\kappa$ is often called absorption coefficient.

Now consider the scattering of a plane wave (as equation 2-44) by a certain particle. The scattered field $E_s$ is linearly related to the incoming field $E_0$ through:

$$E_s = S(\theta, \phi) \frac{\exp(-jkr)}{jkr} E_0$$ (2-46)

where $S$ is the amplitude function, which is a function of scattering angles, and $r$ is a vector in space. The intensity of the scattered field is then given by:
Let the total energy, scattered in all directions, be equal to the energy of the incident wave falling on an area $\sigma_s$ (the scattering cross section of the particle). Then,

$$\sigma_s = k^{-2} \int_{4\pi} |S(\theta, \varphi)|^2 d\Omega$$  \hspace{1cm} (2-48)

where $d\Omega = \sin \theta d\theta d\phi$ is an element of solid angle. If the amplitude in the forward direction $S(0,0)$ is known, the extinction cross section can be determined from the forward scattering theorem [7,8]:

$$\sigma_e = \frac{4\pi}{k^2} \text{Re}[S(0,0)]$$  \hspace{1cm} (2-49)

The coefficients can be made dimensionless by dividing them by the geometrical cross section; the resulting quantity is called the extinction (scattering, absorption) efficiency $Q$. Finally, the scattering anisotropy $g$, which is defined as the expectation value of the cosine of the scattering angle, can be calculated from:

$$g = \sigma_e^{-1} \int_{4\pi} \cos \theta |S(\theta, \varphi)|^2 d\Omega$$  \hspace{1cm} (2-50)

Mie theory provides a formal solution to Maxwell's equations (2-43) for a homogeneous sphere of radius $a$. The complex refractive index already appears in equation 2-43, but the parameter $x = k_m - a$ is equally important, since the equations have to fulfill boundary conditions at the surface of the sphere. Furthermore, due to the symmetry of the problem the amplitude function $S(\theta, \varphi)$ can be split into two contributions $S_1(\theta)$ and $S_2(\theta)$ corresponding to parallel and perpendicular polarization directions, respectively. They are given by:

$$S_1(\theta) = \sum_{i=1}^{\infty} \frac{2i+1}{i(i+1)} \left( a_i \frac{P_i(\cos \theta)}{\sin \theta} + b_i \frac{d}{d\theta} P_i(\cos \theta) \right)$$

$$S_2(\theta) = \sum_{i=1}^{\infty} \frac{2i+1}{i(i+1)} \left( b_i \frac{P_i(\cos \theta)}{\sin \theta} + a_i \frac{d}{d\theta} P_i(\cos \theta) \right)$$  \hspace{1cm} (2-51)

where $P_i$ are the associated Legendre functions, and $a_n$ and $b_n$ are the Mie coefficients, expressed in terms of Ricatti-Bessel functions $\psi$, $\xi$ and their derivatives $\psi'$ and $\xi'$ as

$$a_i = \frac{\psi'(xm)\psi(x) - m\psi'(xm)\psi'(x)}{\psi'(xm)\xi(x) - m\psi'(xm)\xi'(x)}$$

$$b_i = \frac{m\psi'(xm)\psi(x) - \psi'(xm)\psi'(x)}{m\psi'(xm)\xi(x) - \psi'(xm)\xi'(x)}$$  \hspace{1cm} (2-52)

The scattering and extinction efficiencies follow from equations 2-48 and 2-49 and are expressed in terms of the Mie coefficients as:

$$Q_{\text{ext}} = \frac{2}{x^2} \sum_{i=1}^{\infty} (2i+1) \text{Re}(a_i + b_i)$$  \hspace{1cm} (2-53)
The scattering anisotropy, from equation 2-49, is then given by:

\[ g = \frac{4}{x^2 Q_{\text{scat}}} \sum_{i,j} \left( \frac{2i+1}{i+1} \right) \text{Re}(a_i a_j + b_i b_j^*) + \frac{2i+1}{i+1} \text{Re}(a_i b_j^*) \]  

(2-55)

When the scattering particle is imbedded in a medium with non-unity refractive index, \( m \) in the preceding equations has to be replaced by the relative refractive index \( m_{\text{rel}} \) given by

\[ m_{\text{rel}} = \frac{m_{\text{particle}}}{m_{\text{medium}}} \]  

Even though the results of this section appear complicated, all calculations can be performed numerically because it is not necessary to carry out the summations to infinity to achieve accurate results. Computer code to perform Mie calculations is readily available. Most computer codes work with real-valued refractive indices, and consequently absorption properties cannot be calculated. To serve as a tool in the subsequent chapters, the code by Zijp et al [9] was modified to include complex arguments. A small web-based calculator using this code is (usually) available from http://www.lasercentre.org/miecalculator. Mie theory is the numerical "gold standard" for calculating scattering properties. These calculations are needed to verify the accuracy of the extracted optical properties, and are also used to estimate the optical properties of biological tissues e.g. red blood cells in relation to oxygen saturation in chapter 6.

REFERENCES

8. Because the imaginary unit in the denominator term of equation 2-45 is often combined with \( S \), equation 2-49 is often found having \( \text{Im}{} \) instead of \( \text{Re}{} \).